CLINICAL APPLICATION AND EVALUATION OF ROBOT-ASSISTED SURGERY IN CHILDREN

Thomas P Cundy MBBS BMedSci(Hons) DCH

The Hamlyn Centre, Institute of Global Health Innovation, Imperial College London

Division of Surgery, St Mary's Hospital, Imperial College London

2014

This thesis is submitted to Imperial College of Science, Technology and Medicine in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Except for where indicated, it presents entirely my own work and describes the results of my own research.

DECLARATION OF ORIGINALITY

This thesis presents original work of the titled author.
That which is not is referenced accordingly.

The copyright of this thesis rests with the author and is made available under a Creative Commons Attribution Non-Commercial No Derivatives license. Researchers are free to copy, distribute or transmit the thesis on the condition that they attribute it, that they do not use it for commercial purposes and that they do not alter, transform or build upon it. For any reuse or redistribution, researchers must make clear to others the license terms of this work.

To my son, Douglas Thomas Cundy, born on the 12th of August 2014.
For joyfully bringing the purpose of this thesis into context at the most opportune time.

With Love,
Dad, 20th August 2014

Abstract

Minimally invasive surgery (MIS) in children is epitomised by delicate and complex reconstructive procedures undertaken on diminutive anatomy within constrained operative workspaces. Conventional MIS equipment imposes restrictions on a surgeon's ability that may limit the eligibility, safety and effectiveness of keyhole surgery in paediatric settings. Enhancements provided by medical robotics may restore and augment operative capabilities to overcome these limitations. This thesis represents a detailed healthcare technology assessment of robotic technologies in paediatric MIS.

Systematic review of the first decade of clinical adoption identifies a progressive diffusion pattern. Fundoplication and pyeloplasty procedures stand out as dominant target applications. Meta analyses of comparative effectiveness literature for these procedures identified outcomes to be either comparable or marginally better, but at higher financial cost. An international survey was conducted to understand perceptions of paediatric surgeons towards robotic technologies. To address a deficiency in dedicated education resources, an inaugural European workshop was hosted. Large prospective fundoplication and pyeloplasty series were then analysed to determine multi-dimensional learning curves.

Other features of robots in paediatric surgery were explored in further detail, specifically dextrous 'wristed' instruments and haptic feedback loss. In a pre-clinical randomised study of robotic versus non-robotic instruments a threshold workspace size of $<200cm^3$ was identified for which existing larger robotic instruments are less well suited for advanced bimanual tasks. Investigation of *in vivo* suture damage revealed that experience-related factors compensate for haptic loss. A force-sensing paediatric laparoscopy simulator was developed and validated to provide a platform for compensatory haptic skills to be acquired.

Overall, first-generation robotic systems can safely be used to perform all paediatric procedures currently undertaken with conventional MIS techniques. However, cost-effectiveness is not sustainable in most healthcare settings. If genuinely disruptive clinical improvements are to be achieved, creative new procedural approaches need to be considered that are facilitated by purpose-designed technology. To pursue this agenda, the application of two novel single-shaft flexible robotic system prototypes are investigated for future roles in advancing surgical care in children.

Acknowledgements

"We are like dwarfs on the shoulders of giants, so that we can see more than them, and things at a greater distance, not by virtue of any sharpness of sight on our part, or any physical distinction, but because we are carried high and raised up by their giant size."

John of Salisbury, 1159 AD (in reference to the ancient scholars of Greece and Rome).

A modern re-incarnation of this quote was penned by Isaac Newton in a 1675 AD in a letter to a rival colleague, saying *"If I have seen further, it is by standing upon the shoulders of giants"*. The latter part of this quote is now immortalised on the British two-pound coin and, to me, symbolises the fundamental iterative process of knowledge gain in science. This thesis represents a pursuit of new knowledge that builds on existing knowledge that precedes it. The experience gained through this thesis has been humbling in allowing me to increasingly respect those who have contributed to the foundations of science that allow us to seek further advancement.

Through the Hamlyn Centre, I have been privileged to be exposed to the global cusp of surgical innovation and technology. I have been fortunate to be granted the academic freedom and resources to pursue this personally fulfilling thesis topic. For this, I am grateful to my supervisors, *Professor Lord Ara Darzi* and *Professor Guang-Zhong Yang*, for their trust and support in my enthusiasm for this topic.

To my father, *Associate Professor Peter Cundy*, thank you for introducing me to academic surgery and serving as a luminary role model in life and profession. To my mother, *Jenny Cundy RN*, who works tirelessly as a devoted emergency department nurse, thank you for continuing to inspire me with your inexhaustible compassion and kindness as an exemplary health professional.

To *Mr Christopher Kirby*, *Dr Hilary Boucaut, Mr Warwick Teague*, and *Dr Cathy Cord-Udy,* thank you for igniting and fuelling my passion towards my chosen career specialty path and for your ongoing mentorship that, through this study period abroad, has proven not to be at all limited by geographical distance.

I have undertaken my doctoral studies as a John Monash Scholar and am tremendously grateful to the *General Sir John Monash Foundation* for their support that has financially enabled my studies. I owe special thanks to *Dr Peter Binks* for the pastoral support that he continues to selflessly provide to my family and myself. Leadership is a fundamental principle of the John Monash

Scholarship programme. For this reason, I specifically sought to relocate to London to undertake studies under the tutelage of Professor Ara Darzi. The experience under his guidance and supervision has exceeded my expectations. I leave with matured and diversified leadership skills that are inspired by his outstanding example of quality and leadership co-existing at the very highest level between clinical surgery and surgical research. I am especially grateful for his trust, patience and teaching during my time under his direct clinical supervision in my final 12 months at St Mary's Hospital.

To *Mr Azad Najmaldin*, thank you for guiding me through various clinical and ethical aspects related to this thesis, and for allowing me the opportunity to maintain the Leeds paediatric robotic surgery database. Azad has been an international pioneer of paediatric laparoscopic surgery, and later robot-assisted laparoscopic surgery. His fierce determination to commit to technology that he believes in has, in the end, served him well throughout his career. The challenges associated with this approach reminds me of the Winston Churchill quote *"You have enemies? Good. That means you've stood up for something, sometime in your life."* I greatly admire his tenacious persistence, contagious enthusiasm and integrity to his own values.

To *Dr George Mylonas, Dr Valentina Vitiello, Dr Jianzhong Shang, Chris Payne* and *Hedy Rafii-Tari*, thank you for your reliable help. These engineers have dazzled me with their special talents and intellect. I am convinced that their ability to understand clinical problems far exceeds any clinicians' ability to appreciate similarly complex engineering problems. I am particularly thankful to George, a true inventor with an amazing mind for problem solving, who has allowed me to share with him the thrill of working towards and successfully filing an original patent.

To my office colleagues and friends, *Mr Hani Marcus, Mr Archie Hughes-Hallett*, and *Dr Richard Kwasnicki*, your company is something that I will always cherish and fondly remember. We always enjoyed celebrating our successes together, reliably united to support each other during challenging times, and motivated each other in many ways. This has been a standout highlight of my PhD experience. I am also greatly appreciative to *Dr Karen Kerr* and *Raphaele Raupp* for their steadfast support and friendship.

Lastly, and most importantly, I remain deeply indebted to my beautiful wife, *Joanna*. Her support and tolerance of my ambitions towards this thesis has been absolutely remarkable. The period associated with this thesis has seen us become married, and become parents – both triumphant moments that will always remain my proudest achievements in life.

Exact Details of Contributions

The content of this thesis represents my original work, although such is the nature of academic research that I received support from co-authors and collaborators. Unless stated below, contributions of others are either representative of manuscript review prior to submission for peer-reviewed publication, or acknowledged separately in relevant aspects of the thesis text.

Chapter 3	Statistical support was provided by Leanne Harling and Thanos Athanasiou.
Chapter 4	Clinical procedures were performed by Azad Najmaldin. Raw intra-operative data was collected by Azad Najmaldin for transcription to a central database that I maintained during the period associated with this thesis.
Chapter 6	Clinical data for *in vivo* suture damage was prospectively collected by Azad Najmaldin prior to the period associated with this thesis. Hedyeh Rafii-Tari and Christopher Payne provided software and hardware engineering input to assemble the ForSense simulator. Evelyn Thangarajah assisted with participant recruitment and data collection for the ForSense study.
Chapter 7	Thomas MacKinnon assisted with data collection.
Chapter 8	The i-Snake® robot prototype was developed by Guang-Zhong Yang *et al* at Imperial College London. The CYCLOPS robot prototype was developed by George Mylonas *et al* at Imperial College London.

Table of Contents

ABSTRACT **4**

ACKNOWLEDGEMENTS **5**

EXACT DETAILS OF CONTRIBUTIONS **7**

TABLE OF CONTENTS **8**

LIST OF TABLES **11**

LIST OF FIGURES **14**

LIST OF ACRONYMS **19**

CHAPTER 1 INTRODUCTION **21**

1.1 PROLOGUE 21

1.2 AIMS OF THE RESEARCH 22

1.3 THESIS OVERVIEW 23

1.4 ORIGINAL CONTRIBUTIONS OF THIS THESIS 25

1.5 PATENTS, PUBLICATIONS AND PRESENTATIONS FROM THIS THESIS 26

1.5.1 Patents related to this thesis *26*

1.5.2 Publications arising from this thesis *26*

1.5.3 Other publications arising from work related to this thesis *27*

1.5.4 Oral presentations arising from this thesis *28*

1.5.5 Invited oral presentations arising from work related to this thesis *29*

1.5.6 Other oral presentations arising from work related to this thesis *29*

1.5.7 Poster presentations arising from this thesis *30*

1.5.8 Poster presentations arising from work related to this thesis *30*

CHAPTER 2 CLINICAL APPLICATION & ADOPTION OF PAEDIATRIC ROBOTIC SURGERY **31**

2.1 THE HISTORY OF SURGICAL ROBOTICS 32

2.1.1 Robotics in the Renaissance *32*

2.1.2 Robots in the Modern World *33*

2.1.3 Robot-Assisted Surgery *34*

2.2 THE FIRST DECADE OF ROBOTIC SURGERY IN CHILDREN 43

2.2.1 Introduction *43*

2.2.2 Materials and Methods *43*

2.2.3 Results *46*

2.2.4 Discussion *48*

2.3 ROBOT-ASSISTED MINIMALLY INVASIVE SURGERY FOR PAEDIATRIC SOLID TUMOURS 53

2.3.1 Introduction *53*

2.3.2 Methods *53*

2.3.3 Results *54*

2.3.4 Discussion *60*

CHAPTER 3 CLINICAL COMPARATIVE EFFECTIVENESS OUTCOMES IN PAEDIATRIC ROBOTIC SURGERY **65**

3.1 META ANALYSIS OF ROBOT-ASSISTED VERSUS CONVENTIONAL LAPAROSCOPIC AND OPEN PYELOPLASTY IN CHILDREN 66

3.1.1 Introduction *66*

3.1.2 Materials and Methods *66*

3.1.3 Results *70*

3.1.4 Discussion *82*
3.2 META ANALYSIS OF ROBOT-ASSISTED VERSUS CONVENTIONAL LAPAROSCOPIC FUNDOPLICATION IN CHILDREN 87
3.2.1 Introduction *87*
3.2.2 Methods *87*
3.2.3 Results *89*
3.2.4 Discussion *97*

CHAPTER 4 EDUCATION & TRAINING IN PAEDIATRIC ROBOTIC SURGERY 100
4.1 EDUCATION AND TRAINING IN PAEDIATRIC ROBOT-ASSISTED MINIMALLY INVASIVE SURGERY: LESSONS LEARNED FROM AN INAUGURAL MULTINATIONAL WORKSHOP 101
4.1.1 Introduction *101*
4.1.2 Materials and methods *102*
4.1.3 Results *104*
4.1.4 Discussion *106*
4.2 THE LEARNING CURVE OF ROBOT-ASSISTED LAPAROSCOPIC PYELOPLASTY IN CHILDREN 111
4.2.1 Introduction *111*
4.2.2 Materials and Methods *112*
4.2.3 Results *116*
4.2.4 Discussion *126*
4.3 THE LEARNING CURVE OF ROBOT-ASSISTED LAPAROSCOPIC FUNDOPLICATION IN CHILDREN 132
4.3.1 Introduction *132*
4.3.2 Materials and Methods *132*
4.3.3 Results *135*
4.3.4 Discussion *139*

CHAPTER 5 CLINICAL NEEDS ASSESSMENT AND TECHNOLOGICAL GAP ANALYSIS 145
5.1 INTERNATIONAL ATTITUDES OF EARLY ADOPTERS TO CURRENT AND FUTURE ROBOTIC TECHNOLOGIES IN PAEDIATRIC SURGERY 146
5.1.1 Introduction *146*
5.1.2 Methods *147*
5.1.3 Results *149*
5.1.4 Discussion *155*

CHAPTER 6 CLINICAL CONSIDERATIONS FOR HAPTIC FEEDBACK LOSS 160
6.1 EXPERIENCE RELATED FACTORS COMPENSATE FOR HAPTIC LOSS IN ROBOT-ASSISTED LAPAROSCOPIC SURGERY 161
6.1.1 Introduction *161*
6.1.2 Materials and Methods *162*
6.1.3 Results *164*
6.1.4 Discussion *169*
6.2 A FORCE SENSING ENHANCED SIMULATION ENVIRONMENT (FORSENSE) FOR LAPAROSCOPIC SURGERY TRAINING AND ASSESSMENT 176
6.2.1 Introduction *176*
6.2.2 Materials and Methods *177*
6.2.3 Results *180*
6.2.4 Discussion *186*

CHAPTER 7 INSTRUMENTATION FOR SMALL OPERATIVE WORKSPACES 191
7.1 ROBOTIC VERSUS NON-ROBOTIC INSTRUMENTS IN SPATIALLY CONSTRAINED OPERATIVE WORKSPACES – A PRE-CLINICAL RANDOMISED CROSSOVER STUDY 192
7.1.1 Introduction *192*

7.1.2 Methods *192*
7.1.3 Results *197*
7.1.4 Discussion *200*

CHAPTER 8 POSITION STATEMENT & NEXT-GENERATION SURGICAL ROBOTS 205

8.1 ROBOTIC SURGERY IN CHILDREN – ADOPT NOW, AWAIT, OR DISMISS? 206
8.1.1 Introduction *206*
8.1.2 Adopt Now *206*
8.1.3 Dismiss *208*
8.1.4 Await *211*
8.1.5 Position Statement *215*

8.2 PER-ORAL ENDOSCOPIC CARDIOMYOTOMY AND PYLOROMYOTOMY USING A FLEXIBLE SNAKE ROBOT – PROOF OF CONCEPT WITH A PORCINE MODEL 217
8.2.1 Introduction *217*
8.2.2 Methods *219*
8.2.3 Results *225*
8.2.4 Discussion *227*

8.3 EVALUATION OF PRESSURE EFFECT SETTINGS IN WATER-JET ASSISTED OESOPHAGO-GASTRIC SUBMUCOSAL DISSECTION 234
8.3.1 Introduction *234*
8.3.2 Methods *234*
8.3.3 Results *235*
8.3.4 Discussion *236*

8.4 CYCLOPS V1 PROTOTYPE EVALUATION FOR USE IN PAEDIATRIC LAPAROSCOPY 238
8.4.1 Introduction *238*
8.4.2 Materials and Methods *239*
8.4.3 Results *245*
8.4.4 Discussion *247*

CHAPTER 9 CONCLUSIONS & FUTURE WORK 251

9.1 ACHIEVEMENTS OF THIS THESIS 251
9.2 FUTURE WORK 253
9.2.1 Ongoing monitoring and assessment *253*
9.2.2 Education and training in paediatric robotic surgery *254*
9.2.3 Next-generation robotic systems *255*
9.3 CONCLUSION 256

APPENDICES 258

LIST OF REFERENCES 263

List of Tables

Table 2.1 *Key features of open surgery versus conventional minimally invasive surgery (MIS) versus da Vinci® assisted MIS*.....38

Table 2.2 *A summary of paediatric robotic surgery procedures reported in the literature during the review period (n = 137 publications). *(ARM = anorectal malformation, CDH = congenital diaphragmatic hernia, ACE = antegrade continence enema, Mitrofanoff = Mitrofanoff appendicovesicostomy, OA/TOF = oesophageal atresia and tracheo-oesophageal fistula repair)* 49

Table 2.3 *Patient demographics, operative details and patient outcomes for identified cases of robot-assisted MIS for paediatric solid tumours*.....59

Table 3.1 *Quality scoring checklist for the star-based modified Newcastle-Ottawa Scale (mNOS).* 69

Table 3.2 *Characteristics of studies included in the meta-analysis. "-" not reported, * = median (range) values, ** = standard deviation. RC = retrospective cohort study, RCC = retrospective case-control study*.....71

Table 3.3 *Pelvi-ureteric junction obstruction (PUJO) characteristics reported amongst studies included in the meta-anaysis for a) robot-assisted (RP) versus conventional laparoscopic pyeloplasty (LP), and b) robot-assisted (RP) versus open (OP) pyeloplasty. "-" not reported, "re-do" = secondary procedure for recurrent PUJO.*.....72

Table 3.4 *Summary of study quality appraisal using the modified Newcastle-Ottawa Scale (mNOS).*.....73

Table 3.5 *Summary of post-operative complications reported amongst studies included in the meta-analysis for a) robot-assisted (RP) versus conventional laparoscopic pyeloplasty (LP), and b) robot-assisted (RP) versus open (OP) pyeloplasty. "-" not reported, * = incomplete data, n/a = not applicable, PUJ = pelvi-ureteric junction, UTI = urinary tract infection.* 78

Table 3.6 *Characteristics of studies included in the meta-analysis. "-" = not reported. RCC = retrospective case-control study, PC = prospective cohort study, RC = retrospective cohort study.* 90

Table 3.7 *Distribution of patients with neurological impairment and also those requiring concomitant gastrostomy at the time of surgery. "-" = not reported. NI = neurologic impairment.* 90

Table 3.8 *Summary of study quality appraisal using the modified Newcastle-Ottawa Scale (mNOS).*.....91

Table 3.9 *Summary of post-operative complications reported amongst studies included in the meta-analysis. * details not reported or incomplete, n/a = not applicable.* 94

Table 4.1 *Summary of responses (n = 12) to the question "what are your attitudes towards the following programme topics and themes?". Data are displayed as descending order mean-rating scores (± standard deviation) generated from a 5-point level-of-interest Likert scale (1 = not at all interested, 2 = not very interested, 3 = neutral, 4 = somewhat interested, 5 = very interested).* 105

Table 4.2 *Summary of responses (n = 18) to the question "what is your impression of the following aspects of the workshop programme?". Data are displayed as descending order mean-rating scores (± standard deviation) generated from a 5-point level-of-value Likert scale (1 = not valuable, 2 = limited value, 3 = average value, 4 = valuable, 5 = very valuable).* 105

Table 4.3 *Patient demographic information and clinical characteristics (n = 90).* 117

Table 4.4 *Operating times for the overall series (n = 88) and segmented phases of respective learning curves.* 123

Table 4.5 *Post-operative complications graded according to the Clavien-Dindo classification [126]*.....124

Table 4.6 *Summary of literature base for studies investigating learning curves in robot-assisted laparoscopic pyeloplasty (RP). LP = conventional laparoscopic pyeloplasty, LOS = length of hospital stay, OP = open pyeloplasty, OT = operating time.* 127
Table 4.7 *Patient demographic information and clinical characteristics (n = 57). FTT = failure to thrive, LF = conventional laparoscopic fundoplication, RF = robot-assisted laparoscopic fundoplication.*....134
Table 4.8 *Operating times for the overall series (n = 57) and segmented phases of respective learning curves.*....138
Table 4.9 *Post-operative complications graded according to the Clavien-Dindo classification. POD = post-operative day* 139
Table 5.1 *Summary of responses to the question "What are your attitudes toward the following features of robot-assistance that are perceived as benefits in paediatric minimally invasive surgery". Data are displayed as mean-rating scores (± standard deviation) generated from a 5-point level of agreement Likert scale (1 = strongly disagree, 2 = disagree, 3 = neither, 4 = agree, 5 = strongly agree).* 151
Table 5.2 *Summary of responses to the question "What are your attitudes toward the following features of robot-assistance that are perceived as limitations in paediatric minimally invasive surgery". Data are displayed as mean-rating scores (± standard deviation) generated from a 5-point level of agreement Likert scale (1 = strongly disagree, 2 = disagree, 3 = neither, 4 = agree, 5 = strongly agree). * = borderline statistically significant.*....152
Table 5.3 *Itemised responses to questions regarding preferred hardware specifications and costs of robotic systems for paediatric minimally invasive surgery. * statistically significant (P < 0.05) compared to all other response items, and ** compared to all other items except the most closely matched response item.* 154
Table 6.1 *Patient demographic and clinical information for sequential quartile periods, and overall cohort. * Significant difference compared to both Q1 and Q2, ** Significant difference compared to Q2. SD = standard deviation, RPD = moderate or severe renal pelvis dilatation, AI = acute inflammation, LPV = lower pole renal vessel, MR = malrotation, Stones = renal stone disease.* 164
Table 6.2 *Suture characteristics for robot-assisted laparoscopic pyeloplasty amongst sequential quartile periods, and overall cohort. * Significant difference compared to Q1, Q2 and Q3, ** Significant difference compared to both Q2 and Q4, *** Significant difference compared to between Q3 and Q4.*....165
Table 6.3 *Summary of suture damage for amongst sequential quartile periods, and overall cohort. † Jonckheere Trend Test ‡ effect size estimate using Kendall's tau-b correlation (τ). I:C = incomplete:complete suture damage.* 167
Table 6.4 *Demographic characteristics of the study cohort.* 180
Table 6.5 *Time, force, and score metric outcomes amongst levels of experience for the peg transfer and suture tasks. N = Newtons, N/s = Newton/seconds, NS = not statistically significant, r = Pearson correlation coefficient, P = p value, * Mann-Whitney U test, ** Kruskall-Wallis test.*....181
Table 6.6 *PLS and fPLS scores amongst groups of experience level. For each scoring metric, comparisons between all combinations of two experience level groups were statistically significant (P < 0.001 - 0.038, Mann-Whitney U). β = unstandardised regression coefficient.* 184
Table 6.7 *Time and force results for suture subtasks. All values represent mean or mean ± SD for time (seconds) and force (Newtons or Newton/seconds) variables. N = novices, I = intermediates, E = experts, P = P value.* 185
Table 7.1 *Participant demographic information (n = 23).* 197
Table 7.2 *PLS task scores (higher score = superior performance) for non-robotic and robotic instruments in various workspace sizes. IQR = interquartile range, ∅ = diameter* 198

Table 7.3 *Workspace boundary breaches for non-robotic and robotic instruments in various workspace sizes. IQR = interquartile range, ∅ = diameter* 200
Table 7.4 *PLS task scores (higher score = superior performance) for horizontal and vertical suture directions performed with non-robotic and robotic instruments. IQR = interquartile range.* 200
Table 8.2 *Identified problems and proposed solutions for i-Snake®-assisted POEM and POEP procedures.* 232
Table 8.3 *Technical needs and non-technical barriers that are required to be addressed for successful single-shaft bimanual surgical platforms.* 239

List of Figures

Figure 2.1 *Technical drawing from a notebook of Leonardo da Vinci depicting what is probably the actuated arm mechanism for a semi-automatic knight warrior. This drawing is believed to be the earliest design for a robot. It is one drawing amongst many that comprises the Codex Atlanticus, the largest single collection of da Vinci's drawings. Picture courtesy of Google.* *32*

Figure 2.2 *A model of Leonardo's robotic knight demonstrating the exterior suit of armor and interior workings for the upper limbs and head. Picture courtesy of Wikipedia.* *33*

Figure 2.3 *Conventional laparoscopic surgery (written informed consent for clinical photography was obtained from the patient).* *35*

Figure 2.4 *ZEUS Master-Slave Robotic System. (picture courtesy PRWeb http://ww1.prweb.com/prfiles/2007/05/10/525578/iBotA.bmp)* *36*

Figure 2.5 *The illusion of a fully immersive operative experience with the da Vinci® Surgical System. The top image would represent the entire field of view for the surgeon at the master console. Picture courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).* *38*

Figure 2.6 *The da Vinci® instruments replicate the degrees-of-freedom possessed by the human hand (a), and (b) are controlled using an instinctive interface that can be calibrated to various motion scaling settings to suit procedural needs. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).* *39*

Figure 2.7 *Schematic overview of a typical operating theatre set-up for the da Vinci® Surgical System. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).* *40*

Figure 2.8 *A visual timeline of da Vinci® Surgical System models including the a) 3-armed da Vinci Standard®, b) 4-armed da Vinci S®, c) da Vinci Si® with dual master consoles, and d) da Vinci Single-Site®. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).* *41*

Figure 2.9 *The da Vinci Xi® Surgical System. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).* *42*

Figure 2.10 *A Prisma flow diagram outlining the systematic search strategy.* *45*

Figure 2.11 *An illustrative overview of the operative set-up for paediatric transperitoneal pyeloplasty using the da Vinci® master-slave robotic platform, displaying the a) docked slave component, b) master console, c) port configuration with patient in modified flank position, d) camera view at commencement of ureteral anastomosis.* *46*

Figure 2.12 *Representation of the geographical origin of paediatric robotic surgery publications across major continents. Overall, 220 publications were represented from 18 countries, across 52 institutions.* *47*

Figure 2.13 *Published case volumes of robotic surgical procedures in children, categorised by twelve-month periods from April 2001 to March 2012 (n = 137 publications).* *50*

Figure 2.14 *The published literature reporting robotic surgery in children, categorised by quality of evidence in twelve-month intervals. During the 11-year review period, the published literature comprises 34% case reports, 52% case series, and 14% non-randomised comparative studies (n= 220 publications).* *50*

Figure 2.15 *A Prisma flow diagram [63] depicting the systematic process undertaken using the search strategy "Neoplasms"[MeSH] AND ("Surgery, Computer-Assisted"[MeSH] OR "robotics"[MeSH] OR "da Vinci" OR "telerobotic" OR "telesurgery" OR "robotic surgery") AND ("Pediatrics"[MeSH] OR "Infant"[MeSH] OR "Child"[MeSH] OR "Adolescent"[MeSH]). Case series were regarded as articles reporting ≥ 3 relevant cases that met inclusion criteria.* *55*

Figure 3.1 *Prisma flow diagram outlining the systematic search strategy and study selection process.* 70
Figure 3.2 *Forest plot comparisons of success rates for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.* 74
Figure 3.3 *Forest plot comparisons of re-operation rates for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.* 75
Figure 3.4 *Forest plot comparisons of Clavien Grade 1 – 5 complications for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.* 76
Figure 3.5 *Forest plot comparisons of urinary leakage complications for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.* 77
Figure 3.6 *Forest plot comparisons of estimated blood loss for a) all studies, and b) high quality studies only (≥ 9 median mNOS score) comparing robot-assisted versus open pyeloplasty in children.* 79
Figure 3.7 *Forest plot comparisons of length of hospital stay for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.* 80
Figure 3.8 *Forest plot comparisons of operating time for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.* 81
Figure 3.9 *Prisma flow diagram outlining the systematic search strategy and study selection process.* 89
Figure 3.10 *Forest plot comparisons of a) age, and b) weight for studies comparing RF versus LF in children.* 92
Figure 3.11 *Forest plot comparisons of conversions for studies comparing RF versus LF in children.* 93
Figure 3.12 *Forest plot comparisons of length of hospital stay for studies comparing RF versus LF in children.* 94
Figure 3.13 *Forest plot comparisons of post-operative complications for studies comparing RF versus LF in children.* 95
Figure 3.14 *Forest plot comparisons of a) total operating time for studies comparing RF versus LF in children, and b) sub-group analysis of high quality studies only.* 96
Figure 4.1 *Example of a structured robotic surgery training curriculum framework based on those proposed by Chitwood et al [144] and Lee et al [143].* 102
Figure 4.2 *Skills laboratory (a) for practical stations that included hands-on wet lab training (b), hardware familiarisation and port placement strategies (c), and robot docking (d).* 106
Figure 4.3 *Hands-on stations included a robot-assisted laparoscopic fundoplication using a porcine model in the EASIE-R™ Simulator (EndoSim, MA) (a), robot-assisted laparoscopic pyeloplasty using a porcine model (b), dV-Trainer® virtual reality robotic surgery simulator (c), and augmented reality image-guided surgery demonstration (d).* 107
Figure 4.6 *Time-based schematic for surgical workflow during a typical case, indicating definitions for recorded intervals. * representing anaesthesia set-up and patient positioning.* 113
Figure 4.7 *CUSUM chart (a) and test (b) for set-up time.* 118
Figure 4.8 *CUSUM chart (a) and test (b) for docking time.* 119
Figure 4.9 *CUSUM chart (a) and test (b) for console time.* 120
Figure 4.10 *CUSUM chart (a) and test (b) for operating time.* 121
Figure 4.11 *CUSUM chart (a) and test (b) for total operating room time.* 122
Figure 4.12 *CUSUM chart (a) and test (b) for post-operative complications. Stepped interpolation lines are used for exaggerated effect of individual cases.* 125
Figure 4.13 *Raw console time data chronologically represented as a line graph (a), and scatter plot with both linear (dotted line) and quadratic (solid line) trend lines (b).* 128
Figure 4.14 *Typical port configuration consisting of (clockwise from top) 3mm left sub-xiphisternal Nathanson liver retractor, left upper quadrant anterior axillary line 5mm -8mm working instrument (slightly lower than right upper quadrant port), left lumbar*

region 3.5mm bedside assistant instrument (e.g. conventional laparoscopic grasper for introducing suture/retracting tissue, and scissors for cutting suture), periumbilical 12mm optical port, and right upper quadrant mid-clavicular line 5mm - 8mm working instrument. 133
Figure 4.15 *CUSUM chart for docking time (a), and scatter plot of raw docking time data (b) with linear (dotted) and quadratic trend lines (solid).* 136
Figure 4.16 *CUSUM charts for console time (solid line) and total operating time (dotted line) (a), and scatter plot of raw time data (b) with linear (dotted) and quadratic trend lines (solid).* 137
Figure 4.15 *Operative images highlighting the dexterity of wristed instruments for a) retro-oesophageal dissection, b) intracorporeal suturing of the fundoplication wrap, and c) preparation of the gastrostomy site with intracorporeal placement of anchoring hitch purse-string suture.* 141
Figure 4.18 *Schematic of a smoothed bi-phasic CUSUM learning curve chart indicating learning and skill maintenance phases either side of a central inflection point (*). Further segmentation of the curve into sub-phases may be conceptually represented by 1) an early-accelerated learning period, 2) consolidation of learning plateau, 3) skill refinement period, and 4) skill mastery or "automaticity" period. Examples of alternate slope gradients are indicated in light grey, and these may also be skewed in various phases or sub-phases.* 143
Figure 5.1 *The bell-shaped distribution and categorisation of innovation adopters, determined on the basis of 'innovativeness' (adapted from Rogers et al [194]). The targeted sample population for this study is shaded grey.* 147
Figure 5.2 *Geographical distribution of survey respondents (n = 48) by country of origin.* 150
Figure 5.3 *Graphical summary of responses to the question "what are your attitudes toward the following next-generation robotic technologies?". Data values are presented as percentages of responses.* 153
Figure 5.4 *Selection of robotic (top two) and non-robotic (bottom three) laparoscopic instrument sizes currently available for paediatric minimally invasive surgery, manufactured by Intuitive Surgical Inc and Karl Storz respectively.* 157
Figure 6.1 *Example of incomplete Vicryl® suture damage viewed at 100x magnification (VHX-2000 Series Digital Microscope) following handling with a Cadiere forceps instrument.* 163
Figure 6.2 *Box plot of overall suture usage per case across quartile sub-group periods (Q1 – Q4). Median values for each period (n = 13 cases each) are represented by the horizontal box line and indicated numerically above the upper whisker end. *Suture usage was significantly lower in Q4 compared to each other period ($P \leq 0.002$).* 165
Figure 6.3 *Suture damage frequencies amongst quartile periods of surgeon experience (n = 13 cases in each group). * Significant differences in suture damage frequency were observed between Q1 versus Q2 - Q4 (χ^2, $P < 0.001$) and also Q2, Q3, and Q4 (Fisher's Exact, P = 0.002, 0.005, 0.009 respectively). No significant differences were detected between Q2, Q3 and Q4 periods.* 167
Figure 6.4 *Suture damage frequencies for all individual cases in the study cohort (n = 52). Dotted and solid lines represent linear trend lines and cubic curvilinear regression lines respectively.* 168
Figure 6.5 *End-effector grip surfaces of Cadiere forceps (top) and large needle driver (bottom) instruments viewed at 20x magnification (VHX-2000 Series Digital Microscope).* 173
Figure 6.6 *Overview of the ForSense and experimental set-up, showing the replacement base and sensitized plate (a), attachment of existing peg board (b), and reverse angle views of the peg transfer and suture tasks (c and d).* 178
Figure 6.7 *Force signatures of low scoring peg transfer and suture task repetitions by a novice (Figures 6.7a and 6.7b respectively) and high scoring peg transfer and suture task*

repetitions by an expert (Figures 6.7c and 6.7d respectively). The dotted horizontal line represents the threshold for force error (1.5 N). *182*

Figure 6.8 *Correlations between task completion time and force magnitude, with least-squares linear regression lines.* *183*

Figure 6.9 *Force signature for an intermediate level participant undertaking a suture task. Events corresponding to various force peaks are illustrated.* *185*

Figure 7.1 *Overview of the experimental set-up demonstrating a participant engaged with the non-robotic instrument task (A), interior view of the task assembled within the PLS box trainer (B), and reverse angle view of the robot docked to the modified PLS box trainer (C).* *194*

Figure 7.2 *Illustrative depiction of the 3 cylindrical workspace sizes (constant height of 40mm and diameters of 40mm, 60mm and 80mm) drawn to scale alongside singular items of the 3 instrument pairs investigated (3mm non-robotic, 5mm robotic and 8mm robotic) that are each in maximum positions of distal angulation. All measurement values in millimetres.* *196*

Figure 7.3 *Objective task scores (higher score = superior performance) (A), workspace breach counts (B), and perceived task workload scores (higher NASA TLX score = higher workload) (C) for instrument pairs amongst the workspace sizes investigated.* *199*

Figure 8.1 *The theoretical S-shaped diffusion of innovation curve that is based on the seminal work of Everett Rogers (grey sigmoid curved line) [194]. A 'tipping point' region of the curve is shaded that typically represents a point of rapid and irrevocable adoption, often triggered when 15-20% overall adoption is reached [22].* *207*

Figure 8.2 *The Gartner Hype Cycle curve is a graphical tool that represents the maturity, adoption and social application of specific technologies (Gartner Inc., CT). It categories the predicted evolution of a technology into 5 key life cycle phases.* *209*

Figure 8.3 *IBM launched the 305 RAMAC in September 1956. This was the first computer with a hard disk drive. To demonstrate its impressive portability at the time, this 5 MB computer weighing over 1000kg is captured being loaded into a Pan-American Airways plane. Portable hand-held 1,000,000 MB (1 TB) USB flash drives are now commonly available and affordable for everyday community use.* *212*

Figure 8.4 *First prototype master console and slave component for the da Vinci® Surgical System, pictured in 1996.* *213*

Figure 8.5 *Schematic diagram illustrating the speculative effect of different evaluation intervals on comparative outcomes when established techniques of plateaued learning curve status are compared with new techniques that require further experience to overcome the learning curve. Adapted from Ramsay et al [191].* *213*

Figure 8.6 *The da Vinci® Sp™ System that is due to be commercially available in 2015.* *214*

Figure 8.7 *Schematic representation of the progression of minimally invasive surgery, transitioning from A) laparotomy, B) multi-port laparoscopy, C) single-port laparoscopy, and to D) 'incisionless' natural orifice endoscopic surgery. Crucial technological innovation intervals are numbered 1 to 3.* *217*

Figure 8.8 *The i-Snake® prototype used for the experiment, featuring 1) proximal rigid shaft, 2) semi-flexible mid-shaft, and 3) modular joint based robotic distal shaft.* *221*

Figure 8.9 *Ex-vivo porcine upper gastro-intestinal specimens with a) oesophagus detubularised and b) stomach transected in mid-coronal plane, demonstrating procedural configurations of the i-Snake® for POEM and POEP respectively. Thickness of luminal muscle layers were 3mm, 4mm and 10mm for the c) oesophagus, d) stomach and pylorus respectively.* *222*

Figure 8.10 *Overview of the ex vivo experimental set-up including a) specimen assembled within the EASIE-R™ simulator with docked i-Snake®, b) view of the control system cart for the i-Snake®, c) i-Snake® positioned on gastric mucosa with HybridKnife multi-function probe extending from the larger 3mm internal channel, and d) intra-gastric*

view of the i-Snake® entering through the gastro-oesophageal junction into the cardia of the stomach. *223*
Figure 8.11 *Five essential procedural steps for POEM and POEP were undertaken, defined by a) creation of a 15 – 20mm transverse mucosal incision, b1) & b2) submucosal tunneling using the HybridKnife, c) intubation of submucosal tunnel, d) myotomy using the HookKnife (Olympus Corporation, Tokyo) (mucosal tunnel opened for illustrative purpose only), and e) extubation of submucosal tunnel in preparation for mucosal closure (i.e. with endoclip).* *224*
Figure 8.12 *The mechanically actuated assistive arm robot supporting the i-Snake® shaft, actuation pack and cabling weight during the in vivo trial. For sterility reasons, a clear protective drape is covering the robotic arm. The linear drive controller is visible as the red joystick.* *225*
Figure 8.13 *Attempted retroflexion of the i-Snake® as confirmed on a) antero-posterior and, b) lateral fluoroscopy imaging* *227*
Figure 8.14 *The HybridKnife entering the oesophageal submucosal space with views from the a) on-board camera, and b) separate graphic interface screen proving joint position feedback.* *228*
Figure 8.15 *Positions of maximal retroflexion for a 12mm gastroscope and the 13mm i-Snake® prototype used in this study (NB: flexible mid-shaft segment not articulated)* *231*
Figure 8.16 *Overview of the experimental set-up involving a) cadaveric porcine upper gastrointestinal tract specimen, 2) ERBE VIO® 2 Electrosurgical Generator and ERBEJET™ 2 water pump console unit, and 3) HybridKnife T-type multi-function probe.* *235*
Figure 8.17 *Detubularised esophagus with water-jet probe tip in situ demonstrating submucosal elevation length and width at effect setting 20.* *236*
Figure 8.18 *The effect of water-jet pressure effect settings on submucosal elevation.* *237*
Figure 8.19 *Digitally enhanced concept image of the CYCLOPS system mounted on a flexible endoscope.* *238*
Figure 8.20 *Schematic of the CYCLOPS deployed within the stomach cavity for natural orifice endoluminal surgery.* *239*
Figure 8.21 *Digitally enhanced concept image of the CYCLOPS system mounted on a laparoscope.* *240*
Figure 8.22 *Stylistic impression of the CYCLOPS attached to a flexible endoscope, featuring a flexible over-sheath, inflated peripheral structure and tendon-driven manipulated instruments. (Image courtesy of Dr George Mylonas)* *241*
Figure 8.23 *Overview of the experimental set-up demonstrating the a) stereoscopic monitor, b) VisionSense III scope camera, c) CYCLOPS tendon driving unit, d) passive 3D glasses, e) motorised actuation mechanisms for endoscopic forceps, f) Geomagic® Touch™ haptic devices, g) Pediatric Laparoscopic Surgery (PLS) box trainer, and h) CYCLOPS peripheral scaffold attached to the VisionSense scope.* *242*
Figure 8.24 *Assembled paediatric sized CYCLOPS prototype positioned above an open-roof PLS box trainer.* *243*
Figure 8.25 *Individual components of the CYCLOPS prototype system demonstrating a) reverse angle view of the CYCLOPS end-effectors performing the peg transfer task, b) the CYCLOPS tendon driving unit with tendons (yellow) and 1.9mm Bowden cables (silver) attached to each of the 12 motors, c) motorised control mechanism for one of the two endoscopic forceps, and d) the master control interface provided by Geomagic® Touch™ haptic devices.* *244*
Figure 8.26 *Sequence of the CYCLOPS performing the peg transfer task demonstrating a) far right lateral reach, b) far left lateral reach, c) coordinated instrument triangulation and bimanual control to exchange the peg ring, and d) crossover of instruments into the contralateral workspace hemisphere of the peripheral scaffold.* *246*
Figure 8.27 *CYCLOPS on-board camera view during the peg transfer task.* *247*

List of Acronyms

AESOP	Automated Endoscopic System for Optimal Positioning
ANOVA	Analysis of variance
ASN	Mr Azad Najmaldin
BT	Box trainer
CUSUM	Cumulative summation
CT	Computer tomography
DOF	Degrees-of-freedom
EBL	Estimated blood loss
EUR	Euro currency
FDA	United Stated Food and Drug Administration
FLS	Fundamentals of Laparoscopic Surgery simulator
ForSense	Force sensing enhanced simulation environment
F/T	Force/Torque
FTT	Failure to thrive
GORD	Gastro-oesophageal reflux disease
Hz	Hertz
IBM	The International Business Machines Corporation (computer hardware company)
IDEAL	Idea, Development, Exploration, Assessment, Long-term follow-up
IQR	Inter-quartile range
LED	Light emitting diode
LOS	Length of hospital stay
LC	Learning curve
LP	Laparoscopic pyeloplasty
MAG3	Technetium-99m mercaptoacetyltrigylcine isotope renogram study
MIS	Minimally invasive surgery
MISTELS	McGill Inanimate System for Training and Evaluation of Laparoscopic Skills
mNOS	Modified Newcastle Ottawa Scale
NASA-TLX	National Aeronautics and Space Administration Task Load Index
OP	Open pyeloplasty
OR	Odds ratio
OT	Operating time
N	Newton (unit)
NI	Neurological impairment

NOES	Natural orifice endoluminal surgery
NOTES	Natural orifice transluminal endoscopic surgery
pCLE	Probe-based confocal laser endomicroscopy
PEG	Percutaneous endoscopic gastrostomy
PC	Prospective cohort study
PLS	Pediatric Laparoscopic Surgery simulator
POD	Post-operative day
POEM	Per-oral endoscopic myotomy
POEP	Per-oral endoscopic pyloromyotomy
PRISMA	Preferred Statement for Reporting Systematic Reviews and Meta-Analyses
PUJO	Pelvi-ureteric junction obstruction
R&D	Research and development
RCM	Remote centre of motion
RF	Robot-assisted laparoscopic fundoplication
RP	Robot-assisted laparoscopic pyeloplasty
RC	Retrospective cohort study
RCC	Retrospective case-control study
SBTA	Simulation based training and assessment
SAGES	Society of American Gastrointestinal and Endoscopic Surgeons
SD	Standard deviation
SPLS	Single port laparoscopic surgery
US	United States of America
USD	United States currency (dollars)
VR	Virtual reality
WMD	Weighted mean difference

CHAPTER 1 INTRODUCTION

1.1 Prologue

In 1964 at the World Fair in New York, the renowned scientist and author Isaac Asimov broadly outlined his vision of future technologies. Many of these predictions have proved astoundingly accurate. Asimov had a special affinity for robotic technology and is eponymously credited with The Three Laws of Robotics. His forecast for this field was that *"robots will neither be common nor very good in 2014, but they will be in existence"*. In describing primitive IBM computers on exhibition at the same World Fair, Asimov also stated that *"...it will be such computers, much miniaturized, that will serve as the 'brains' of robots"*. Although he has not lived to self-evaluate the exactness of his 50-year prediction for robotics, his prescient words serve as a testable statement that underpins the primary hypothesis for this thesis that is a comprehensive healthcare technology assessment for the use of robot-assisted surgery in children.

Robotic systems for minimally invasive surgery have arguably been the most dominant technology item to be introduced to paediatric surgery in recent years. Existing robotic technology serves to empower surgeons with computer-enhanced abilities to perform multi-port laparoscopic or thoracoscopic surgical procedures. It remains uncertain what direction the diffusion trajectory of robot-assisted surgery will follow in years to come and what its eventual fate might evolve towards. What is certain is that this technology has developed an undeniable clinical and academic presence. Dedicated content on the topic of robot-assisted surgery appears in the latest editions of all authoritative paediatric surgery textbooks. This sense of cemented status has largely occurred without the technology being subjected to comprehensive processes of critical evidence-based assessment in order to determine true clinical and cost-effectiveness value. Across healthcare in general, a scenario of inadequate evidence is automatically imposed whenever something new is introduced. Accumulation of evidence takes time and demands resources. Typically the highest level of evidence data requires the most intensive scientific effort. A recurring narrative throughout this thesis is that technology evolution and evidence-based evaluation must occur simultaneously in order to promote and safeguard effective clinical translation of robotic innovations. Following a sufficient period of over 10 years that robot-assisted surgery has been allowed the opportunity to mature in the paediatric clinical arena, the time is appropriate to critically evaluate whether this technology is indeed "*neither common nor very good in 2014*".

1.2 Aims of the Research

The aims of this thesis are to 1) investigate the application of robot-assistance in paediatric minimally invasive surgery, to 2) empirically evaluate its clinical role and, to 3) explore potential for greater clinical impact through development of future innovation in surgical robotics.

By figuratively looking backwards in order to look forwards, the aims of this thesis are addressed by structuring the work into two chronologically orientated components. Firstly, a detailed appraisal of *past and present* robotic systems is undertaken using a mixed methodology approach of systematic literature reviews, meta-analyses of comparative effectiveness data, a social science theory orientated survey study, cumulative summation learning curve analysis studies, a prospective *in vivo* clinical study, simulation laboratory construct validity study, and a pre-clinical randomised cross-over study. And secondly, to address clinical and technical shortcomings associated with current technology, *future* robotic system prototypes developed at Imperial College London will be evaluated for several novel paediatric procedure specific applications.

Primary hypotheses to be tested in this thesis are as follows:

- Global adoption trends for paediatric robot-assisted surgery are measurable and reflect growing uptake (Chapter 2).
- Clinical outcomes for robot-assisted procedures are better than outcomes for open or conventional laparoscopic procedures (Chapter 3).
- There is unmet demand for basic educational resources in paediatric robot-assisted surgery and this can be provided by an intensive hands-on workshop (Chapter 4).
- Learning curves for paediatric robot-assisted laparoscopic procedures are multi-dimensional and can be defined with clear transition points that signal progression beyond the learning phase (Chapter 4).
- Existing features of putative benefit and limitation in robotic surgery are perceived by paediatric surgeons with widely varied weightings (Chapter 5).
- Consensus amongst paediatric surgeons is that design specifications and cost of currently available robotic systems are insufficient for optimal usage in paediatric minimally invasive surgery (Chapter 5).
- Experts are less aware and concerned by haptic feedback loss in robot-assisted minimally invasive surgery due to experience related non-tactile adaptive skills that compensate for this sensory deficit (Chapter 6).

- Measurements of tool-tissue interaction force can be used to discriminate between level of surgeon experience and may be used as an objective outcome for skills based training and assessment in paediatric robot-assisted and conventional laparoscopy (Chapter 6).
- If robotic and non-robotic instruments are compared for use in small workspaces, robotic instruments will be superior due to features of improved dexterity and precision (Chapter 7).
- There is a workspace size threshold that defines a limit for which larger diameter robotic instruments become less well suited compared to smaller non-robotic instruments (Chapter 7).
- Creative new less invasive procedures may be permitted with robotic technologies that are customised to specific patient populations or procedures (Chapter 8).

1.3 Thesis Overview

The opening chapter provides a historical narrative of robotics and robot-assisted surgery before systematically interrogating the literature in order to quantitatively expose adoption patterns and trends that have occurred throughout the first decade of paediatric robot-assisted surgery.

In recognising the need for progression beyond an early phase of application and clinical dispersion, and into an era of critical assessment, Chapter 3 comprises a thorough review of comparative effectiveness literature including the undertaking of meta-analyses for the two highest volume robot-assisted laparoscopic procedures currently performed in children.

Acknowledging that new surgical technologies or techniques generate new requirements for education and training, Chapter 4 reports on a Paediatric Robotic Surgery Inaugural European Workshop that was hosted to fulfil an unmet need for dedicated hand-on pre-clinical educational resources. Quantitative and qualitative delegate feedback is examined to understand preferences for pre-clinical training resources and ways to improve their provision. One of the priorities in establishing structured goal-orientated clinical phase training is knowledge of procedure specific learning curves. In Chapter 4, learning curves for paediatric robot-assisted laparoscopic fundoplication and pyeloplasty are defined by using the cumulative summation (CUSUM) analysis technique to process data from the largest prospective single-surgeon series for these procedures.

To understand the specific needs of robotic technology in paediatric surgery, Chapter 5 forms a clinical needs assessment and technical gap analysis. This is achieved through a social science theory based survey study that was distributed to early adopter paediatric surgeons. Results of this survey hierarchically identify specific features of robotic surgery that are driving its appeal, reveals

attitudes toward limiting factors to adoption that are acting as barriers to diffusion, and captures opinions toward future robotic technologies. Insight provided by survey responses serves to generate valid hypotheses for subsequent chapters.

One of the most frequently cited drawbacks of robotic surgery is loss of haptic feedback. This is particularly relevant in paediatric surgery as operative tasks invariably require delicate handling of small anatomy. Without tactile sensory input there is increased theoretical risk of inadvertent tissue damage. In the survey study described above, haptic feedback loss was the only perceived limitation of robot-assisted surgery for which a significantly different response was observed between experts and non-experts. The implication that experts might acquire non-tactile skills that compensate for haptic loss is investigated further in Chapter 6 by measuring frequency of *in vivo* suture damage. After demonstrating that adaptive perceptual skills are able to partially compensate for the technological deficit of haptic feedback loss, a force-sensing enhanced paediatric laparoscopy simulator was developed and validated to provide a resource for these skills to be acquired in the pre-clinical setting.

Paediatric surgeons anecdotally identify dexterous wristed instruments as one of the most advantageous features of robotic surgery systems, however this lacks evidence-based support. Robotic instruments are generally larger than non-robotic instruments by virtue of actuation mechanism components that must be accommodated in the instrument design. Instinctively, smaller instruments are better suited for use in small workspaces that are abundant in paediatric patients. Chapter 7 comprises a laboratory-based randomised crossover study that compares robotic versus non-robotic instruments for a validated paediatric intra-corporeal suturing task, and investigates the influence of both workspace size and instrument characteristics on task performance.

Lastly, Chapter 8 will candidly distill the controversial argument about the role of robot-assistance in paediatric surgery into an evidence informed decision-making taxonomy; whether to adopt this technology 1) now, 2) later, or 3) not at all. In finding the most compelling position to be in support of awaiting and engaging with promising next-generation robotic technologies, two novel single-shaft robotic platform prototypes are introduced that are under development at Imperial College London. Pre-clinical feasibility and proof-of-concept experiments are described, with specific consideration towards disruptive applications for pathologies encountered in young children.

1.4 Original Contributions of this Thesis

- Quantitatively determining the adoption chronology and procedure-based breakdown of clinical application for paediatric robot-assisted minimally invasive surgery.
- Identifying the comparative effectiveness of robot-assisted pyeloplasty and fundoplication versus existing alternative techniques through data synthesis of the available literature.
- Highlighting the value of the cumulative summation analysis technique for learning curve analysis by using this methodology to define multi-dimensional learning curves for robot-assisted laparoscopic pyeloplasty and fundoplication.
- Addressing deficiencies in pre-clinical educational resources for paediatric robot-assisted minimally invasive surgery by inaugurating a multinational hands-on workshop programme.
- Capturing global attitudes of the early adopter paediatric surgeon community to define specialty-specific perceptions towards perceived benefits and limitations of robot-assisted surgery, as well as unambiguous specification requirements for next-generation robots.
- Demonstrating for the first time using *in vivo* data that experience related non-tactile adaptive skills compensate for haptic feedback loss in robot-assisted minimally invasive surgery.
- Developing and validating a force sensing enhanced paediatric laparoscopy simulator as a platform to permit haptic compensatory skills to be acquired in the pre-clinical setting.
- Investigating the performance of robotic versus non-robotic instruments in spatially constrained operative workspaces and identifying a workspace threshold of $200cm^3$ for which smaller non-robotic instruments are better suited for advanced bimanual tasks such as suturing.
- Exploring proof-of-concept and early feasibility assessment for two novel single-shaft robotic platform prototypes to be used in paediatric surgery.

1.5 Patents, Publications and Presentations from this Thesis

1.5.1 Patents related to this thesis

1. Title: CYCLOPS: A Smart Versatile Robotic Tool for Single-Port Access and Natural Orifice Endoscopic Surgery
   Inventor: G Mylonas, **TP Cundy**, GZ Yang, AW Darzi
   Applicant: Imperial College Innovations Ltd
   Patent number: 1316333.2
   Filed: 13th September, 2013.

1.5.2 Publications arising from this thesis

1. **TP Cundy**, K Shetty, J Clark, TP Chang, K Sriskandarajah, NE Gattas, AS Najmaldin, GZ Yang, A Darzi. The first decade of robotic surgery in children. Journal of Pediatric Surgery. 2013 April;48:858–865.
2. **TP Cundy**, HJ Marcus, J Clark, A Hughes-Hallett, EK Mayer, AS Najmaldin, GZ Yang, A Darzi. Robot-assisted minimally invasive surgery for pediatric solid tumors – a systematic review of feasibility and current status. European Journal of Pediatric Surgery. 2014;24(2):127-135.
3. **TP Cundy**, L Harling, HJ Marcus, T Athanasiou, AW Darzi. Meta analysis of robot-assisted versus conventional laparoscopic fundoplication in children. Journal of Pediatric Surgery. 2014;49(4):646-652.
4. **TP Cundy**, NE Gattas, GZ Yang, AW Darzi, AS Najmaldin. Experience related factors compensate for haptic loss in robot-assisted laparoscopic surgery. Journal of Endourology. 2014;28(5):532-528.
5. **TP Cundy**, L Harling, A Hughes-Hallett, EK Mayer, AS Najmaldin, T Athanasiou, GZ Yang, A Darzi. Meta analysis of robot-assisted versus conventional laparoscopic and open pyeloplasty in children. British Journal of Urology International. 2014;114(4):582-594.
6. **TP Cundy**, HJ Marcus, A Hughes-Hallett, AS Najmaldin, GZ Yang, A Darzi. International attitudes of early adopters to current and future robotic technologies in pediatric surgery. Journal of Pediatric Surgery. 2014;49(10):1522-1526.
7. **TP Cundy**, E Thangaraj, H Rafii-Tari, CJ Payne, G Azzie, MH Sodergren, GZ Yang, AW Darzi. Force sensing enhanced simulation environment (ForSense) for laparoscopic surgery training and assessment. Surgery. [in press]

8. **TP Cundy**, NE Gattas, A White, GZ Yang, A Darzi, AS Najmaldin. Learning curve evaluation using CUSUM analysis – a clinical example of pediatric robot-assisted laparoscopic pyeloplasty. Journal of Pediatric Surgery. [in press]
9. **TP Cundy**, SP Rowland, NE Gattas, AD White, AS Najmaldin. The learning curve of robot-assisted laparoscopic fundoplication in children – a prospective evaluation and CUSUM analysis. The International Journal of Medical Robotics and Computer-Assisted Surgery. [in press]
10. **TP Cundy**, EK Mayer, JI Camps, LH Olsen, G Pelizzo, GZ Yang, A Darzi, AS Najmaldin. Training and education in pediatric robot-assisted minimally invasive surgery: lessons learned from an inaugural multinational workshop. Journal of Robotic Surgery. [in press]
11. **TP Cundy**, HJ Marcus, A Hughes-Hallett, T MacKinnon, AS Najmaldin, GZ Yang, A Darzi. Robotic versus non-robotic instruments in spatially constrained operative workspaces – a pre-clinical randomized crossover study. British Journal of Urology International. [in press]

1.5.3 Other publications arising from work related to this thesis

1. V Vitiello, SL Lee, **TP Cundy**, GZ Yang. Emerging robotic platforms for minimally invasive surgery. IEEE Reviews in Biomedical Engineering. 2013;6:111–126.
2. G Mylonas, V Vitiello, **TP Cundy**, A Darzi, GZ Yang. CYCLOPS: a versatile robotic tool for bimanual single-access and natural-orifice endoscopic surgery. Proceedings of the 2014 IEEE International Conference on Robotics and Automation.
3. HJ Marcus, A Hughes-Hallett, **TP Cundy**, D Nandi, GZ Yang, A Darzi. Robotic surgery: not everything that counts can be easily counted. British Medical Journal. 2013 April; 346: f2461.
4. J Clark, D Noonan, V Vitiello, MH Sodergren, J Shang, CJ Payne, **TP Cundy**, GZ Yang, A Darzi. A novel flexible hyper-redundant surgical robot: prototype evaluation using a single incision flexible access pelvic application as a clinical exemplar. Surgical Endoscopy. [in press]
5. SP Rowland, **TP Cundy**, JA Harikrishnan, AS Najmaldin. Pediatric robot-assisted laparoscopic heminephroureterectomy. Journal of Pediatric Urology. [under peer review]

1.5.4 Oral presentations arising from this thesis

1. **TP Cundy**, K Shetty, J Clark, TP Chang, K Sriskandarajah, NE Gattas, A Najmaldin, GZ Yang, A Darzi. The first decade of robotic surgery in children. International Pediatric Endosurgery Group (IPEG) 22nd Annual Congress, Beijing, China. June, 2013.
2. **TP Cundy**, NK Patel, J Shang, CA Seneci, CJ Payne, V Vitiello, J Clark, JP Teare, AW Darzi, GZ Yang. Per-oral endoscopic cardiomyotomy and pyloromyotomy using a flexible snake robot – proof of concept with a porcine model. 6th Hamlyn Symposium on Medical Robotics, London, UK. June, 2013.
3. **TP Cundy**. Horizon scanning future robotic platforms for pediatric minimally invasive surgery. Paediatric Robotic Surgery Inaugural European Workshop, 6th Hamlyn Symposium on Medical Robotics, London, UK. June, 2013.
4. **TP Cundy**, E Thangaraj, MH Sodergren, AS Najmaldin, SA Clarke, GZ Yang, A Darzi. Development, integration and preliminary validation of a sensing enhanced simulation environment (SEnSE) for paediatric minimally invasive surgery. Trainee Session, British Association of Paediatric Surgery (BAPS), Bournemouth, UK. July, 2013. ** Best Presentation Award
5. **TP Cundy**, NE Gattas, AS Najmaldin. Robot-assisted minimally invasive fundoplication in infants and toddlers – is age a limitation? 3rd European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Marseille, France. September 2013 .
6. **TP Cundy**, HJ Marcus, A Hughes-Hallett, AS Najmaldin, GZ Yang, A Darzi. International attitudes of early adopters to current and future robotic technologies in pediatric surgery. International Pediatric Endosurgery Group (IPEG) 23rd Annual Congress, Edinburgh. July, 2014.
7. **TP Cundy**, GZ Yang, A Darzi, AS Najmaldin. Learning curve analysis in pediatric surgery using the cumulative sum (CUSUM) method – a statistical primer and clinical example. International Pediatric Endosurgery Group (IPEG) 23rd Annual Congress, Edinburgh. July, 2014.
8. **TP Cundy**, EK Mayer, JI Camps, LH Olsen, G Pelizzo, GZ Yang, A Darzi, AS Najmaldin. Education and training in pediatric robot-assisted minimally invasive surgery: lessons learned from an inaugural multinational workshop. 4th European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Bratislava, Slovakia. October, 2014.
9. **TP Cundy**, HJ Marcus, A Hughes-Hallett, T MacKinnon, AS Najmaldin, GZ Yang, A Darzi. Robotic versus non-robotic instruments for minimally invasive surgery in spatially constrained operative workspaces. 7th Hamlyn Symposium on Medical Robotics, London, UK. July, 2014.

1.5.5 Invited oral presentations arising from work related to this thesis

1. Debate panel member. "Why robotic surgery is the future in paediatrics". 4th European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Bratislava, Slovakia. October, 2014.

1.5.6 Other oral presentations arising from work related to this thesis

2. NK Patel, **TP Cundy**, GZ Yang, J Teare, A Darzi. A novel flexible snake robot for endoluminal upper gastrointestinal surgery. Digestive Diseases Week (DDW), Chicago. May, 2014.
3. G Mylonas, V Vitiello, **TP Cundy**, A Darzi, GZ Yang. CYCLOPS: a versatile robotic tool for bimanual single-access and natural-orifice endoscopic surgery. IEEE International Conference on Robotics and Automation, Hong Kong. June, 2014.
4. O Jackson, **TP Cundy**, AS Najmaldin. A technique for minimally invasive gastrostomy tube insertion in children using an intracorporeal purse-string anchoring hitch suture. 3rd European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Marseille, France. September 2013. ** Best Presentation Award
5. V Vitiello, **TP Cundy**, A Darzi, GZ Yang, GP Mylonas. Augmented instrument control for the CYCLOPS robotic system. 7th Hamlyn Symposium on Medical Robotics, London, UK. July, 2014.
6. SP Rowland, **TP Cundy**, AS Najmaldin. Instrument selection in robot-assisted paediatric surgery: an insight into consumables usage and costs in the European setting. 4th European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Bratislava, Slovakia. October, 2014.
7. M Phillips, **TP Cundy**, AS Najmaldin. Hiatal repair and fundoplication using the da Vinci system: a video presentation. 4th European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Bratislava, Slovakia. October, 2014.
8. JQ Tay, **TP Cundy**, AS Najmaldin. Laparoscopic lower urinary tract and genital surgery in children – appraising the role of robot-assistance. 4th European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Bratislava, Slovakia. October, 2014.

1.5.7 Poster presentations arising from this thesis

1. **TP Cundy**, K Sriskandarajah, K Shetty, TP Chang, MH Sodergren, J Clark, GZ Yang, A Darzi. Water-jet assisted esophago-gastric submucosal dissection: a feasibility study and exploration of pressure effect settings. Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Annual Meeting, Baltimore, United States.
2. **TP Cundy**, NE Gattas, SM Whiteley, A Springer, AS Najmaldin. Robot-assisted laparoscopic surgery in paediatric urology – a seven year single surgeon experience. 6th Hamlyn Symposium on Medical Robotics, London, UK. June, 2013.
3. **TP Cundy**, AS Najmaldin. Haptic loss of compensated by experience related factors in robot-assisted minimally invasive surgery. European Robotic Urology Congress (ERUS), Stockholm, Sweden. September 2013.
4. **TP Cundy**, SP Rowland, AS Najmaldin. Success and limitations of robotic surgery in infants. 7th Hamlyn Symposium on Medical Robotics, London, UK. July, 2014.

1.5.8 Poster presentations arising from work related to this thesis

1. NK Patel, **TP Cundy**, J Shang, CJ Payne, CA Seneci, V Vitiello, J Clark, J Teare, A Darzi, GZ Yang. Endoscopic submucosal dissection for gastric lesions using a flexible snake robot – early assessment and feasibility study. 6th Hamlyn Symposium on Medical Robotics, London, UK.
2. SP Rowland, **TP Cundy**, J Harikrishnan, AS Najmaldin. Paediatric robot-assisted laparoscopic heminephroureterectomy. 7th Hamlyn Symposium on Medical Robotics, London, UK. July, 2014.

CHAPTER 2 CLINICAL APPLICATION & ADOPTION OF PAEDIATRIC ROBOTIC SURGERY

Content from this chapter was published as:

TP Cundy, K Shetty, J Clark, TP Chang, K Sriskandarajah, NE Gattas, AS Najmaldin, GZ Yang, A Darzi. The first decade of robotic surgery in children. Journal of Paediatric Surgery. 2013 April;48:858–865.

TP Cundy, HJ Marcus, J Clark, A Hughes-Hallett, EK Mayer, AS Najmaldin, GZ Yang, A Darzi. Robot-assisted minimally invasive surgery for paediatric solid tumours – a systematic review of feasibility and current status. European Journal of Paediatric Surgery. 2014;24(2):127-135.

Content from this chapter was presented as:

TP Cundy, K Shetty, J Clark, TP Chang, K Sriskandarajah, NE Gattas, A Najmaldin, GZ Yang, A Darzi. The first decade of robotic surgery in children. International Paediatric Endosurgery Group (IPEG) 22nd Annual Congress, Beijing, China. June, 2013.

2.1 The History of Surgical Robotics

A robot is broadly defined as a mechanical device which often mimics a biological form and is capable of performing tasks on command or in a pre-programmed automated fashion. Amongst the general public, when one thinks of robotic technology it generally provokes emotive associations of modernism and futuristic science in which elements of human life are replaced by unemotional but highly intelligent autonomous humanoid objects. Science fiction films that attempt to portray a vision of the future are heavily decorated with countless forms of robots. The common belief is that the future world and robots are inseparably linked.

2.1.1 Robotics in the Renaissance

Surprisingly, robots are not exactly modern. In circa 1495 AD, a 26 year-old Leonardo da Vinci designed the earliest known robot [1] (Figure 2.1). The sophisticated humanoid robot that he envisioned was a grand mechanical knight-in-armor for warfare. Similar to his manned flying machine that replicated avian flight, Leonardo's fascination with a deeper understanding of anatomy and natural biology is felt to have inspired his pursuit to animate an automated humanoid device.

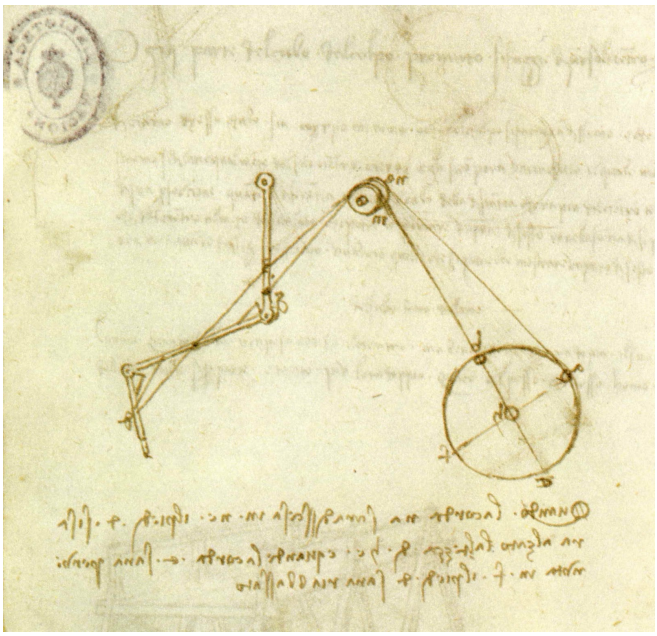


Figure 2.1 Technical drawing from a notebook of Leonardo da Vinci depicting what is probably the actuated arm mechanism for a semi-automatic knight warrior. This drawing is believed to be the earliest design for a robot. It is one drawing amongst many that comprises the *Codex Atlanticus,* the largest single collection of da Vinci's drawings. Picture courtesy of Google.

To the unassuming enemy or observer, Leonardo's planned robot had the external appearance of a regular Germanic knight suited in armor traditionally worn by Milanese militia [1] (Figure 2.2). Internally, there would be a complex mechanical system with independent operating systems for both upper and lower limbs. The lower limb joints actuated with 3 degree-of-freedom (DOF) and were powered by an external crank arrangement that tensioned cable-tendon joints. Each upper limb joint actuated with 4 DOF and was powered and controlled by a mechanical analog-programmable controller within the chest compartment. Breakthroughs in electrical energy science were not to occur for at least another 300 years so the mechanical devices in the da Vinci robot are presumed to have been intended as human-powered, but automatically operated [1]. It is believed to have been able to stand, sit up, wave its arms, move its head, raise its visor, open its jaws and produce sound akin to battle cry drums. Historians believe that Leonardo first publically displayed his robotic knight in 1945 during a celebration at the Sforza Castle in Milan.

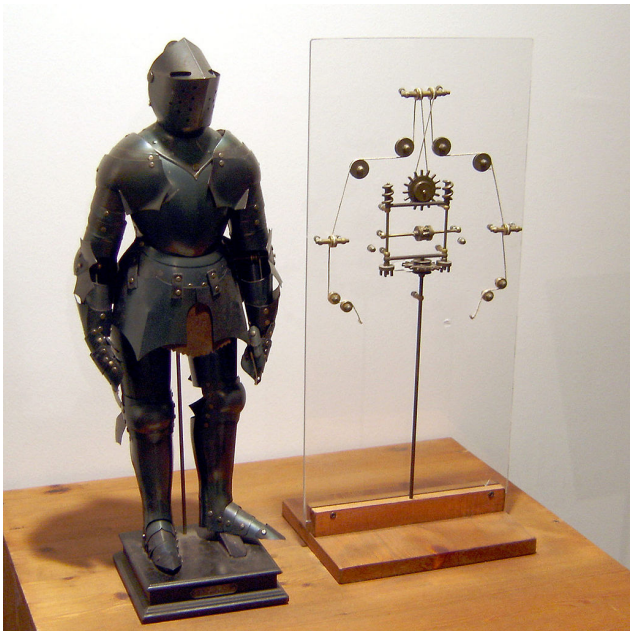


Figure 2.2 A model of Leonardo's robotic knight demonstrating the exterior suit of armor and interior workings for the upper limbs and head. Picture courtesy of Wikipedia.

2.1.2 Robots in the Modern World

The term "*robot*" is credited to the Czech playright Joseph Capek who, in 1917, first used the word to describe fictional automata characters in the short story *Opilec* that was later adapted by his brother Karel into the theatre play "*Rossum's Universal Robots*". The origin of the word robot is therefore based on a Czech word "*robata*" that means "*laborer*". Modern use of robotics is

predominantly for industrial tasks such as production line assembly or packaging. These tasks are labor-intensive and repetitive. Robotic arms can perform tasks such as automobile assembly with far greater strength, speed, safety, precision and reliability. Unlike a human, robots can function 24 hours a day without physical fatigue or fallibility. In 1961, the Unimate robot (Unimation Inc., NJ) was developed as a 6 DOF mechanical arm to handle molten die-castings and perform spot welding. This was the earliest industrial robot and since this time robots have continued to radically transform the efficiency and ability of many industries around the globe.

2.1.3 Robot-Assisted Surgery

During the late 1980s, rapid advances in robotics were occurring at the same time as the revolutionary introduction of minimally invasive surgery. For many of the same reasons that robots augmented or substituted human insufficiencies to be advantageous in major industry, the use of robot-assistance was explored in minimally invasive surgery. For surgeons, the transition from open surgery to minimally invasive surgery demanded necessary compromises in almost all innate sensory and physical faculties (Figure 2.3). Vision became two-dimensional from three-dimensional, and low resolution from high-resolution quality. Dexterity for tissue manipulation became limited to 4 DOF per upper limb from 7 DOF. Sense of touch for appreciation of tissue characteristics became crude and almost absent. Visuomotor coordination was greatly disturbed by motion parallax and scaling by virtue of long instruments articulated around a fulcrum point. Robot-assistance was proposed as a technological solution to restore many of these impediments towards those appreciated in open surgery and also to venture beyond the natural abilities of human performance.

Surgical robots are generally classified into three main categories according to the level of control that the surgeon has over the robot [2]. Firstly, *active autonomous robotic systems* perform pre-defined operative tasks such as image-guided biopsy or bone milling without any real-time master control. Secondly, *semi-active robotic systems* allow the surgeon and robot to share control predominantly as surgical assist devices. Thirdly, *master-slave teleoperator robotic systems* involve the surgeon (master) having complete control over a bed-side operating device (slave). These modular systems are also known as *teleoperator, telemanipulator* or *telepresence* robots. The common prefix "*tele*" denotes that the surgeon (master) and robot (slave) operate at a distance from one another, either wirelessly or connected through electronic cabling.



Figure 2.3 Conventional laparoscopic surgery (written informed consent for clinical photography was obtained from the patient).

The earliest in-human use of surgical robots involved active or semi-active robotic systems. In the late 1980s, the PUMA 560 (Programmable Universal Manipulation Arm, Unimation Inc., NJ) was used for image-guided brain biopsy and the PROBOT (Imperial College London, UK) was used for image-guided transurethral prostatectomies. In 1992, the ROBODOC (Integrated Surgical Systems, CA) was introduced for image-guided total hip arthroplasty. In 1996, the AESOP 1000 (Automated Endoscopic System for Optimal Positioning 1000, Computer Motion, CA) became the first robotic system to receive FDA approval for use in general surgery. As a surgical assist robotic system, the AESOP replaced the need for a human camera-holder in laparoscopic surgery with a table-mounted robotic camera holder arm that was under surgeon control through a voice activation interface named the HERMES Control Center.

Teleoperator robotic systems are the most common and well-known surgical robots in clinical use today. Initial development of these systems was heavily funded by the National Aeronautics and Space Administration (NASA) in the United States with the goal of a robotic arm being used by astronauts in space exploration. Computer Motion released the ZEUS® system (Computer Motion, CA) in 1998 once FDA clearance was obtained for use in laparoscopic surgery (Figure 2.4). At the time this was the first commercially available teleoperator robotic system for surgery. The slave component of the ZEUS® consisted of three robotic arms that were rail-mounted to the operating table. One of the arms was the AESOP laparoscope holder and the other two arms provided 4 DOF

each for working instrument (Figure 2.4). To control the ZEUS® robot, the surgeon sat comfortably at a separate master console with a video monitor and operated the AESOP via a voice headset and used two egg shaped manipulators to actuate the working instrument arms.



Figure 2.4 ZEUS Master-Slave Robotic System. (picture courtesy PRWeb http://ww1.prweb.com/prfiles/2007/05/10/525578/iBotA.bmp)

In 2001, a transatlantic telepresence robot-assisted laparoscopic cholecystectomy was performed on a 68 year-old lady using the ZEUS robotic system. This highly publicised procedure attracted worldwide attention and was an emphatic demonstration of the ability and reliability of the telepresence surgery concept. The patient was located in the Strasbourg Civil Hospital in Eastern France and the team of French surgeons led by Professor Jacques Marescaux were located in New York. A dedicated high speed 155 millisecond bandwidth fibreoptic telecommunications channel was set up by France Telecom with only 150 milliseconds latency. The symbolic procedure was successfully completed in 54 minutes and was termed "*Operation Lindburgh*" in recognition of Charles Lindburgh who was the first person to fly solo across the Atlantic Ocean.

Computer Motion merged with Intuitive Surgical in 2003. Details surrounding this merger are rich in rumour and speculation. Some believe that Intuitive Surgical acquired Computer Motion out of desire to end incessant litigation over accusations of intellectual property infringement. Following the dissolution of Computer Motion, the ZEUS® system ceased to be manufactured or marketed.

While Computer Motion was financially supported by NASA, the beginnings of Intuitive Surgical was made possible through investment by the United States military. A prototype developed by

Green, Rosen, Fisher, Satava *et al* at the Stanford Research Institute was demonstrated to the Association of Military Surgeons in the United States. The prototype explored new horizons in battlefield telepresence emergency surgery whereby an armored vehicle was fitted with robotic arms and vision systems. This Medical Forward Area Surgical Team (MEDFAST) vehicle would rapidly locate itself to the battlefield victim and once safely loaded on scene, the surgeon could operate without delay at a Mobile Advanced Surgical Hospital (MASH) up to 30km away. The military supported ongoing research and development (R&D) for this project and appointed the renowned military surgeon Richard Satava to manage it through the Defense Advanced Research Projects Agency (DARPA). Years later after the project established maturity and proof-of-concept, Frederick Moll, a surgeon and entrepreneur, bought out the patent license for the telepresence robotic system and founded Intuitive Surgical Incorporated with Robert Younge and Joseph Freund. Based on the much of the fundamental early work of the battlefield robot, the company developed the da Vinci® Surgical System for mainstream use in clinical surgery.

The da Vinci® Surgical System has become synonymous with the field of robotic surgery. Following the ZEUS® system being made obsolete, the da Vinci® has been the dominant and only approved surgical robot for thoracic and abdominal minimally invasive surgery. Since FDA approval was granted in 2000, over 3000 da Vinci® Surgical Systems have been installed worldwide, of which approximately two-thirds are located in the United States. Cardiac surgery was proposed as one of the primary target applications for the da Vinci®. Exciting new cardiac procedures were performed such as the closed chest coronary artery bypass graft, yet overall uptake in cardiothoracic surgery has been curiously disappointing. Instead, application of the da Vinci® has flourished in urology and more recently in gynaecology.

The ZEUS® and the da Vinci® are similar in that they are both master-slave teleoperator robotic systems, but the two robotic systems differ in many other aspects (Table 2.1). All da Vinci® system models consist of 3 components; 1) a master console, 2) patient side cart, and 3) 3D vision cart. The da Vinci® master console offers a truly immersive and comfortable operating experience by aligning orientation of the field of view and instrument tips with the surgeons body posture (Figure 2.5). This delivers the remarkable illusion of being physically within the magnified operative field and with instrument dexterity that is almost exactly as responsive as having both hands also within the operative field (Figure 2.5). Instinctive dexterity is facilitated by the EndoWrist® instrument design that replicates the 7 DOF that the human hand possesses (Figure 2.6). These DOF include XYZ axis, pitch, yaw, roll and grasp movements.

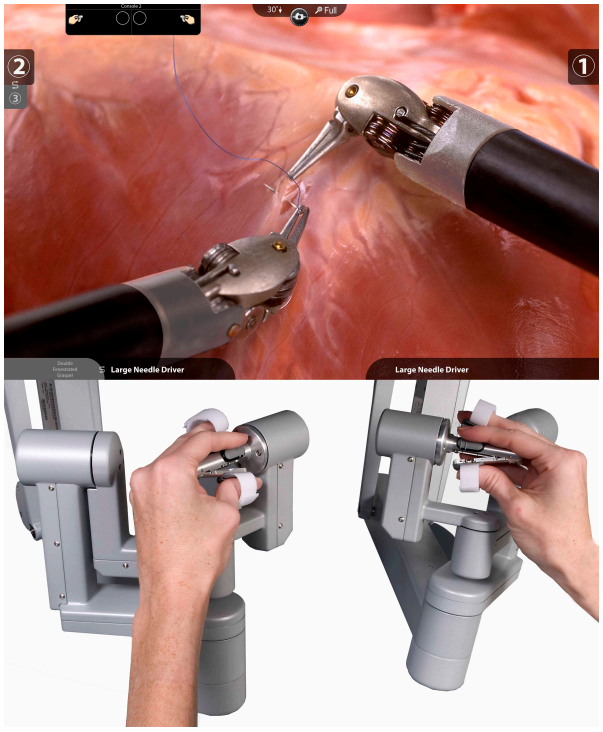


Figure 2.5 The illusion of a fully immersive operative experience with the da Vinci® Surgical System. The top image would represent the entire field of view for the surgeon at the master console. Picture courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).

	Open surgery	Conventional MIS	da Vinci® MIS
Vision	3D HD	2D SD	3D HD
DOF	7	4	7
Visuomotor coordination	Unimpaired	Motion parallax	Restored
Ergonomy	Comfortable	Compromised	Restored
Haptic feedback	Essentially unaffected	Impaired	Absent
Tremor	Natural	Exacerbated	Eliminated

Table 2.1 Key features of open surgery versus conventional minimally invasive surgery (MIS) versus da Vinci® assisted MIS.

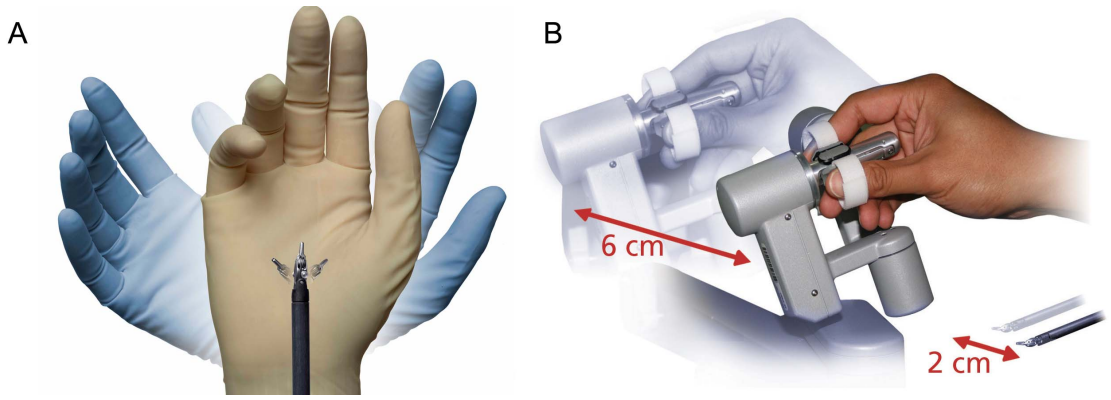


Figure 2.6 The da Vinci® instruments replicate the degrees-of-freedom possessed by the human hand (a), and (b) are controlled using an instinctive interface that can be calibrated to various motion scaling settings to suit procedural needs. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).

Unlike the ZEUS, the da Vinci® patient side cart is a large floor-mounted portable structure. Before the surgeon commences at the master console, the patient side cart is maneuvered to a desired position alongside the operating table where instrument arms are then docked in specially designed ports (Figure 2.7). Early da Vinci® models were 3-armed but later models have all included a 4th arm for tissue retraction. The camera arm is under complete control of the surgeon using the master console hand interface. An electronic pedal clutch mechanism allows the surgeon to alternate between digitized control of the camera arm and instrument arms. A stereoscope is mounted to the robotic camera arm. These stereoscopes consist of two separate endoscopes that are housed together in a single outer casing. The video feed of each scope is independently transmitted to the left or right eye viewer within the master console so that the surgeon views a binocular image. The video system allows 10x or 15x magnification.

Digitizing surgeon hand movements permits computer-assisted enhancements to be transferred to the instruments. Motion parallax is eliminated with the da Vinci® system through computer reversal of the fulcrum effect such that hand movement in a left direction will correspond to movement the instrument tip to the left and not vice-versa as occurs with conventional minimally invasive surgery. Computer control also allows any physiological tremor of the surgeon hand to be filtered out.

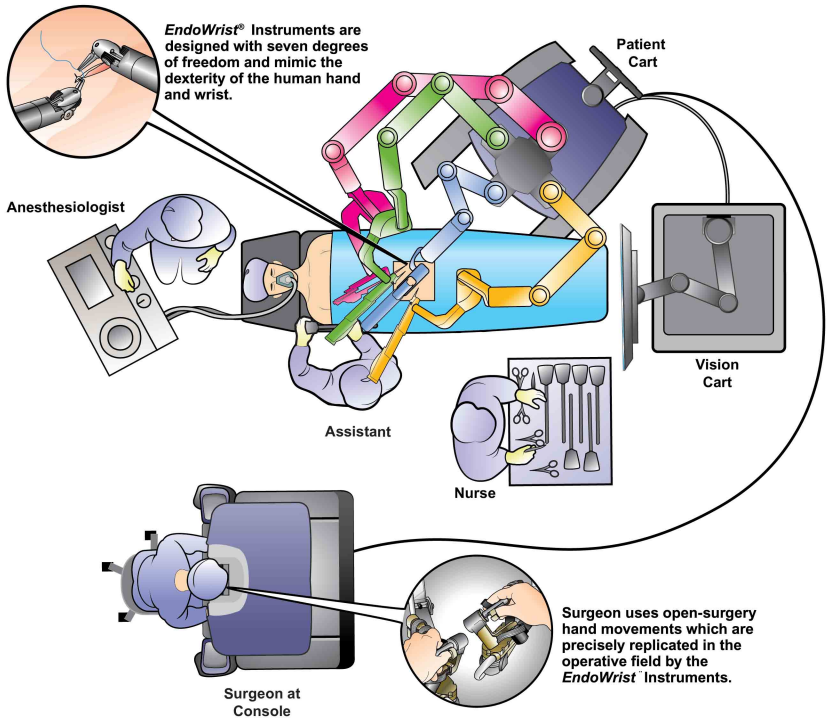


Figure 2.7 Schematic overview of a typical operating theatre set-up for the da Vinci® Surgical System. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).

Several da Vinci® Surgical System models have been released since the da Vinci Standard® became available in 1999 (Figures 2.8 and 2.9). In 2006, the da Vinci S® was released that offered upgraded features of high-definition vision and the TilePro® multi-image display feature. In 2009, the da Vinci Si® was released that offered a dual console option for better pedagogy capabilities as well as the Firefly™ Fluoresence Imaging Vision System. In 2011, the da Vinci® Single-Site® was released as a compatible add-on to the da Vinci Si®. The Single-Site® sought to capitalise on emerging interest for single-port laparoscopy and made this possible with robot-assistance through customised semirigid instruments that are inserted through curved cannulae. Lastly, the da Vinci Si-e® and da Vinci Xi® have been announced for market release in late 2014 or early 2015. The da Vinci Si-e® is promoted as a "*lower-cost system for less complex procedures*" and the da Vinci Xi® is described as a new advanced system with added features that include an overhead boom arm to aid re-positioning for multi-quadrant laparoscopic surgery and ability to dock the endoscope in any of the 4 instrument arms. In general each model has been less bulky, easier to maneuver around the operating theatre, and able to be stored in a more compact way.



Figure 2.8 A visual timeline of da Vinci® Surgical System models including the a) 3-armed da Vinci Standard®, b) 4-armed da Vinci S®, c) da Vinci Si® with dual master consoles, and d) da Vinci Single-Site®. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).

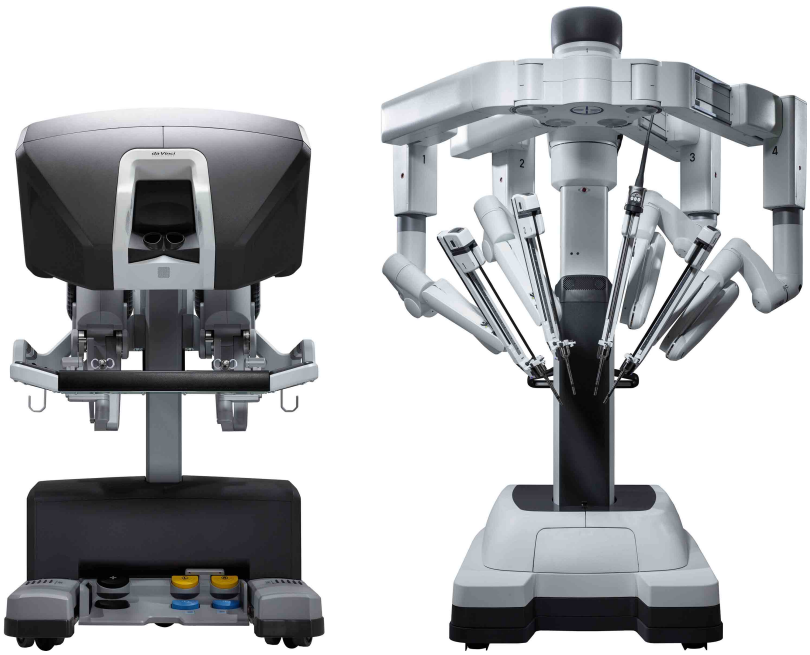


Figure 2.9 The da Vinci Xi® Surgical System. Pictures courtesy of Intuitive Surgical (© 2014 Intuitive Surgical, Inc. with permissions).

2.2 The First Decade of Robotic Surgery in Children

2.2.1 Introduction

The perceived benefits of robotic surgical technology are well suited to paediatric minimally invasive surgery. Design features of present day robotic surgical platforms include motion scaling, greater optical magnification, stereoscopic vision, increased instrument tip dexterity, tremor filtration, instrument indexing, and elimination of the fulcrum effect [2-4]. Individually and collectively, these robotic enhancements offer improvements to conventional minimally invasive surgery, permitting technical capabilities beyond existing threshold limits of human performance for delicate and precise surgery within spatially constrained operative workspaces in children [2, 5-12].

Historically, in the mid-1990's Okada *et al* and Partin *et al* first described the use of robot assistance for surgery in children in the form of an extracorporeal camera holder [13, 14]. Robotic surgical technology has since evolved to more established master-slave platforms, such as the da Vinci® Surgical System. In April 2001, Meininger *et al* published the first cases of robotic surgery in children using a fully-integrated platform [15]. The first of these two Nissen fundoplication procedures was reported as occurring in July 2000 [15-17]. Shortly afterwards, in March 2002, Peters *et al* performed a pyeloplasty using the da Vinci®, understood to have been the first robotic urological procedure in child (personal communication, July 2012) [18, 19].

The evolution of laparoscopic surgery highlights the transitory stages that follow adoption and diffusion of surgical innovation [20-22]. Robotic surgery was introduced to the specialty of paediatric surgery following initial case reports in the early 21st century. Subsequently, this promising surgical technology has undergone a formative ten-year period of introduction, development, early dispersion, exploration and preliminary assessment. In recognition of this important milestone, this chapter aims to provide a comprehensive review of the literature to investigate overall global case volumes, trends, and quality of evidence for the first decade of robotic surgery in children.

2.2.2 Materials and Methods

2.2.2.1 Search methods

A systematic literature search of multiple electronic databases and grey literature sources was performed to retrieve all reported cases of robot-assisted minimally invasive surgery in children (Figure 2.10).

The search period ranged from April 2001 to March 2012. This period spans 10 years from the publication date of the first reported robotic surgical procedure in a child, with an additional 11th year for contemporaneous update. Where available, electronic publication dates were regarded as the dates of publication for classification of retrieved articles to twelve-month periods between the months of April to May. Two reviewers screened identified articles independently for relevance, with disagreements resolved by consensus.

A comprehensive search strategy included the following sources; 1) PubMed, 2) Ovid MEDLINE, 3) EMBASE, 4) PubMed related articles feature, 5) hand searching reference lists from retrieved publications, 6) individual search of a relevant but non-indexed journal, and 7) published abstracts from annual congresses of the International Pediatric Endosurgery Group.

2.2.2.2 Inclusion and exclusion criteria

Robot-assisted general, urological and thoracic surgical procedures were included only, reflective of the specialty remit of paediatric surgery. In an attempt to capture all reported robot assisted procedures in children, exclusion criteria were kept as minimal as possible, detailed in Figure 2.10. No language restrictions were used. Procedures performed using robotic surgical assist systems were excluded, such as those undertaken with the AESOP®. All identified cases performed using robotic master-slave operative platforms were included (Figure 2.11).

Publications were classified into sub-groups based on senior author and institutional affiliation in order to screen for repetition of data. In the event of a larger series being reported that accounted for cases reported in a smaller series from the same institution, the smaller published series was excluded. Where repetition of data could not be determined with complete certainty, exclusion was not undertaken.

2.2.2.3 Data extraction

Bilateral procedures undertaken under than same general anaesthetic were regarded as two independent procedures (i.e. bilateral pyeloplasties and ureteral reimplantations). Similarly, multiple procedures undertaken synchronously under the same general anaesthetic were regarded as independent procedures (i.e. fundoplication *with* gastrostomy, hiatus hernia repair *with* fundoplication, Mitrofanoff appendicovesicostomy *with* antegrade continence enema).

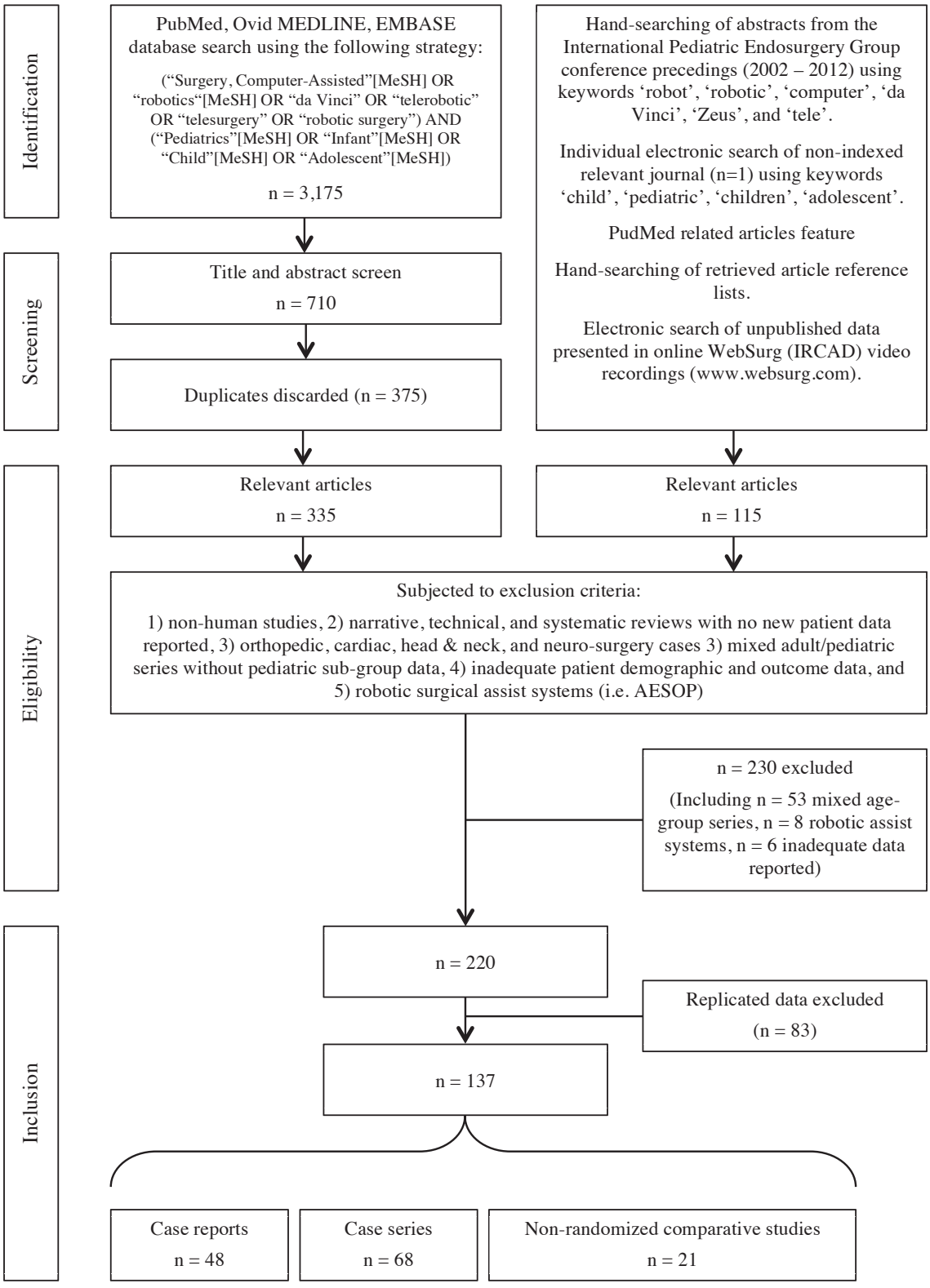


Figure 2.10 A Prisma flow diagram outlining the systematic search strategy.

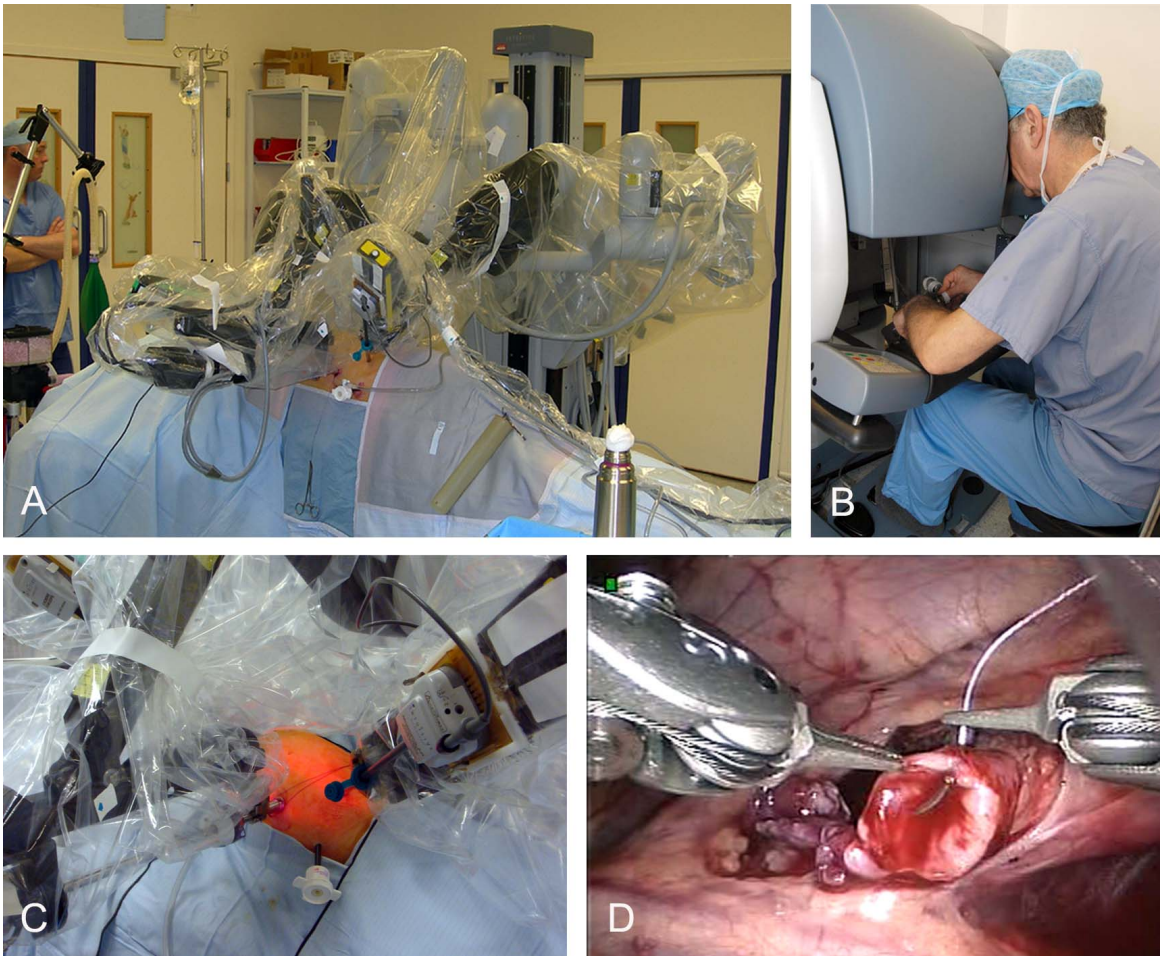


Figure 2.11 An illustrative overview of the operative set-up for paediatric transperitoneal pyeloplasty using the da Vinci® master-slave robotic platform, displaying the a) docked slave component, b) master console, c) port configuration with patient in modified flank position, d) camera view at commencement of ureteral anastomosis.

2.2.3 Results

A total of 220 relevant publications were retrieved. Following exclusion of replicated data, 137 publications were identified, reporting 2393 cases in 1840 patients (Figure 2.10).

The most prevalent abdominal, genitourinary and thoracic procedures reported were fundoplication (n = 424), pyeloplasty (n = 672) and lobectomy (n = 18) respectively (Table 2.2). Overall, the most reported robotic procedure in children to date is pyeloplasty. For both pyeloplasty and ureteral reimplantation procedures, a 9:1 reporting ratio was observed in favour of transperitoneal versus retroperitoneal approach (603:69/672 and 431:48/479 respectively). The youngest reported patient was a 1-day-old neonate, and the smallest reported patient weighed 2.2kg [23].

Analysis of total published case volume by country of origin revealed that publications from the United States comprised a 79% majority (Figure 2.12).

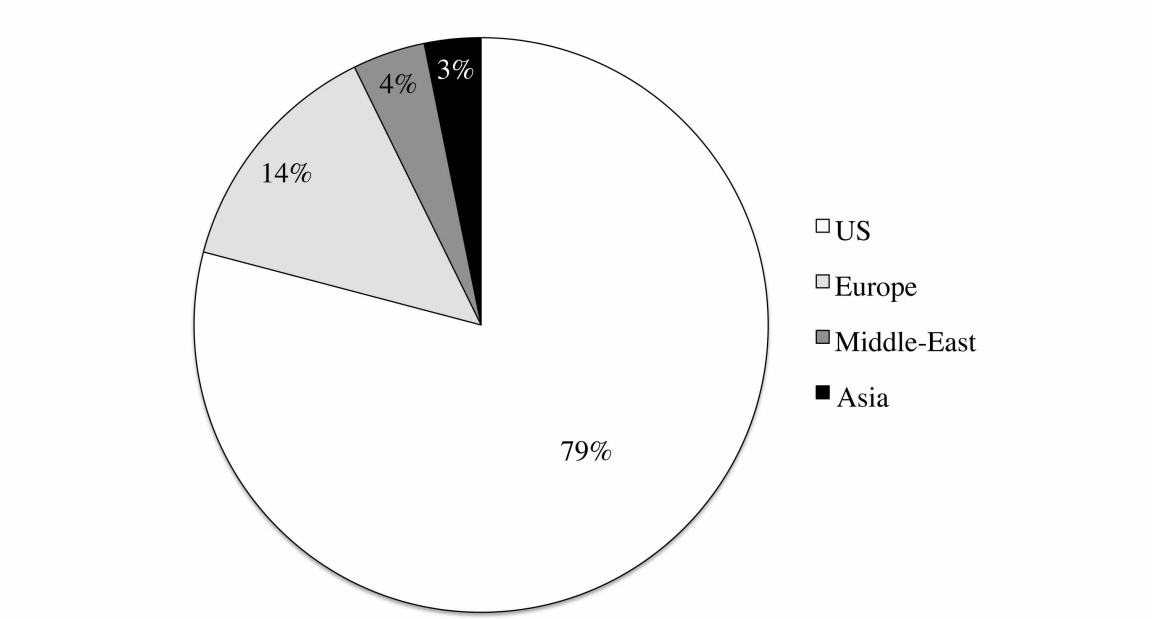


Figure 2.12 Representation of the geographical origin of paediatric robotic surgery publications across major continents. Overall, 220 publications were represented from 18 countries, across 52 institutions.

The da Vinci® Surgical System was the most frequently published platform (n=122/137, 89%), with the remainder of publications reporting cases using the ZEUS® Surgical System (Computer Motion Inc, CA) (n= 5/137, 3.5%) or not citing the robotic platform used.

There was an overall progressive trend of increasing total reported case volume over time (Figure 2.13). The most recently evaluated twelve-month period (April 2011 to March 2012) saw a 37.5% increase in number of publications and a 124% increase in total reported case volume compared to the highest values for earlier periods. Subgroup analysis of case volumes by anatomical region revealed that genitourinary procedures most closely reflected the total reported case volume over time (Figure 2.13). The quality of evidence did not appear to improve over time, however the number of higher quality of evidence publications did increase proportionally to total number of publications (Figure 2.14). No randomised controlled trials involving robotic surgery in children were identified.

The net reported conversion rate was 2.5% (n= 61/2398). The net conversion rates amongst subgroups of abdominal, genitourinary and thoracic procedures were 3.9%, 1.3%, and 10% respectively. The rate of reported robot malfunctions or failures was 0.6% (15/2398).

2.2.4 Discussion

There is moral and professional obligation to closely monitor clinical practice and outcomes for safe implementation of new surgical technology. These prerequisite activities apply to individual surgeons, institutions, regions, countries and global specialty communities, with tendencies to concentrate towards the former. This review is understood to be the largest collation of global case volume data in paediatric robotic surgery to date.

Robotic surgery has been applied to many abdominal, genitourinary and thoracic procedures in children. Most, if not all, procedures that are currently undertaken using conventional laparoscopic or thoracoscopic approaches have been performed using a robotic approach. In this review, it was noted that more complex procedures were reported over time, including Kasai portoenterostomy, Mitrofanoff appendicovesicostomy, and thoracic tumour resection. These procedures demonstrate the potential role of robotic surgery as an enabling innovation, permitting previously intangible minimal access surgical approaches for complex reconstructive procedures in children.

A recent survey of the international paediatric surgical community by Jones *et al* revealed a majority opinion that robotic surgery has a future role in the specialty, despite less than 20% of respondents having any previous experience with robotic surgery [24]. Results of this review support this consensus opinion, identifying increasing numbers of paediatric robotic surgery publications and reported case volumes over time. The accelerated rate of publications and reported case volumes in the most recent twelve-month period reviewed might be interpreted as a sentinel sign of an imminent tipping point for adoption of robotic surgery in paediatric surgery [20, 22]. Interesting trends were also seen among case volumes classified by anatomical regions, with genitourinary procedures comprising greater proportions of total case volumes in recent years. This is in contrast to earlier years, when abdominal procedures such as fundoplication and cholecystectomy predominated the literature. Additionally, widespread geographical distribution of paediatric robotic surgery services was observed, with publications represented from 18 countries, inclusive of several developing countries. The number of institutions represented in the literature was 52; a number that might be considered concentrated given the global nature of net publications in the field.

Gastrointestinal		Genitourinary		Thoracic	
n	**Procedure**	**n**	**Procedure**	**n**	**Procedure**
424	Fundoplication	672	Pyeloplasty	18	Lobectomy
95	Gastrostomy	479	Ureteral reimplantation	14	Thymectomy
92	Cholecystectomy	51	Ureteroureterostomy	9	Benign mass excision
33	Splenectomy	38	Nephrectomy	8	CDH*
26	ARM* reconstruction	34	Mitrofanoff*	5	Oncological
25	Gastric banding	29	Partial nephrectomy	5	Diaphragmatic plication
21	Oesophagomyotomy	18	Augmentation cystoplasty	5	Bronchogenic cyst excision
18	Choledochal cyst excision and Roux-en-Y hepatico/ choledochojejunostomy reconstruction (EC 15/18, IC 3/18)*	16	Retrovesical remnant excision	4	Thoracic sympathectomy
17	Gynaecological	16	Nephroureterectomy	3	Segmentectomy
16	Hiatus hernia repair	15	Ureterocalicostomy	3	OA/TOF* repair
13	CDH*	14	Orchidopexy	2	Duplication cyst excision
12	Oncological	8	Varicocelectomy	1	Cystic hygroma excision
11	Kasai portoenterostomy	7	Ureteropyelostomy		
10	Colectomy	7	Bladder neck sling cystourethropexy		
9	Adrenalectomy	6	Pyelolithotomy		
9	Appendectomy	5	Oncological		
8	Pyloromyotomy	5	Urachal remnant excision		
7	Pyloroplasty	4	Bladder diverticulectomy		
6	Entero-enterostomy	3	Fibroepithelial polyp excision		
5	Small bowel resection	2	Heminephroureterectomy		
4	ACE*	1	Renal vascular hitch		
4	Ladd's procedure	1	Distal ureterectomy (ectopic ureteral stump)		
4	Inguinal hernia repair	1	Hypospadias repair		
3	Duodenal atresia repair	1	Sigmoid vaginoplasty		
2	Duodenojejunostomy for SMA syndrome	1	Gonadal vein ligation (gonadal vein syndrome)		
2	Liver cyst excision				
2	Duplication cyst excision				
1	Pancreaticojejunostomy				
1	Ingested foreign body retrieval				
1	Meckel's diverticulectomy				
1	Rectopexy				
Total = 882		Total = 1,434		Total = 77	

Table 2.2 A summary of paediatric robotic surgery procedures reported in the literature during the review period (n = 137 publications). *(ARM = anorectal malformation, CDH = congenital diaphragmatic hernia, ACE = antegrade continence enema, Mitrofanoff = Mitrofanoff appendicovesicostomy, OA/TOF = oesophageal atresia and tracheo-oesophageal fistula repair)

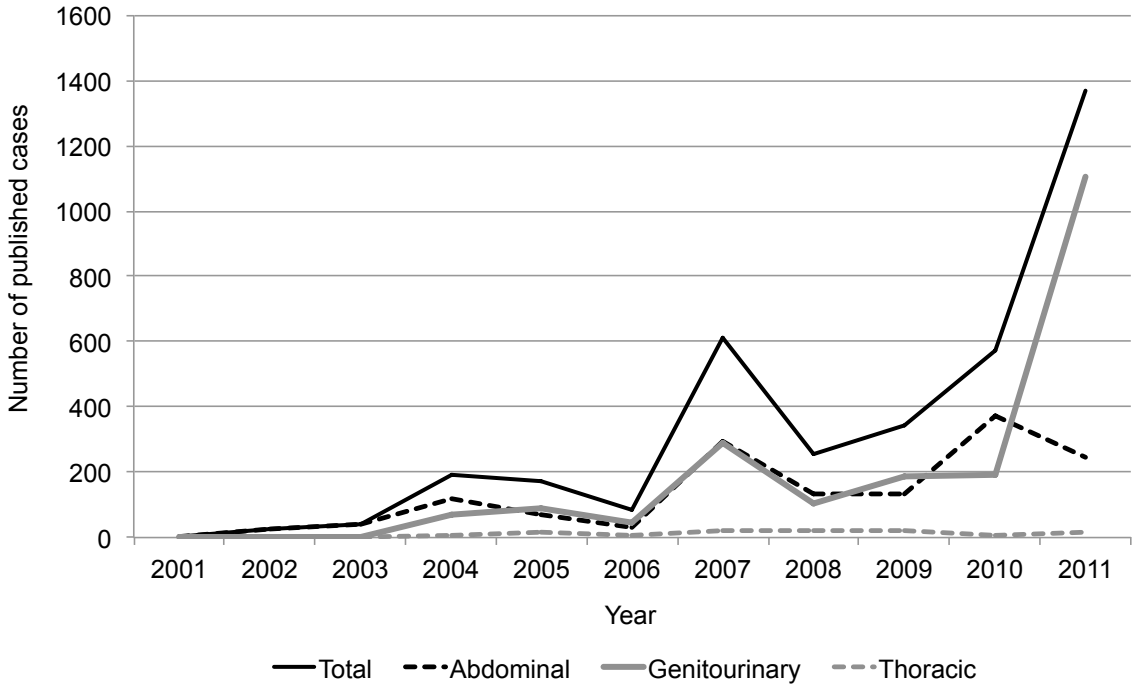


Figure 2.13 Published case volumes of robotic surgical procedures in children, categorised by twelve-month periods from April 2001 to March 2012 (n = 137 publications).

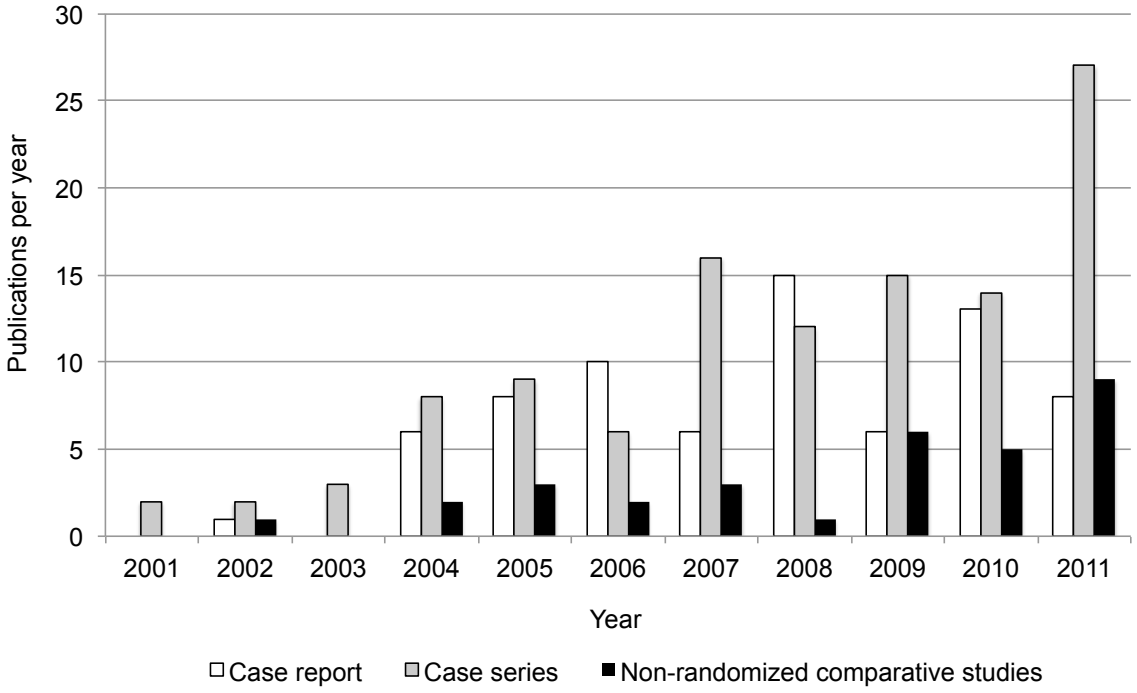


Figure 2.14 The published literature reporting robotic surgery in children, categorised by quality of evidence in twelve-month intervals. During the 11-year review period, the published literature comprises 34% case reports, 52% case series, and 14% non-randomised comparative studies (n= 220 publications).

The rate of reported robot malfunctions or failures was low, providing reassuring evidence for the stability of robotic system software and hardware in the operative environment. The overall conversion rate was found to be comparable with conventional paediatric minimal access surgery [25]. It should be noted that this conversion rate is comprised of cases that would represent the far left of many surgeons' robotic surgery learning curves. Higher net conversion rates for thoracic procedures are suspected to be due to small subgroup sample size and learning curve effect. Of note, 25% (2/8) of converted thoracic procedures were successfully completed using conventional thoracoscopic technique.

Six large case series reporting over one hundred procedures each were included in this review [23, 26-30]. There was a trend of larger series being reported over time, with four of these six larger studies being published in the most recent twelve-year review period [27-30]. The largest series identified was by Katsuri *et al*, who reported 300 extravesical ureteral reimplantations undertaken in 150 patients [28]. The remaining five large series ranged in size from 101 – 161 procedures. Although outside this review period, several abstracts have recently been published by Meehan *et al* and Najmaldin *et al*, both reporting single institution case volumes of over three hundred procedures [31, 32].

The field of robotic surgery in general is rapidly evolving. Already within this review period, three models of the da Vinci® Surgical System have been released. Included in this review is the first reported robotic da Vinci® Single-Site™ procedure to be undertaken in a child [33].

In 2009, the Balliol Collaboration defined a framework to identify the stages that follow the evolution of surgical innovations [20]. The four stages comprising this framework include 1) Innovation, 2a) Development, 2b) Early Dispersion and exploration, 3) Assessment and 4) Long-term implementation and monitoring ('IDEAL') [20]. The first decade of robotics in paediatric surgery has been plentiful in reports that demonstrate safety and feasibility, a characteristic that would allocate current status within Stage 2b of the IDEAL framework. It is recognised that different study designs are appropriate at different stages of innovation [20]. Evidence-based advancement of surgical technology through all stages of innovation in paediatric surgery has traditionally relied on less than desired qualities of evidence, predominantly in the form of case studies [21, 34, 35]. This study reports encouraging trends towards larger volume case series being reported, however this is not reflected by trends of higher quality evidence. The majority of existing literature is Level 3b quality evidence or lower. Randomised controlled trials (RCTs) are considered the gold-standard method of comparative assessment for new surgical techniques and technology. Timing of RCTs during stages of surgical innovation is important and may influence

trial outcome [34, 36]. Recognised barriers to undertaking randomised controlled trials in surgical disciplines are heightened in paediatric surgery by additional ethical and scientific challenges [34, 37-39]. The proportion of RCTs in the paediatric surgery literature is reported as ranging between 0.05 – 3% [35, 40, 41]. No randomised controlled trials were identified in this review.

Although beyond the scope of this review, equipoise is arguably now established for many robotic surgical procedures in children, signaling a need for more prospective controlled trials to move beyond the era of early dispersion and development (Stage 2b), and into an era of assessment (Stage 3) through critical appraisal. While RCTs in paediatric robotic surgery should certainly now be encouraged and supported, at the same time emphasis should be focused on improving standard and rigor of case studies and non-randomised comparative studies [38]. These studies should ideally be prospective in design with carefully considered methodology and selection of procedure specific process or outcome variables [38, 41]. In this review, a considerable degree of data heterogeneity was observed in reporting measures for patient demographic information, operative details and outcomes. Standardisation of these reporting measures would benefit future efforts of data synthesis for systematic review and meta-analysis.

It is acknowledged that this review is limited by reporting bias; specifically publication, duplication and time lag biases. Efforts were made to eliminate duplication bias, with screening and subsequent exclusion of 83 papers or abstracts that contained data repetition. Despite these potential sources of bias, comprehensive review of the available literature provides the most tangible surrogate measure of global case volumes and trends for paediatric robotic surgery.

In conclusion, robotics holds exciting promise to overcome many of the barriers associated with current surgical technology in paediatric surgery, while retaining all the benefits. It also offers opportunity as an enabling innovation to broaden the remit of minimally invasive surgery to include more complex procedures in children. By comprehensively examining literature to quantify publication output and case volume trends, this review reveals expanding global adoption and diffusion of innovation during the first decade of robotic surgery in children. Future evolution and evaluation should occur simultaneously within the next decade of paediatric robotic surgery, such that wider and broader clinical uptake is led by higher quality evidence.

2.3 Robot-Assisted Minimally Invasive Surgery for Paediatric Solid Tumours

2.3.1 Introduction

Surgical resection is a key component of multimodal treatment strategies for many paediatric solid tumours. With overall cure rates for childhood tumours approaching 80% [42], there is an incentive to seek further means for improved quality of life through reduced surgery-related morbidity. The first reports of minimally invasive surgery (MIS) in paediatric oncology appeared in the mid-1990s [43-45]. Well-recognised advantages of MIS include decreased post-operative pain, expedited recovery, earlier feeding and reduced wound-related complications. For oncological indications, MIS might enable more specific patient benefits such as less blood loss [46, 47], earlier transition to post-operative adjuvant therapy [47-50], and possible biological gains at a cellular level [51, 52].

While diagnostic and staging purposes of MIS have become well defined [53-55], therapeutic roles remain less accepted and even controversial [49, 54-59]. This might be considered surprising given the widespread popularity and experience with MIS for non-oncological indications. Attributing exact reasons for such cautious clinical uptake is mostly speculative but might be partly explained by a perceived threat to safe oncological principles posed by the high degree of technical difficulty associated with these complex procedures [55, 58, 60, 61]. Solutions to these challenges might be met through a range of technical and ergonomic enhancements offered by robotic surgical technology.

The aim of this chapter is to systematically review the current status of robot-assisted MIS for paediatric solid tumours and to critically appraise whether the evidence supports further exploration and adoption.

2.3.2 Methods

The review protocol was registered on the PROSPERO international prospective database of systematic reviews (CRD42013003752).

2.3.2.1 Search methods

A systematic search of multiple electronic databases was undertaken (PubMed, Ovid Medline and EMBASE) (Figure 2.15). The search period was for the years 2002 to 2012 inclusively. Two

reviewers independently undertook title and abstract screen, with disagreements resolved by consensus discussion.

The primary search strategy was supplemented by 1) electronic search of abstracts from annual congresses of the International Society of Paediatric Oncology and International Pediatric Endosurgery Group between 2003 – 2012 using the keyword 'robot', 2) reference lists of retrieved articles, and 3) PubMed related articles feature.

2.3.2.2 Eligibility criteria

Inclusion criteria were defined as 1) clinical procedures in children (<18 years or treated with internationally recognised paediatric oncology protocols i.e. Children's Oncology Group or European Paediatric Oncology Group), 2) therapeutic MIS for resection of benign or malignant solid tumour(s), and 3) utilisation of a robotic surgical platform. Studies were excluded if they exclusively involved computer-assisted image guidance, stereotactic procedures (i.e. CyberKnife®), reported duplicated data, contained insufficient clinical data, or were non-clinical. No language restrictions were imposed.

2.3.2.3 Data extraction

Patient demographic information, operative details, oncological outcomes, and surgical complications were retrieved from included studies. Corresponding authors were contacted in the event of insufficient data being reported in studies, such as mixed adult/paediatric series without age category sub-classification.

2.3.3 Results

A total of 40 robot-assisted solid tumour resection procedures were identified (Table 2.3).

Varied tumour biology was observed, with 21 different pathologies reported. Pathology was benign in 37.5% (15/40), malignant in 35% (14/40) and intermediate or indeterminate in 27.5% (11/40). Aside from two cases [62], all indications were for treatment of primary tumours. Anatomical location of tumours was abdominal (52.5%), pelvic (20%), mediastinal (12.5%), neck (7.5%), and thoracic (7.5%). Although retroperitoneoscopic approaches were not described, tumours involved retroperitoneal structures in more than one-third of all cases.

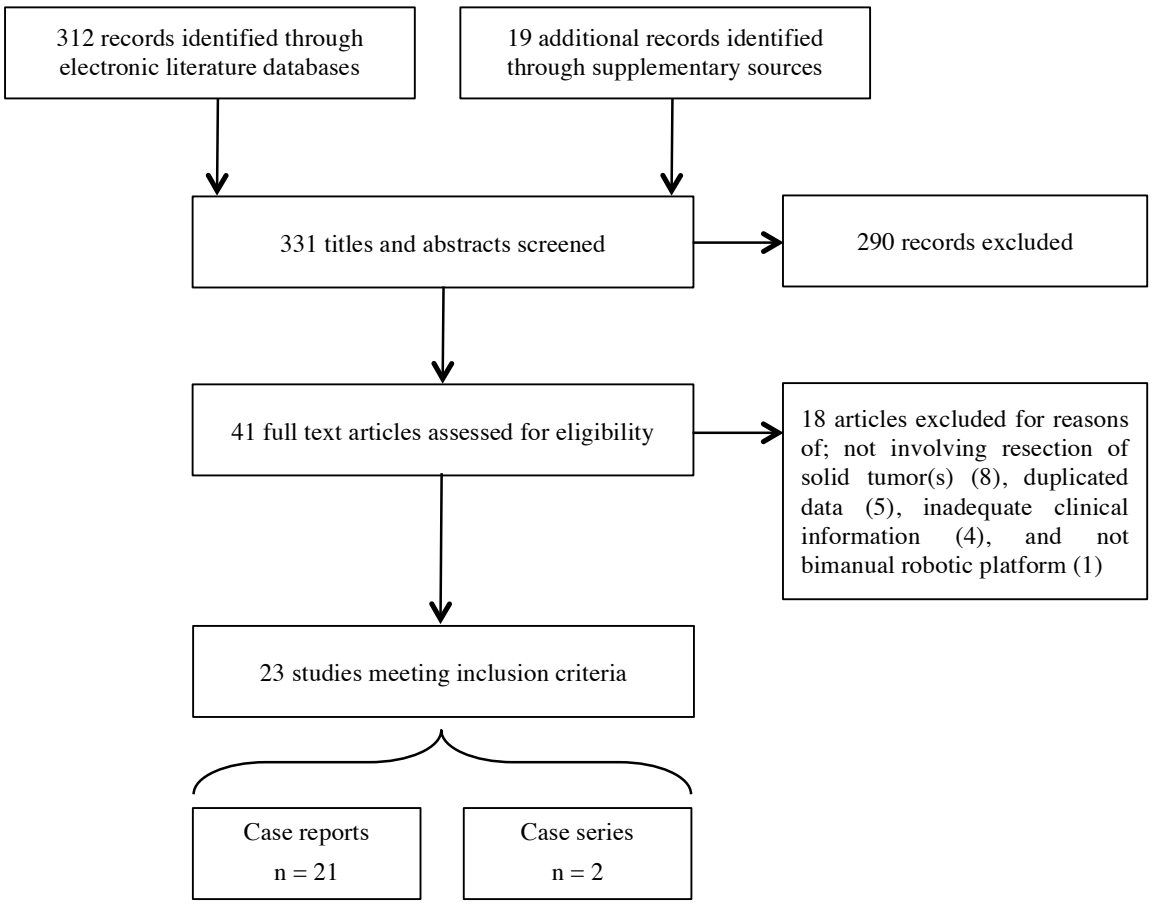


Figure 2.15 A Prisma flow diagram [63] depicting the systematic process undertaken using the search strategy "Neoplasms"[MeSH] AND ("Surgery, Computer-Assisted"[MeSH] OR "robotics"[MeSH] OR "da Vinci" OR "telerobotic" OR "telesurgery" OR "robotic surgery") AND ("Pediatrics"[MeSH] OR "Infant"[MeSH] OR "Child"[MeSH] OR "Adolescent"[MeSH]). Case series were regarded as articles reporting ≥ 3 relevant cases that met inclusion criteria.

Tumour size ranged from 10 – 110mm maximal cross-sectional diameter. Among tumour sizes that were reported (23/40), subgroup analysis assigned by maximum measurements of 10 – 30mm, 30 – 50mm, 50 – 80mm and > 80mm, revealed distributions of 39%, 13%, 43.5% and 4.5% respectively. Interestingly, the majority of cases involved adolescent patients with less than 15% of children being younger than teenage years at the time of surgery (Table 2.3). The youngest patient identified was a 1-year old boy [58].

The da Vinci® Surgical System was the robotic platform utilised in all cases. There were no documented events of robot malfunction or failure. Real-time image guidance was reported for two

cases only, described by Volkin *et al* who used intra-operative ultrasound to aid definition of pheochromocytoma resection margins during partial adrenalectomy [64].

2.3.3.1 Study details

The relevant literature was limited to Level 4 clinical evidence, comprised of case reports and several case series (Figure 2.15). Mixed adult/paediatric series represented 22% (5/23) of publications that met inclusion criteria, and 50% (2/4) of publications from which inadequate data could be obtained (Figure 2.15). The earliest reported case may be attributed to Gutt and Heller *et al* [16], who are also credited with the first robot-assisted procedure performed in a child.

2.3.3.2 Oncological outcomes

The operative goal for all procedures was for full tumour clearance with curative intent. Neoadjuvant chemotherapy was reported as part of the treatment strategy in three cases [58, 65, 66]. There were no reports of positive microscopic tumour margins. Although length of follow up differed considerably amongst studies (range 2 – 72 months), no local tumour recurrence or port-site metastases were recognised. Where relevant, all specimens were satisfactorily retrieved in bags without the need for tissue morcellation.

2.3.3.3 Complications

Overall conversion rate was 12.5% (5/40) (Table 1). All conversions were to an open surgical approach and involved abdominal pathology. The indications for conversion were anatomical difficulty (2), unexpected malignant pathology suspected macroscopically (2) and acute hypertensive crisis during pheochromocytoma resection (1). Other intra-operative complications included contained tumour spillage during dissection of a thin-walled cystic component of an adrenal Ewing's sarcoma/primitive neuroectodermal tumour. This patient subsequently underwent whole-abdominal radiation therapy and chemotherapy with no recurrence at 14 months follow up. Post-operative complications included singular events of transient hypotension and hypocalcaemia following pheochromocytoma resection and total thyroidectomy for papillary thyroid carcinoma respectively. Residual disease was reported in one case (Table 2.3). In this adrenalectomy procedure for neuroblastoma, post-operative CT imaging revealed residual tumour that prompted return to theatre for open exploration.

Author	n	Age	Anatomical Region	Diagnosis	Procedure	Tumour size (mm)	OT (mins)	Follow up (months)	Conversions or complications
Akar et al [31]	1	17	Pelvis	Juvenile cystic adenomyoma	Uterine myomectomy	48 x 34 x 30	-	-	Nil
Anderberg et al [41]	1	1	Pelvis	Embryonal rhabdomyosarcoma	Radical cystoprostatectomy	-	185	-	Nil
Backes et al [24]	1	18	Pelvis	Embryonal rhabdomyosarcoma	Radical hysterectomy with right salpingo-oophorectomy and pelvic lymphadenectomy	60 x 32 x 30	177	-	Nil
Camps et al [49]	1	16	Abdomen	Ganglioneuroma	Left adrenalectomy	51 x 37 x 24	-	-	Nil
Choy et al [27]	1	14	Abdomen	Mixed epithelial and stromal tumour	Partial nephrectomy	20 x 15 x 8	-	9	Nil
Cost et al [28]	1	14	Abdomen	Clear cell renal cell carcinoma	Partial nephrectomy with extended lymph node dissection (aortic and hilar)	15	180	6	Nil
Cost et al [21]	1	15	Abdomen	Mature para-aortic/left renal hilum teratoma	Metastasectomy and bilateral retroperitoneal lymph node dissection	21	527 *	12.5	Nil
	1	15	Abdomen	Paratesticular rhabdomyosarcoma	Retroperitoneal lymph node dissection	-	357 *	16	Nil
DeUgarte et al [26]	1	17	Mediastinum	Complex massive retro-cardiac oesophageal leiomyoma	Thoracoscopic extra-mucosal tumour resection with flexible endoscope assistance	70 x 70 x 55	-	24	Nil
Dumitrascu et al [50]	1	16	Abdomen	Pancreatoblastoma	Central pancreatectomy	60	-	-	Early conversion on high macroscopic suspicion of malignancy
Gutt et al [23]	1	16	Pelvis	Gonadoblastoma	Bilateral salpingo-oophorectomy	-	95 *	-	Nil
Hassan et al [31]	1	16	Mediastinum	Cardiac myxoma (left ventricular)	Tumour excision (left atriotomy transmitral approach)	15 x 16	-	-	Nil
Hsu et al [51]	1	15	Abdomen	Ectopic pancreas presenting as a gastric submucosal tumour	Gastric wedge resection with flexible gastroscopy assistance	15	-	-	Nil

Lee et al [33]	1	16	Neck	Papillary thyroid carcinoma	Total thyroidectomy with central compartment lymph node dissection via a bilateral axillo-breast approach	-	-	12	-
Lee et al [32]	1	14	Neck	Papillary thyroid carcinoma with extracapsular invasion	Total thyroidectomy with central compartment lymph node dissection	14	132	-	Transient post-operative hypocalcaemia spontaneously resolving within 3 months
	1	13		Papillary thyroid carcinoma		10	121	-	Nil
Meehan et al [19]	3	-	Abdomen	Neuroblastoma	-	-	-	-	Return to theatre for laparotomy after residual disease discovered on post-operative CT scan (1)
	1	-	Abdomen	Pheochromocytoma	Adrenalectomy	-	-	-	Converted following intraoperative acute hypertensive crisis (1)
	1	2	Abdomen	Adrenal carcinoma	Adrenalectomy				
	1	-	Abdomen	Benign adrenal mass					
	1	-	Pelvis	Ovarian teratoma	-	-	-	-	
	1	-	Abdomen	Ganglioneuroma (retroperitoneal)	-	-	-	-	Converted due to anatomical difficulty
	1	-	Abdomen	Pancreatic mass	-	-	-	-	Converted due to anatomical difficulty
	1	7	Abdomen	Adenocarcinoma	Total proctocolectomy	-	-	-	Converted following unexpected discovery of large colon tumour invading anterior abdominal wall
Meehan et al [20]	5	4	Mediastinum	Ganglioneuroma	Resection of tumour in posterior mediastinum, approximating vena cava	40 x 20 x 25	22	26	Nil
		2	Mediastinum	Ganglioneuroblastoma	Resection of tumour in	65 x 42 x	56	30	Nil

					posterior right mediastinum, adherent to azygous vein and superior vena cava	17			
		17	Thorax	Mature teratoma	Resection of tumour, densely adherent to left lung and aorta	56 x 47 x 29	140	19	Nil
		11	Mediastinum	Germ cell tumour	Resection of tumour in anterior mediastinum, adherent to superior vena cava, right lung, phrenic nerve and pericardium	78 x 63 x 54	131	2	Nil
		16	Thorax	Non-specific inflammatory mass (unable to be pathologically excluded as necrotic benign tumour)	Resection of necrotic mass adherent to carina and compressing bronchus	60 x 40 x 20	143	28	Nil
Nakib et al [35]	1	13	Pelvis	Teratoma	Right oophorectomy	-	120 *	-	Nil
	1	8	Pelvis	Teratoma	Left oophorectomy	-	130 *	-	Nil
Rogers et al [29]	1	14	Abdomen	Hereditary pheochromocytoma (associated with VHL)	Left partial adrenalectomy and excision of adjacent extra-adrenal tumour	30 & 9	180 *	-	Nil
Park et al [52]	1	12	Thorax	Typical carcinoid lung tumour (left lower lobe)	Left lower lobectomy	21	-	72	Nil
St Julien et al [30]	1	18	Abdomen	Hereditary pheochromocytoma	Right partial adrenalectomy (previous left adrenalectomy)	17 x 16 x 20	-	12	Nil
Stephenson et al [36]	1	17	Abdomen	Ewing sarcoma/primitive neuroectodermal tumour (adrenal)	Right adrenalectomy	50	-	14	Intra-operative tumour spillage
Volkin et al [22]	1	15	Abdomen	Metachronous bilateral pheochromocytoma	Left partial adrenalectomy	55	245	24	Post-operative hypotension requiring corticosteroids
	1				Right partial adrenalectomy	-	300		
Wright et al [53]	1	14	Pelvis	Leiomyoma	Uterine myomectomy	110	-	12	Nil

"-" = not available, * = total operative time, VHL = Von Hippel-Lindau syndrome, OT = operative time (console time).

Table 2.3 Patient demographics, operative details and patient outcomes for identified cases of robot-assisted MIS for paediatric solid tumours.

2.3.4 Discussion

Minimally invasive surgery has been established as a safe, feasible, and effective operative approach for many oncological indications in adult specialties such as urology, gynaecology, thoracic, and general surgery. In these same specialty areas, robot-assisted MIS has been most widely adopted for therapeutic roles in benign and malignant tumour disease. The extent that this technology has diffused clinical practice is most apparent in the United States, where robot-assisted prostatectomy is now regarded as the standard of care for example [67]. When considered in this context, the overall case volume of robot-assisted paediatric solid tumour MIS reported in the literature is remarkably low. However, the considerably smaller tumour incidence, unique tumour biology and obvious anatomical size differences in children poses a very different setting for which the roles of MIS need to be carefully considered in paediatric patient populations.

2.3.4.1 Technical advantages

Radical resection or local excision of tumours in children is generally characterised by high-risk surgery in poorly accessible, difficultly visualised and spatially constrained anatomical spaces. Technical challenges of these domains are noted as a major limiting factor for conventional MIS [47]. In other series of MIS for paediatric solid tumour resection, Chan *et al* reported 88% (7/8) of conversions to be for limited intra-corporeal space [57], while Metzelder ascribed 86% (12/14) to limited tumour exposure or visibility [54].

Roles for robot-assisted MIS are felt to be most relevant for complex procedures that demand restoration of organic faculties enjoyed by open surgery, such as three-dimensional vision, highly redundant manual dexterity and innate control. In such circumstances, robot-assistance is able to reproduce these features in an immersive manner at distant intra-corporeal sites. Examples of operative locations identified in this review include the posterior mediastinum [60, 68], retroperitoneal space [62, 64, 69-71], endocardial left ventricular apex [72], central neck compartments [73, 74] and deep pelvis [23, 58].

Almost universally, authors commented that the dexterity of 7 DOF articulated instruments, along with intuitive master-slave control permitted more meticulous dissection during tumour extirpation [58, 60, 62, 65, 68, 70-73, 75-77]. Tremor filtration and motion scaling capability were also noted to facilitate greater instrument control and precision [61, 68, 74]. When intra-corporeal suturing was required, this was considered an easier and quicker task to perform [62]. Several

procedure-specific benefits were described. For mediastinal surgery, enhanced instrument dexterity aided circumferential dissection around structures such as the oesophagus and rigid masses [60, 68]. For myomectomy, it was felt that better multilayer hysterectomy might translate to safer future pregnancies [75].

High-definition stereoscopic optics was reported to contribute to enhanced recognition of the operative field and subsequent tissue manipulation [23, 58, 62, 65, 68, 70-73, 75-78]. These remarks are supported by findings of a comprehensive bench-top experiment by Jourdan *et al* who established that stereoscopic vision improves task performance and accelerates the learning curve [79]. These benefits became more apparent as the complexity of simulated MIS tasks increased [79].

The longest operative duration identified in this review was almost 9 hours [66]. The master-slave set-up of robot-assisted platforms permits the surgeon to assume a comfortable seated position throughout the procedure. This has obvious ergonomic benefits, particularly for longer cases in which fatigue might compromise operative performance [60, 65].

2.3.4.2 Patient safety and benefit

The case reported by Anderberg *et al* best illustrates the potential gains that might be achieved. In this case, a 1 year old boy with a pelvic rhabdomyosarcoma underwent radical cystoprostatectomy without complication [58]. The infant was mobilising and feeding on the first post-operative day, with little opiate analgesia requirement. He commenced adjuvant chemotherapy on the sixth post-operative day and was discharged home three days later [58].

In order for robot-assisted MIS to be considered viable against existing standards, then either equivalent or superior outcomes must be achieved for the priority operative goal – safe and complete tumour clearance. For the vastly diverse range of indications in this review, the low overall oncological complication rate (5%, 2/39: n =1 contained tumour spillage, n = 1 residual disease) indicates that acceptable oncological outcomes are attainable in carefully selected cases.

Through a variety of reasons, it seems robot-assistance may make MIS more tangible for select paediatric solid tumour resections. Backes *et al* considered MIS to be a preferable treatment option, but concern for compromise in surgical and oncological principles guided their decision to utilise robot-assistance [65]. As contributor of over 50% of the cases identified

in this review, Meehan *et al* were able to undertake many cases that they had not yet performed using conventional MIS [23].

Surgical complication rates for abdominal tumour surgery in general are reported to be as high as 30% [80], and conversion rates for solid tumour resection using conventional MIS range from 21% [57] to 23% [54] to 56% [48] in the paediatric literature. Given the high degree of heterogeneity amongst these study cohorts as well as in this review, genuine attempt at meaningful outcome data comparison is limited. However, collective complication (10%) and conversion (12.5%) rates for cases in this review do seem at least comparable, if not lower. Risk of port-site recurrence has been noted as an ongoing concern with the use of MIS in paediatric oncology [47, 55, 56]. No port-site metastases were identified.

2.3.4.3 Limitations

Lack of tactile feedback (haptics) was frequently cited as a primary technical concern [23, 58, 65, 68]. Several authors commented that this was partially compensated by visual cues provided through the enhanced optics [58, 76] and experience related factors [65]. Both of the two major oncological complications were discussed as possibly contributed by diminished tactile feedback [23, 77].

Weighing over half a metric tonne, the robot slave component dwarfs a small child when docked in position. The large system footprint in the operating theatre and unavailability of appropriately sized paediatric instruments were described as limiting factors for usability in younger patients due to port-site clustering and robot arm conflicts [58]. This might partly explain the observation that most procedures in this review were undertaken in larger adolescent patients. Emergency access to the patient for conversion or anaesthetic reasons might also be impeded by system size and configuration, although robot undocking has been reported as quick with appropriate theatre team training and awareness [9, 23, 76, 81]

Robot-assisted surgery is currently expensive. Outlay costs for a new da Vinci® Si™ Surgical System exceed £1,500,000 without including limited usage instruments that are priced at approximately £2,000 each. Some authors have commented that if indirect cost savings involved with reduced length of hospital stay are taken into account, then robot-assisted surgery in children may be cost-effective compared to open surgery [66, 82, 83].

Low case volume makes progression through learning curves an obstacle [56, 62]. The adult literature reports surgical and oncological outcomes for robot-assisted prostatectomy to improve along a surgeons' learning curve [84], with plateau occurring after 25 to 120 cases [84, 85]. In an effort to bridge the learning curve, Cost *et al* and Anderberg *et al* described using a shared team approach in which more experienced adult robot-assisted surgical oncologist colleagues act as proctors [58, 66]. Lastly, paediatric surgeons have commented that learning curves are shorter and steeper than those for conventional MIS [23, 86, 87].

2.3.4.4 Evidence

The highest quality of evidence in this review was provided by small case series. Without comparative data against control groups, it is difficult to confidently attribute any objectively measured positive or negative patient outcomes to robot-assistance. It is also difficult to assert that robot-assisted MIS for paediatric solid tumours can be considered safe and feasible given that over 20 different indications for surgery are reported among a relatively small number of overall cases with mostly short-term follow up. At present, there is no obvious index procedure for which robot-assisted paediatric tumour surgery can be assumed to have a favoured role. What is demonstrated is 1) the versatility of robot-assistance for thoracic and abdominal tumour surgery in children and 2) oncological and surgical complications as well as conversion rates seem acceptably low in the context of similar quality data from open and conventional MIS literature. Without major concerns highlighted, there is little justification to discourage further exploration of roles for robot-assisted surgery in this setting. Future studies should seek to address the limited amount of long-term oncological follow up that is currently available.

A recent Cochrane Review by de Lijster *et al* revealed an absence of controlled clinical trials investigating conventional MIS for paediatric thoracic or abdominal solid tumours [56]. Interestingly, a previously initiated randomised controlled trial was abandoned due to inadequate patient recruitment, insufficient MIS expertise, and lack of equipoise amongst participating surgeons [88]. Clearly, there are considerable barriers to pursuing high quality evidence in this field. Some of these might be overcome through efforts to establish multi-centre collaborative trial groups [56, 80], central prospective registers or databases, and further centralisation of specialist services [58]. Internal study validity would be strengthened by trial protocols that define case selection criteria and risk stratification for tumour type, size, location, resectability, and adjuvant therapies. Understandably, this would necessitate multi-

disciplinary consensus [53, 54] in order to navigate the diverse, dynamic and often individualised care in paediatric oncology [56].

In conclusion, the current status of robot-assisted surgery for paediatric solid tumours is small and relatively static, with no clearly apparent index procedures. Perceived benefits of robot-assisted MIS in this setting seem subjectively compelling, but remain unsubstantiated by evidence. The ongoing adoption of robot-assisted MIS in adult oncological surgery sets an interesting precedence; especially given the similar lack of strong supportive evidence from high quality trials [67].

CHAPTER 3 CLINICAL COMPARATIVE EFFECTIVENESS OUTCOMES IN PAEDIATRIC ROBOTIC SURGERY

Content from this chapter was published as:

TP Cundy, L Harling, A Hughes-Hallett, EK Mayer, AS Najmaldin, T Athanasiou, GZ Yang, A Darzi. Meta analysis of robot-assisted versus conventional laparoscopic and open pyeloplasty in children. British Journal of Urology International. [in-press]

TP Cundy, L Harling, HJ Marcus, T Athanasiou, AW Darzi. Meta analysis of robot-assisted versus conventional laparoscopic fundoplication in children. Journal of Paediatric Surgery. 2014;49(4):646-652.

3.1 Meta Analysis of Robot-Assisted versus Conventional Laparoscopic and Open Pyeloplasty in Children

3.1.1 Introduction

As identified in Chapter 2.2, pyeloplasty is the most prevalently reported and highest volume application of robot-assisted minimally invasive surgery in children [89]. A recent study examining population weighted United States Nationwide Inpatient Sample (NIS) data reported that for the period 2008 – 2010, the distribution of open (OP), robot-assisted (RP) and conventional laparoscopic (LP) approaches for paediatric pyeloplasty was approximately 83.5%, 13.5% and 3% respectively [90]. This data also indicated that adoption of RP has surpassed that of the conventional laparoscopic technique (LP), and that RP now comprises >80% of minimally invasive paediatric pyeloplasties [90]. The utility of RP seems to be preferred for older children at present, with most young children undergoing OP [90].

It remains largely unclear how the many technological enhancements offered by robot-assistance might translate into clinically measurable outcome benefits. As RP becomes more established, this application of robotic surgery will inevitably transition towards an era of critical assessment [20, 91]. Accordingly, comparative studies are increasingly emerging [89] and this allows opportunities for quantitative data synthesis to more definitively evaluate effectiveness of RP against established best-practice techniques. The aim of this chapter is therefore to undertake a meta-analysis of robot-assisted versus conventional laparoscopic and open pyeloplasty in children.

3.1.2 Materials and Methods

The study protocol was registered on the PROSPERO international prospective database of systematic reviews (CRD42013003969) and analysis was performed in accordance with recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [63].

3.1.2.1 Search strategy

Systematic literature searches were undertaken of the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Ovid Medline and EMBASE electronic databases using the following search strategy (“Surgery, Computer-Assisted”[MeSH] OR

"robotics"[MeSH] OR "da Vinci" OR "telerobotic" OR "telesurgery" OR "robotic surgery") AND ("Pediatrics"[MeSH] OR "Infant"[MeSH] OR "Child"[MeSH] OR "Adolescent"[MeSH]) AND ("Kidney"[MeSH] OR "Pelviureteric Junction Obstruction" OR "Pyeloplasty"). The search was conducted up to December 2013. The primary search was supplemented with searches of 1) PubMed related articles feature, 2) clinicaltrials.gov registry using the keyword "pyeloplasty", and 3) abstracts of the International Pediatric Endosurgery Group Annual Congresses (2002 – 2013), the American Urological Association Annual Meetings (2006 – 2013), Section of Urology Program of the American Association of Paediatrics National Conference (2007 – 2012), and World Congress of Endourology (2008 – 2013).

3.1.2.2 Inclusion and exclusion criteria

All included studies satisfied the following criteria: 1) comparing RP versus LP and/or open pyeloplasty (OP), 2) involving paediatric patients with mean study group ages < 18 years, 3) reporting ≥ 5 patients in each study group, 4) involving singular pathologies or procedures, and 5) investigating objective clinical outcome measures or cost. No language restrictions were imposed. In the event that duplication of data was observed, more recent studies or those with larger sample sizes were preferentially considered.

3.1.2.3 Outcomes of interest

Primary outcomes of interest were operative success, requirement for re-operation, conversion rates, post-operative complications, and urinary leakage complication rates. Operative success was regarded as 1) resolution of pre-operative clinical symptoms, 2) improvement or complete resolution of hydronephrosis on follow-up radiologic studies, 3) stable hydronephrosis with improved drainage on diuretic renogram (i.e. t1/2 < 10 minutes) and, 4) stabilisation of function in renal imaging if performed. Secondary outcome measures were estimated blood loss, length of hospital stay, operating time, analgesia requirement, and cost. Operating time was preferentially considered as the time from first skin incision to skin closure.

3.1.2.4 Data extraction and synthesis

Two reviewers independently undertook literature searches, screened abstracts, and assessed eligible articles against inclusion criteria. There was 90% agreement on identification of articles and discrepancies were resolved by consensus, or arbitrated by a third reviewer.

The number of renal units undergoing surgical intervention was regarded as the denominator value for assessment of complication rates, success rates, and urine leak complication rates. Corresponding authors were contacted regarding any missing data.

The methodological quality of studies was appraised using a star-based modified Newcastle-Ottawa Scale (mNOS) that considers patient selection, inter-group comparability, and outcome assessment (maximum 3, 10, and 2 stars respectively; total /15) [92]. The 10 single-star variables used to grade comparability amongst study groups included study group periods, surgeons, age (or weight), gender, indication criteria, pelvi-ureteric junction obstruction (PUJO) aetiology, PUJO laterality, re-do cases, operative approach, and ureteric stent use (Table 3.1). Quality scoring of included studies was independently assessed by two reviewers, with 83% inter-rater agreement. Patient demographic and outcome data was extracted from all included studies.

Statistical analysis was conducted using Review Manager® Version 5.1.7 for Windows (The Cochrane Collaboration, Software Update, Oxford, UK) and STATA v.11 statistical analysis software (StataCorp LP, TX, USA). A weighted random-effects model was used for all analyses. Pooled odds ratios (OR) were calculated as the summary statistic for dichotomous variables and weighted mean difference (WMD) calculated for continuous variables. Both OR and WMD are reported with 95% confidence intervals (CI). A P value < 0.05 was considered statistically significant. Determination of heterogeneity was undertaken using the χ^2 test (Cochran's Q) and I^2 value; with $I^2 \geq 75\%$ denoting high degree of statistically significant heterogeneity. Risk of publication bias was assessed by visual inspection of funnel plots in addition to statistical estimation with both Begg and Mazumdar's test and Egger's test for small study effects.

Selection	
Group assignment	Allocation criteria reported? (1 star)
Representativeness	Either or both study groups are fairly representative of the general paediatric population requiring pyeloplasty (1 star)? All study groups are well representative of the general paediatric population requiring pyeloplasty (2 stars)?
Comparability	
Study group period	Study period synchronous for both study groups? (1 star)
Surgeons	Same surgeons performed procedures in both study groups? (1 star)
Age (or Weight)	Mean or median patient age comparable between study groups? (1 star)
Gender	Patient gender distribution comparable between study groups? (1 star)
Indication criteria	Clear description or work-up criteria and indications for surgery in both study groups? (1 star), or presenting symptoms described and generally comparable between study groups? (1 star)
PUJO aetiology	Study groups comparable for proportions of intrinsic and extrinsic pathology? (1 star)
PUJO laterality	Study groups comparable for proportions of left, right and bilateral cases? (1 star)
Re-do cases	Study groups comparable for proportions of primary and secondary cases? (1 star)
Operative approach	All cases clearly transperitoneal? (1 star), or all cases clearly dismembered technique? (1 star)
Ureteric stent	Study groups comparable for proportions of cases having retrograde or antegrade ureteral stent insertion? (1 star)
Outcome assessment	
Defined outcomes	Definition of operative success clearly described? (1 star)
Follow-up	Mean or median follow up time comparable between study groups? (1 star)
mNOS total (/15)	

Table 3.1 Quality scoring checklist for the star-based modified Newcastle-Ottawa Scale (mNOS).

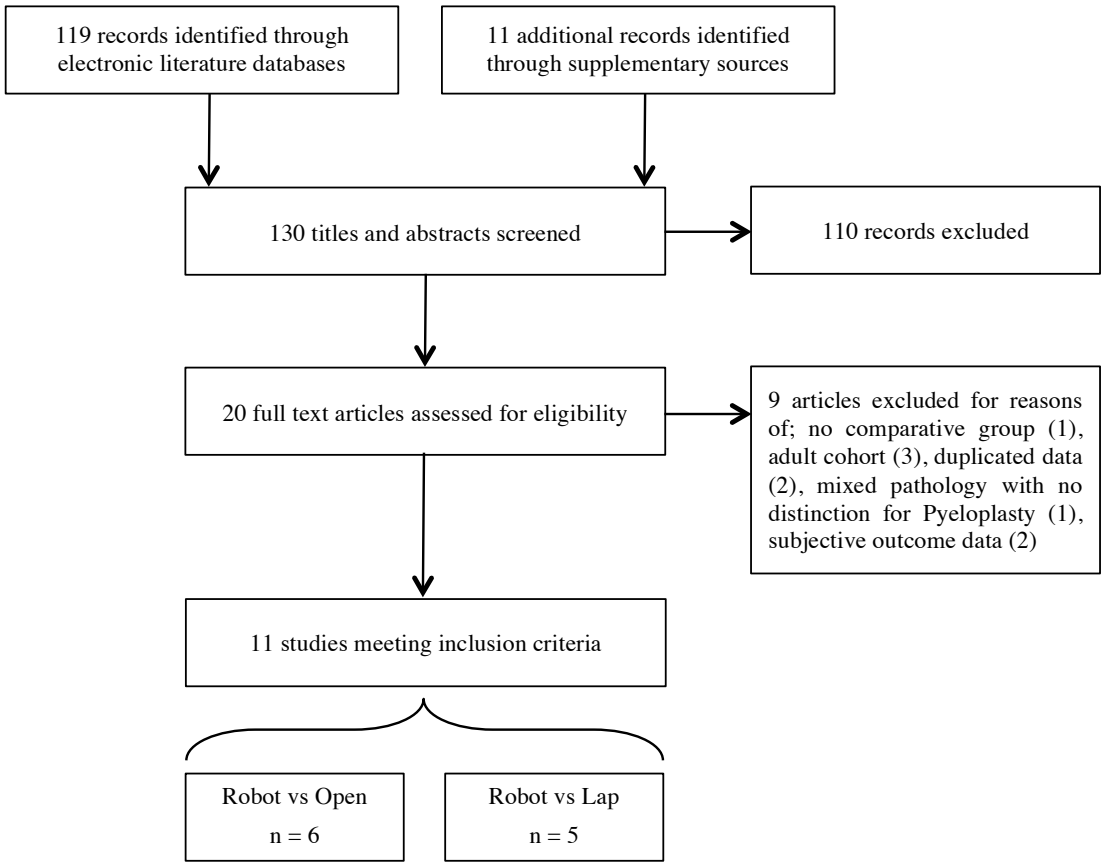


Figure 3.1 Prisma flow diagram outlining the systematic search strategy and study selection process.

3.1.3 Results

Twelve studies met inclusion criteria, involving 384 robot-assisted, 131 laparoscopic, and 164 open pyeloplasty procedures (Figure 3.1, Table 3.2) [93-104].

3.1.3.1 Study characteristics and appraisal of quality of evidence

No randomised controlled trials were identified. Five of the included studies were cohort studies and the remaining seven studies were case-controlled studies (Table 3.2). All studies were retrospective in design and single-institution in origin. All reported RP cases were undertaken using the da Vinci Surgical System®.

	Study design	Study period	Country of study origin	n			Min months follow up *[mean(range)]*
				RF	**OP**	**LP**	
Franco et al [95]	RC	-	USA	15	n/a	12	9 (-)
Kim et al [96]	RCC	2004 – 2007	USA	84	n/a	58	10.1 (6 – 28)
Subotic et al [100]	RC	2006 – 2010	Switzerland	19	n/a	20	10 (6 – 24)
Casella et al [103]	RC	2008 – 2012	USA	23	n/a	23	-
Riachy et al [98]	RC	2007 – 2012	USA	46	n/a	18	22* (2 – 36)
Lee et al [97]	RCC	2000 – 2004	USA	33	33	n/a	10 (0.4 – 28)
Yee et al [102]	RCC	1997 – 2004	USA	8	8	n/a	14.7 (2 – 24)
Swana et al [101]	RCC	2003 – 2009	USA	24	20	n/a	-
Sorensen et al [99]	RCC	2006 – 2009	USA	33	33	n/a	17 (9**)
Behan et al [94]	RCC	2008 – 2010	USA	37	7	n/a	-
Barbosa et al [93]	RCC	2001 – 2008	USA/Brazil	52	53	n/a	34* (12.2 – 92)
Dangle et al [104]	RC	2011 – 2013	USA	10	10	n/a	9.0 (4 – 24)

Table 3.2 Characteristics of studies included in the meta-analysis. "-" not reported, * = median (range) values, ** = standard deviation. RC = retrospective cohort study, RCC = retrospective case-control study.

The median mNOS score was 9 (range 4 – 14, Table 3.4). Study characteristics are summarised in Tables 3.2 and 3.3. Seven studies described method of allocation for patients to undergo RP, LP or OP [93, 98-100, 102, 104]. Yee *et al*, Sorensen *et al*, and Dangle *et al* assigned allocation chronologically, with patients having RP after initiation of respective robotic surgical services [99, 102, 104]. In the studies by Barbosa *et al* and Riachy *et al*, selection of surgical technique was made via shared decision-making between the clinician and family [93, 98]. Subotic *et al* implemented age-based allocation (< 4 years old LP, ≥ 4 years old RP) [100]. No studies reported pre-hoc power calculations to justify adequate sample size. Six studies explicitly described inclusion and/or exclusion criteria. Barbosa *et al*, Subotic *et al* and Riachy *et al* outlined clear respective institutional indications for pyeloplasty [93, 98, 100]. Barbosa *et al* also employed exclusion criteria of absent ultrasound evaluation, post-operative follow up < 1 year, prior pyeloplasty, in-situ ureteric stents, and concomitant urological co-morbidities [93]. Lee *et al* excluded all patients with previous urinary tract surgery [97] and Behan *et al* excluded all patients < 2 years of age [94]. Dangle *et al* included infants only and excluded patients with concomitant vesicoureteral junction reflux [104]. Seven studies reported intentional case matching. Yee *et al*, Swana *et al,* Behan *et al*, and Kim *et al* matched cases by age [94, 96, 97, 101], and Lee *et al* and Sorensen *et al* matched cases by both age and gender [99]. Barbosa *et al* utilised a hierarchical case-matching strategy that incorporated PUJO aetiology, age, pre-operative grade of hydronephrosis, and gender [93].

Amongst the studies that reported satisfactory patient age data, children in the RP groups tended to be older than those in the LP groups (overall mean age 10.0 years for RP versus 6.5 years for LP) and OP groups (overall mean age 8.1 years for RP versus 7.0 years for OP). Pooled analysis identified no overall difference in weight amongst the four studies that reported this data for RP versus OP (P = 0.27). The youngest patients reported were 2.0 months, 1.0 month and 1.0 month of age amongst RP, LP, and OP groups respectively [12, 14, 18]. The smallest patients reported were 5.1 kg, 5.9 kg, and 4.8 kg amongst RP, LP, and OP groups respectively [94, 98].

	Aetiology of PUJO *(intrinsic:extrinsic)*			**Laterality** *(left:right:bilateral)*	
a)	**RP**	**LP**	**Comments**	**RP**	**LP**
Franco et al [95]	-	-	-	6:9:0	8:4:0
Kim et al [96]	-	-	-	-	-
Subotic et al [100]	11:10	20:0	4 re-do (2 RP, 2 LP)	14:5:2	16:4:0
Casella et al [103]	-	-	-	-	-
Riachy et al [98]	24:22	7:12	1 re-do (RP)	29:17:0	8:9:1
b)	**RP**	**OP**	**Comments**	**RP**	**OP**
Lee et al [97]	22:11	18:15	-	22:11:0	17:16:0
Yee et al [102]	-	-	1 re-do (RP group)	4:4:0	5:3:0
Swana et al [101]	-	-	-	-	-
Sorensen et al [99]	-	-	3 re-do (2 RP, 1 OP) 5 pyelolithotomy (3 RP, 2 OP) 1 ruptured PUJ (OP) 1 horseshoe kidney (OP)	-	-
Behan et al [94]	-	-	-	11:26:0	2:5:0
Barbosa et al [93]	38:14	39:14	-	-	-
Dangle et al [104]	-	-	3 re-do (1 RP, 2 OP)	6:4	7:3

Table 3.3 Pelvi-ureteric junction obstruction (PUJO) characteristics reported amongst studies included in the meta-anaysis for a) robot-assisted (RP) versus conventional laparoscopic pyeloplasty (LP), and b) robot-assisted (RP) versus open (OP) pyeloplasty. "-" not reported, "re-do" = secondary procedure for recurrent PUJO.

	Franco et al [95]	Kim et al [96]	Subotic et al [100]	Casella et al [103]	Riachy et al [98]	Lee et al [97]	Yee et al [102]	Swana et al [101]	Sorensen et al [99]	Behan et al [94]	Barbosa et al [93]	Dangle et al [18]
Selection												
Group assignment			*		*		*		*		*	*
Representativeness	*	*	**	*	**	**	**	*	**	*	**	*
Comparability												
Study group period	*	*	*	*	*	*		*		*	*	
Surgeons	*			*							*	*
Age (or Weight)	*	*		*	*	*	*	*	*	*	*	
Gender			*	*	*	*			*	*	*	*
Indication criteria			*		*				*		*	*
PUJO aetiology					*	*	*		*		*	
PUJO laterality			*	*	*	*	*			*	*	*
Re-do cases			*			*			*		*	*
Operative approach	*		*	*			*		*		*	*
Ureteric stent	*		*		*		*					*
Outcome assessment												
Defined outcomes			*		*	*	*	*	*		*	
Follow-up									*		*	*
mNOS total (/15)	6	3	11	7	11	9	9	4	11	5	14	10

Table 3.4 Summary of study quality appraisal using the modified Newcastle-Ottawa Scale (mNOS).

3.1.3.2 Operative technique

Where described, all RP and LP cases were carried out as transperitoneal dismembered pyeloplasties, with the exception of 1 case in the cohort reported by Lee *et al* that was performed using a retroperitoneal approach. Yee *et al* and Franco *et al* used a somewhat hybrid RP technique in that the initial dissection for exposure of the renal pelvis was performed using conventional laparoscopy [95, 102]. In studies describing operative technique for OP, this was reported as involving either a subcostal flank incision or dorsal lumbotomy [97, 99, 102, 104]. All descriptions of operative technique involved matched placement of retroperitoneal drains between study groups, aside from Sorensen *et al* who placed drains in 91% OP cases and only 3% RP cases [99].

The main source of variance in technique related to placement of ureteric stents. Of the 7 studies that described stent placement (of which all were trans-anastomotic double J stents or cutaneous-pyelo-ureteral stents), 4 studies placed stents in all cases [95, 100, 102-104], and 2 studies

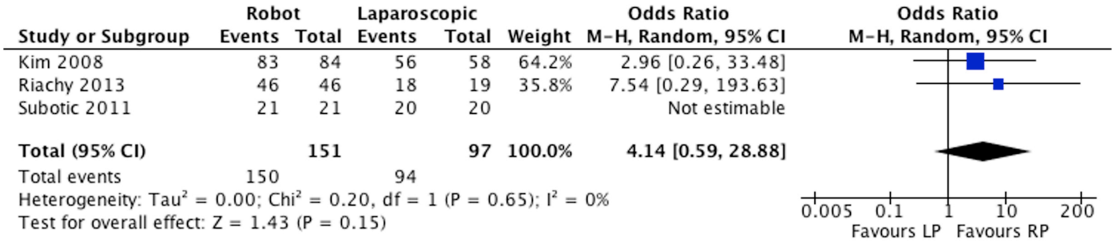
used stents more often in RP cases compared to OP cases (61% versus 7% [97], and 97% versus 36% [99]). Stents were inserted antegrade with the exception of Franco *et al* (RP and LP) and Subotic *et al* (LP only) who inserted stents retrograde, and Casella *et al* who inserted stents retrograde in 56% RP cases and 100% OP cases [103].

3.1.3.3 Primary outcomes; operative success, re-operation rate, conversion rates, post-operative complications, urinary leakage

3.1.3.3.1 Operative success

Nine studies reported success rates. Overall success rates for studies comparing RP and LP were 99.3% and 96.9% respectively (Figure 3.2a). Overall success rates for studies comparing RP and OP were 87.3% and 88.5% respectively (Figure 3.2b). No statistically significant differences were observed in pooled analysis of success rates (Figure 3.2). No statistical evidence of heterogeneity (I^2 = 0%) or publication bias (Begg and Mazumdar: P = 0.317 for RP vs LP and P = 1.0 for RP vs OP) was detected.

(a)



(b)

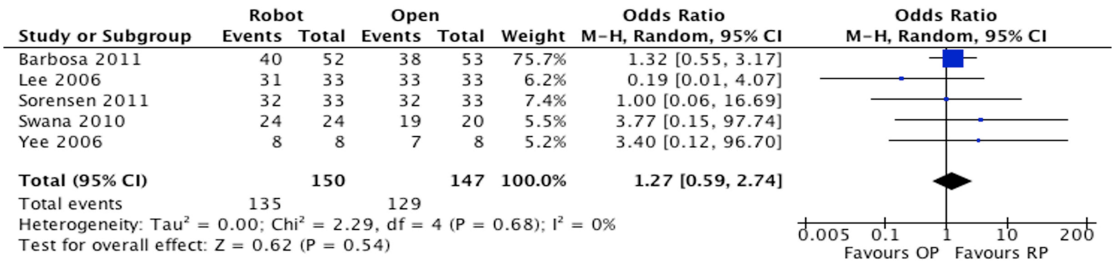


Figure 3.2 Forest plot comparisons of success rates for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.

3.1.3.3.2 Re-operation rate

Eight studies reported data for requirement of re-operation due to recurrent PUJO. While overall re-operations rates were lower in RP compared to LP and OP, these did not reach statistical significance (Figure 3.3).

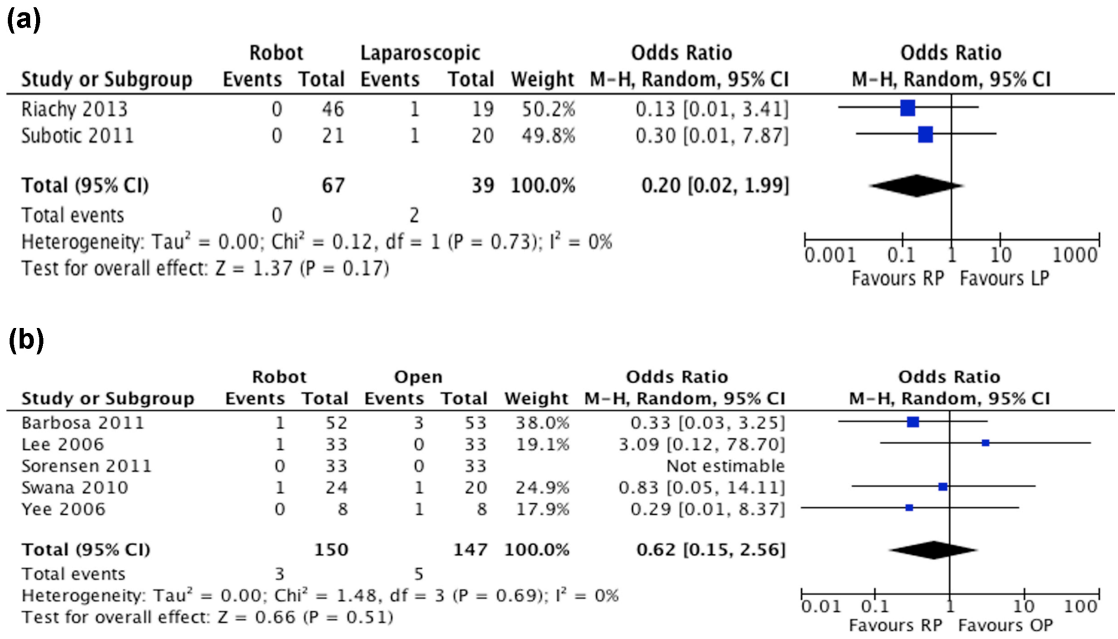
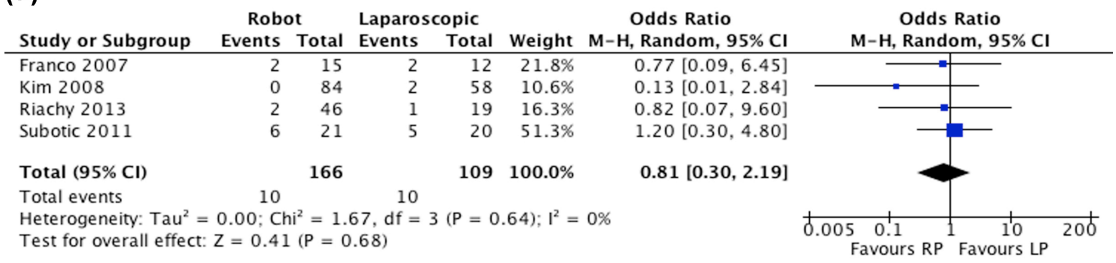


Figure 3.3 Forest plot comparisons of re-operation rates for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.

3.1.3.3.3 Conversion rates

There was insufficient data for pooled analysis of conversions between RP and LP. In studies comparing RP and LP, the overall conversion rate for RP was 2.4% (4/164) and no LP conversions were reported (0/131). Both conversions reported by Franco *et al* were to open technique (2/15) [95], and both conversions reported by Kim *et al* were to conventional laparoscopic technique (2/84) [96]. Reasons for conversion reported by Franco *et al* were for technical difficulty in a case with co-existing renal stone disease (n = 1), and mechanical failure of a robotic arm (n = 1) [95]. In the 4 studies comparing RP and OP that reported conversion rates, the net overall conversion rate for RP was 3.6% (3/84) [97, 99, 102]. All three conversions were to conventional laparoscopic technique and due to mechanical failure of robotic arms [99]. Incidentally, there were 2 other reports of robot malfunction or failure that did not result in conversion [100, 102].

(a)



(b)

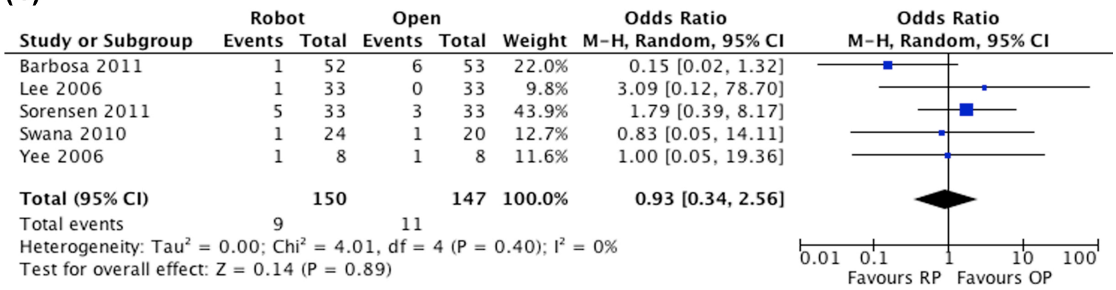


Figure 3.4 Forest plot comparisons of Clavien Grade 1 – 5 complications for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.

3.1.3.3.4 Post-operative complications

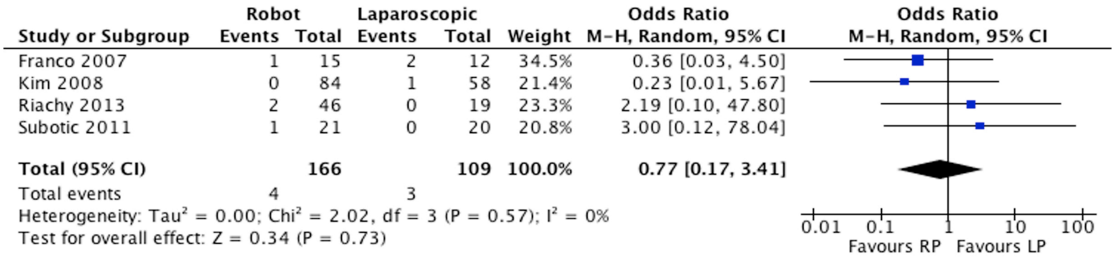
Four studies comparing RP and LP reported post-operative complications. The overall frequency of post-operative complications for RP and LP groups was 6.1% (10/164) and 9.2% (10/109) respectively, however this was not statistically significant (Figure 3.4a, OR = 0.81; 95% CI = 0.30 – 2.19; $P = 0.68$). No statistical evidence of heterogeneity ($I^2 = 0\%$) or publication bias (Egger's Test = -1.38, $P = 0.16$; Begg and Mazumdar: $P = 0.31$) was detected. The overall frequency of post-operative complications in the six studies reporting this data for RP compared to OP was 8.3% (9/108) and 4.8% (5/104) respectively, and this was also not statistically significant (Figure 3.4b, OR = 1.68; 95% CI = 0.57 – 4.94; $P = 0.35$) and without significant heterogeneity.

All reported complications are summarised in Table 3.5. No cases of mortality were identified. Further analysis of complications categorised into sub-groups of minor (Clavien Grade 1 – 2) and major (Clavien Grade 3 – 5) events according to the Clavien-Dindo classification identified no significant differences between RP versus LP groups, and RP versus OP groups ($P = 0.47 – 0.88$).

3.1.3.3.5 Urinary leakage

Of the 10 studies that reported complication data, post-operative urine leak was encountered in 7 study cohorts (Table 3.5). No significant differences were observed between RP and LP groups (Figure 3.5a). There was insufficient data for pooled analysis of RP and OP groups (Figure 3.5b).

(a)



(b)

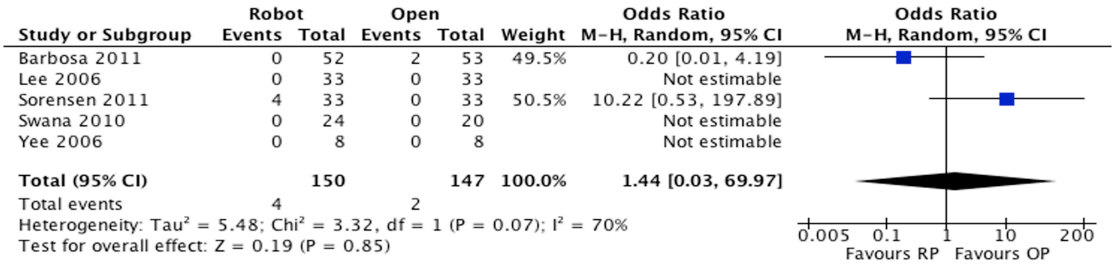


Figure 3.5 Forest plot comparisons of urinary leakage complications for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.

a)	RP		LP	
	% (n)		% (n)	
Franco et al [95]	13.3% (2/15)	Urinary leakage (1), Transient flank pain > 1 year post-op without radiological evidence of PUJO (1) *	16.7% (2/12)	Urinary leakage (2) *
Kim et al [96]	0% (0/84)	n/a	3.4% (2/58)	Urinary leakage (1), *
Subotic et al [100]	31.6% (6/19)	Omentum prolapse through port incision (1), macrohematuria (1), stent dislodgement (1), UTI (2), urinary leakage (1)	25.0% (5/20)	Stent dislodgement (2), severe post-operative dilation of renal pelvis requiring temporary nephrostomy (1), UTI (2)
Casella et al [103]	-	-	-	-
Riachy et al [98]	4.3% (2/46)	Urinary leakage (2)	5.3% (1/19)	Stent dislodgement (1)
TOTAL	**6.1% (10/164)**			**9.2% (10/109)**

b)	RP		OP	
	% (n)		% (n)	
Lee et al [97]	3.0% (1/33)	Missed crossing vessel (retroperitoneal approach) requiring later re-do (1)	0% (0/33)	n/a
Yee et al [102]	12.5% (1/8)	Post-operative ileus (1)	12.5% (1/8)	PUJ stricture (1)
Swana et al [101]	4.2% (1/24)	Stent dislodgement requiring re-operative surgery for re-positioning (1)	5.0% (1/20)	PUJ stenosis with failed balloon dilation and subsequent re-do (1)
Sorensen et al [99]	15.2% (5/33)	Gross hematuria with clot obstruction of ureteral stent (1), urinary leakage (4)	9.1% (3/33)	Pyelonephritis (1), re-presentation with flank pain, vomiting, dehydration (1), asymptomatic stent migration managed conservatively (1)
Behan et al [94]	-	-	-	-
Barbosa et al [93]**	1.7% (1/58)	Re-do pyeloplasty (1)	3.9% (6/154 **)	Post-operative urinoma (2), re-do pyeloplasty (3), unspecified perirenal collection (1)
Dangle et al [12]	10% (1/10)	Port site omental hernia (1)	0% (0/10)	n/a
TOTAL	**6.0% (10/166)**			**4.0% (11/278)**

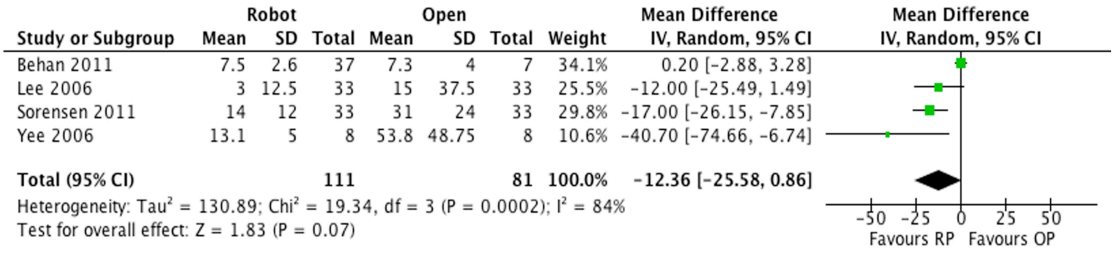
Table 3.5 Summary of post-operative complications reported amongst studies included in the meta-analysis for a) robot-assisted (RP) versus conventional laparoscopic pyeloplasty (LP), and b) robot-assisted (RP) versus open (OP) pyeloplasty. "-" not reported, * = incomplete data, n/a = not applicable, PUJ = pelvi-ureteric junction, UTI = urinary tract infection.

3.1.3.4 Secondary outcomes; estimated blood loss, length of hospital stay, operating time, analgesia, cost

3.1.3.4.1 Estimated blood loss (EBL)

EBL was reported in 5 studies comparing RP and OP. Overall, EBL was lower in RP and this was borderline statistically significant (Figure 3.6a, WMD = -5.7 mL; 95% CI -11.89 – 0.49; $P = 0.07$). No instances of transfusion requirement were identified. Significant heterogeneity was detected ($I^2 = 82\%$). Sub-group analysis of high quality studies only (≥ 9 median mNOS score) increased the overall estimated effect (WMD = -12.30 mL; 95% CI -26.23 – 1.62; $P = 0.08$) but did not improve heterogeneity ($I^2 = 87\%$).

(a)



(b)

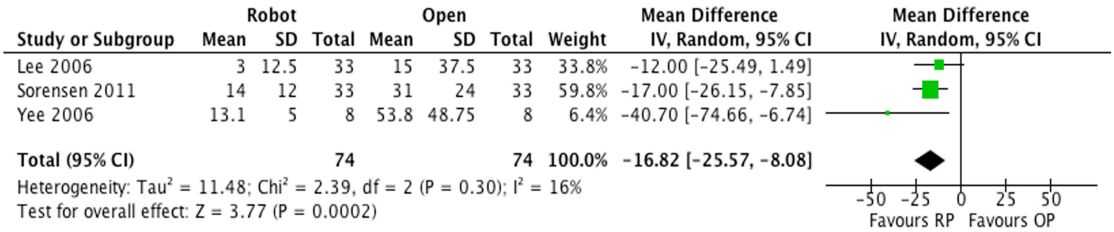


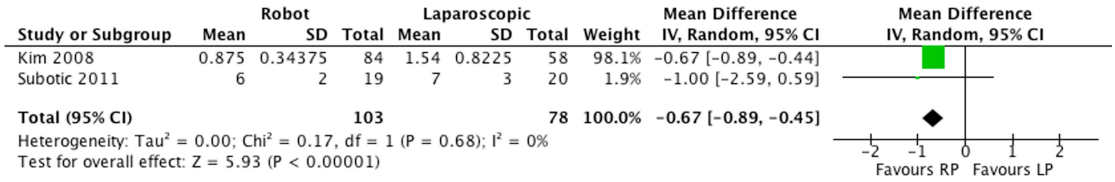
Figure 3.6 Forest plot comparisons of estimated blood loss for a) all studies, and b) high quality studies only (≥ 9 median mNOS score) comparing robot-assisted versus open pyeloplasty in children.

3.1.3.4.2 Length of hospital stay (LOS)

Two studies reported comparative LOS in RP versus LP. Overall, LOS was significantly shorter for RP (Figure 3.7a, WMD = -0.67 days; 95% CI -0.89 – -0.45; $P < 0.001$), however when sub-analysis of high quality studies only was undertaken (≥ 9 median mNOS score) this did not remain significant ($P = 0.22$). Six studies reported comparative LOS data in RP versus OP. Suitable data for pooled analysis was available for 5 of these studies, and this

demonstrated a significantly shorter overall LOS for RP by almost 1 full day (Figure 3.7b, WMD = -0.75 days; 95% CI -1.28 – -0.22; *P* = 0.005).

(a)



(b)

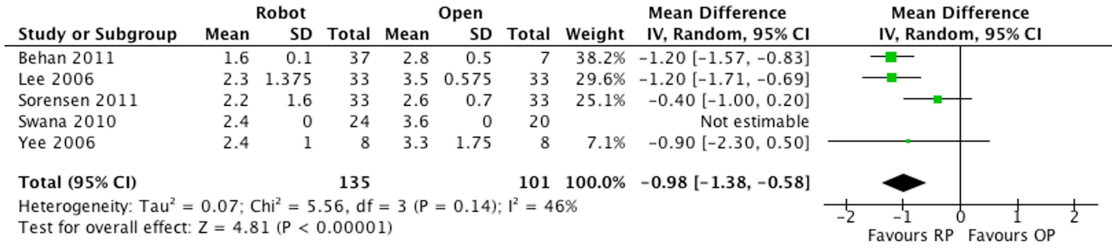


Figure 3.7 Forest plot comparisons of length of hospital stay for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.

3.1.3.4.3 Operating time (OT)

Three studies reported OT for RP versus LP. Overall, a 33 minute shorter OT was observed for RP, however this was not significant (Figure 3.8a, WMD = -33.0 mins; 95% CI -72.42 – 6.42; *P* = 0.10). In contrast, pooled analysis of 5 studies that reported sufficient OT data for RP versus OP identified a statistically significant 57 minute longer OT for RP (Figure 3.8b, WMD = 57.13 mins; 95% CI 34.2 – 80.07; *P* < 0.001). OT time included peripheral time for cystoscopy and patient re-positioning in the studies by Yee *et al* (RP only), Franco *et al* (RP and LP), Subotic *et al* (LP only), and Casella *et al* (56% RP cases and 100% LP).

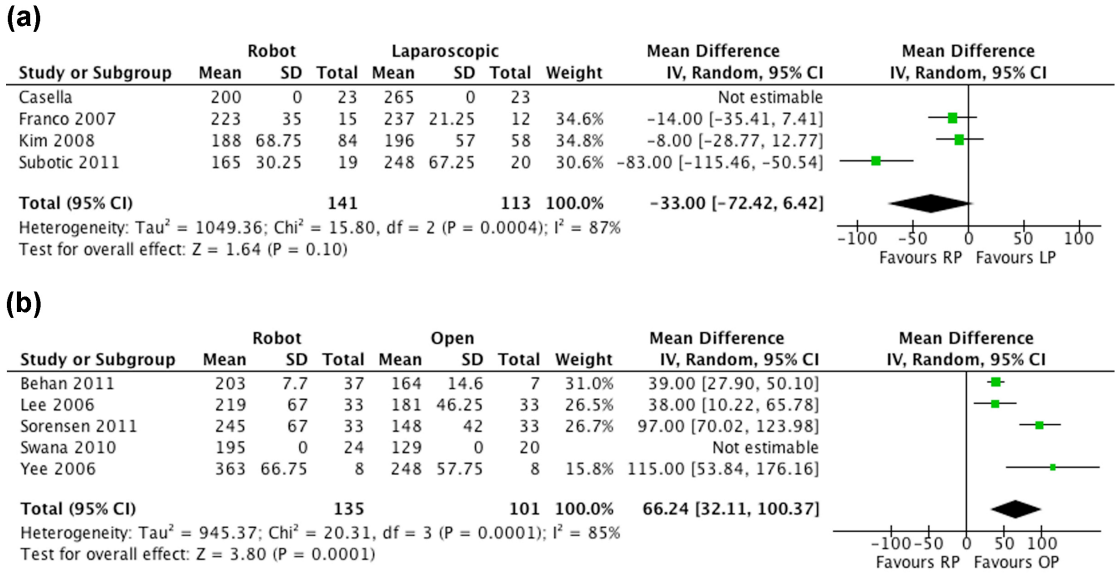


Figure 3.8 Forest plot comparisons of operating time for studies comparing robot-assisted versus a) laparoscopic and b) open pyeloplasty in children.

3.1.3.4.4 Analgesia requirement

There was insufficient data for pooled analysis of analgesia requirement. In the only study reporting post-operative opiate analgesia requirement for RP versus LP, Riachy *et al* observed lower median morphine equivalent requirement in RP, however this was not statistically significant (0.052 mg/kg/hospital day versus 0.067 mg/kg/hospital day, $P = 0.42$) [98]. Three studies reported post-operative morphine usage for RP versus OP. Lee *et al* found a significantly lower mean morphine requirement for their RP group compared to OP group (0.8 mg/kg versus 2.5 mg/kg, $P < 0.001$) despite 55% (18/33) in the OP receiving additional epidural analgesia [97]. Lower mean morphine requirement for RP compared to OP was also found by Yee *et al* (7.4 mg versus 22.0 mg) and Dangle *et al* (0.22 versus 0.32mg), however these findings were not statistically significant [102, 104].

3.1.3.4.5 Cost

Comparative cost data was reported in 3 studies for RP versus OP [94, 102, 104], and 1 study for RP versus LP [103]. This data indicates considerably higher total costs for RP versus OP, and comparable costs for RP versus LP.

Yee *et al* reported cost estimations of $5,466 for RP and $2,410 for OP, although it is unclear whether these values represent total cost or direct costs only [102]. Dangle *et al* found direct

costs of RP to be only $569 more expensive than OP ($4,979 versus $4,410, $P = 0.10$) [104]. Behan *et al* applied a detailed and previously validated mathematical model to estimate direct procedure-related costs and incorporate indirect amortized fixed costs (i.e. capital outlay and maintenance expenses) as well as human capital gains costs (i.e. loss of parental employment productivity and associated salary) [94]. Costs were comparable between RP and OP when amortized robot costs were excluded ($6,008 versus $5,079 respectively, $P = 0.064$). When 5-year and 10-year amortization costs were included, this increased RP costs to $9808 and $8408 respectively, with calculations based on an annual case volume of 100. Shorter LOS with RP contributed to $90 human capital savings and $612 less direct hospitalisation expenses per procedure compared to OP. Findings of lower direct costs, but higher total costs for robot-assisted paediatric urologic surgery have been also reported by Rowe *et al*, however calculations were based on a mixed procedure cohort without sub-group cost analysis for RP versus OP [83]. In the only available comparative cost study for RP versus LP, Casella *et al* found comparable total costs ($15,337 versus $16,067 respectively, $P = 0.46$) that were considered greatly influenced by shorter OT as LOS was standardised for both groups [103].

3.1.4 Discussion

This meta-analysis has identified no significant differences between RP and LP or OP for primary outcome variables of operative success, requirement for re-operation, conversion rates, post-operative complications, and urinary leakage. Significant differences in favour of RP were found for LOS (versus LP and OP). Borderline significant differences in favour of RP were found for EBL (versus OP). Operating time was found to be significantly longer for RP versus OP. Limited evidence from observational studies indicates lower opiate analgesia requirement for RP (versus LP and OP), but considerably higher direct costs (versus OP).

The main technical benefits of robot-assistance in minimally invasive surgery are consistently attributed towards the more demanding procedural steps, namely the ureteral spatulation, pelvis reduction, and uretero-pelvic anastomosis. The motion-scaled EndoWrist® instruments enable parallel alignment of scissors with the proximal ureter for more accurate and controlled linear spatulation. Similarly, the enhanced manual dexterity with these instruments and stereoscopic vision contribute to a lower degree of difficulty for the challenging task of intra-corporeal suturing within small anatomical workspaces.

3.1.4.1 Additional outcome measures

Some additional variables have been assessed in comparative studies of RP. Barbosa *et al* found that children undergoing RP had significantly faster time to sonographic resolution of hydronephrosis compared to an OP cohort (P = 0.004) [93], and Swana *et al* reported significantly quicker return to full activity for children having RP compared to OP (16 days versus 31 days respectively, P = 0.002) [101]. Several studies have also examined parent- and patient-reported outcome measures for RP versus OP using various surveys and subjective assessment tools [93, 105]. These studies demonstrate RP to be associated with greater cosmetic satisfaction and quality of life improvement [93, 105]. Many studies report data to confirm a favourable learning curve for RP [97-99, 101, 102]. It has been estimated that statistically similar operating times to OP can be achieved with case volume experience of 15 to 30 RP procedures [97, 99, 101]. In comparing the learning curves of RP versus LP, Riachy *et al* have demonstrated that the curve is less steep with RP and seems to plateau earlier [98]. The learning curve for RP will be explored in further detail in Chapter 4.

3.1.4.2 Not everything that counts can be easily counted

There are certain perceived advantages of RP that are not easily amenable to quantitative assessment. LP requires advanced skill and is difficult to learn and maintain as a complex reconstructive technique. Robot-assisted surgery offers valuable potential as a '*great leveler*' by shortening learning curves and making minimally invasive surgery more widely accessible [106]. Additionally, ergonomic comfort and efficiency for the surgeon is undeniably superior in RP compared to LP or OP, however the impact of this is difficult to quantify and therefore remains only supported by limited anecdotal and survey-type evidence [107].

3.1.4.3 Quality and level of evidence

Clinical evidence must be appreciated in the context of respective chronological stages that occur within a typical evolution cycle of surgical innovation. There is an inherent risk of bias in undertaking high level of evidence studies that compare established technique(s) with new alternatives. Surgeons are more likely to have developed mastery in OP and/or LP, while those adopting RP may still be progressing through their learning curve. This threatens to favour results towards the former. The window of time to conduct high quality prospective observational studies or clinical trials is therefore short and ideally must be judged to occur once satisfactory time has elapsed since introduction of the new technique, and before

equipoise becomes absolved [108]. Timing for meta-analyses should adhere to similar principles. In recognising that more than 10 years has elapsed since paediatric application of RP was first introduced, the timing for data synthesis is probably appropriate, but it must be stressed that repeat future attempts at meta-analysis should occur at staged intervals as new comparative evidence becomes available.

The reliance upon less robust retrospective data is inadequate and represents a major weakness in the current literature base for paediatric robot-assisted surgery [89]. Given the similarly high success rates amongst all techniques, future studies with larger sample sizes would be required to determine any significance for an anticipated small effect size. To this end, prospective national (or indeed, multinational) registries have been suitably proposed as much needed strategies to ensure that continuous, transparent, and large-scale post marketing surveillance and outcome evaluation of new technology occurs as it is implemented [91, 108, 109]. Length of follow up is another factor that should be addressed in future studies to ensure that outcome assessment extends beyond the early and medium-term post-operative period [29].

Two previous meta-analyses have investigated RP with other techniques [110, 111]. Both these studies heavily focus on adult pyeloplasty. Braga *et al* investigated RP versus LP and included 2 studies from the paediatric literature, however there was no sub-group analysis for paediatric pyeloplasty [111]. A more recent meta-analysis by Autorino *et al* investigated OP versus minimally invasive pyeloplasty (MIP) [110]. There was no distinction between RP and LP. Pooled analysis of operative success, complications, OT and LOS demonstrated significant differences for OT only (WMD = 71.48 mins in favour of OP; $P < 0.001$) [110].

The recent NIS database analysis study by Monn *et al* provides a valuable and informative perspective of the evolving status of RP [2]. For the clinical outcomes and cost variables investigated for RP versus OP, their findings were similar to those reported in this meta-analysis. Children undergoing RP were older than those having OP, mean LOS was half a day shorter for RP compared to OP, and RP was more expensive than OP [2]. By interrogating nationwide or international datasets such as the NIS, outcomes (or health services) research can be a powerful assessment strategy for evaluating large-scale trends and variations in clinical practice. Outcomes research is however dependently influenced by the quality and availability of data from which extractive analysis is conducted. Uncontrollable deficiencies and inadequacies in data may be challenging to statistically correct for. As highlighted by Monn *et al*, the NIS database captures only 20% of all in-patient hospitalisations in the United States, contains data for single inpatient episodes only (i.e. no

outpatient follow up data is available for assessment of outcomes beyond the hospitalisation period), and only began recording data for RP from 2008. Ongoing appraisal of robotic technology for selective indications such as paediatric pyeloplasty, as well as the broader setting, should incorporate both outcomes research and clinical research such that respective advantages and drawbacks of these investigative approaches may be complementary.

3.1.4.4 Standardisation of outcome measures, and operative technique

We identified only 2 comparative studies that reported post-operative complications using the Clavien-Dindo classification [98, 100]. Utilisation of this generic grading system should be encouraged to improve standardisation in reporting of this important outcome variable. Of note, Clavien-Dindo grading may be up-scaled in paediatric pyeloplasty as complications such as those requiring stent re-positioning/replacement usually require a procedure under general anaesthesia.

There is need for consensus regarding definition of '*operating time'* in the robotic surgery literature. There are numerous permutations of '*operating time'*, depending on whether time for cystoscopy, patient positioning, and robot docking/un-docking are included. Link *et al* clearly outline the typical workflow of LP and RP procedures using a time-based schematic [112]. It is important that authors design future comparative studies to employ parity in defining equal and fair '*operating time'* definitions for study groups, as well as clearly communicating these definitions in methodology reporting. If opportunity permits multiple time parameters to be measured, this would be preferable. As a single preferred parameter, skin incision to skin closure time seems most suitable definition of *'operating time'*, as it represents the best defined, fixed, and most prevalent existing measure.

Measurement of EBL is often criticised as being particularly subjective and vulnerable to bias. This might explain the significant heterogeneity detected in pooled analysis of this variable. The reliability of this outcome measure may be improved by more transparent reporting of how it was measured (e.g. suction canister volume, estimation based on blood soaked swabs) and who was involved in data collection (e.g. anaesthetist, surgeon, assistant).

The technique for RP in children is now reasonably refined [113], however minor variations will always persist due to differences in surgeon preference and patient characteristics. Retroperitoneal [114], stentless [115], and da Vinci® Single-Site® pyeloplasty are examples of modified techniques that are emerging. Improvements in study quality will come from

concerted prospective efforts to minimise operative technique variation, and achieve homogeneity in inter-group patient characteristics (Tables 3.1 and 3.4) such that the effects of known and unknown confounders are attenuated. The existing literature base compares techniques in a broader sense, with further investigation of stratified patient sub-groups remaining under-explored. Priorities for focused comparative investigation are paediatric age sub-categories (i.e. infants or teenagers) [29, 90, 97] and more complex cases such as secondary (re-do) pyeloplasties.

In conclusion, meta-analysis of the current literature identifies no significant differences between RP and LP or OP for the 5 primary outcome variables assessed. Significant differences in favour of RP were found for secondary outcome variables of EBL (versus OP) and LOS (versus LP and OP). Operating time was found to be significantly longer for RP versus OP. Limited evidence from observational studies indicates lower opiate analgesia requirement for RP (versus LP and OP), higher total costs for RP versus OP, and comparable costs for RP versus LP. There is a strong need for higher quality evidence in the form of prospective observational studies and clinical trials, as well as further cost-effectiveness analyses.

3.2 Meta Analysis of Robot-assisted versus Conventional Laparoscopic Fundoplication in Children

3.2.1 Introduction

Fundoplication is a high volume surgical procedure in the paediatric patient population. Indications are assorted and invariably related to symptoms or signs of gastro-oesophageal reflux disease (GORD) [116]. Following the advent of endoscopic surgery, a minimally invasive approach to this anti-reflux procedure is now increasingly favoured as standard of care [116].

Initial reports of laparoscopic ant-reflux surgery in infants and children were published in the early 1990's [117, 118]. Almost ten years thereafter, robot-assisted minimally invasive surgery was first described in these age groups [17] [16] and as identified in Chapter 2, fundoplication remains the most prevalently reported application of this technology in paediatric general surgery [89].

The role of robotic surgery in this setting remains unclear, generating a growing sentiment of polarised opinion amongst the surgical community, which is without a well-defined evidence base. The aim of this chapter is to critically appraise the literature comparing robot-assisted versus conventional laparoscopic MIS for fundoplication in order to further elucidate the comparative safety and efficacy of these techniques.

3.2.2 Methods

The study protocol was registered on the PROSPERO international prospective database of systematic reviews (CRD42013003971). Analysis was performed in accordance with recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [63].

3.2.2.1 Search strategy

Systematic literature searches were undertaken of PubMed and EMBASE electronic databases using the following search strategy ("Surgery, Computer-Assisted"[MeSH] OR "robotics"[MeSH] OR "da Vinci" OR "telerobotic" OR "telesurgery" OR "robotic surgery") AND ("Pediatrics"[MeSH] OR "Infant"[MeSH] OR "Child"[MeSH] OR "Adolescent"[MeSH]) AND ("Fundoplication"[MeSH] OR "Gastro-oesophageal

reflux"[MeSH]). The search period was defined as June 2001 to June 2013 inclusively. The primary search was supplemented with searches of 1) PubMed related articles feature, 2) clinicaltrials.gov registry using the keyword "fundoplication", and 3) abstracts of the International Pediatric Endosurgery Group annual congress from 2002 to 2013.

3.2.2.2 Inclusion and exclusion criteria

All included studies satisfied the following criteria: 1) comparing robot-assisted (RF) versus conventional laparoscopic fundoplication (LF), 2) involving paediatric patients with mean or median study group ages < 18 years, 3) reporting ≥ 5 patients in each study group, and 4) investigating either objective clinical outcome measures or GORD symptoms via standardised questionnaires. No language restrictions were imposed. In the event that duplication of data was observed, more recent studies or those with larger sample sizes were preferentially considered, with subsequent exclusion of earlier, smaller studies.

3.2.2.3 Outcomes of interest

Primary outcomes of interest were operative success, requirement for re-operation (i.e. due to wrap failure, post-operative symptoms related to surgery) and post-operative morbidity (defined as dysphagia, retching, belching). Operative success was regarded as improvement or resolution of GORD that was measured either objectively using upper gastrointestinal contrast studies, 24-hour pH monitoring studies, oesophageal manometry, or oesophagoscopy with or without biopsy; or subjectively using validated questionnaires such as the Paediatric GORD Symptom and Quality of Life Questionnaire [119, 120]. Secondary outcome measures of interest were intra-operative conversions, intra-operative complications, length of hospital stay (LOS), post-operative complications, operating time (OT), analgesia requirement and cost. Operating time was regarded as the 'total' time from first skin incision to skin closure.

3.2.2.4 Data extraction and synthesis

Two reviewers independently undertook literature searches, screened abstracts and assessed articles against eligibility criteria. Discrepancies were resolved by consensus and discussion with a third reviewer. Corresponding authors were contacted regarding any missing data. The methodological quality of studies was appraised using the same mNOS tool described in Chapter 3.1 [92]. The 10 single-star variables used to grade comparability amongst study groups included age, weight, gender, indication for surgery, severity of GORD, major co-morbidities

(including neurological impairment), proportion of re-do cases, proportion of cases involving concomitant procedures (i.e. gastrostomy), operative technique (including number of wrap sutures), and surgeon experience (or number of operating surgeons in each study group). Patient demographic and outcome data was extracted from included studies. For data synthesis, studies were weighted based on sample size and quality of study scoring. Statistical analysis was performed using the same methodology described in Chapter 3.1.

3.2.3 Results

Six studies met inclusion criteria, involving 135 robot-assisted and 162 conventional laparoscopic fundoplication procedures (Tables 3.6 and 3.7) [82, 121-125]. A summary of the results of the search strategy is shown in Figure 3.9.

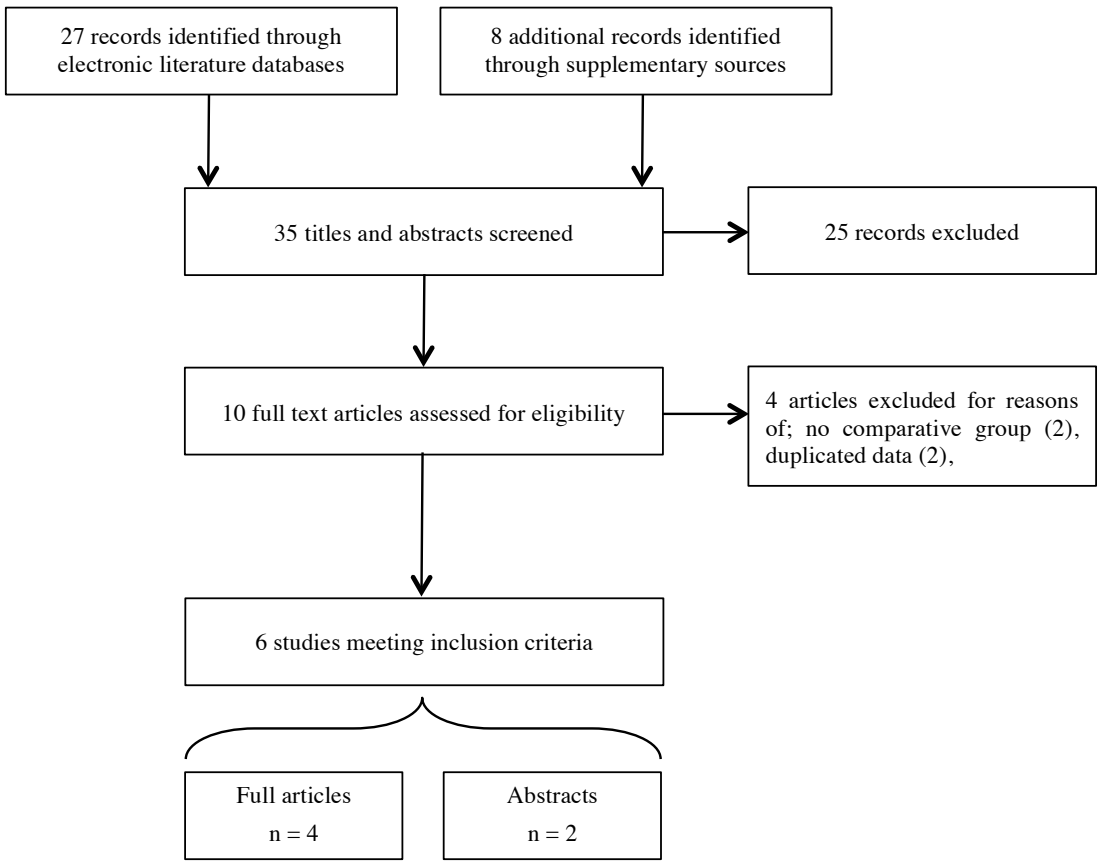


Figure 3.9 Prisma flow diagram outlining the systematic search strategy and study selection process.

	Study	Study period	n		Fundo-plication	Min months follow up [mean (range)]	Surgeons	
			RF	LF			RF	LF
Ivascu 2004 [125]	RCC	2002 – 2003	17	34	Nissen	-	-	-
Lehnert 2006 [123]	PC	2001 – 2003	10	10	Thal	14 (-)	1	1
Copeland 2008 [122]	RCC	1994 – 2005	50	50	Nissen	1 (-)	7	3
Al-Bassam 2009 [121]	RC	2005 – 2008	25	25	Nissen	14 (1 – 48)	2	2
Anderberg 2009 [82]	RC	2006 – 2008	14	10	Nissen	12 (-)	1	2
Antao 2010 [124]	RC	1999 – 2009	19	33	Nissen	-	-	-

Table 3.6 Characteristics of studies included in the meta-analysis. "-" = not reported. RCC = retrospective case-control study, PC = prospective cohort study, RC = retrospective cohort study.

	NI (%)			Gastrostomy (%)		
	RF	LF	*P* value	RF	LF	*P* value
Ivascu 2004 [125]	53%	53%	0.99	41%	46%	0.77
Lehnert 2006 [123]	0%	0%	n/a	0%	0%	n/a
Copeland 2008 [122]	-	-	-	34%	48%	0.34
Al-Bassam 2009 [121]	64%	72%	0.55	60%	64%	-
Anderberg 2009 [82]	79%	80%	-	-	-	-
Antao 2010 [15]	32%	45%	-	47%	58%	-

Table 3.7 Distribution of patients with neurological impairment and also those requiring concomitant gastrostomy at the time of surgery. "-" = not reported. NI = neurologic impairment.

3.2.3.1 Study characteristics and appraisal of quality of evidence

No randomised controlled trials were identified. Four of the included studies were cohort studies and the remaining two studies were case-controlled studies (Table 3.6). All reported RF cases were undertaken using the da Vinci Surgical System®. All included studies reported utilisation of the Nissen fundoplication technique, with the exception of the study by Lehnert *et al*, who performed Thal fundoplications [14].

Only one included study was prospective in design, with patient allocation determined by parent preference following detailed explanation of both surgical techniques [123]. All other studies were retrospective and observational [82, 121, 122, 124, 125]; mostly with study group periods that were not synchronous and using historical LF controls [82, 122, 124]. All studies were single-institution in origin. No studies reported pre-hoc power calculations to justify adequate sample size. The median mNOS score was 8 (range 5 – 14, Table 3.8).

Three studies explicitly described inclusion and exclusion criteria. The prospective cohort study by Lehnert *et al* strictly limited their cohort to children with clinically relevant GORD, without co-existing disease (including neurological impairment) or recurrent GORD, not requiring gastrostomy and with no prior history of major congenital anomalies such as oesophageal atresia, abdominal wall defects or diaphragmatic hernia [123]. Al-Bassam *et al* and Anderberg *et al* described inclusion criteria based on indications for fundoplication that consisted of GORD that was refractory to medical management and standardised diagnostic work-up findings [82, 121]. Two studies reported intentional case matching. Ivascu *et al* matched cases by age [125] and Copeland *et al* reported case-matching with controls, however these factors were not clear [122]. Amongst the five studies that reported patient age data, children in the RF groups tended to be older than those in LF groups (overall mean age 8.44 years, RF versus 6.40 years, LF) and this approached overall statistical significance (Figure 3.10a, WMD = 2.1 years; 95% CI -0.10 – 4.32; P = 0.06). Pooled analysis identified no overall difference in weight amongst the three studies that reported this data (P = 0.65, Figure 3.10b). The youngest patients reported were 2 months and 3 months of age for RF and LF groups respectively [121]. The smallest patients reported were 3.5 kg and 3.0 kg for RF and LF groups respectively [121].

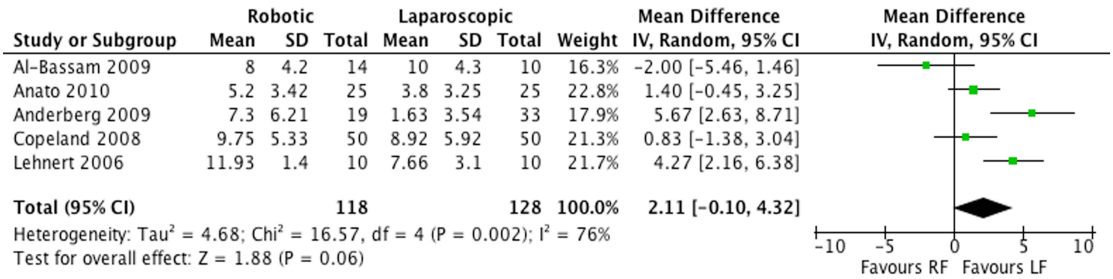
	Ivascu et al [125]	Lehnert et al [123]	Copeland et al [122]	Al-Bassam et al [121]	Anderberg et al [82]	Antao et al [124]
Selection						
Group assignment		*				
Representativeness	*	**	**	**	**	**
Comparability						
Age	*			*	*	
Gender				*		
Weight				*		
Indication				*	*	
GORD severity		*			*	
Co-morbidities	*	*		*	*	*
Re-do cases		*		*		
Other procedures	*	*	*	*		*
Technique		*	*	*	*	
Surgeons				*	*	
Outcome assessment						
Defined outcomes	*	*	*	*	*	*
Follow-up		*	*	*		
mNOS total (/15)	6	10	6	14	9	5

Table 3.8 Summary of study quality appraisal using the modified Newcastle-Ottawa Scale (mNOS).

3.2.3.2 Primary Outcomes: Operative success, re-operation rate and post-operative morbidity

In general, length of follow up was short, with all studies focusing on peri-operative and short-term post-operative outcomes (Table 3.6). No studies clearly defined criteria or endpoints for operative success. As such, there was no standardised or protocoled follow up beyond the early post-operative period to enable data synthesis for the primary outcomes of interest outlined above.

(a)



(b)

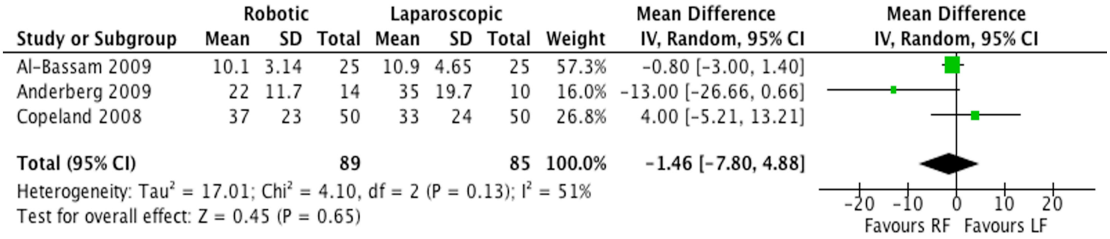


Figure 3.10 Forest plot comparisons of a) age, and b) weight for studies comparing RF versus LF in children.

Antao *et al* reported 3 GORD recurrences, 2 in patients having undergone LF and 1 in a patient having undergone RF [124]. No other cases of recurrence were identified and no requirement for re-operation was reported in any of the included studies. During routine clinical follow up at undefined intervals within a median 14 month period post-operatively, Al-Bassam *et al* observed complete symptom resolution in 64% of RF patients and 60% of LF patients [121]. Improvement in symptoms was noted in 36% and 40% of RF and LF patients in this same cohort respectively [121]. At 30-day clinical follow up, Copeland *et al* observed comparable rates of transient symptoms (30% RF versus 28% LF) that included dysphagia, abdominal pain, feeding aversion and gas bloating [122].

3.2.3.3 Secondary outcomes: Conversions, length of hospital stay, post-operative complications, operating time, analgesia requirement, cost

3.2.3.3.1 Conversions

All 6 studies reported conversion data. Overall conversion rates were 3.0% (4/135) for RF and 6.2% (10/162) for LF, with combined estimate indicating 51% lower conversion rate in RF that was not statistically significant (OR = 0.49; 95% CI 0.14 – 1.72; P = 0.27, Figure 3.11). No statistical evidence of heterogeneity (I^2 = 0%) or publication bias (Egger's Test = -1.87, P = 0.69; Begg and Mazumdar: P = 1.00) was detected.

In the RF group, reasons for conversions were due to intraoperative hypotension and arrhythmia (n = 1) [122], technical difficulty in a re-do case (n = 1) [122], and unclear anatomy associated with hiatus hernia (n = 1) [121]. In the LF group, reasons for conversion were due to gastric perforation (n = 1) [122], incidental discovery of Morgagni hernia (n = 1) [82], "instrument problems" (n = 1) [82], and technical difficulty in re-do cases (n = 2) [121]. Although detailed reasons for conversions were not described by Antao *et al*, it was reported that most events in LF cases were due to technical difficulties related to spatially confined workspaces in smaller children [124].

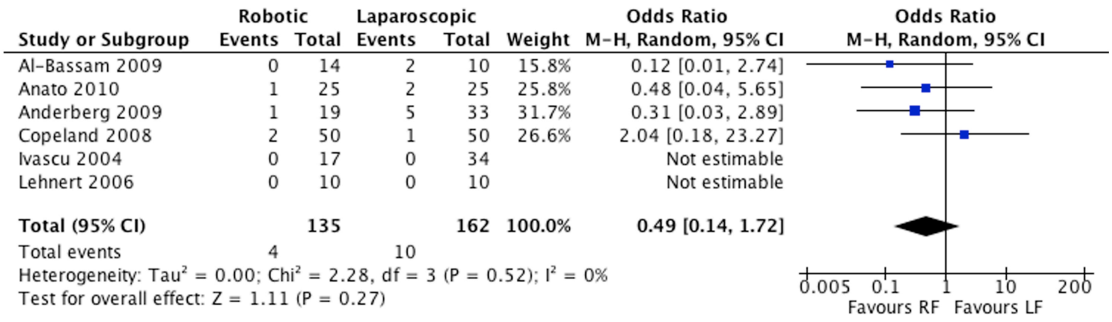


Figure 3.11 Forest plot comparisons of conversions for studies comparing RF versus LF in children.

3.2.3.3.2 Length of hospital stay

Duration of post-operative hospital stay was reported in 5 studies. No statistically significant difference was observed between RF and LF groups (WMD = -0.02 days; 95% CI -1.10 – 1.06; P = 0.98), with no heterogeneity detected (Figure 3.12).

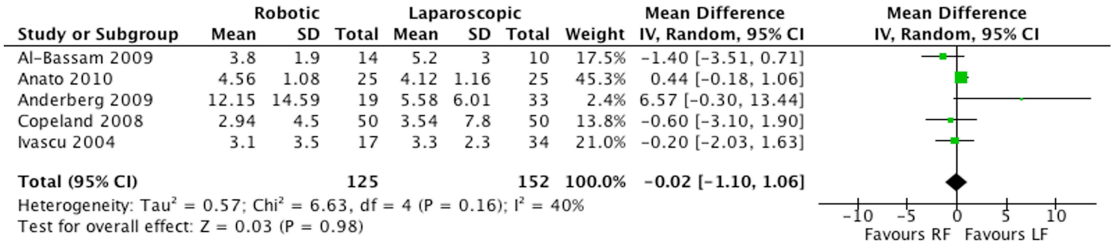


Figure 3.12 Forest plot comparisons of length of hospital stay for studies comparing RF versus LF in children.

3.2.3.3.3 Post-operative complications

The overall frequency of post-operative complications was 12/135 (8.9%) and 13/162 (8.0%) for RF and LF groups respectively. No cases of mortality were identified. Reported complications are summarised in Table 3.9. Inadequate reporting detail prohibited categorisation and analysis of complications according to the Clavien-Dindo classification [126]. There was no significant difference observed between RF and LF groups for complication frequency (Figure 3.13, OR = 1.13; 95% CI = 0.47 – 2.70; *P* = 0.78), again without significant heterogeneity.

	RF		LF	
	n (%)	Details	n (%)	Details
Ivascu 2004 [125]	0/17 (0%)	n/a	0/34 (0%)	n/a
Lehnert 2006 [123]	0/10 (0%)	n/a	0/10 (0%)	n/a
Copeland 2008 [122]	7/50 (14%)	Tight wrap requiring dilatation (4), *	8/50 (16%)	Tight wrap requiring dilatation (3), *
Al-Bassam 2009 [121]	2/25 (8%)	Delayed gastric emptying (2)	2/25 (8%)	Delayed gastric emptying (1), dysphagia (1)
Anderberg 2009 [12]	2/14 (14%)	Umbilical port-site hernia (1), wound infection (1)	1/10 (10%)	Wound infection (1)
Antao 2010 [124]	1/19 (5%)	Recurrence (1)	2/33 (6%)	Recurrence (2)

Table 3.9 Summary of post-operative complications reported amongst studies included in the meta-analysis. * details not reported or incomplete, n/a = not applicable.

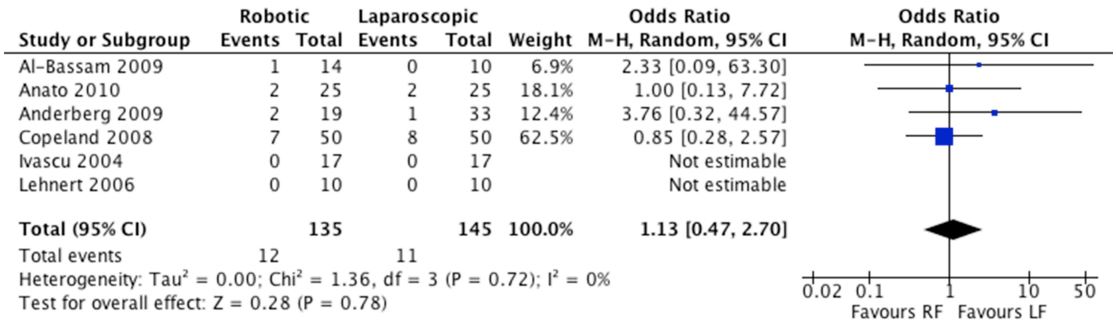


Figure 3.13 Forest plot comparisons of post-operative complications for studies comparing RF versus LF in children.

3.2.3.3.4 Operating time

Total operating time was reported in all 6 studies. No statistically significant difference was revealed between RF and LF groups, although the estimated effect favoured RF (Figure 3.14a, WMD 11.2 minutes; 95% CI -14.85 – 37.28; $P = 0.4$). Significant heterogeneity was detected (I^2= 88%), as well as small study effect publication bias (Egger's test = -3.88, P = 0.028). Sub-group analysis of high quality studies only (> 8 median mNOS score) improved heterogeneity (I^2= 83%), however with minor effect on overall estimate (Figure 3.14b, WMD = 15.97 minutes; 95% CI -18.55 – 50.49; $P = 0.36$). Statistical publication bias assessment of this subgroup was not possible due to the low number of high-quality studies.

In evaluating breakdown of operative times for defined procedural stages, Lehnert *et al* found initial time from skin incision to start of hiatal region dissection to be significantly longer in the RF group ($P = 0.002$) [123]. Inversely, they also found that for the more technically difficult aspect of the procedure, hiatal dissection was significantly shorter in the RF group (P = 0.005) [123]. No significant time differences were found for hiatal repair and fundoplication stages. In the only study reporting comparative time data that examined set-up or robot 'docking' time, Antao *et al* found total operating room time to be more contrasting between RP and LP, compared to operating time [15].

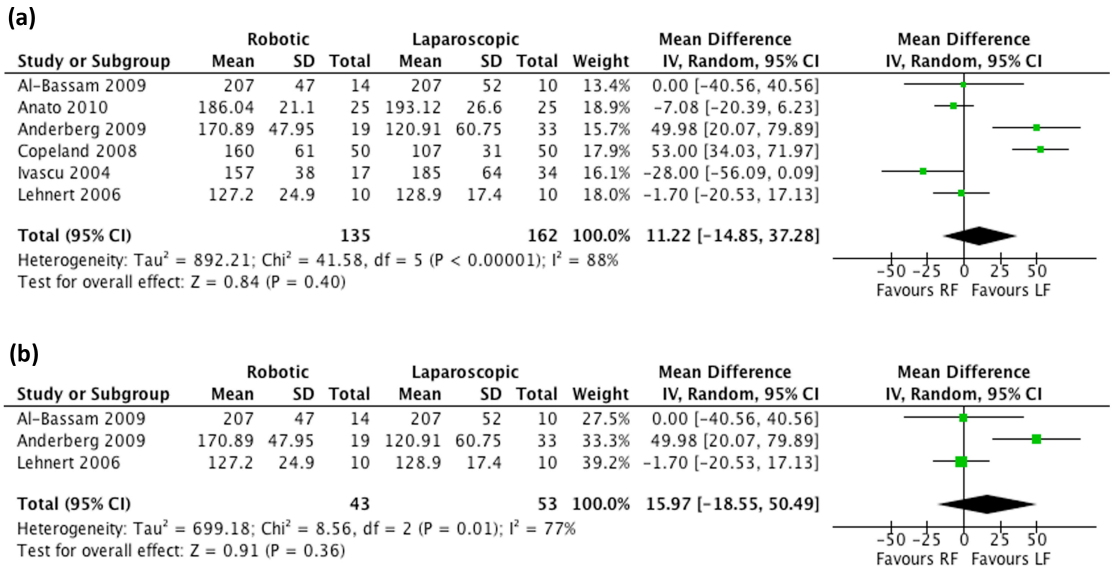


Figure 3.14 Forest plot comparisons of a) total operating time for studies comparing RF versus LF in children, and b) sub-group analysis of high quality studies only.

3.2.3.3.5 Analgesia requirement

Two studies reported comparative opiate analgesia requirements, although each used different methods of measurement that precluded quantitative data synthesis [82, 121]. Al-Bassam *et al* found no significant difference in the proportion of patients that required 1 – 2 doses of opiate analgesia post-operatively (36% RF versus 28% LF, $P = 0.173$) [121]. In this study, analgesia requirement was subjectively assessed in the context of vital sign measurements. Using a more objective and standardised Visual Analogue Scale (VAS) method to assess post-operative pain, Anderberg *et al* found patients had shorter post-operative duration of opiate requirement (1.1 ± 0.9 days RF versus 1.6 ± 0.7 days LF) [82]. These findings are somewhat unexpected given that larger abdominal wall incisions are needed to accommodate 8mm instruments in RF cases, compared to 3mm-5mm instruments used in LF cases.

3.2.3.3.6 Cost

Cost analysis by Anderberg *et al* revealed 29% higher per case cost for RF compared to LF [82]. When indirect fixed costs such as capital outlay and maintenance service were excluded, RF remained more expensive on a per case basis (EUR 9,584 versus EUR 8,982). Of note, LF instrument costs were not included in these economic calculations as pre-existing reusable instruments were used during the study period.

3.2.3.3.7 Post-hoc sub-analysis

Clinical outcomes are known to vary amongst the assorted laparoscopic fundoplication techniques (i.e. Nissen, Thal, Toupet, Dor). To explore the effect of fundoplication technique as a potential confounder in our results, a sub-analysis was performed of studies involving Nissen fundoplication only. The only outcome measure affected in pooled analysis was operating time, with estimated effect marginally increasing from WMD = 11.22 minutes (95% CI -14.85 – 37.28, $P = 0.40$) to WMD = 13.95 minutes (95% CI -19.03 – 46.94, $P = 0.41$).

3.2.4 Discussion

This meta-analysis has identified no significant difference between robot-assisted and conventional laparoscopic fundoplication for short-term outcomes of intra-operative conversion, length of hospital stay, post-operative complications and total operating time. Limited evidence from observational studies also indicates higher direct costs for RF, and post-operative analgesia requirement that is either comparable or lower than that for LF. There is a distinct lack of longer-term follow up data in the literature that limits comparative evaluation of anti-reflux surgery success, post-operative morbidity, and re-operation rates. The importance and relevance of these under-reported outcome measures is emphasised by recent high quality long-term follow-up studies of LF cohorts that reveal GORD symptom recurrence rates of 19.3% - 26.8% and re-operation rates of 10.5% - 14.0% [120, 127].

3.2.4.1.1 Adult evidence

Four recent meta-analyses have investigated RF versus LF in adult patients, with each including no fewer than 4 RCTs [128-131]. No significant differences were identified for conversions [128], LOS [128-130] and cost [128, 131]. Both Markar *et al*, Mi *et al*, and Wang *et al* found increased total operative times with RF (WMD range = 3.17 to 24.05 mins) [129-131]. Mi *et al* found post-operative complications to be 65% lower in RF ($P = 0.04$) [130], however significant differences were not seen in two other separate pooled analyses [128, 129]. Longer-term outcomes of post-operative GORD, dysphagia, quality of life, and requirement for re-operation were assessed in many RCTs and observational studies included in these studies, with no significant difference between RF and LF determined in any available pooled analyses [128-131].

3.2.4.1.2 Evidence discrete roles of robot-assisted fundoplication

The impact of conventional laparoscopic fundoplication over the traditional open surgical technique was clearly *disruptive*, with well-described patient benefits justifying widespread adoption and progressive acceptance towards standard of care [116, 132, 133]. Given that all skin incisions, port sites, port numbers and operative steps are essentially indifferent between RF and LF approaches; it could be argued that RF should be considered as an adjunct to conventional laparoscopy, rather than a *de novo* surgical approach in itself. In this regard, any expected patient benefit associated with robot-assistance would more *incremental* when performed by expert surgeons, and therefore less discernable or even 'hidden' when evaluated using familiar discriminators in small comparative studies. Furthermore, some perceived benefits of robot-assistance might not be measurable by quantitative data obtained through clinical trials [106].

The enhanced features of robot-assistance are felt to offer a greater role in more difficult or high-risk cases such as those involving previous fundoplication or preservation of pre-existing gastrostomy [7, 134]. Currently, there is no evidence to guide patient selection in these circumstances and this might be a focus of future research. Several authors also describe an attractively short and steep learning curve for RF in which proficiency can be attained after only 5 – 10 cases [82, 121, 122, 135]. The RF learning curve is explored in detail in Chapter 4.

3.2.4.2 Cost-benefit

From an exclusively evidence-based standpoint, it is challenging to robustly defend a cost-benefit argument for RF in the context of presently available outcome and economic data. This scenario is certainly not unique to this particular indication and seems reflected across most adult and paediatric settings [67, 136]. The high cost of robotic surgical technology is a major barrier to adoption, driven by a lack of market competition and expenses generally associated with early phase technology [67]. While affordability presently seems static at best, cost-benefit evaluations will obviously need to be periodically re-visited as pricings inevitably are driven down. In the meantime, costs of increasingly popular disposable laparoscopic instruments should not be ignored. On a per case cost basis, the expense of these single-use instruments approaches that of robotic instruments [9].

3.2.4.3 Limitations and future directions

The majority of comparative effectiveness literature is comprised of small retrospective studies with historical controls. The strength of this meta-analysis is therefore limited by inherent vulnerability of these study designs to multiple sources of bias and both known and unknown confounders. Many important outcome variables also remain unaccounted for in the literature. More high quality prospective studies and clinical trials are indisputably warranted to better inform the debate of RF versus LF for fundoplication in children. Future studies should strive towards methodological quality that satisfies criteria of; 1) prospective design, 2) patient selection criteria accounting for many of the comparability variables outlined above (Table 3.8), 3) regular protocoled follow up with clearly delineated outcome measures, 4) attention towards more procedure and pathology orientated outcomes, and 5) length of follow up that extends beyond the early post-operative period. Rigor of post-operative complication monitoring and recording might be improved with adherence to the Clavien-Dindo classification [126].

In conclusion, neta-analysis of the current literature identifies comparable safety and short-term efficacy for robot-assisted laparoscopic fundoplication when compared to conventional laparoscopic fundoplication in children. However, there is insufficient evidence to assess comparative effectiveness for important procedure and pathology specific outcome measures such as success rate, post-operative surgery related morbidity and re-operation rates. Higher quality and longer-follow up studies are now required to more definitively and comprehensively determine the role of robotic-assisted techniques in this setting. Equipoise in short-term clinical outcomes emphasises the need for further cost-effectiveness analysis to also be undertaken.

CHAPTER 4 EDUCATION & TRAINING IN PAEDIATRIC ROBOTIC SURGERY

Content from this chapter was published or submitted as:

TP Cundy, EK Mayer, JI Camps, LH Olsen, G Pelizzo, GZ Yang, A Darzi, AS Najmaldin. Training and education in paediatric robot-assisted minimally invasive surgery: lessons learned from an inaugural multinational workshop. Journal of Robotic Surgery. [in press]

TP Cundy, SP Rowland, NE Gattas, AD White, AS Najmaldin. The learning curve of robot-assisted laparoscopic fundoplication in children – a prospective evaluation and CUSUM analysis. The International Journal of Medical Robotics and Computer-Assisted Surgery. [in press]

TP Cundy, NE Gattas, A White, GZ Yang, A Darzi, AS Najmaldin. Learning curve evaluation using CUSUM analysis – a clinical example of paediatric robot-assisted laparoscopic pyeloplasty. Journal of Pediatric Surgery. [under peer review]

Content from this chapter was presented as:

TP Cundy, EK Mayer, JI Camps, LH Olsen, G Pelizzo, GZ Yang, A Darzi, AS Najmaldin. Education and training in paediatric robot-assisted minimally invasive surgery: lessons learned from an inaugural multinational workshop. 4th European Society of Paediatric Endoscopic Surgeons Congress (ESPES), Bratislava, Slovakia. October, 2014.

TP Cundy, GZ Yang, A Darzi, AS Najmaldin. Learning curve analysis in paediatric surgery using the cumulative sum (CUSUM) method – a statistical primer and clinical example. International Paediatric Endosurgery Group (IPEG) 23rd Annual Congress, Edinburgh. July, 2014.

4.1 Education and Training in Paediatric Robot-Assisted Minimally Invasive Surgery: Lessons Learned from an Inaugural Multinational Workshop

4.1.1 Introduction

Surgical innovation should be introduced into clinical practice with rigorous attention to salient skills training and education of relevant healthcare team members. This principle is paramount to safe, responsible, and ethical clinical translation of technology [137-139]. The emerging interest and roles for robotic surgery has created a need for creative new approaches to surgical training and education [140]. Paediatric robot-assisted minimally invasive surgery has many unique considerations that demand dedicated training opportunities in addition to generic specialty non-specific training resources that are emerging. Some examples of factors that deserve focused training in this field are the numerous operative indications that occur exclusively or predominantly in children, adaptation strategies for widely varied patient ages and sizes, and emphasis on reconstructive rather than extirpative surgical techniques [9, 10, 27, 141].

At present, there is no standardised validated training curriculum for any specialty field in which robotic surgery is being adopted [142]. This is recognised as a major priority and leading representative societies such as the American Urological Association (AUA) and European Association of Urology (EAU) are in the process of actively addressing the issue, as well as establishing proficiency-based credentialing standards [142, 143]. In the interim, the modular and stepwise curriculum framework described by Chitwood *et al* seems to be the preferred approach to training [144]. This educational model was implemented at the original international training centre for robotic surgery and has been replicated by many others since [144, 145]. Broadly, it involves a 2-stage process that consists of preclinical and clinical phases (Figure 4.1) [10, 143, 144]. In the initial pre-clinical phase, informal hands-on workshops or courses are regarded as integral [143]. Such events are typically the first thing that surgeons or clinical teams seek when interested in a new technology or technique. It is important that these resources are available and accessible in themselves, and also for organised curricula to follow in a succeeding manner.

This chapter reports on the outcome of a European-based paediatric robotic surgery workshop and critically reflects on lessons learned from this experience. The event was a hands-on focused event intended to offer an exposure rich environment for delegates to familiarise with, and learn basic principles of robotic surgery in a maximally efficient manner.

Pre- and post-workshop delegate feedback is presented in order to 1) improve the understanding of paediatric surgeons' learning needs and preferences for these style of training events, and 2) to explore the capacity for improvement of the educational experience offered. The feasibility and sustainability of such events are further evaluated by introspectively examining the financial and practical challenges encountered.

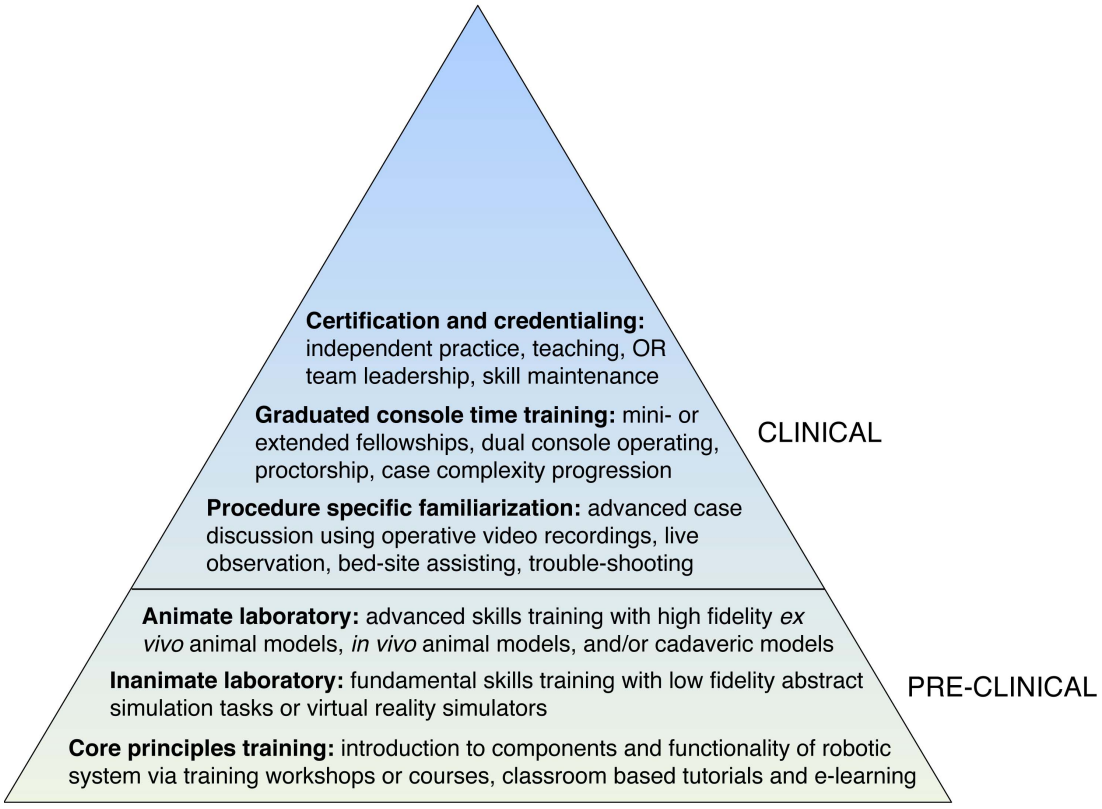


Figure 4.1 Example of a structured robotic surgery training curriculum framework based on those proposed by Chitwood *et al* [144] and Lee *et al* [143].

4.1.2 Materials and methods

The Paediatric Robotic Surgery Inaugural European Workshop was hosted at the 6th Hamlyn Symposium on Medical Robotics in London (United Kingdom) in June 2013. The workshop was held in association with the European Society of Paediatric Endoscopic Surgeons (ESPES). Advertisement was circulated online via the websites of ESPES, British Association of Paediatric Endoscopic Surgeons (BAPES), Paediatric Surgery On Line Society, Trainees in Paediatric Surgery, European Society for Paediatric Urology, Swiss Society for Paediatric Urology, and Journal of Paediatric Surgical Specialties (Appendices 1

and 2). An announcement of the workshop was also distributed via an international email registry of paediatric surgeons maintained by the workshop convener (ASN).

4.1.2.1 Programme

The workshop was held over one full day at St Mary's Hospital, London. The workshop program was comprised of interactive classroom-based short tutorials and hands-on practical components, with emphasis on the latter. Delegates rotated through four 90-minute practical stations with a minimum 2:4 faculty to delegate ratio. The station sequence was different for each group. Stations ranged from basic to intermediate level and consisted of 1) hardware familiarisation and docking, 2) virtual reality simulation training, 3) robot-assisted laparoscopic fundoplication using a porcine model, and 4) robot-assisted laparoscopic pyeloplasty.

Structured tutorial topics included; 1) setting up a robotic surgical service and theatre team (paediatric and adult perspectives), 2) economic and ethical considerations, 3) specific gastrointestinal, hepato-biliary, and urological procedures, 4) retroperitoneal access for paediatric robotic surgery, 5) image guided paediatric minimally invasive surgery, 6) horizon scanning next-generation robotic platforms, and 7) an augmented reality live demonstration using an upper urinary tract phantom model. The practical stations involved three da Vinci® Surgical Systems and one dV-Trainer® (Mimic Technologies Inc, WA). Classroom based teaching comprised 25% of the program time, and hands-on sessions for the remaining 75%. Mini-tutorials were conducted in an impromptu fashion during practical sessions to suit delegates' learning needs. Examples of such mini-tutorials included port placement strategies, a "5 minute dock" technique, and tips for judicious instrument selection. All delegates were presented with a certificate of attendance.

4.1.2.2 Qualitative and quantitative survey feedback

Registered delegates were asked to complete online pre-workshop and post-workshop surveys. These surveys were designed using an online survey software and questionnaire tool (SurveyMonkey®, CA). Questions were designed to enquire about background clinical practice, perceptions towards possible workshop topics, and both overall and specific feedback on the workshop program. Ordinal response questions were assessed using 5-point level-of-interest, level-of-satisfaction, or level-of-value Likert scales. Finally, delegates were given a free-text answer option to provide suggestions for how the workshop could be

improved. Ratings were coded from 1 to 5 to enable mean aggregate rating scores to be computed (e.g. 1 = not at all interested, to 5 = very interested). Surveys were distributed and collated by the workshop organiser (TPC).

4.1.3 Results

A total of 29 surgeons (11 faculty, 18 delegates) participated in the workshop. Countries represented included England, Denmark, Italy, USA, Belgium, Australia, and Turkey. Interest in the workshop exceeded the quota of registration places, with 6 surgeons reserving places on a short-list for cancellations (Germany, Slovenia, Kuala Lumpur, and United Kingdom). The majority of delegates were consultant surgeons (67%, 12/18), with the remaining delegates being senior trainees. One-third of surgeons attended with colleagues from their own clinical team. In describing their background clinical setting and motivation for attending the workshop, 26% (5/19) were actively involved in a paediatric robotic surgery service, and the remaining delegates were either considering establishing a robotics surgical service or had an academic interest in robotic surgery. All delegates had performed <10 paediatric robotic procedures as primary surgeon and 17% (3/18) had experience with 30 – 50 cases as bedside assistant.

The pre-survey response rate was 67% (12/18). Most delegates expressed favourable interest in all 20 hands-on or classroom based curriculum components that were nominated (Table 4.1), although there was variance in the appeal of each individual item. The most highly rated topics were hands-on robotic console time training (dry and wet laboratory), virtual reality simulation, and hardware familiarisation (Table 4.1).

In response to the question "*what is your overall level of satisfaction with the workshop?*", 94% (17/18) responded "*very satisfied*". All delegates indicated that they would recommend the workshop to a colleague. When presented with options for preferred time allocation for a future similar workshop, 0% indicated a ½ day duration, 67% indicated 1 full day, 33% indicated 2 full days, and 0% indicated 3 full days. All delegates felt that the faculty:delegate ratio was satisfactory, with the majority responding that an ideal breakdown of classroom:practical time allocation would be 20:80 (61% response). The hands-on practical components of the workshop were rated the most valuable (Table 4.2, Figures 4.2 and 4.3).

Topic	Mean rating ± SD
Console time simulation and training (dry lab)	4.8 ± 0.4
Console time simulation and training (wet lab)	4.8 ± 0.4
Virtual reality simulation and training	4.8 ± 0.4
Hardware familiarisation	4.8 ± 0.6
Basic principles	4.7 ± 0.7
Procedure specific training (urology)	4.7 ± 0.7
Emergency un-docking	4.7 ± 0.7
Trouble shooting with experience faculty	4.7 ± 0.7
Complications – how to avoid	4.7 ± 0.7
Tips and tricks for efficient theatre workflow	4.7 ± 0.9
Robot docking	4.6 ± 0.8
Procedure specific training (general surgery)	4.6 ± 0.8
Image guided surgery demonstration	4.5 ± 0.7
Bedside assisting tips	4.5 ± 1.0
Horizon scanning next-generation robotic platforms	4.4 ± 0.7
Procedure specific training (thoracic)	4.4 ± 0.8
Setting up a robotics service – lessons learned	4.3 ± 1.1
Establishing and maintaining a robotics theatre team	4.3 ± 1.1
Ethical and medico-legal considerations	4.2 ± 0.9
Cost considerations	4.1 ± 0.9

Table 4.1 Summary of responses (n = 12) to the question "*what are your attitudes towards the following programme topics and themes?*". Data are displayed as descending order mean-rating scores (± standard deviation) generated from a 5-point level-of-interest Likert scale (1 = not at all interested, 2 = not very interested, 3 = neutral, 4 = somewhat interested, 5 = very interested).

Topic	Mean rating ± SD
Hands-on dry laboratory skills on da Vinci system	4.9 ± 0.3
Hands-on wet laboratory skills on da Vinci system	4.8 ± 0.4
Mini-tutorials with faculty during hands-on sessions	4.8 ± 0.4
Virtual reality simulation and training	4.4 ± 0.6
Classroom based teaching	4.1 ± 0.8

Table 4.2 Summary of responses (n = 18) to the question "*what is your impression of the following aspects of the workshop programme?*". Data are displayed as descending order mean-rating scores (± standard deviation) generated from a 5-point level-of-value Likert scale (1 = not valuable, 2 = limited value, 3 = average value, 4 = valuable, 5 = very valuable).

Numerous free-text responses were provided with suggestions for workshop improvement. Several delegates expressed that "*more robots for the groups*" and "*as much time on practical skills as possible*" would be of benefit. In terms of program structure, delegates recommended a more sequential and modular approach such as "*an initial classroom lecture,*

followed by simulation, then docking, dry lab, and wet lab", or "*doing experimental animal model teaching…on the second day after completion of the first day*", or "*a day of dry lab and basics followed by a full day of wet lab*" in order "*…to put acquired knowledge into context*".



Figure 4.2 Skills laboratory (a) for practical stations that included hands-on wet lab training (b), hardware familiarisation and port placement strategies (c), and robot docking (d).

4.1.4 Discussion

The positive and constructive feedback indicates that training and educational needs can be met with a workshop of this kind. The fact that the number of registration requests exceeded the quota of available places also demonstrates that there is interest amongst the paediatric surgical community for such an event within the European region. As future adoption of robot-assisted minimally invasive surgery appears to be showing no indications of slowing, it is anticipated that demand for education and training will continue to grow.

Numerous delegates identified that their motivation for attending was because they were considering setting up a robotic surgery program. Embarking on the establishment of a paediatric robotic surgical service requires considerable financial and administrative commitment [9, 27, 146, 147]. We feel it is important that individuals or groups in this scenario are

able to access an opportunity to freely discuss and familiarise with this technology amongst a relevant peer-group, without the presence of direct industry marketing pressure. Following purchase of a da Vinci® system, the manufacturer is mandated by the FDA to provide surgical teams with formal training before clinical use commences [144, 148]. This on-site or off-site training is often brief and it is should be acknowledged that extensive further training requirements are the obligation of surgeons and their clinical teams.



Figure 4.3 Hands-on stations included a robot-assisted laparoscopic fundoplication using a porcine model in the EASIE-R™ Simulator (EndoSim, MA) (a), robot-assisted laparoscopic pyeloplasty using a porcine model (b), dV-Trainer® virtual reality robotic surgery simulator (c), and augmented reality image-guided surgery demonstration (d).

Training in robotic surgery requires attention towards both non-technical and technical skills [149-151]. Our delegate feedback almost unanimously emphasised preference and satisfaction for hands-on technical skills training. This was not unexpected as natural curiosity towards new technology is best satisfied via personal hands-on interaction. Non-technical skills should not however be overlooked, especially in the early phase of learning when establishment of a solid theoretical and applied knowledge base is critical for confident progression up the metaphorical training pyramid (Figure 4.1). Much of this content is better suited to teaching in a didactic setting of interactive tutorials, lectures, or e-learning modules. As this pre-clinical workshop was targeted at a basic and intermediate level, it was essential to

complement practical hands-on content with necessary classroom based teaching despite this not being perceived as particularly appealing program content [152].

The status of paediatric robotic surgery in the USA is considerably more prominent that the rest of the world [89]. Multiple institutional groups in the USA have previously described successful processes of clinical service implementation [12, 23, 29, 146, 153]. In alignment with growth of the field on a national and regional level, several North American courses in paediatric robotic surgery are available. The most established is the "*Annual Pediatric Robotic Urology – Updated and Live Case Demonstration*". This 2-day course is now in its 5th successive year and is hosted by the University of Chicago. A recent survey of paediatric urologists in the USA indicates that despite available resources, robotic surgery training needs are still unfulfilled [152]. In this study by Wang *et al*, robotic surgery was one of the most frequently cited topics that specialist training program graduates wished they had gained more experience with during training [152].

4.1.4.1 Feasibility and sustainability of a robotic surgery training course or workshop

There are inherent challenges in coordinating any practical training event in robotic surgery, and also specific challenges in purposefully dedicating an event to the paediatric specialty. The master-console based nature of existing robotic system means that only 1 person can actively be engaged with the master interface at any one time. This has a restrictive influence on the number of delegates that can be accommodated on a practical training event. Physical co-location of more than 1 da Vinci® system or virtual reality simulator is dependent on the available resources of the host institution or willingness of industry to support a training event with loan equipment. Unlike open surgery or conventional minimally invasive surgery, all equipment items relating to robotic surgery are significantly more expensive and less transportable.

The highest fidelity training resource will always involve the clinical da Vinci® systems, although the fidelity of training tasks that they may be used for will evidently vary (e.g. simple abstract tasks, *in vivo* animal models, or cadavers). Assigning da Vinci® systems for use in a training course or workshop obviously renders them unavailable for clinical use. This requires planning and support of both clinical teams and hospital management who would normally allocate the robot for clinical sessions. Many institutions have upgraded their da Vinci® systems to later models. Redundant earlier models are typically either traded in with

the manufacturer, or are decommissioned from clinical use for re-purposing in a training capacity. This latter option will become more difficult in the near future as Intuitive Surgical has announced that instruments compatible with the inaugural systems (i.e. the Standard model) will become obsolete from production. This is an unfortunate circumstance, as wet lab training involving animal specimens tends to be reliant upon availability of non-clinical systems in order to avoid risks of contamination and zoonotic disease. As an alternative, simulators are an excellent utility to make basic and intermediate level training more accessible and affordable. Five simulator platforms are commercially available and these include the 1) da Vinci® Skills Simulator (Intuitive Surgical, CA), 2) dV-Trainer® (Mimic Technologies Inc, WA), 3) robotic surgical simulator "RoSS™" (Simulated Surgical Systems, NY), 4) SimSurgery® Educational Platform "SEP-Robot" (SimSurgery, Oslo, Norway), and 5) ProMIS™ Surgical Simulator (Haptica, Ireland, United Kingdom). Although each has been validated to various extents, it is unclear which is more effective as a training and assessment tool [140, 154, 155]. The costs for these simulators range from between USD 62,000 and USD 158,000 [154].

Due to the relative immaturity of the field, geographical concentration and critical mass of experienced faculty members is not in abundance. The enthusiastic response from invited faculty for this workshop was however very encouraging, with incurred travel costs being willingly self-funded and teaching provided *pro bono*. The experience of assembling faculty from multiple institutions and countries adds value of regional practice perspectives and shared experiences. An example of this occurred during one tutorial session in which an insightful debate arose on the appropriate minimum age cut-off for open versus robot-assisted minimally invasive pyeloplasty.

Conscious effort was made to keep the cost of this workshop to an absolute minimum and competitive with similar workshops that are orientated to adult specialties. The individual registration fee was £280 and this price was budgeted on a break-even costing. The greatest expenses were derived from da Vinci® instruments, animal tissue specimens, and catering. Industry support was kindly received from Mimic Technologies Inc who provided a loaned dV-Trainer®.

4.1.4.2 Future

Future efforts at repeat or alternate pre-clinical training events should seek to iteratively improve on the educational quality by incorporating all aspects of feedback received.

Workshop program designs should be modified to give more consideration towards stepwise transition from didactic teaching, to basic hands-on training using simulators, and then basic-to-intermediate hands-on training using da Vinci® systems. Recognising the essential role of nurses, anaesthetists, and other staff that form a robotic operating room team, there would be merit in advertising such workshops to all these healthcare professional groups. As the program becomes more established, it would also seem appropriate to aim to offer CME (Continuing Medical Education) credit for those involved. This recognition would hopefully contribute towards eventual points-based standardised credentialing systems. The descriptive and survey-response outcomes of our event will hopefully serve to inform future training events and curricula that will arise.

Finally, it is important to realise the scope and limitations of pre-clinical workshops and that these events serve to provide a foundation for more advanced proficiency-based training. As outlined in Figure 4.1, *pre*-clinical training should be followed by *clinical phase training*. One of the first priorities in clinical phase training is procedure specific familiarisation. Some procedures are obviously more complex than others and each procedure tends to have individualised learning curves. Detailed understanding of procedure specific training requirements is needed in order to establish *clinical training* structure and targets. Chapters 4.2 and 4.3 seek to identify procedure specific training requirements by evaluating the learning curves for the two highest volume procedures in paediatric robot-assisted surgery; pyeloplasty and fundoplication. Also investigated are the methodological approaches to best measure the learning curve, with focus on highlighting the unique value of the under-utilised cumulative summation (CUSUM) analysis technique.

4.2 The Learning Curve of Robot-Assisted Laparoscopic Pyeloplasty in Children

4.2.1 Introduction

The "*learning curve*" concept was first described in the aircraft manufacturing industry where it was recognised that performance improves with both time and experience, and subsequently leads to increased productivity [156, 157]. In general, proficiency improvement tends to be most rapid in the initial phase, followed by a tapering period that eventually leads to a stable performance plateau [157]. Learning curve principles apply equally to surgical disciplines and are becoming more relevant as new technology-based developments continue to rapidly emerge that influence surgeons at all levels. A detailed understanding of the learning curve for any given technique or technology is vital due to the many direct implications on clinical outcomes, training needs, patient safety and healthcare economics.

The learning curve is especially relevant in the setting of paediatric laparoscopic pyeloplasty. A low and stable rate of adoption persists for this technique despite it thriving in the adult setting [90, 158]. One of the most frequently cited barriers to more widespread uptake is the challenging and prohibitive learning curve. Robot-assisted minimally invasive surgery has helped to make the advanced technical skill requirements for complex reconstructive elements of this procedure to be more achievable, such as abundant fine intra-corporeal suturing [159, 160]. As such, the proportion of paediatric pyeloplasties performed with a minimally invasive technique has increased since the introduction of robotic technology. Over 80% of these minimally invasive procedures are now performed using a robot-assisted approach [90]. Capabilities of robot-assistance to favourably influence the learning curve has therefore led to this technology being referred to as an "*enabling*" innovation [106].

Cumulative sum (CUSUM) analysis is a statistical process control tool for quantitative assessment of consecutive performances over time with reference to an agreed standard. An early application of this analysis technique was for quality assurance monitoring of ammunition production lines during the Second World War [161, 162]. It was not until the 1970s that application of the CUSUM analysis was later introduced to medical and surgical fields [163, 164]. The CUSUM analysis is now appreciated as a preferred statistical method for monitoring and evaluating outcomes following introduction of any newly implemented surgical technique or technology, and particularly for individual surgeons [165-167]. Despite its ostensive virtues, the CUSUM method remains under-utilised in the surgical literature in

general, and is described in only a small number of publications within the field of paediatric surgery [168, 169].

This chapter aims to introduce the CUSUM analysis technique and apply this statistical method to evaluate the learning curve for paediatric robot-assisted laparoscopic pyeloplasty (RP).

4.2.2 Materials and Methods

Consecutive paediatric robot-assisted pyeloplasty (RP) procedures undertaken between March 2006 and October 2013 at Leeds Teaching Hospitals NHS Trust were included in the study cohort. Since the introduction of a paediatric robotic surgical program at this tertiary referral hospital in February 2006, the robot-assisted approach has been preferentially used for all minimally invasive pyeloplasty cases. A single surgeon (ASN) performed all cases. This surgeon had extensive background experience in conventional paediatric laparoscopic surgery, including pyeloplasty. The inaugural surgical team received a short period of formal pre-clinical training with the da Vinci® Surgical System prior to commencement of clinical service. All intra-operative and post-operative clinical data was prospectively recorded in an electronic database.

4.2.2.1 Operative Technique

Indications for RP were symptomatic pelvi-ureteric junction obstruction (PUJO), increasing antero-posterior renal pelvis diameter, or deteriorating renal function with or without urinary tract infection. All patients were investigated pre-operatively with renal ultrasonography and diuretic MAG3 renogram studies. The standard procedure utilised a transperitoneal Anderson-Hynes dismembered reduction pyeloplasty technique with placement of a percutaneous trans-renal trans-anastomotic nephroureterostomy tube. From 2010, an additional percutaneous extra-renal retroperitoneal drain was used in most cases. No patients underwent on-table cystoscopy immediately prior to RP.

4.2.2.2 Follow-up

Patients were routinely followed up with renal ultrasound imaging at 1 and 4 months post-operatively, and then with outpatient clinic review at 6 months and yearly ultrasound thereafter, with isotope renogram studies as necessary.

4.2.2.3 Outcome Measures

The learning curve effect of surgeon experience on multiple outcomes was investigated, including 1) operating room time variables, 2) post-operative complications, and 3) conversions. To measure operating room times, numerous time stamps were prospectively logged during the surgical workflow. Definitions of these time stamps and corresponding intervals are schematically summarised in Figure 4.6 that is adapted from that reported by Link *et al* [170]. Set-up time, docking time, console time, operating time, and total operating room time were evaluated. Avoidable and unavoidable operating room delays were also recorded and 'total operating time' was corrected to account for avoidable delays. Complications were regarded as any deviation from the expected post-operative course and graded according to the Clavien-Dindo classification [126]. Consensus studies were referred to in the event of uncertainty regarding assignment of grading classifications [171, 172].

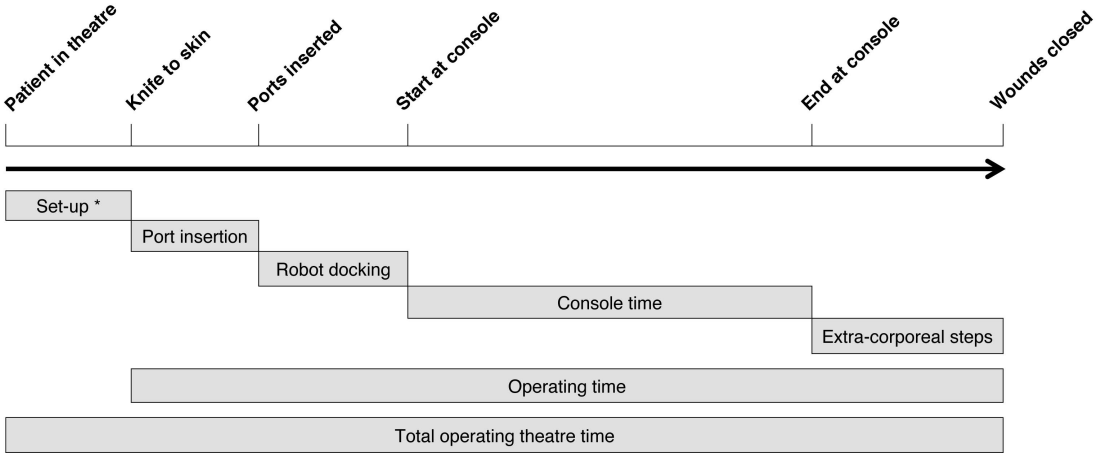


Figure 4.4 Time-based schematic for surgical workflow during a typical case, indicating definitions for recorded intervals. * representing anaesthesia set-up and patient positioning.

4.2.2.4 Data Analysis

There were missing data for 3.8% (17/450) of time stamp data points. The influence of missing data was extrapolated during time interval segmentation, as two time stamps were required to determine any time interval measurement. To avoid listwise deletion of patients from the dataset for often-singular data point omissions (i.e. only one of six time stamps not recorded for a single patient), a Missing Value Analysis procedure was conducted and expectation-maximisation (EM) algorithm applied. Little's Missing Completely At Random (MCAR) test was performed to demonstrate missing data occurred at random before replacing missing data with EM imputed values.

The CUSUM method was used for learning curve analysis and both CUSUM charts and CUSUM tests were generated. The parameters assessed were set-up time ($CUSUM_{SET\text{-}UP}$), docking time ($CUSUM_{DOCKING}$), console time ($CUSUM_{CONSOLE}$), operating time ($CUSUM_{OT}$), total operating room time ($CUSUM_{TOTAL\text{-}OT}$), and complications ($CUSUM_{COMPLICATIONS}$). All cases that were converted from robot-assisted technique to either conventional laparoscopic or open technique were excluded in analysis of operating room time variables.

The observed-minus-expected CUSUM chart is a graphical representation of binary or continuous data for a series of consecutive procedures. It involves transformation of raw data to a running cumulative sum of differences between individual measured values and a pre-defined target. Similar to previously described methods [173-176], the CUSUM score of the first case was the difference between the first case outcome and the target outcome for all cases. The CUSUM for the second case was the summation of the previous case's CUSUM added to the difference between the second case outcome and target outcome of all cases. This process continued until the CUSUM for the last case is computed as a zero value. Mathematically, the CUSUM scores were therefore determined using the following formula, with $C_0 = 0$:

$$C_n = \sum_{j=1}^{n} (X_j - X_E)$$
$$= (X_O - X_E) + C_{n-1}$$

Where C = cumulative sum; n = chronological procedure number; X_O = outcome measures for the nth procedure; X_E = expected (target) outcome value. "$X_O - X_E$" represents the deviation of the outcome from the target. For time-based continuous data, X_E = group mean

value. Complications were regarded as a dichotomous variable, with $X_O = 0$ assigned for cases with no complications, and $X_O = 1$ cases in which a post-operative complication(s) occurred. The $CUSUM_{COMPLICATIONS}$ target value was assigned as $X_E = 0.15$, based on the recent editorial by Ficarra *et al* who described an acceptable RP complication rate of <15% [110, 159].

In the CUSUM charts generated, chronological rank ordered cases are plotted on the x-axis, and cumulative sum scores on the y-axis. A trend in the process results in a change in slope. An upward (positive) sloped segment occurs during a period in which outcomes tend to exceed the pre-defined target, and a downward (negative) slope occurs when outcomes are achieved that are below the target. The degree of slope can indicate a measure of progress, such that a steeper slope reflects a more accelerated progress. Transition beyond the learning phase was identified as an inflection point on the CUSUM chart, and defined as the case after which three consecutive negative CUSUM scores were subsequently recorded [177]. A stable process tends to be represented by a consistently downward trend or fluctuation around a horizontal axis, and this may be interpreted as a proficiency status.

To quantitatively determine whether the processes were "*in-control*", a two-sided tabular CUSUM test was applied for each operating time parameter investigated. This test consists of computing two modified CUSUM charts simultaneously on either side of a horizontal axis that represents the target value. One of these CUSUM charts is positive (upper) and the other negative (lower), and each is reactive in their respective directions if accumulated deviations from target value exceed a reference value (k). If each line crosses a decision limit (h) then the process is deemed "out of control". Theoretically, the process should re-set at either zero or as the h value when the limit is reached; however in practice no re-set value was applied such that a learning curve pattern was not disrupted. Mathematically, the upper (C^+) and lower (C^-) CUSUMs were determined using the following formulas [176]:

$$C_n^+ = \max\left(0, X_O - (X_E + k) + C_{n-1}^+\right)$$
$$C_n^- = \max\left(0, (X_E - k) - X_O + C_{n-1}^-\right)$$

The reference values (k) and decision limits (h) were assigned using the principles described by Montgomery [176]. The reference value (k) was chosen halfway between the target value and the positive or negative shift of mean. The mean shift is usually chosen as 0.5 to 1.5 standard deviation (σ) of the process mean, of which 1.0 was utilised in this study [176]. The reference value was therefore calculated as one half the magnitude of mean shift to detect, using the formula:

$$k = \frac{1.0\ \sigma}{2}$$

The decision limit (h) is usually chosen as 4 or 5 times the process standard deviation (σ), of which a multiplicative factor of 5 was utilised in this study with the formula [176]:

$$h = 5\sigma$$

Selection of 1σ for calculating k and 5σ for computing h generally provides a CUSUM that has good average run length (ARL) properties for detection of shift of approximately 1σ in the series mean.

Comparisons between case experience and normally distributed operating room time outcomes were assessed using the two-tailed Student's t-test for bi-phasic learning curves, and one-way ANOVA for multi-phasic learning curves. Comparison between case experience and complication frequency was assessed using the Kruskal-Wallis test. Statistical significance was regarded as $P < 0.05$. Statistical analysis was undertaken using SPSS version 19.0 (IBM Corp, NY).

4.2.3 Results

A total of 93 cases were eligible for inclusion. Three cases were excluded from analysis; one that involved a concomitant procedure on the contralateral urinary tract, and two for unrecorded time data. The study cohort was therefore represented by 90 RP cases. Demographic information and clinical characteristics are summarised in Table 4.3. The youngest patient in the series was 1 month of age, and the smallest patient weighed 4.1 kilograms. No patients were lost to follow up. The median duration of follow up was 3.9 years (range 0.6 – 7.9 years).

Age	Overall (mean ± SD)	6.96 ± 5.10 years
	0 – 1 years	n = 14
	1 – 3 years	n = 13
	3 – 5 years	n = 9
	5 – 8 years	n = 17
	8 - 13 years	n = 21
	13 – 18 years	n = 16
Gender	Male:Female	57:33
PUJO etiology	Intrinsic:Extrinsic	70:20
	Primary:Secondary	86:4
Laterality	Left:Right	55:35

Table 4.3 Patient demographic information and clinical characteristics (n = 90).

The $CUSUM_{SET\text{-}UP}$ and $CUSUM_{DOCKING}$ charts demonstrated multi-phasic learning curves that shared very similar patterns (Figures 4.7a and 4.8a). Steep initial learning curves were seen that had inflection points at cases 10 and 15 for $CUSUM_{SET\text{-}UP}$ and $CUSUM_{DOCKING}$ respectively. This was followed by extended periods of proficiency (downward trend followed by stabilisation around a horizontal axis), before trend changes and repeat inflections occurred at cases 71 and 72 respectively. The $CUSUM_{DOCKING}$ test signalled an out-of-control process at the 10th case (Figure 4.7b).

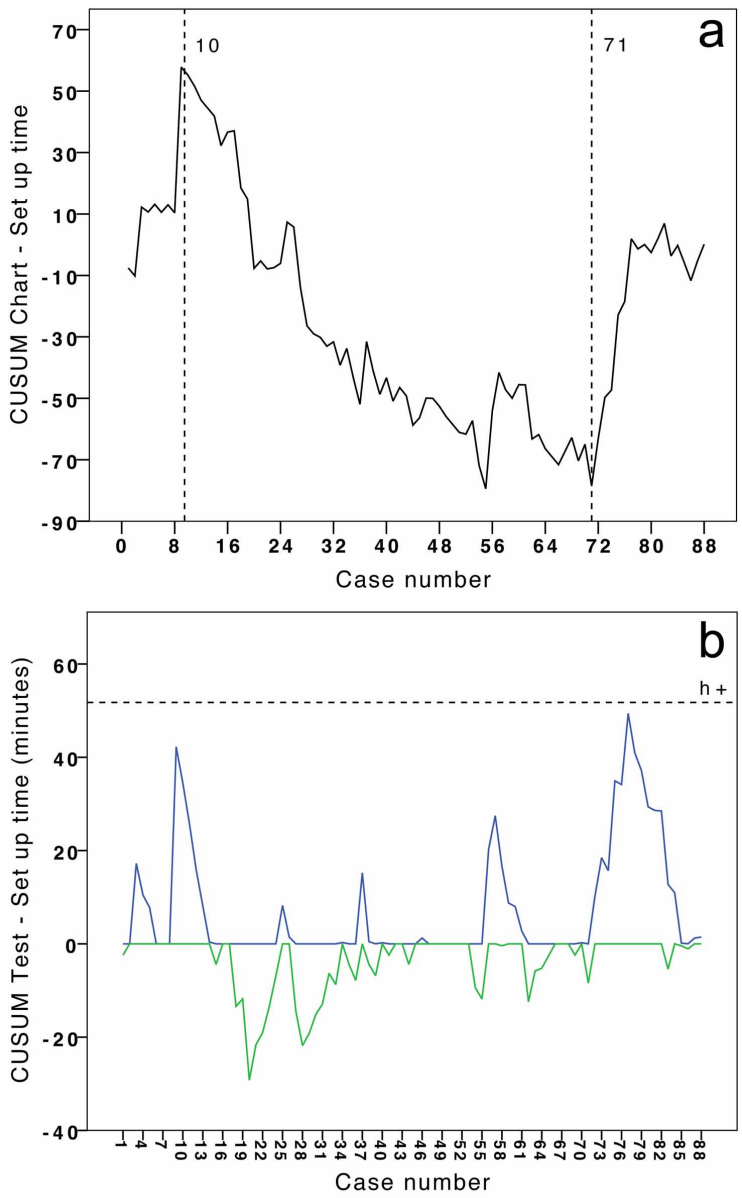


Figure 4.5 CUSUM chart (a) and test (b) for set-up time.

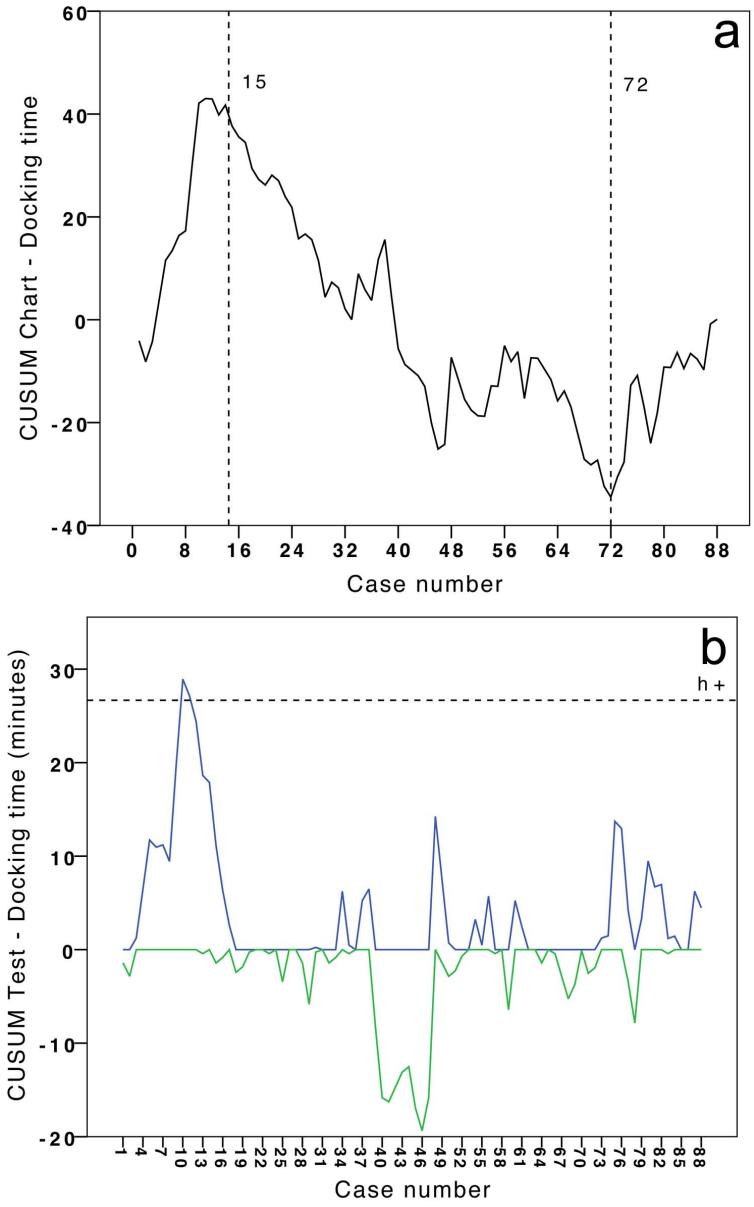


Figure 4.6 CUSUM chart (a) and test (b) for docking time.

4.2.3.1 Operating times

The $CUSUM_{CONSOLE}$, $CUSUM_{OT}$, and $CUSUM_{TOTAL\text{-}OT}$ charts demonstrated bi-phasic learning curves with inflection points at cases 42, 57, and 58 respectively (Figures 4.9a, 4.10a, and 4.11a). The $CUSUM_{CONSOLE}$ chart had a clearly defined pyramidal pattern; with mirrored upward and downward segments indicating a relatively constant rate of proficiency gain during the learning phase, followed by a similarly constant rate of proficiency refinement and/or maintenance (Figure 4.9a). In comparison, the $CUSUM_{OT}$ and $CUSUM_{TOTAL\text{-}OT}$ charts displayed flatter and more prolonged proficiency gain phases (Figures 4.10a and 4.11a). The upper $CUSUM_{TOTAL\text{-}OT}$ tests signalled an out-of-control process from cases 10 – 17 (Figure 4.11b).

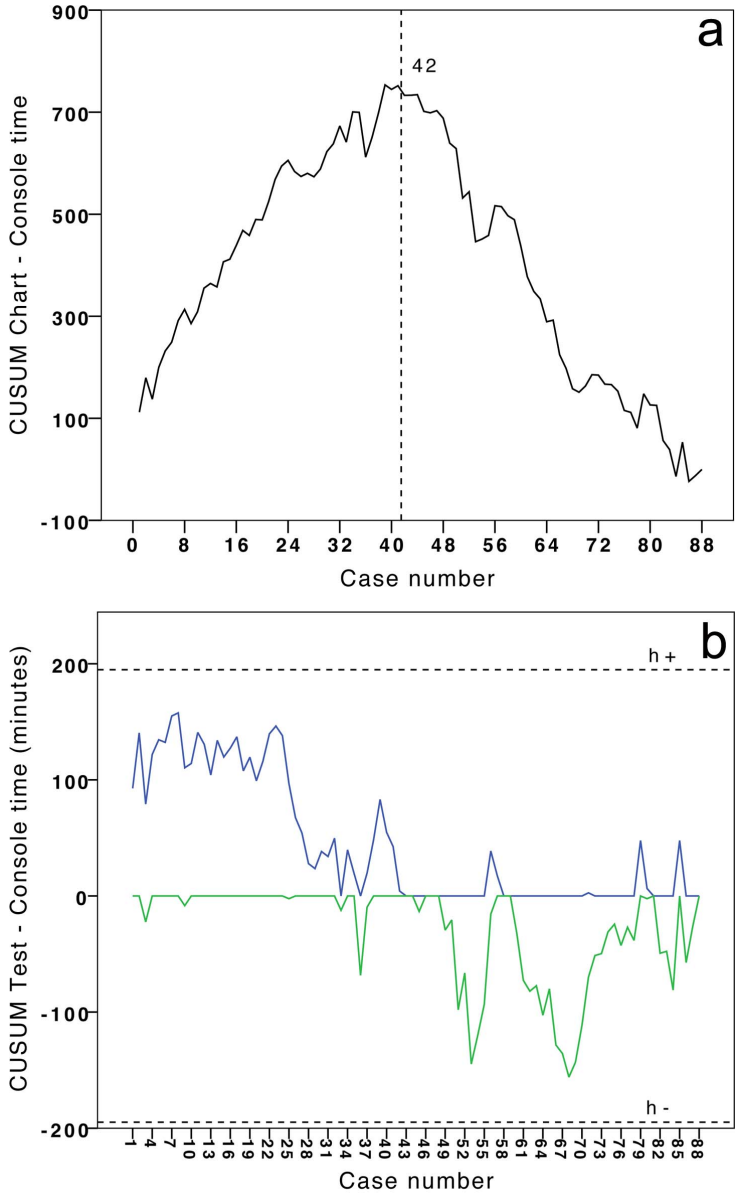


Figure 4.7 CUSUM chart (a) and test (b) for console time.

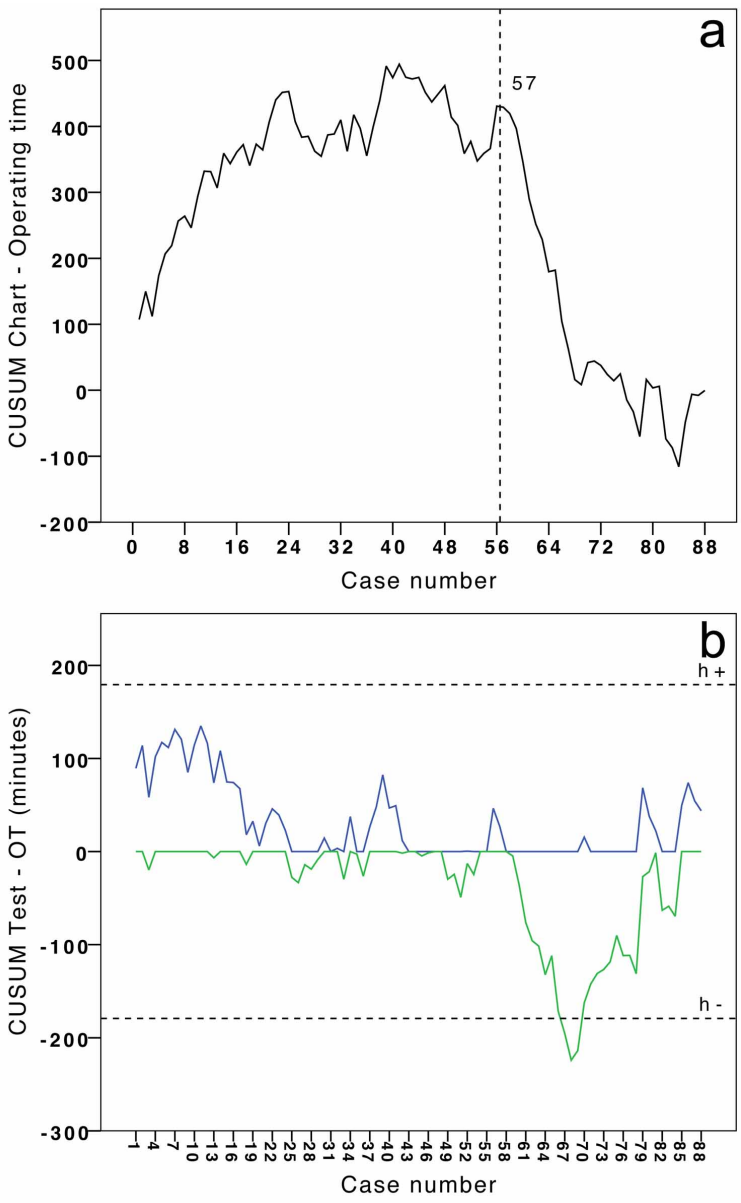


Figure 4.8 CUSUM chart (a) and test (b) for operating time.

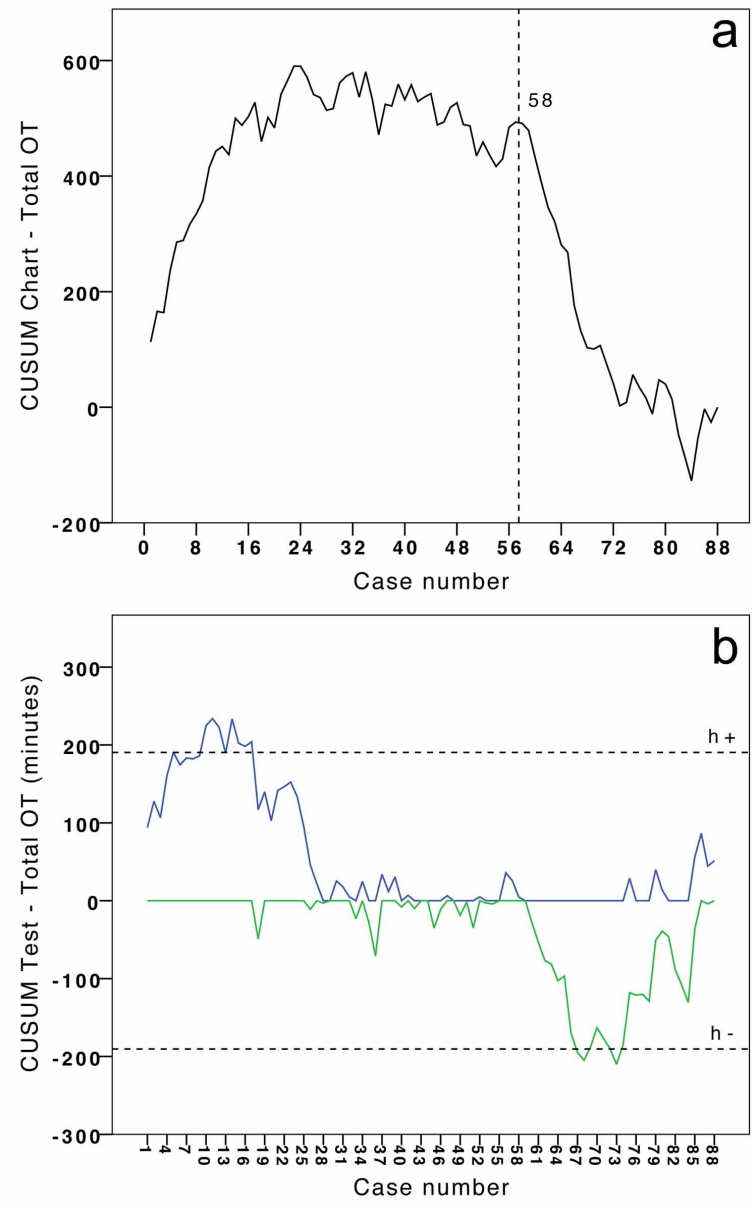


Figure 4.9 CUSUM chart (a) and test (b) for total operating room time.

All comparisons of Phase 1 and Phase 2 operating times for bi-phasic learning curve phases were statistically different (Table 4.4). For multi-phasic curves, separate analyses of Phase 1 and Phase 2, or Phase 2 and Phase 3 were all statistically significant (P = 0.027 – 0.006, Student's t-test). Improvements in console time had the greatest impact on OT and total operating room time, with mean console time in Phase 2 being 33.4 minutes shorter. Avoidable delay was recorded in 53% of cases (46/88) with mean (± SD) delay time of 26.6 (± 12.3) minutes. The causes of delay were attributed to surgical assistant inexperience or error (39%), equipment unavailability or malfunction (29%), nursing scrub staff inexperience or error (22%), anaesthesia issues (7%), and robot malfunction or failure (3%). The most disruptive cause of avoidable delay arose from circumstances in which the surgeon was

required to scrub and carry out procedural steps that would normally be performed by an experienced bedside surgical assistant. There was no significant difference between case experience and avoidable delay ($P = 0.48$, Kruskal-Wallis test).

	Phase 1 Case numbers Mean ± SD (mins)	**Phase 2** Case numbers Mean ± SD (mins)	**Phase 3** Case numbers Mean ± SD (mins)	***P***	**Overall** Case numbers Mean ± SD (mins)
Set-up time	1 – 10 28.1 ± 16.8	11 – 71 20.6 ± 8.5	72 – 88 27.2 ± 9.4	0.01	1 – 88 22.6 ± 10.4
Docking time	1 – 15 14.6 ± 5.6	16 – 72 10.8 ± 4.8	73 – 88 14.3 ± 5.7	0.009	1 – 88 12.1 ± 5.3
Console time	1 – 42 185.3 ± 34.7	43 – 88 151.9 ± 36.0	-	< 0.001	1 – 88 167.8 ± 39.0
OT	1 – 57 240.2 ± 33.2	58 – 88 218.8 ± 37.0	-	0.007	1 – 88 232.6 ± 35.8
Total OT	1 – 58 250.6 ± 36.1	59 – 88 225.7 ± 37.0	-	0.003	1 – 88 242.1 ± 38.1

Table 4.4 Operating times for the overall series (n = 88) and segmented phases of respective learning curves.

4.2.3.2 Complications

Post-operative complications are summarised in Table 4.5. No significant differences were observed between case experience and frequency of complications ($P = 0.125$). Three cases required repeat procedures for PUJO recurrence (3.4%, 3/87). These occurred as cases 28, 52, and 79. All re-do cases were successfully performed as RP procedures and are included in this series. We regard the overall success rate of this series as 96.7% (3/90).

For the first 78 cases, the $CUSUM_{COMPLICATIONS}$ chart demonstrated a general downward trend indicative of sustained acceptable complication frequency and proficiency for this outcome. Although not satisfying criteria for a learning curve inflection point, the chart slope deviated to an upward trend for the last 12 cases in which there was a cluster of complications (Figure 4.12a). The one-sided upper $CUSUM_{COMPLICATIONS}$ test signalled an out-of-control process only at case 30 (Figure 4.12b).

4.2.3.3 Conversions

Two cases were converted to open procedures (2.2%, 2/90). Case 8 was converted due to inability to pass either the nephrostomy tube or a guidewire through the distal dismembered ureter segment. Case 86 was a separate re-do case (previous open pyeloplasty in a different country) that was converted due to poor visualisation related to gaseous bowel distension.

Clavien Grade	n	Description
I	8	Post-operative nausea and vomiting (1), temporary ileus (2), port site surgical emphysema (1), shoulder tip pain (1), re-admission 3 days post discharge for mild frank haematuria that was managed conservatively (1), re-admission for blocked nephro-ureterostomy stent that was successfully managed with saline flush (1), urinary retention requiring urethral catheterisation (1).
II	0	
IIIa	0	
IIIb	4	Acute hydronephrosis due to renal pelvis clot obstruction that proceeded to unremarkable diagnostic laparoscopy following free sub-diaphragmatic gas finding on CT (1), symptomatic PUJO recurrence that required re-do procedure (3).
IVa	0	-
IVb	0	-
V	0	-

Table 4.5 Post-operative complications graded according to the Clavien-Dindo classification [126].

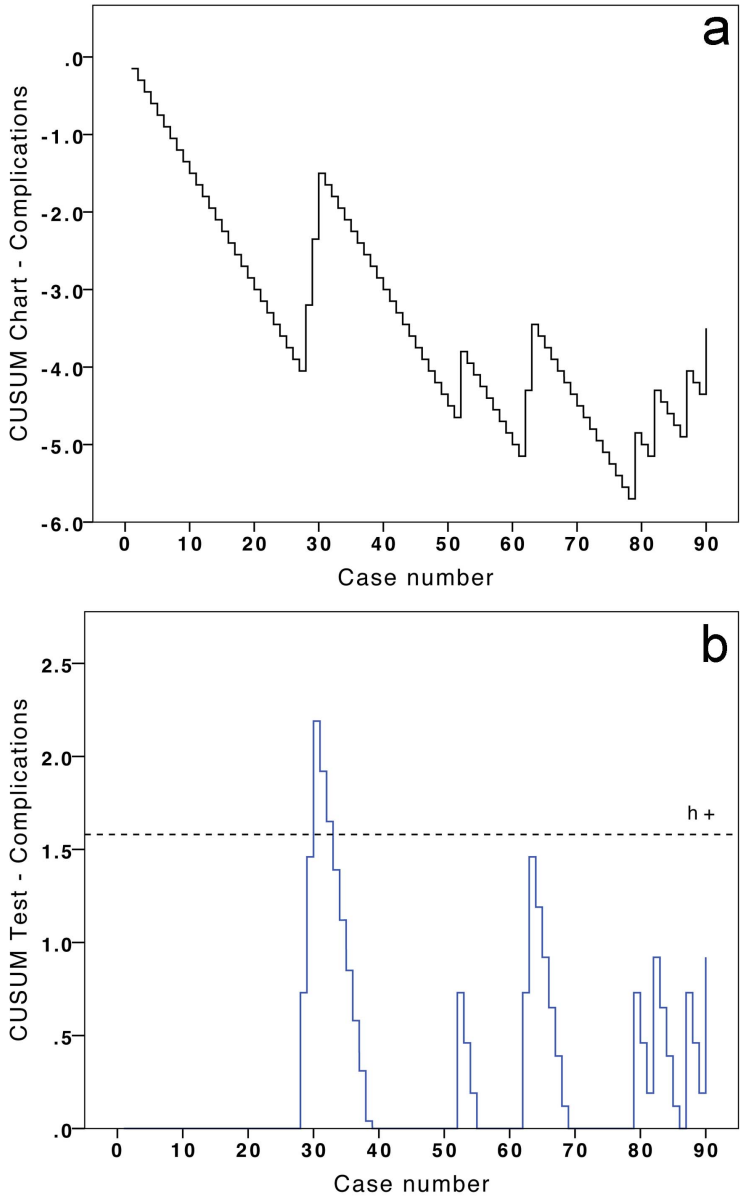


Figure 4.10 CUSUM chart (a) and test (b) for post-operative complications. Stepped interpolation lines are used for exaggerated effect of individual cases.

4.2.4 Discussion

Numerous studies have previously reported learning curve data for adult and paediatric RP [18, 29, 98, 99, 114, 146, 170, 178, 179]. This current literature base is generally based on clinical data that are collected retrospectively and sampled from individual surgeons' series that are < 45 cases, with diverse but generally limited statistical analysis methodology (Table 4.6).

4.2.4.1 Measuring the learning curve

The most common method for evaluation of surgical learning curves consists of simple chronological raw data plots that may include various regression models and lines-of-best-fit for visual or quantitative trend detection. Natural variance in data greatly obscures detection of trends using this approach. This is demonstrated in Figure 4.13a, where a simple line plot of the data set for the variable in our results with the most clear-shaped CUSUM learning curve fails to indicate any apparent trend or pattern. Similarly, the lines-of-best-fit in Figure 4.13b can be seen to be far less informative than the corresponding CUSUM chart and test in Figure 4.9. Importantly, the often-used linear regression lines-of-best-fit will fail to show many characteristic features usually expected in learning curves, such as peaks and plateaus.

Another frequently utilised approach involves group splitting of a patient cohort into block sub-groups based on arbitrary mathematical convenience (i.e. 100 consecutive patients divided into four groups of 25 patients). Univariate statistics are often used to then compare outcomes between selected sub-groups. While this approach is often reported in the literature, it should be avoided as it carries inadequate sensitivity to define the case experience quota for which important learning curve transitions occur [154, 156].

The CUSUM analysis was originally designed for two purposes; to evaluate the learning curve and to monitor quality control [165]. CUSUM charts are a useful and reliable method to detect learning curve patterns that otherwise would not be as apparent with simple plots. The recursive nature of the statistical process allows early identification of expected or unexpected deviations (i.e. < 1.5σ) as they are occurring and also accounts for random variation in data [154, 156, 180]. Similarly, CUSUM tests are able to sensitively detect when outcome processes deviate from pre-defined 'quality control' thresholds. Several studies have previously applied hierarchical decision intervals to signal at "*alert*" and "*alarm*" limits [181-183]. In this regard, more conservative "*alert*" limits can serve as early-warning indicators to prompt vigilance over threats to unacceptable outcome deviation, or pre-emptive remedial action for trainees. Ideally, these decision intervals would be assigned based on international

benchmark standards, however the nascence of paediatric RP and associated literature limited suitability of this approach for the present study.

	Maximum individual surgeon case n	**Learning curve analysis technique**	**Findings**
Link et al 2006 [170]	10	Simple column graph.	No learning curve for console time.
Lee et al 2006 [97]	32	Scatter plot with linear regression analysis and ANOVA.	Significant learning curve for OT ($P = 0.003$), such that outcome comparable between RP and OP after approximately 28 cases.
Olsen et al 2007 [114]	67	Scatter plot with linear regression analysis.	Significant learning curve for OT ($P = 0.007$, retroperitoneal approach)
Passerotti et al 2009 [178]	14	Scatter plot with linear regression analysis and ANOVA (time), and group splitting with univariate analysis (quality).	Significant learning curve for anastomosis time ($P = 0.02$) and quality ($P < 0.01$, comparing first 5 cases with last 5 cases) * *in vivo* porcine survival study.
Sorensen et al 2011 [99]	24	Group splitting with univariate analysis based on year of surgery.	Learning curve for OT such that after 15 – 20 cases there no statistical difference between RP and OP. LOS significantly decreased between 3 successive years from 3.5 days, to 2.0 days and 1.2 days ($P = 0.01$).
Minnillo et al 2011 [29]	154	Group splitting with univariate analysis based on year of surgery.	OT and LOS significantly decreased between block periods of the first 5 years of practice and last 3 years in large 8-year multi-surgeon series ($P < 0.01$ and $P < 0.05$ respectively).
Riachy et al 2013 [98]	45	Scatter plot with linear regression analysis.	No significant learning curve for OT. Significant learning curve for OT in LP, implying less steep learning curve for RP.
Tasian et al 2013 [179]	20	Scatter plot with linear regression for trend line fitting only.	Learning curve trend seen for console time in closely mentored trainees. Projected estimate that 37 cases required for trainee to achieve comparable console times to an experienced paediatric urologist.
de Lambert et al 2013 [146]	17	Scatter plot with linear trend line	No statistical analysis but down-sloping linear trend line for OT.

Table 4.6 Summary of literature base for studies investigating learning curves in robot-assisted laparoscopic pyeloplasty (RP). LP = conventional laparoscopic pyeloplasty, LOS = length of hospital stay, OP = open pyeloplasty, OT = operating time.

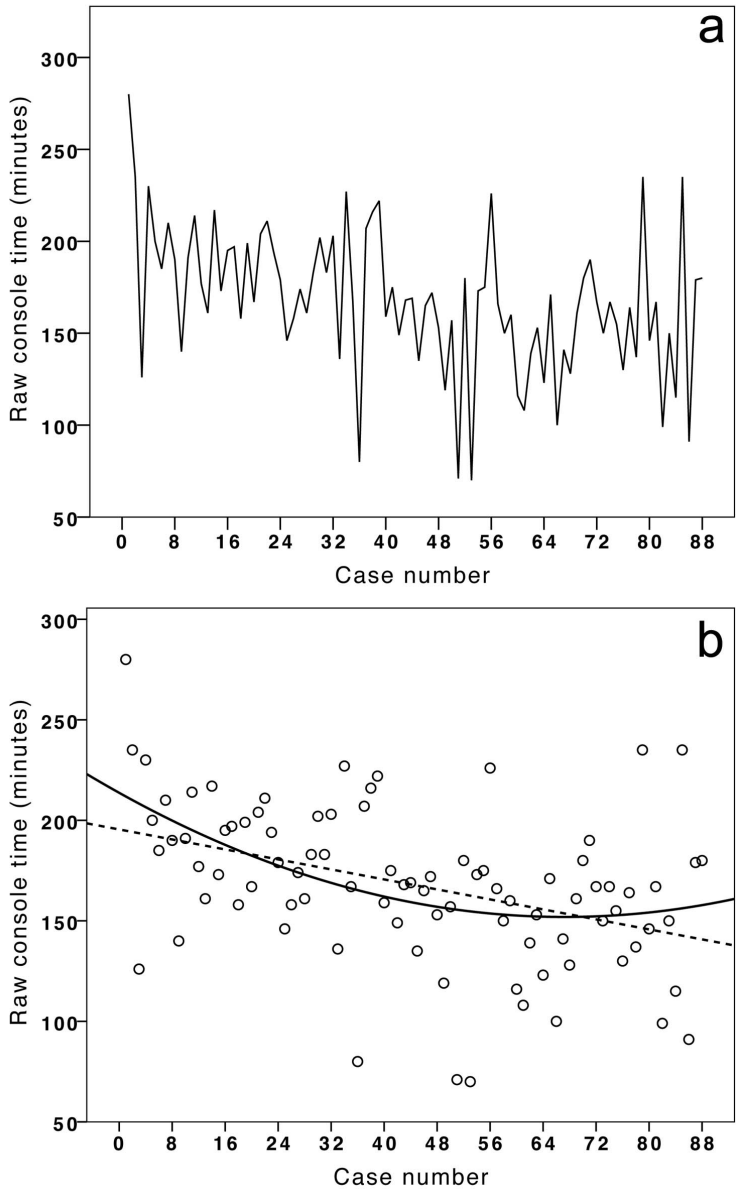


Figure 4.11 Raw console time data chronologically represented as a line graph (a), and scatter plot with both linear (dotted line) and quadratic (solid line) trend lines (b).

In learning curve evaluation, variables may be sampled from two possible clusters, 1) the surgical process, and 2) patient outcomes [156]. Variables are measured from each of these clusters in this chapter. Operating time is the most favoured outcome variable in the learning curve literature and this is undoubtedly related to ease of data collection. The lack of definition standardisation for "*operating time*" is an unresolved issue that influenced the preference for analysing multiple time measures in this chapter. Patient outcome variables are a more reliable and relevant measure of skill quality and competency. Binary outcomes such as mortality are often used; however in specialties such as paediatric surgery, the infrequency of these events makes this impractical for use. Similarly, the high success rate (>95%) of all

modes of pyeloplasty limits the appropriateness of success as an outcome variable for use in learning curve analysis, hence the selection of post-operative complications as the focus patient outcome variable. With the Clavien-Dindo classification becoming more widely used, it is envisaged that weighted $CUSUM_{COMPLICATION}$ scores will become more feasible in the future and bring important advantages of appropriately stratifying complication severity in learning curve analysis.

4.2.4.2 Interpreting the learning curve

Learning curves can be separated into labeled phases. The first "*learning*" phase is often the steepest and consists of an initial period of maximal proficiency gain that is incurred with familiarisation of a technique or technology. An ideal "*learning*" phase will be both short and steep, although these characteristics are reflective of the complexity of a task such that a less complex task will contextually be shorter and less steep. Results in this chapter demonstrate clear transition points in the learning curves for each of the 5 operating room time variables investigated. The case experience period to the left of the first transition point represents the learning phase. Statistical confirmation of a learning curve effect was observed by significant differences seen between mean values for each Phase 1 and the respective subsequent Phase 2. A learning curve trend was not observed for post-operative complications. This result could be encouragingly interpreted as evidence that no measurable patient morbidity occurred within the introductory period of robot-assistance in our series. It is also demonstrated that the learning curve is distinctly different depending on the outcome variable assessed. These findings reinforce a message that one cannot presume surgical proficiency or "*mastery*" beyond the learning phase to be based on singular outcome components, and that these tenets are very much multi-faceted [168].

As overall confidence and proficiency builds towards the tail end of the learning curve, there is a natural tendency to progress from selected to unselected patients, and to cases of increasing complexity. Previous studies have cited these as reasons for a multi-phasic learning curve in which unexpected upward CUSUM chart trends are seen late in the series [173, 175, 184, 185]. It is felt that this explains the $CUSUM_{COMPLICATIONS}$ chart trend change for the last 12 cases in our series. In these 12 cases, 25% were re-do procedures, and 50% were procedures in children ≤ 6 months of age.

The complex human and equipment environment of an operating room can lead to many potential confounders in learning curve evaluation. Consistent make-up of a dedicated

surgical team certainly contributes to a productive environment in which each staff member synchronously complements the overall workflow [29, 99, 146]. The unexpected second transition points in the $CUSUM_{SET\text{-}UP}$ and $CUSUM_{DOCKING}$ charts are attributed to an interval that coincides with re-location of the paediatric robotic surgical service to a different hospital with re-installation of the robot and turnover of staff. Interestingly, these variables are those most reflective of team-based performance. Conversely, the variable that is most reflective of individual (surgeon) performance is console time, and in this chapter the CUSUM chart for this learning curve to be the most classically shaped, perhaps contributed by a relative absence of human confounders.

4.2.4.3 Augmenting the learning curve

Simulation and training are the most perceivable strategies to efficiently re-shape the learning curve inside and outside of the operating room [156]. As described in Chapter 4.1, there is a variety of training resources that are available. Organisation and structuring of modular training curricula should incorporate objective learning curve data from a multitude of relevant outcome variables such that evidence-based expectation standards can be assigned. It remains unclear which individual or combination of different training resources is most effective in beneficially augmenting the learning curve. As such, this field remains an important and active area of academic interest.

Case frequency, variety and complexity are likely contributing factors to the shape of the learning curve. A surgeon performing one RP per week would be expected to progress along a steeper and more accelerated learning curve than a surgeon who performs only several RP cases per year. This lends support to the somewhat controversial argument that robotic surgery services should at least initially be set up in high volume tertiary referral centers. In this series, the surgeon (ASN) maintained an active robot-assisted surgery caseload with variety in many different paediatric general surgery and urology procedures. This benefited fundamental skill retention for not only the surgeon, but also that of entire peri-operative team.

4.2.4.4 Limitations and future work

Learning curves must be appreciated in context. These results reflect the specific learning curve pattern for a single surgeon with extensive background experience in conventional paediatric laparoscopic surgery. Future work is needed to broaden the understanding of

learning curves for RP in trainees and other surgeons with varying background experience in minimally invasive surgery. There is also a need to also investigate comparative learning curves for open and conventional laparoscopic pyeloplasty in order to definitively determine whether RP does in indeed have an advantageous learning curve. Measurable effects of the RP learning curve likely apply to many other surgical process and patient outcome variables such as length of hospital stay, analgesia requirement, estimated blood loss, and patient (or parent) satisfaction. These variables remain largely un-investigated.

As per-minute operating theatre time has been shown to be one of the major components of direct costs in cost-effectiveness studies of RP, it would be fair to assume there is a financial expense associated with the learning curve [83, 170]. Steinberg *et al* have estimated overall costs of the average robot-assisted prostatectomy learning curve to be $217,000 based on a theoretical model [186]. This form of cost analysis is yet to be calculated for RP. While results in this chapter did not demonstrate difference between case experience and avoidable delay, this factor might represent a tangible way for per-minute operating theatre time expense to be minimised.

Lastly, given that the more defined procedural learning curves in urology (e.g. robot-assisted prostatectomy) transition at > 50 cases [168], it is surprising that much of the pre-existing learning curve evidence for RP consists of such small series. To capture the learning curve in its entirety, future studies should ensure adequate sample size.

4.3 The Learning Curve of Robot-Assisted Laparoscopic Fundoplication in Children

4.3.1 Introduction

Gastric fundoplication is among the commonest elective procedures performed by paediatric surgeons [116, 187]. Approaches to this operation have further diversified following the recent introduction of robot-assisted technology for laparoscopic surgery. In addition to fundoplication being one of the leading applications of robotic surgery in children [89], this procedure is often targeted for generic skills training in robotic surgery and considered suitable for case-mix prioritisation when initiating a robotic surgery clinical service [135]. The learning curve for paediatric robot-assisted laparoscopic fundoplication remains ill-defined. As such, this chapter aims to evaluate the learning curve for this procedure by examining a prospective single-surgeon clinical database and applying the cumulative summation analytical technique to identify salient learning curve transition points.

4.3.2 Materials and Methods

A prospectively maintained electronic database was examined to identify all robot-assisted laparoscopic fundoplication (RF) cases performed at Leeds Teaching Hospitals NHS Trust during an 8-year period from February 2006 to February 2014. The inaugural robot-assisted minimally invasive procedure performed at this institution was a laparoscopic fundoplication that occurred in February 2006. Subsequently, the robot-assisted laparoscopic fundoplication has been the preferred approach for this operation. A single surgeon (ASN) performed all cases using the da Vinci® Standard Surgical System.

4.3.2.1 Patient selection

Patients considered for RF were those with gastro-oesophageal reflux disease (GORD) that was non-responsive to medical treatment or with clinically significant sequelae. Patients were referred by gastroenterologists, respiratory physicians or nephrologists and often had co-morbid illnesses. Due to heterogeneity in presenting features and co-morbidities (Table 4.7), diagnostic work-up was variable and consisted of one or more of the following investigations as indicated; oesophago-gastroscopy, upper gastrointestinal biopsy, upper gastrointestinal contrast studies, gastric emptying studies, oesophageal pH monitoring, and impedence

studies. There were no exclusion criteria for RF, and this included previous fundoplication or pre-existing gastrostomy.

4.3.2.2 Operative Technique

Typical port placement configuration is outlined in Figure 4.14. Port sites were placed more caudally in younger children in order increase intra-corporal instrument length, maximise dexterity and avoid external robot arm collisions. Pre-existing gastrostomy tracts were either left undisturbed or refashioned to improve access. The usual robotic instrument size was 8mm and scope size 12mm. The standard Nissen fundoplication technique involved adequate mobilisation of the intra-abdominal oesophagus and proximal stomach. If necessary, the superior short gastric arteries were divided using the PK™ Dissecting Forceps instrument. Fundoplications were performed with short, loose wraps secured by 3 to 5 non-absorbable interrupted sutures, and hiatal defects were repaired with 2 to 3 non-absorbable interrupted sutures (3/0 or 4/0 ETHIBOND®, Ethicon, NJ). In cases that involved concomitant gastrostomy formation, this was performed using a robot-assisted intracorporeal purse-string anchoring hitch stitch approach with a Seldinger technique Peel-Away® system (Cook Medical, IN) for placement of a gastrostomy tube or button device.

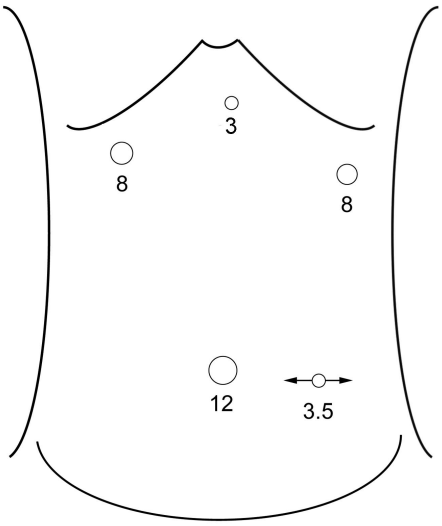


Figure 4.12 Typical port configuration consisting of (clockwise from top) 3mm left sub-xiphisternal Nathanson liver retractor, left upper quadrant anterior axillary line 5mm -8mm working instrument (slightly lower than right upper quadrant port), left lumbar region 3.5mm bedside assistant instrument (e.g. conventional laparoscopic grasper for introducing suture/retracting tissue, and scissors for cutting suture), periumbilical 12mm optical port, and right upper quadrant mid-clavicular line 5mm - 8mm working instrument.

4.3.2.3 Outcome Measures

Similar to Chapter 4.2, surgical process outcomes that were evaluated included robot docking time, console operating time, and total operating time. Definitions of time-based variables were the same as described in Chapter 4.1. Patient outcomes that were evaluated included conversions, intra-operative complications, and post-operative complications. Post-operative complications were regarded as any deviation from the expected post-operative course and graded according to the Clavien-Dindo classification [126].

Age	Overall (mean ± SD)	7.6 ± 6.0 years
	0 – 1 years	n = 6
	1 – 3 years	n = 16
	3 – 5 years	n = 3
	5 – 8 years	n = 7
	8 - 13 years	n = 9
	13 – 18 years	n = 16
Gender	Male:Female	27:30
Presenting features	Vomiting or retching	44% (25/57)
	Respiratory complications	33% (19/57)
	Feeding difficulty or FTT	16% (9/57)
	Choking or apnea	2% (1/57)
Co-morbid illnesses	Cystic fibrosis	23% (13/57)
	Neurological impairment	18% (10/57)
	Failure to thrive	18% (10/57)
	Renal failure	14% (8/57)
	Achalasia	7% (4/57)
	Musculoskeletal deformity	4% (2/57)
	Hypoaldosteronism	4% (2/57)
	Oncological	4% (2/57)
	Cystinosis	2% (1/57)
Concurrent procedures	Hiatus hernia repair	67% (38/57)
	Gastrostomy	60% (34/57)
	Heller myotomy	7% (4/57)
Re-do procedures	Previous LF	7% (4/57)
	Previous RF	2% (1/57)

Table 4.7 Patient demographic information and clinical characteristics (n = 57). FTT = failure to thrive, LF = conventional laparoscopic fundoplication, RF = robot-assisted laparoscopic fundoplication.

4.3.2.4 Data Analysis

There were missing data for 5.3% (15/285) of time stamp data points. Missing data was handled using the Missing Value Analysis procedure and expectation-maximisation (EM) algorithm described in Chapter 4.1.

Cumulative sum (CUSUM) charts were generated to evaluate the learning curve for operating time variables ($CUSUM_{DOCKING}$, $CUSUM_{CONSOLE}$, and $CUSUM_{TOTAL\text{-}OT}$) using the methodology described in Chapter 4.1. Comparisons between case experience and normally distributed operating time outcomes were assessed using the two-tailed Student's t-test for bi-phasic learning curves, and one-way ANOVA for multi-phasic learning curves. Statistical significance was regarded as $P < 0.05$. Statistical analysis was undertaken using SPSS version 20.0 (IBM Corp, NY).

4.3.3 Results

A total of 59 cases were eligible for inclusion. Two cases were excluded from analysis due to intra-operative and post-operative outcome data that was not recorded prospectively. The study cohort was therefore represented by 57 RF cases. Demographic information and clinical characteristics are summarised in Table 4.8. The youngest patient in the series was 1 month of age (Case 28), and the smallest recorded patient weight was 6.4 kilograms (Case 27). No patients were lost to follow up. The median duration of follow up was 4.2 years (range 0.5 – 8.0 years).

4.3.3.1 Operating times

The $CUSUM_{DOCKING}$ chart demonstrated a bi-phasic learning curve with an inflection point at case 42 (Figure 4.15a). Comparison of Phase 1 and Phase 2 docking times was statistically significant ($P = 0.038$, Table 4.8). Parenthetically, there was a steep initial portion of the $CUSUM_{DOCKING}$ chart from cases 1 – 12 that was followed by stabilisation around a horizontal axis from cases 13 – 42. Although not fulfilling inflection point criteria, it is felt that the steep initial learning curve phase is relevant and in this series was able to be overcome after the first 12 cases.

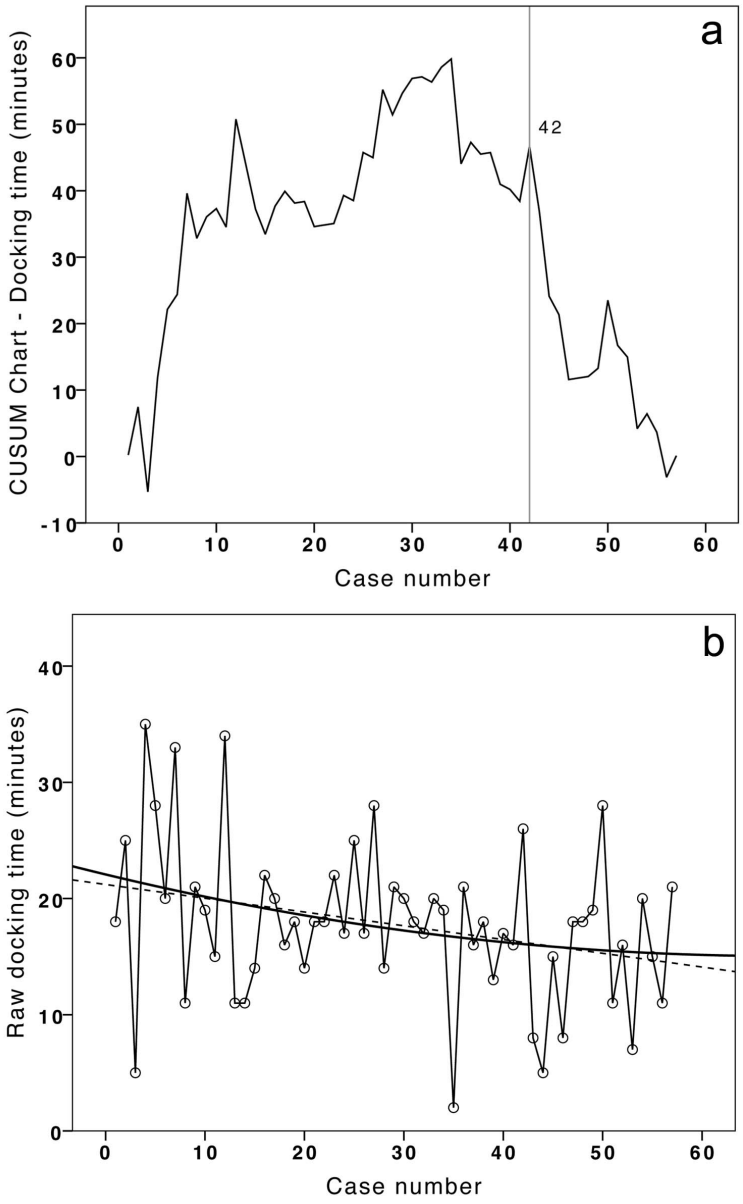


Figure 4.13 CUSUM chart for docking time (a), and scatter plot of raw docking time data (b) with linear (dotted) and quadratic trend lines (solid).

The $CUSUM_{CONSOLE}$ and $CUSUM_{TOTAL\text{-}OT}$ charts were multi-phasic with dual inflection points at cases 34 and 37, and at cases 47 and 48 respectively (Figure 4.16a). There was strong positive correlation between console time and total operating time ($r = 0.59$, $P < 0.001$) that accounts for the CUSUM chart patterns being very similar for these variables. There was a significant difference in console times between learning curve phases ($P < 0.001$), and a borderline significant difference in total operating times between phases ($P = 0.053$).

Mean temporal improvements between the learning phase (Phase 1, Table 4.8) and the subsequent learning curve phase(s), were 4.2 minutes for docking time, 23.1 minutes for console time, and 12.6 minutes for total operating time.

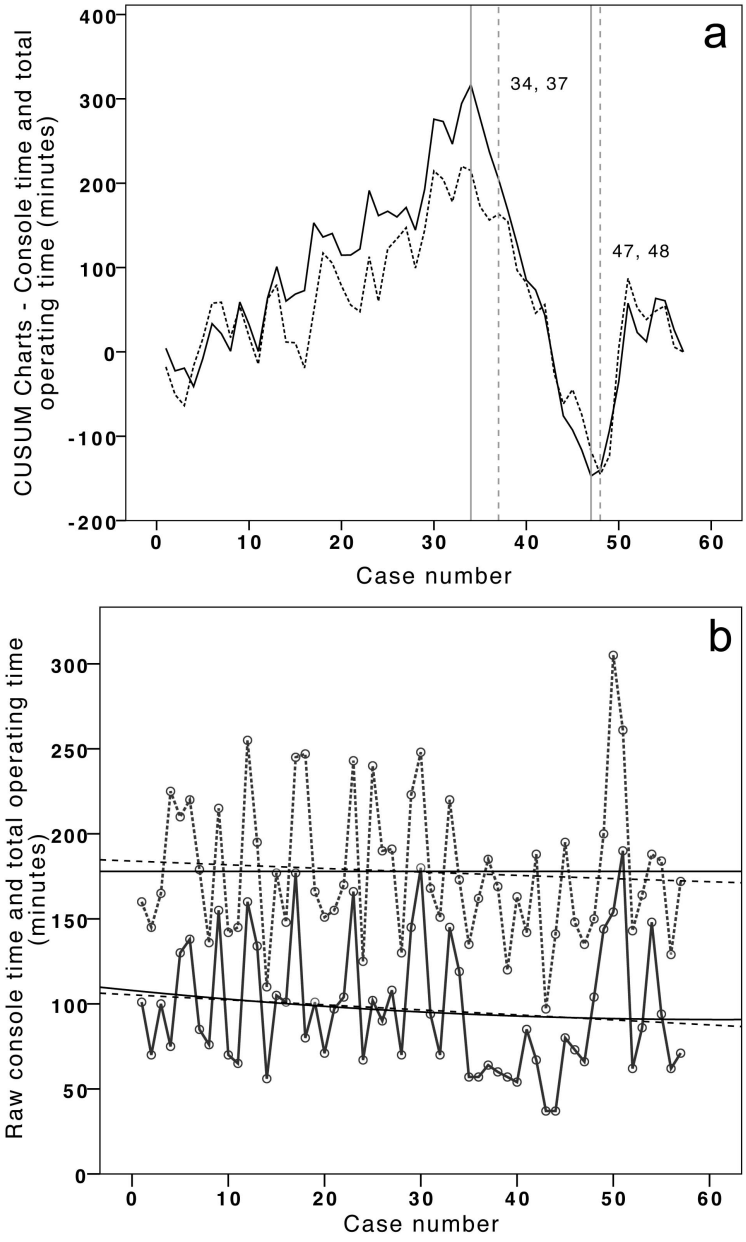


Figure 4.14 CUSUM charts for console time (solid line) and total operating time (dotted line) (a), and scatter plot of raw time data (b) with linear (dotted) and quadratic trend lines (solid).

4.3.3.2 Conversions

No conversions to open or conventional laparoscopic fundoplication occurred, although one conversion to mini-laparotomy was required in a 1.6-year-old child for exploration following posterior gastric wall perforation during percutaneous gastrostomy (Case 18). No injury was identified that required repair.

	Phase 1 Case numbers Mean ± SD (mins)	**Phase 2** Case numbers Mean ± SD (mins)	**Phase 3** Case numbers Mean ± SD (mins)	***P***	**Overall** Case numbers Mean ± SD (mins)
Docking time	1 – 42 18.9 ± 6.7	43 – 57 14.7 ± 6.3	-	0.038	1 – 57 17.8 ± 6.8
Console time	1 – 34 106.1 ± 35.1	35 – 47 61.1 ± 14.1	48 – 57 111.5 ± 44.6	< 0.001	1 – 57 96.8 ± 38.4
Total OT	1 – 37 182.3 ± 40.5	38 – 48 149.8 ± 28.4	49 – 57 194.0 ± 56.1	0.053	1 – 57 177.9 ± 43.1

Table 4.8 Operating times for the overall series (n = 57) and segmented phases of respective learning curves.

4.3.3.3 Complications

In addition to the above, the only other intra-operative complication included a seromuscular tear that occurred during a re-do case of previous conventional laparoscopic fundoplication (Case 17).

Post-operative complications are summarised in Table 4.9. Two patients required elective re-do fundoplication, prompted by persistent retching. Both patients were infants that weighed less than 10kg weight at the time of their original surgery and had respective co-morbidities of hypoaldosteronism and renal impairment secondary to cystinosis. Both patients underwent successful and uneventful robotic re-do procedures. At the time of re-do surgery, intact fundoplication wraps were found but had loosened in one and herniated into the mediastinum in the other. Given their symptoms, the fundoplication, hiatus hernia repair and gastrostomy site were taken down and re-fashioned.

Clavien Grade	n	Description
I	5	Transient retching that resolved spontaneously by POD 4 (1), prolonged ileus (1), dysphagia that resolved spontaneously (3)
II	2	Pulmonary infection (2)
IIIa	0	-
IIIb	3	Upper gastrointestinal bleed on POD 8 that required gastroscopy (unremarkable) and non-urgent blood transfusion (1), re-do procedure for failed fundoplication and/or hiatal repair (2)
IVa	0	-
IVb	0	-
V	0	-

Table 4.9 Post-operative complications graded according to the Clavien-Dindo classification. POD = post-operative day

4.3.4 Discussion

This prospective series summarises the initial 8-year clinical experience of a single-surgeon commencing paediatric robot-assisted laparoscopic fundoplication. Similar to Chapter 4.2, clear learning curve effects are demonstrated for docking time, console time and total operating time such that experience leads to significant temporal improvements.

There is an absence of literature that directly compares the learning curve for robot-assisted versus conventional laparoscopic fundoplication in children. Indeed, a prospective study design to address this evidence gap would be almost prohibitive for practical and ethical reasons. Some authors subjectively report that the learning curve for RF is more favourable compared to conventional laparoscopic fundoplication [121, 135, 188]. Existing paediatric literature estimates the learning curve for conventional laparoscopic fundoplication to be between 20 – 50 cases [116, 187, 189]. Our findings indicate that the learning curve for RF is at least comparable to these figures.

The subjective opinion of many of those who perform RF is that robot-assistance facilitates more accurate, resolute, and efficient surgery for the more challenging procedural steps, specifically; dissection of the hiatal and retro-oesophageal regions, as well as placement of crural and fundoplication wrap sutures (Figure 4.17). Lehnert *et al* have previously demonstrated that hiatal dissection is able to be undertaken 34% faster ($P < 0.05$) with robot-assistance compared to conventional laparoscopy [123]. This somewhat supports the impression that advanced technical features of robot-assistance become more apparent in more complex

cases, such as those involving previous fundoplication, abnormal anatomy, or pre-existing gastrostomy [134].

A dedicated and cooperative operating room team undoubtedly has a positive effect on overall workflow [190]. This is particularly relevant in robot-assisted surgery as equipment is unique in many ways and often demands coordinated activity from multiple staff members. Docking time is perhaps the variable that is most indicative of operating room team efficiency and proficiency. It is encouraging that the docking time learning curve had a short and steep initial phase that could be overcome within the first 12 cases before subsequent stabilisation or improvement. This suggests that successful team building can be achieved within a short period.

The mean post-learning phase console and total operating times of 61 minutes and 150 minutes respectively seem acceptable and comparable with conventional laparoscopic fundoplication operating times [189]. The secondary upward inflections seen in the $CUSUM_{CONSOLE}$ and $CUSUM_{TOTAL\text{-}OT}$ charts were unexpected and prompted close examination of cases that occurred in this period. A cluster of 4 consecutive cases (48 to 51) was observed to be responsible for the curve trend change (Figure 3). These cases specifically involved; 1) a 2-year-old patient with large aberrant hepatic vessel that obscured the operative view, 2) a re-do case in a 19-month-old child with pre-existing gastrostomy and intra-abdominal adhesions, 3) a 3-year-old patient with pre-existing PEG that was taken down and revised to button gastrostomy, and 4) an adolescent with achalasia that underwent a Heller myotomy with fundoplication and hiatus hernia repair. The increased technical complexity of these cases is felt to have contributed to longer console and total operating times, and therefore bimodal CUSUM charts. Multiple studies have previously described similar multiphasic learning curves and attribute this pattern to surgeons progressing toward more challenging cases as skill proficiency and confidence develops [173, 174, 184, 185]. This scenario confounds evaluation of learning curves and disturbs learning effect trends [157]. Complex statistical risk-adjustment techniques have been reported that account for case-mix heterogeneity and variation that occurs with transition from selected to unselected case-mixes, however this relies on the availability of validated risk stratification scoring systems [162, 191, 192].

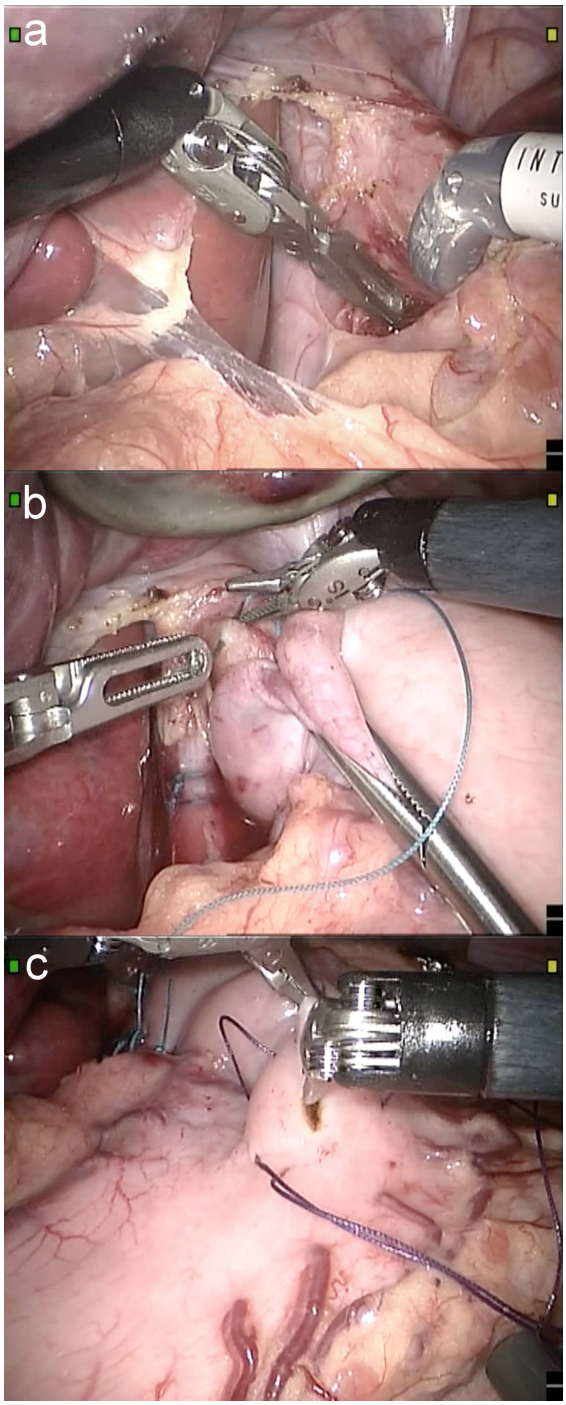


Figure 4.15 Operative images highlighting the dexterity of wristed instruments for a) retro-oesophageal dissection, b) intracorporeal suturing of the fundoplication wrap, and c) preparation of the gastrostomy site with intracorporeal placement of anchoring hitch purse-string suture.

One of the most pertinent items of information that a surgeon seeks from a learning curve analysis is the expected case experience that is needed to overcome the curve. Accurate identification of this case quota is not forthcoming in the literature due to limited analytical

methods that are generally described as being inconsistent and of variable quality [157]. CUSUM analysis techniques are under-represented despite ostensive virtues for monitoring surgical performance [157]. Smoothing of natural data variance ("*noise*") by CUSUM charts makes trends more apparent, and the recursive nature of cumulative summation data processing is better suited for early and sensitive detection of both small process changes and curve inflection points [164]. To highlight how these advantages confer more visually informative displays of data, Figures 4.15 and 4.16 depict both CUSUM charts and scatterplots for the same sets of data.

It is important to quantify learning curve transition point(s) for new technologies or techniques. Identifying the point at which the asymptote is reached allows more comprehensive studies such as prospective controlled clinical trials to be undertaken with the reassurance that learning effect will not bias results. Knowledge of inflection points is also valuable for appropriate structuring of training policies and appreciation of economic costs to these processes. Learning curve related reductions in operating room times have tangible cost-reduction implications that must be considered when assessing the cost-effectiveness of robotic surgery.

Confusion persists as to how the learning curve should be defined, when it concludes, and how certain phases should be categorised and measured. In this chapter, CUSUM charts are interpreted in the context of a conceptual bell-shaped curve that may be sub-divided into various phases (Figure 4.18). In reality this curve will seldom be symmetrical and will differ in height, slope, and length amongst all sub-phases. For bi-phasic curves, the inflection point signifies transition from a learning phase to a skill maintenance phase. The learning phase may be further sub-divided into a steep early phase of accelerated and maximal proficiency gain, and then a subsequent learning sub-phase of skill consolidation that is represented by a relatively stable plateau (Figure 4.18).

The post-inflection point period is likely to be initially concentrated on technical skill refinement (4.18). In this phase, surgeons will explore and implement various optimisation strategies for their practice. This may range from simple adjustments or learned "*tricks*", to more substantial modifications for enhanced surgical process efficiency or patient outcome benefit. An example of a technical refinement that iteratively evolved in this series is a revised method for robot-assisted laparoscopic gastrostomy. This entails preparation of an intracorporeal purse-string anchoring hitch suture. Untied loose ends of the purse-string are then delivered extracorporeally by introducing a conventional laparoscopic grasper

instrument through the planned gastrostomy site under direct vision (robotic port site or alternative site). The robot is then un-docked immediately afterwards. The un-docked scope is returned to the optical port to guide gastrostomy tube insertion under direct vision using a Peel-Away® Introducer Set (Cook Medical, IN). After tying off the purse-string around the gastrostomy tube, the loose ends are tied off again around the gastrostomy flange. In addition to avoiding interference with robot arms at the patient bedside when securing the gastrostomy at skin level, this technical refinement also offers the advantages of a safer, more secure, and better-positioned gastrostomy device.

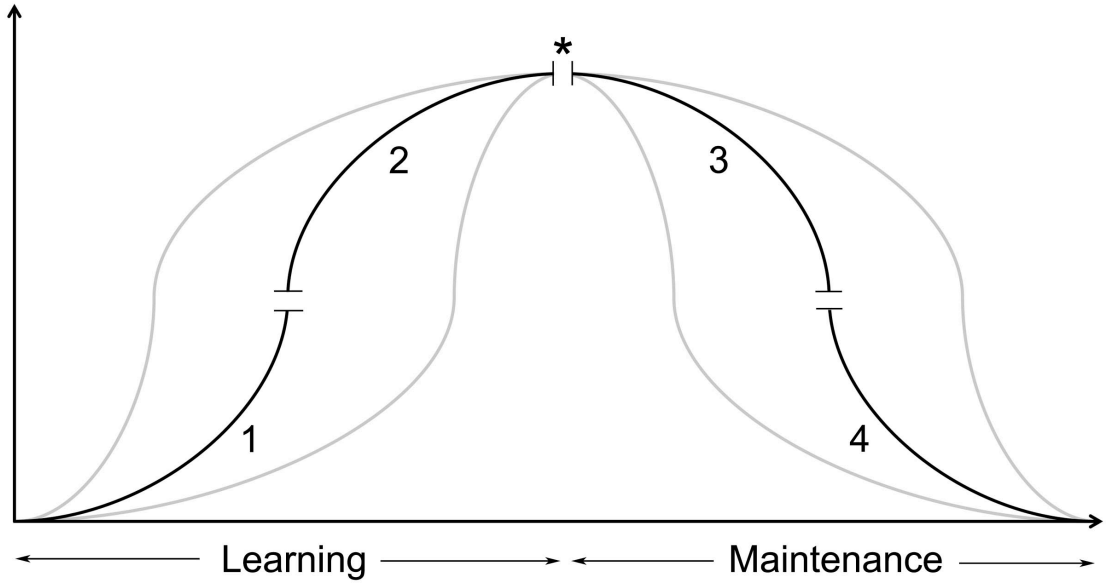


Figure 4.16 Schematic of a smoothed bi-phasic CUSUM learning curve chart indicating *learning* and skill *maintenance* phases either side of a central inflection point (*). Further segmentation of the curve into sub-phases may be conceptually represented by 1) an early-accelerated learning period, 2) consolidation of learning plateau, 3) skill refinement period, and 4) skill mastery or "*automaticity*" period. Examples of alternate slope gradients are indicated in light grey, and these may also be skewed in various phases or sub-phases.

4.3.4.1 Limitations

As learning curve patterns will be somewhat unique for individual surgeons, our results should be interpreted in the context of a single surgeon with considerable background experience in conventional paediatric laparoscopy. Further studies are needed to establish a broadly representative impression of the learning curve for RF in children. It should be noted however, that there are abundant difficulties in comparing learning curves between studies due to lack of standardisation in study design, analysis methods, surgical technique, surgeon

experience, and surgeon number. In this regard, large prospective single-surgeon series (or multiple-surgeon series with individualised outcome analysis) should be encouraged as this study design helps to eliminate surgeon bias and provides truer learning curve estimates.

The CUSUM method used in this study assigned the target outcome as the group mean value. While this approach is internally valid and previously described [173-175, 185], it lacks external validity. Preferred externally valid targets are international benchmark standards and these are presently unavailable for paediatric RF, hence our use of group mean values. Another limitation of using central tendency values as target outcomes is that small early learning curve series will have higher mean values compared to those values that would be obtained if the series were extended and outcomes improved or stabilised for a longer period along the tail of the curve. For this reason, small sample size studies may distort the estimated inflection point by using an overly conservative central tendency value to weight samples in the CUSUM analysis. This emphasises the need for learning curve studies to ensure adequate sample size.

In conclusion, the CUSUM method has valuable potential for learning curve evaluation and outcome quality monitoring in surgery. In applying this statistical technique to the largest reported single-surgeon series of paediatric RP and RF, Chapters 4.2 and 4.3 demonstrate numerous distinctly shaped learning curves and well-defined learning phase transition points. CUSUM analysis results highlight that experience leads to significant temporal improvements. By evaluating numerous parameters, it is revealed that a granular perspective is needed when considering learning curves. It is an oversimplification to holistically describe a procedural learning curve as a fixed number of cases. It is likely that many procedure-related process and outcome measures have separate learning curve patterns as well as distinct curve inflection points.

CHAPTER 5 CLINICAL NEEDS ASSESSMENT AND TECHNOLOGICAL GAP ANALYSIS

Content from this chapter was published as:

TP Cundy, HJ Marcus, A Hughes-Hallett, AS Najmaldin, GZ Yang, A Darzi. International attitudes of early adopters to current and future robotic technologies in paediatric surgery. Journal of Paediatric Surgery. [in press]

Content from this chapter was presented as:

TP Cundy, HJ Marcus, A Hughes-Hallett, AS Najmaldin, GZ Yang, A Darzi. International attitudes of early adopters to current and future robotic technologies in paediatric surgery. International Paediatric Endosurgery Group (IPEG) 23rd Annual Congress, Edinburgh. July, 2014.

5.1 International Attitudes of Early Adopters to Current and Future Robotic Technologies in Paediatric Surgery

5.1.1 Introduction

Robot-assisted minimally invasive surgery has been one of the most recent major innovations to be introduced to paediatric surgeons. Anecdotally, paediatric surgeons' views on this technology are polarised at the extremes but nevertheless the technology remains in an ongoing early state of global adoption [89]. Current robotic technology is in a first-generation phase, defined by the various master-slave da Vinci® Surgical System models. Future robotic and computer-assisted technology will become more advanced and is forecast to become better suited for clinical use in the paediatric setting [139, 193].

Social science theory provides illuminating insight into why some innovations ultimately succeed, why some become quiescent, why some fail, and the rates for which all adoption processes occur [22]. Innovation is seldom adopted en masse in a universal and rapid fashion. Instead, adoption progressively occurs over time and it is well-established that adopter groups can be classified based on cognitive and attitudinal traits that lead to overt behavioural responses of when and whether to adopt [194]. Adopter categories are allocated by an individual's "*innovativeness*" – the degree to which they are relatively earlier in adopting new ideas than their respective peers [194]. Because all physical and behavioural human traits are inherently normally distributed, the variable of innovativeness is expected to follow a bell-shaped curve [194]. This permits categorisation of a relevant population into discrete conceptual adopter groups; the first of which are "*innovators*" and "*early adopters*" (5.1).

Perceptions of relative advantage and compatibility are the most important innovation attributes that influence an individual's innovation-decision process and the technology's overall rate of adoption [194]. Cross-sectional surveys are therefore essential tools for understanding and tracing the diffusion of an innovation such as robotic surgery. This focused survey chapter aims to capture international attitudes of early adopter paediatric surgeons to current and future robotic technologies in order to 1) examine what specific features are driving its appeal and enthusiasm, 2) to explore attitudes toward limiting factors to adoption that are acting as barriers to diffusion, and 3) to investigate opinions toward future robotic technologies for paediatric surgery and the detailed needs of this technology end-user community.

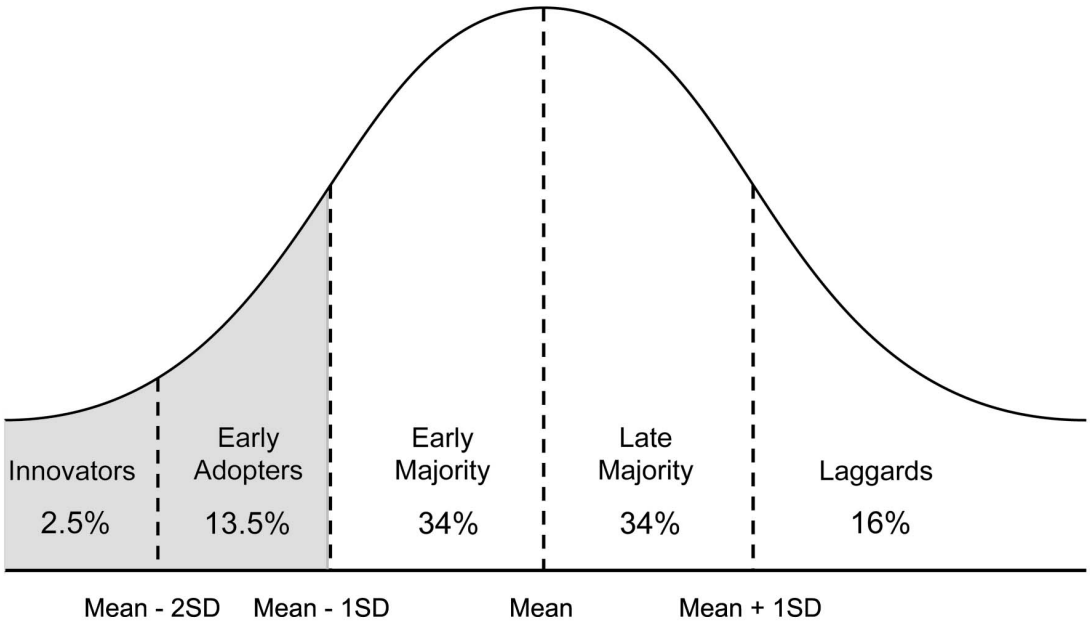


Figure 5.1 The bell-shaped distribution and categorisation of innovation adopters, determined on the basis of 'innovativeness' (adapted from Rogers et al [194]). The targeted sample population for this study is shaded grey.

5.1.2 Methods

5.1.2.1 Survey

The survey design and implementation was undertaken with reference to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) statement [195]. An electronic survey was generated via a subscription-based online survey software and questionnaire tool (SurveyMonkey®, CA; Appendix 3). The survey was constructed into 4 sections; 1) participant demographic and robotic surgery clinical practice information, 2) attitudes toward current perceived *benefits* of robot-assistance in paediatric MIS, 3) attitudes toward current perceived *limitations* of robot-assistance in paediatric MIS, and 4) attitudes toward future robotic technologies in paediatric MIS. All sections were composed of multiple-choice or 5-point Likert scale matrix style closed response questions, supplemented with several free-text open response options. For sections 2 and 3, perceived current benefits and limitations were parsed from a review of the relevant literature and agreed upon following consensus discussion with co-authors. Likert scale question items in sections 2, 3, and 4 were randomised in order such that potential for order bias was limited. The method of randomisation was by computer-generated random order sequencing, an embedded function

enabled by the survey software used. For these questions items, a non-response option of "*don't understand*" was also offered. The survey was piloted amongst surgeons that were ineligible for inclusion as study participants, and non-paediatric general surgeons and urologists at the host institution that had experience with robotic surgery. Piloting indicated that completion of the survey took approximately 15 minutes.

5.1.2.2 Participants

The survey was exclusively distributed to paediatric surgeons with first-hand experience or exposure in robot-assisted MIS. The rationale for targeting this specific group was to ensure that responses were received only from those with appropriate familiarity with the technology. This closed survey approach of selectively sampling a representative population avoided the risk of responder self-selection effect bias. Respondents were classified as experts or non-experts in order to explore differences in attitudes between these sub-groups. The criterion for the former was considered as experience of >30 robot-assisted MIS procedures performed in the paediatric setting as operating surgeon.

5.1.2.3 Distribution

The survey was distributed over the period of one calendar month between June and July 2013. Surveys were circulated in the following three settings; 1) personal approach of recognised experts attending the 22nd International Pediatric Endosurgery Group (IPEG) Annual Congress (Beijing, China), 2) delegates and faculty attending the Inaugural European Paediatric Robotic Surgery Workshop hosted at the 6th Hamlyn Symposium on Medical Robotics (London, United Kingdom), and 3) personal email invitation to corresponding authors of relevant publications in the field that were identified during a recent systematic review [89]. Surgeons approached in person were asked to complete the survey in private on an iPad® (Apple Inc, CA). Surgeons approached via email were able to access the survey via a URL web link to the survey host site. All completed surveys were anonymised as no personal identifying details were requested. Completed surveys were assigned identifying codes based on chronological order of receipt (i.e. Expert 1, Expert 2, Expert 3).

5.1.2.4 Data Processing and Analysis

Survey responses were automatically captured by the online software and exported as a coded summary file. No propensity scoring or weighting of items was used. Analysis of

Likert scale responses was undertaken by assigning scores from 1 – 5 ("1" for "*strongly disagree*" or "*not at all interested*"; "5" for "*strongly agree*" or "*very interested*"). Non-responses of "*don't understand*" were omitted from analysis. The Friedman test was used to compare response items reported by the overall cohort, and if significance was found, then further pairwise comparisons were undertaken using the Wilcoxon Signed Ranks test. Responses between expert and non-expert sub-groups were compared using the Mann-Whitney U test. Remaining closed question response data was analysed using descriptive statistics. Statistical significance was regarded as $P < 0.05$. Statistical analysis was performed using SPSS version 21.0 (IBM Corp, NY).

An emergent theme analysis was performed on free-text responses to the question "*what are the priorities for future robotic platforms in paediatric minimally invasive surgery?*". Three raters individually undertook preliminary screens of these responses to identify themes. Following agreement on themes, the responses were re-screened and binary coded for theme content. The coding allocations of each individual rater were pooled, and discrepancies resolved during a single consensus meeting. As some respondents indicated multiple theme categories, the denominator value for percentage calculations is larger than the number of respondents.

5.1.3 Results

A total of 48 responses were received (22 experts, 26 non-experts), with 14 countries represented overall (Figure 5.2). Survey invitations were sent to 70 valid emails addresses. The email response rate was 30% (21/70), with remaining responses being received from the other two distribution sources.

In the expert group, 86% (19/22) had experience of >50 cases as primary surgeon, with the remaining 14% reporting experience of between 30 – 50 cases. In the non-expert group, 88% (23/26) had experience of <10 cases as primary surgeon, with the remaining 12% reporting experience of 10 – 30 cases. Bedside assistant experience of >10 paediatric robotic surgery cases was reported by 50% (11/22) in the expert group, and 38% (10/26) in the non-expert group. Access to a robotic surgical system (clinical or training) amongst respondents was 3 days per week in 6%, 2 days per week in 10%, 1 day per week in 25%, 0.5 days per week in 38%, and not at all in 21%.

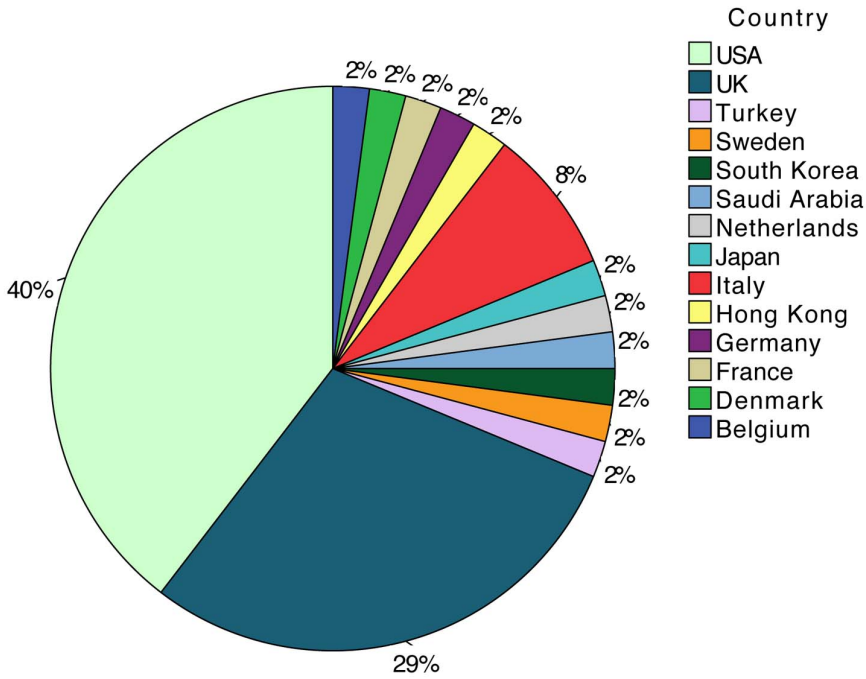


Figure 5.2 Geographical distribution of survey respondents (n = 48) by country of origin.

5.1.3.1 Perceived benefits of robot-assistance

When asked to describe attitudes toward 10 perceived benefits of robot-assistance in paediatric MIS, the mean aggregated 5-point level of agreement Likert scale score was highest for features of wristed instruments, stereoscopic vision, and magnified view (Table 5.1). In comparing responses between the expert and non-expert sub groups, significant differences were found only for the feature of motion scaling with experts being less agreeable that this was of benefit (P = 0.008, Table 5.1). Free-text responses for "*other*" benefits that were not listed included "*less operating room manpower*" (Expert 17) which led to operations being "*less stressful and advantageous to the patient with shorter learning curves and team approach, as compared to laparoscopic operations*" (Non-expert 21). Additionally, robot-assistance was felt to have a "*pedagogical potential*" benefit (Non-expert 2) and opportunities for "*remote surgery*" (Expert 17).

	Experts n = 22	**Non-experts** n = 26	**P**	**Overall** n = 48
Wristed instruments	4.86 ± 0.35	4.77 ± 0.43	NS	4.81 ± 0.39
Stereoscopic vision	4.73 ± 0.55	4.69 ± 0.55	NS	4.71 ± 0.54
Magnified view	4.59 ± 0.73	4.50 ± 0.71	NS	4.54 ± 0.71
Operator comfort	4.64 ± 0.58	4.42 ± 0.70	NS	4.52 ± 0.65
Surgeon controlled camera	4.59 ± 0.59	4.42 ± 0.81	NS	4.50 ± 0.71
Shorter learning curve	4.36 ± 0.79	4.46 ± 0.76	NS	4.42 ± 0.77
Hand-eye coordination	4.38 ± 0.80	4.35 ± 0.94	NS	4.36 ± 0.87
Instrument re-indexing	4.22 ± 0.73	4.13 ± 0.85	NS	4.17 ± 0.79
Tremor filtration	4.05 ± 0.90	4.27 ± 1.00	NS	4.17 ± 0.95
Motion scaling	3.82 ± 0.80	4.38 ± 0.75	0.008	4.13 ± 0.82

Table 5.1 Summary of responses to the question "*What are your attitudes toward the following features of robot-assistance that are perceived as benefits in paediatric minimally invasive surgery*". Data are displayed as mean-rating scores (± standard deviation) generated from a 5-point level of agreement Likert scale (1 = strongly disagree, 2 = disagree, 3 = neither, 4 = agree, 5 = strongly agree).

5.1.3.2 Perceived limitations of robot-assistance

The mean aggregated 5-point level of agreement Likert scale scores for 13 perceived limitations of robot-assistance in paediatric MIS were highest for features of capital outlay expense, instrument size, maintenance expense and consumables expense (5.2). Statistically significant differences in responses between expert and non-expert groups were observed only for haptic feedback loss (P = 0.023), with experts being less agreeable that this was a limitation Table 5.2). Free-text responses indicated a need for "*4mm or even 2mm instruments*" (Expert 6).

	Experts n = 22	**Non-experts** n = 26	**P**	**Overall** n = 48
Capital expense	4.62 ± 0.50	4.35 ± 0.85	NS	4.47 ± 0.72
Instrument size	4.27 ± 0.94	4.19 ± 0.63	NS	4.23 ± 0.78
Consumables expense	4.32 ± 0.72	4.12 ± 0.86	NS	4.21 ± 0.80
Maintenance expense	4.24 ± 0.94	4.19 ± 0.85	NS	4.21 ± 0.88
System size in operating room	4.09 ± 0.81	4.00 ± 0.85	NS	4.04 ± 0.82
Re-positioning for multi-quadrant surgery	3.95 ± 0.95	3.60 ± 0.82	NS	3.77 ± 0.89
Haptic feedback loss	3.18 ± 1.10	3.92 ± 1.16	0.023	3.58 ± 1.18
Instrument range	3.32 ± 1.21	3.50 ± 1.07	NS	3.42 ± 1.13
Set-up and docking time	3.00 ± 1.20	3.62 ± 0.85	NS	3.33 ± 1.06
Access to simulation and training	3.10 ± 0.94	3.50 ± 1.24	0.069*	3.32 ± 1.12
Unclear supportive evidence	3.27 ± 1.16	3.24 ± 1.13	NS	3.26 ± 1.13
Emergency access to patient	2.77 ± 1.11	3.46 ± 1.07	0.052*	3.15 ± 1.13
System instability	2.57 ± 0.93	2.96 ± 1.22	NS	2.79 ± 1.10

Table 5.2 Summary of responses to the question "*What are your attitudes toward the following features of robot-assistance that are perceived as limitations in paediatric minimally invasive surgery*". Data are displayed as mean-rating scores (± standard deviation) generated from a 5-point level of agreement Likert scale (1 = strongly disagree, 2 = disagree, 3 = neither, 4 = agree, 5 = strongly agree). * = borderline statistically significant.

5.1.3.3 Future robotic technologies

When asked, "*is there is a future role for robot-assisted minimally invasive surgery in children?*", 72% (34/47) responded "*definitely*", 26% (12/47) responded "*probably*", 1 respondent was "*unsure*", and 1 did not submit a response to the 5-point likelihood Likert scale options.

Respondents were asked to rate their attitudes toward the following next-generation robotic technologies; 1) hand-held bedside operated robotic instruments, 2) flexible snake robots for natural orifice transluminal endoscopic surgery (NOTES) or single-incision laparoscopic surgery (SILS), 3) da Vinci® Single-Site® Surgery (Intuitive Surgical, CA), 4) micro-bots, 5) image guidance (i.e. augmented reality), and 6) remote-access telesurgery. The technologies that respondents were most interested in were microbots, image guidance, and flexible snake robots (mean aggregated 5-point level of interest Likert scale scores 4.43 ± 0.62, 4.30 ± 0.75, and 4.30 ± 0.72 respectively). Breakdown of responses are further summarised in Figure 5.3.

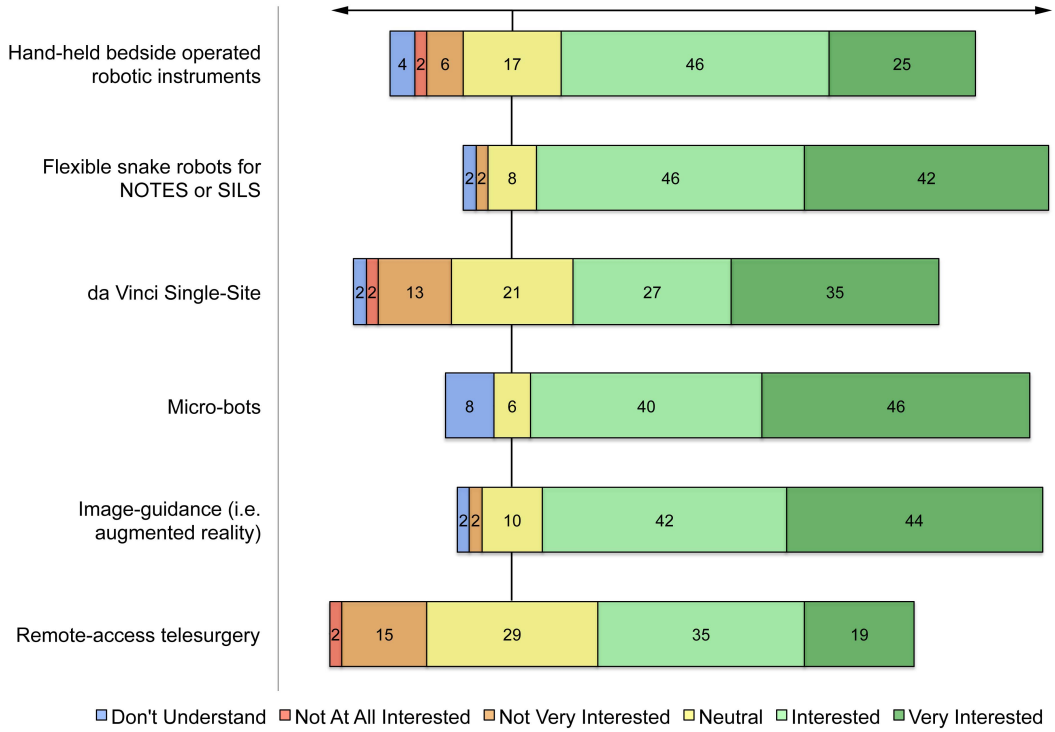


Figure 5.3 Graphical summary of responses to the question "*what are your attitudes toward the following next-generation robotic technologies?*". Data values are presented as percentages of responses.

The most preferred instrument size for paediatric robot-assisted MIS was 3mm (52.2% response), and this response was significantly more favorable compared to all other response items when pairwise comparisons were evaluated (P = 0.03, Table 5.3). The most preferred scope diameter size was 5mm (43.5% response), and again, this response was statistically significant compared to other response items (P < 0.001, Table 5.3). The majority of respondents (51.1%) felt that a price range of €500,000 - €1.0 million was reasonable as capital outlay cost for a new robotic surgical system (Table 5.3). Capital outlay cost for the latest model da Vinci® Si Surgical System would fall within the price range of €1.0 - €2.0 million depending on country of purchase and system model. Only 19% (9/47) of respondents indicated that they felt this price range was reasonable (Table 5.3).

Question	**Response options**	**Response (%, n/total)**
What is the preferred instrument diameter for paediatric robot-assisted minimally invasive surgery?	2 mm	17.4% (8/46)
	3 mm	52.2% (24/46) *
	3.5 mm	23.9% (11/46)
	5 mm	2.2% (1/46)
	8 mm	4.3% (2/46)
What is the preferred scope diameter for paediatric robot-assisted minimally invasive surgery?	3 mm	4.3% (2/46)
	5 mm	43.5% (20/46) *
	8 mm	10.9% (5/46)
	10 mm	32.6% (15/46)
	12 mm	8.7% (4/46)
How much do you feel is reasonable as capital outlay cost for a new robotic surgical system?	€ 250,000 – 500,000	29.8% (14/47)
	€ 500,000 – 1.0 million	51.1% (24/47) **
	€ 1.0 million – 1.5 million	17.0% (8/47)
	€ 1.5 million – 2.0 million	2.1% (1/47)
	€ 2.5 million – 3.0 million	0.0% (0/47)

Table 5.3 Itemised responses to questions regarding preferred hardware specifications and costs of robotic systems for paediatric minimally invasive surgery. * statistically significant (P < 0.05) compared to all other response items, and ** compared to all other items except the most closely matched response item.

Six themes were identified from free-text responses regarding priorities for future robotic platforms in paediatric MIS. The most dominant themes were instrument size (47%, 27/58), cost (24%, 14/58), and system size (17%, 10/58). Many responses commented on the need for miniaturisation of master and slave component hardware "*while retaining the features of adult size instruments*" (Expert 1).

5.1.4 Discussion

The principle aim of those making individualistic impressions of an innovation is to obtain information that reduces levels of uncertainty about an innovation's likely consequences [194]. Simply distilled, this questions is "*what are the innovation's advantages and disadvantages in my situation?*" [194]. Seeking these answers and forming decisions on whether to accept or reject an innovation is a highly social process. Despite our digital age of rapid and largely unrestricted access to scientific literature, diffusion studies demonstrate that most individuals evaluate an innovation based primarily on subjective information conveyed through discussion with like-minded peers or those within shared communication networks [194]. This chapter has carefully deconstructed the salient positive and negative technology attributes in order to demystify what really is influencing, or not influencing, the early adoption of robotic surgery amongst paediatric surgeons.

Several previous loco-regional survey studies have included small components that enquired about overall impressions of robotic surgery [24, 196]. In a web-based survey of Pacific Association of Paediatric Surgeons (PAPS) and Australian and New Zealand Association of Paediatric Surgeons (ANZAPS) members, 54% (63/116) believed that robotic surgery has a role in the future of paediatric MIS [24]. This survey was carried out in 2007 and at this time 17% (20/116) of respondents reported previous experience with robot-assisted MIS [24]. A smaller and earlier survey of North American paediatric surgeons reported that 71% (12/17) felt robotics would play at least an important role in the future, with 47% (8/17) also reporting that a greater emphasis should be placed on robotic surgery training during residency [196].

The rate of adoption of a new technology is affected by the old technology that it supersedes [194]. In the mind of potential adopters, a new technology that is indifferent to existing practice would not be perceived as a genuine innovation [194]. Respondents to this survey would undoubtedly have been making implicit comparisons against conventional MIS. It might therefore be presumed that those who are more satisfied and content with conventional laparoscopy in their clinical practice might have less favorable attitudes toward robot-assistance. This logical assumption might in fact be incorrect. Diffusion theory describes a paradox in that those who have the greatest need for the benefits of a new idea are typically the last to adopt an innovation [194]. That is to say, early adopters will tend to be those who least *need* the innovation.

This survey selectively targeted early adopters. Some generalisable personality values of earlier adopters are that they are less dogmatic, more receptive to change, have grater rationality, and are better able to cope with uncertainty and risk compared to their succedent counterparts [194]. Interestingly, age has been found to not be particularly indicative of whether someone will be an early, middle, or late adopter [194]. Although it was not directly enquired about, it is possible that some respondents may have in fact decided to discontinue their implementation of robotic surgery in their clinical practice and in doing so, might regard the robot at their institution as an expensive "*white elephant*".

Relative advantage of a technology is a ratio of expected benefits and the costs of adoption of an innovation [194]. Costs may be either financial or figurative. Results of this study provide empirical evidence to support the widely recognised view that financial cost is indisputably *the* major prohibitive factor in the diffusion of robotic technology within paediatric surgery. The economic inaccessibility of the da Vinci® platform also creates, or widens, an inequality gap amongst healthcare institutions in the developed and developing world. This innovation consequence generates important ethical debate in itself. Cost has plurality in that it is a not only capital outlay expense that restrains the rate of technology adoption, but it is also high ongoing maintenance and consumables expenses. These latter expenses comprise a profit driven *"razor-and-blades"* recurring revenue model. From a business and industry perspective the financial history of Intuitive Surgical is nothing short of remarkable. After opening on the NASDAQ stock market in April 2003 at USD $11.66, share prices have increased up to 50,714% to a high of USD $588.28 in May 2012. New technology of this type is inherently expensive due to a post-commercialisation phase where many years of preceding and costly research and development is recouped [197]. The niche industry sector does however remain a monopoly market. Without market competition, it is unlikely that costs will become more affordable and this has been demonstrated with consecutive releases of iteratively more expensive da Vinci® Surgical System model updates.

Instrument size was the other standout limiting factor and future priority that was identified. Survey responses very clearly indicated that the preferred robotic instrument size(s) did not at all correspond with those that are presently available for clinical use. The technological gap in instrument sizes for robotic and non-robotic laparoscopic instruments is highlighted in Figure 5.4. Surprisingly, the smaller 5mm diameter size da Vinci® instruments have not been well received by paediatric surgeons [10, 198, 199]. This is due to a '*snake-like*' distal segment design which has a longer articulation axis, rendering it less accommodating in spatially constrained anatomical workspaces that are abundant in infants and young children [10, 11, 146].

On the other hand, the larger 8mm instruments possess the compact EndoWrist® patented design and many paediatric surgeons will compromise on instrument diameter in order to utilise this feature. A similar scenario exists for the da Vinci® laparoscope catalogue. Smaller 5mm scopes exist, but these are monoscopic and paediatric surgeons report preferential use of larger 8.5mm or 12mm scopes that are stereoscopic. The reasons for both instrument and scope size being larger than desired are likely due to fundamental technical barriers of scalability, or resistance to commercialisation due to unsatisfactory current market sales forecasts.



Figure 5.4 Selection of robotic (top two) and non-robotic (bottom three) laparoscopic instrument sizes currently available for paediatric minimally invasive surgery, manufactured by Intuitive Surgical Inc and Karl Storz respectively.

Technological innovations frequently undergo hardware and/or software variation as they diffuse [194, 200]. Robot- and computer-assisted surgical technology are moving targets that are evolving at a fast pace in the pre-commercialisation phase [193]. While the da Vinci® was designed as a generic master-slave surgical platform, the inevitability of digital age technology is that surgical robotics will undergo rapid advancement toward smarter and smaller versions that ultimately become better suited for more specific functions in which they are intended [139, 193, 201]. In their responses to this survey, paediatric surgeons have identified features of existing robotic platforms that should be preserved for system upgrades

or next-generation prototypes, and also features that might be sacrificed for reasons of lesser appeal, as well as factors that must be addressed as major barriers to adoption. In general, the early adopter cohort that was sampled in this study seems most receptive toward future robotic technologies that are smaller, less expensive, more intelligent and flexible. Realisation of these technological ideals would likely draw appeal from current non-adopters and accelerate diffusion of robotic innovation amongst the relevant paediatric surgical specialties.

The clinical value and cost-effectiveness of robotic surgery in children remains unclear, however it should be noted that compelling superiority or non-inferiority affirming evidence played a minor role in the earlier diffusion wave of conventional laparoscopic and thoracoscopic surgery [22, 38]. To this end, it is perhaps unsurprising that lack of supportive evidence was ranked as one of the lowest perceived limiting factors in the survey results (Table 5.2). As previously described by Wilson and embedded within the IDEAL framework, any innovation will eventually face an introspective period of critical objective assessment to determine its genuine clinical value [20, 22].

5.1.4.1 Limitations

The email invitation response rate could be considered relatively low, however this is within expectations of web-based and postal surveys distributed to either closed or open sample groups [195, 202-204]. The small sample size of distributed and returned surveys reflects the small global number of eligible paediatric surgeons for this study. Standard deviation values for most Likert scale scores were small (< 1.0), indicating high levels of agreement that would be unlikely to considerably deviate with a larger sample size.

The nature of the closed survey distribution sources in this study were such that all potential respondents had expressed behaviour that identified themselves as clear enthusiasts. As the awareness and diffusion of robotic surgery in paediatric urology and general surgery is in its early stages, we feel our estimation of sampling only "*innovator*" or "*early adopter*" groups is reasonably accurate despite acknowledging that it is essentially impossible to confirm empirically. It should also be appreciated that in reality innovativeness is a continuous variable and there is no distinct transition point where one adopter falls might into one category, and the next adopter into another [194]. While beyond the purpose and scope of this study, responses from non-adopters or "*non-enthusiasts*" would likely be less extolling of

many perceived virtues of robotic surgery and more critical of perceived limitations, although strong views on some factors such as cost might be shared.

It must also be acknowledged that cognitive and behavioural changes occur in a time-dependent manner following initial exposure or awareness to an innovation. Diffusion scholars have studied this as a multi-staged innovation-decision model [194]. For this study, the perceptions and attitudes of one paediatric surgeon at the time of surveying would likely be different several years later, just as they would likely be if asked the same questions several years earlier. For this reason, any cross-sectional survey of this type must be considered in context of the chronological stage of technology diffusion in which it was carried out, and category of adopter types that were sampled at the time.

In conclusion, future progress in this field requires a clear understanding of critical feedback and respective requirements of the technology end-user community. To address this need, this chapter has captured the attitudes of a representative group of early adopters in paediatric robotic surgery. Insight provided by these responses will help to inform relevant clinical, engineering, and industry groups such that unambiguous goals and priorities may be assigned for the future.

CHAPTER 6 CLINICAL CONSIDERATIONS FOR HAPTIC FEEDBACK LOSS

Content from this chapter was published or submitted as:

TP Cundy, NE Gattas, GZ Yang, AW Darzi, AS Najmaldin. Experience related factors compensate for haptic loss in robot-assisted laparoscopic surgery. Journal of Endourology. 2014;28(5):532-528.

TP Cundy, E Thangaraj, H Rafii-Tari, CJ Payne, G Azzie, MH Sodergren, GZ Yang, AW Darzi. Force sensing enhanced simulation environment (ForSense) for laparoscopic surgery training and assessment. Surgery. [under peer review]

Content from this chapter was presented as:

TP Cundy, AS Najmaldin. Haptic loss of compensated by experience related factors in robot-assisted minimally invasive surgery. European Robotic Urology Congress (ERUS), Stockholm, Sweden. September 2013.

TP Cundy, E Thangaraj, MH Sodergren, AS Najmaldin, SA Clarke, GZ Yang, A Darzi. Development, integration and preliminary validation of a sensing enhanced simulation environment (SEnSE) for paediatric minimally invasive surgery. Trainee Session, British Association of Paediatric Surgery (BAPS), Bournemouth, UK. July 2013.

***** Best Presentation Award presented by Emeritus Professor Lewis Spitz**

6.1 Experience Related Factors Compensate for Haptic Loss in Robot-Assisted Laparoscopic Surgery

6.1.1 Introduction

In Chapter 5, *haptic feedback loss* was found to be the only perceived limitation of robot-assisted surgery in which there was a statistically significant difference between expert and non-expert groups. Prompted by this finding, this Chapter investigates the hypothesis that experience related factors compensate for haptic loss in robot-assisted surgery.

The etymology of the term '*haptic*' may be traced to the Greek verb '*haptesthai'* and noun *'haptikos'* that pertain to a sense of touch. A detailed modern interpretation describes haptic touch as the ability to experience the environment through active exploration, typically with the hands through processes of palpation and manipulation [205]. In the bioengineering vernacular, haptics implies more to the science of interaction between machine and human. The technical craft of traditional open surgery is characterised by intimate haptic relationships between the surgeon's hands and the operative field. The era of minimally invasive surgery necessarily required this relationship to be compromised, with surgeon hands and arms replaced by small diameter, long, rigid, metallic instruments. While some degree of haptic feedback is preserved in conventional MIS, haptic feedback is entirely absent in present day robot-assisted MIS [206]. As such, this complete deficit remains a frequently cited clinical disadvantage in the field of robot-assisted surgery with obvious concerns regarding the potential for attributable surgical complications. Surgeons anecdotally report that following a period of familiarisation with a robotic platform, awareness of non-haptic perceptual substitutes compensate for lack of discriminatory force, tactile cognizance and mechanical arm proprioception [207].

This interesting adaptive process remains under-investigated, poorly understood and hence of unknown clinical impact. Suture damage in robot-assisted MIS is an operative mishap commonly attributed to a haptic feedback deprived sensory state [208-212]. This chapter prospectively investigates this specific operative event in an *in vivo* setting to explore the effect of surgeon experience in overcoming haptic feedback loss.

6.1.2 Materials and Methods

Consecutive cases of children undergoing robot-assisted laparoscopic pyeloplasty at Leeds Teaching Hospitals NHS Trust were included. This procedure was specifically chosen as it requires abundant suturing. All patients had pelvi-ureteric junction obstruction confirmed on renal ultrasound or diuretic MAG3 renogram. Indications for surgery were symptomatic obstruction, deteriorating renal function or increasing grade of hydronephrosis.

6.1.2.1 Operative technique

A single surgeon (ASN) performed all cases using the da Vinci® Surgical System. This surgeon had prior experience with 39 robot-assisted laparoscopic procedures. A standard transperitoneal dismembered Anderson-Hynes reduction pyeloplasty technique was used in all cases as described in Chapter 4.2. In general, 5/0 Vicryl® (Ethicon Endo-Surgery, OH) interrupted sutures were used for the uretero-pelvic anastomosis and 4/0 Vicryl® continuous 'running' sutures used for closure of the pelvis (double-layer), peritoneum and when appropriate, the mesentery. Square surgeon's knots were the default knot, using either 2:1:1 or 2:1:1:1 throws. Robotic instruments used for suturing included either 1) paired needle driver instruments or 2) one forceps (Cadiere or DeBakey) and one needle driver instrument.

6.1.2.2 Primary outcomes

Intra-corporeal suture damage was logged intra-operatively and prospectively recorded. Suture damage was defined as either *incomplete* (i.e. fraying, crushing, crimping, abrasion) or *complete* (i.e. broken thread or de-swaged needle) loss of integrity (Figure 6.1). To account for variation in number of sutures used on an individual case or sub-group basis, *frequency (or rates) of suture damage* were calculated by [(number of damaged sutures/ total number of sutures used) x 100]. Related intra-operative events were also prospectively recorded and graded as involving either major or minor inadvertent tissue damage. Major damage was classified by the need for adjustment (i.e. repeat suture) or intervention, whereas minor damage required no disruption to the surgical workflow.

6.1.2.3 Secondary outcomes

Suture technique (interrupted or continuous), size (4/0 or 5/0) and instruments were subjected to post-hoc analysis. Operative time, intra-operative complications, post-operative complications (early and late), and both clinical and radiological follow up were also

evaluated. Patients were followed with renal ultrasound imaging at one and four months post-operatively, and then with clinical review at six months and yearly thereafter, with isotope renogram as necessary. Operative time was measured as time spent at the master console.

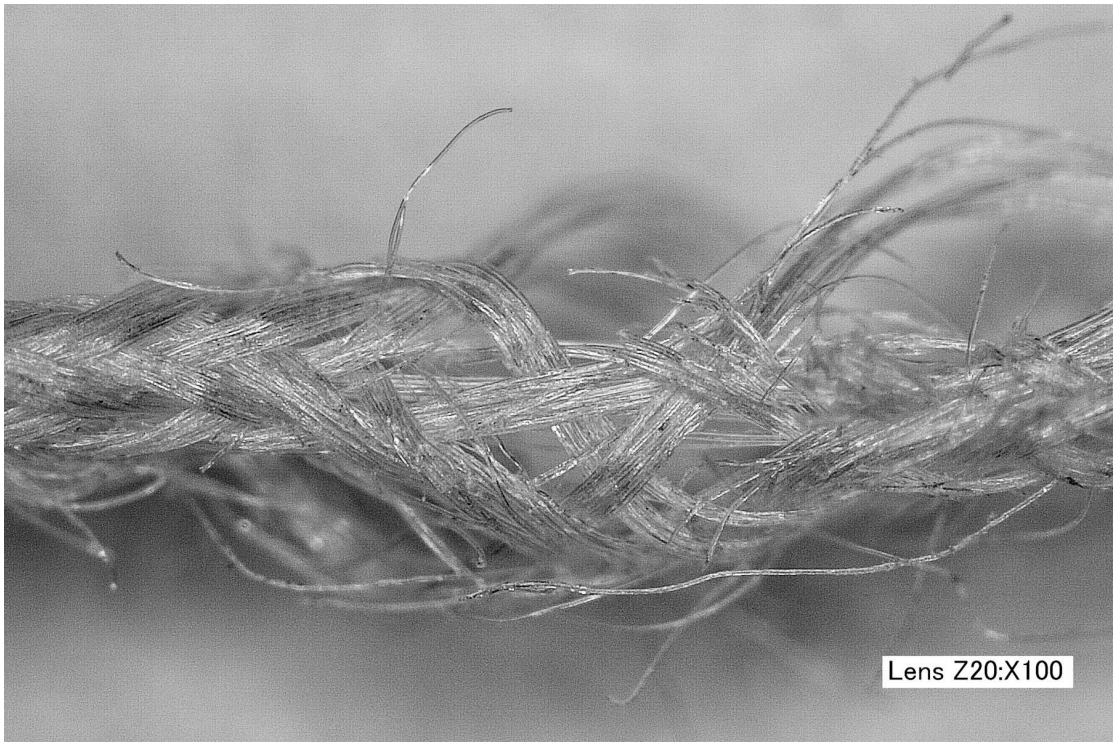


Figure 6.1 Example of incomplete Vicryl® suture damage viewed at 100x magnification (VHX-2000 Series Digital Microscope) following handling with a Cadiere forceps instrument.

6.1.2.4 Statistical analysis

Statistical analysis was undertaken using SPSS version 19.0 (IBM Corp, Armonk NY). Non-parametric tests were used to deal appropriately with skewness of the data. The patient cohort was separated into sequential quartile sub-groups (Q1 – Q4) to determine effect of surgeon experience (number of cases). Analysis of trends across all categorical time periods was undertaken using the Jonckheere Trend Test, with effect size estimated using two-tailed Kendall's tau-b correlation. Post-hoc comparison between any two quartile periods (i.e. Q1 versus Q4) was undertaken using the Wilcoxon Rank-Sum (Mann-Whitney U) or two-sided Pearson Chi-Square tests.

Relationships between surgeon experience, suture damage frequency and operating time were undertaken using two-tailed Pearson's or Spearman's Rank-Order correlation. Stepwise

multiple regression was used to assess suture damage frequency and operating time as possible predictors of surgeon experience. The alpha value for rejection of the null hypothesis was regarded as 0.05.

6.1.3 Results

The study cohort included 52 patients, involving a total of 1,135 sutures. Patient demographic and clinical information is summarised in Table 6.1.

		Q1 n = 13	**Q2 n = 13**	**Q3 n = 13**	**Q4 n = 13**	**Total n = 52**
Age (years)	*Mean ± SD*	8.4 ± 5.0	7.9 ± 5.1	2.5 * ± 2.5	5.2 ± 4.5	6.0 ± 4.9
	Minimum	2.1	0.25	0.42	0.5	0.25
	Maximum	15.7	15.2	9.0	14.0	15.7
Gender	*Male:Female*	9:4	9:4	7:6	8:5	33:19
Laterality	*Left:Right*	9:4	8:5	7:6	8:5	32:20
Pathology	*RPD*	5	6	4	3	18
	AI	3	7	5	1 **	16
	LPV	3	3	2	2	10
	MR	2	1	1	0	4
	Stones	0	1	0	0	1
	Re-do	0	1	0	0	1

Table 6.1 Patient demographic and clinical information for sequential quartile periods, and overall cohort. * Significant difference compared to both Q1 and Q2, ** Significant difference compared to Q2. SD = standard deviation, RPD = moderate or severe renal pelvis dilatation, AI = acute inflammation, LPV = lower pole renal vessel, MR = malrotation, Stones = renal stone disease.

6.1.3.1 Suture usage

The mean number of sutures used for robot-assisted laparoscopic pyeloplasty in this series was 22 (SD ± 6). Mean number of 5/0 and 4/0 suture packets (1 packet = 1 suture needle and thread) used per patient was 5 (SD ± 2) and 2 (SD ± 1) respectively. Characteristics of suture usage are summarised in Table 6.2. Significantly fewer sutures were used per case during the latest quartile period (Q4) compared to each earlier quartile period ($P \leq 0.002$, Figure 6.2). This is accounted for by refinement of surgical technique across the study period to not only be more conservative with number of anastomosis sutures used, but also more preferential use of 5/0 continuous sutures (Table 6.2).

		Q1 n = 13	Q2 n = 13	Q3 n = 13	Q4 n = 13	Total n = 52
5/0	*Interrupted*	314	279	259	150*	1002
	Continuous	0	0	4	22*	26
	Total	314	279	263	172*	1028
4/0	*Interrupted*	0	18	0	0	18
	Continuous	20	25	27	17***	89
	Total	20	43**	27	17***	107
5/0 & 4/0	*Interrupted*	314	297	259	150*	1020
	Continuous	20	25	31	39*	115
	Total	334	322	290	189*	1135

Table 6.2 Suture characteristics for robot-assisted laparoscopic pyeloplasty amongst sequential quartile periods, and overall cohort. * Significant difference compared to Q1, Q2 and Q3, ** Significant difference compared to both Q2 and Q4, *** Significant difference compared to between Q3 and Q4.

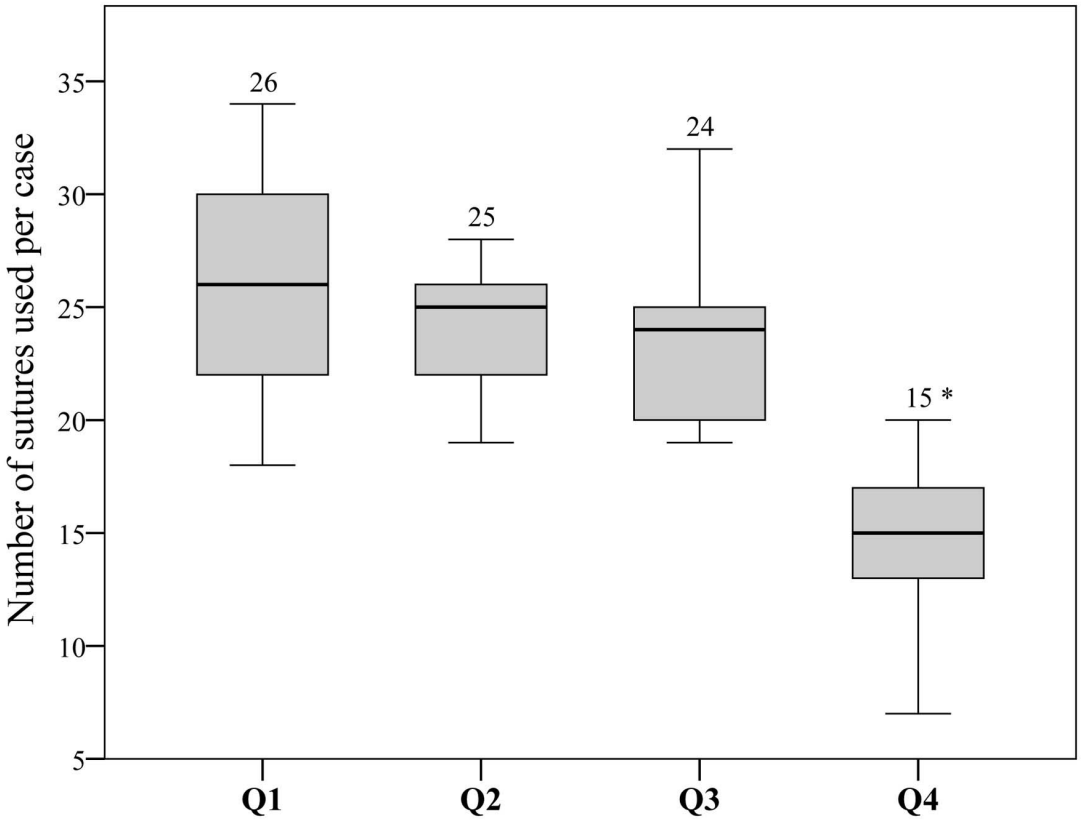


Figure 6.2 Box plot of overall suture usage per case across quartile sub-group periods (Q1 – Q4). Median values for each period (n = 13 cases each) are represented by the horizontal box line and indicated numerically above the upper whisker end. *Suture usage was significantly lower in Q4 compared to each other period ($P \leq 0.002$).

6.1.3.2 Suture damage

The overall frequency of suture damage was 2.6% (Table 6.3). The ratio of incomplete:complete suture damage was 1:6. There was a significant inverse trend between surgeon experience and suture damage frequency overall ($P = 0.014$, $\tau = -0.280$) implying that greater surgeon experience was associated with less suture damage (Table 6.3). The impact of experience on suture damage was most apparent when comparing the earliest quartile sub-group (Q1) with the later three quartile sub-groups (Q2 – Q4) ($P < 0.001$) (Figure 6.3). A non-linear regression curve estimation model demonstrated best line of fit to be cubic ($R^2 = 0.21$, $P = 0.009$), with plateau of suture damage frequency seen after approximately 28 cases (Figure 6.4).

Surgeon experience was associated with shorter operative times ($r = -0.43$, $P = 0.002$), supporting a learning curve period amongst this study cohort. There was a positive correlation between operating time and frequency of suture damage ($\rho = 0.22$), however this was not statistically significant ($P = 0.11$). Operative time and suture damage frequency were both found to be significant predictors of surgeon experience in a stepwise multiple regression model, with the former being a marginally stronger predictive variable (standardised β weights -0.37 versus -0.30, $P = 0.004$ versus $P = 0.18$). Incorporating both operative time and suture damage frequency demonstrated strong predictive strength for surgeon experience ($R^2 = 0.52$)

Continuous sutures had significantly higher damage frequency compared to interrupted sutures ($P = 0.022$) (Table 6.3), presumably due to greater requirement for suture handling. It is suspected that this also accounts for unexpectedly higher damage frequency seen with more resilient 4/0 suture material, compared with 5/0 suture material ($P = 0.038$) (Table 6.3).

In comparing cases in which either paired robotic needle driver instruments or one robotic needle driver with one robotic forceps instrument were used for suturing, significantly higher frequency of suture damage was seen with the latter (1.4% versus 7.1%, $P < 0.001$).

		Suture damage					
		Total Freq (%) n (I:C)	**Q1** Freq (%) n (I:C)	**Q2** Freq (%) n (I:C)	**Q3** Freq (%) n (I:C)	**Q4** Freq (%) n (I:C)	p-value † ‡
5/0	*Total*	2.0% 21 (2:19)	5.4% 17 (2:15)	0.4% 1 (0:1)	0.4% 1 (0:1)	0.6% 2 (0:2)	0.014 -0.299
4/0	*Total*	7.5% 8 (2:6)	10.0% 2 (0:2)	7.0% 3 (0:3)	11.1% 3 (2:1)	0% 0 (0:0)	0.23 -0.232
5/0 & 4/0	*Interrupted*	2.2% 22 (2:20)	5.4% 17 (2:15)	1.0% 3 (0:3)	0.4% 1 (0:1)	0.7% 1 (0:1)	0.002 -0.369
	Continuous	6.1% 7 (2:5)	10.0% 2 (0:2)	4.0% 1 (0:1)	9.7% 3 (2:1)	2.6% 1 (0:1)	0.62 -0.063
	Total	2.6% 29 (4:25)	5.9% 19 (2:17)	1.2% 4 (0:4)	1.4% 4 (2:2)	1.1% 2 (0:2)	0.019 -0.280

Table 6.3 Summary of suture damage for amongst sequential quartile periods, and overall cohort. † Jonckheere Trend Test ‡ effect size estimate using Kendall's tau-b correlation (τ). I:C = incomplete:complete suture damage.

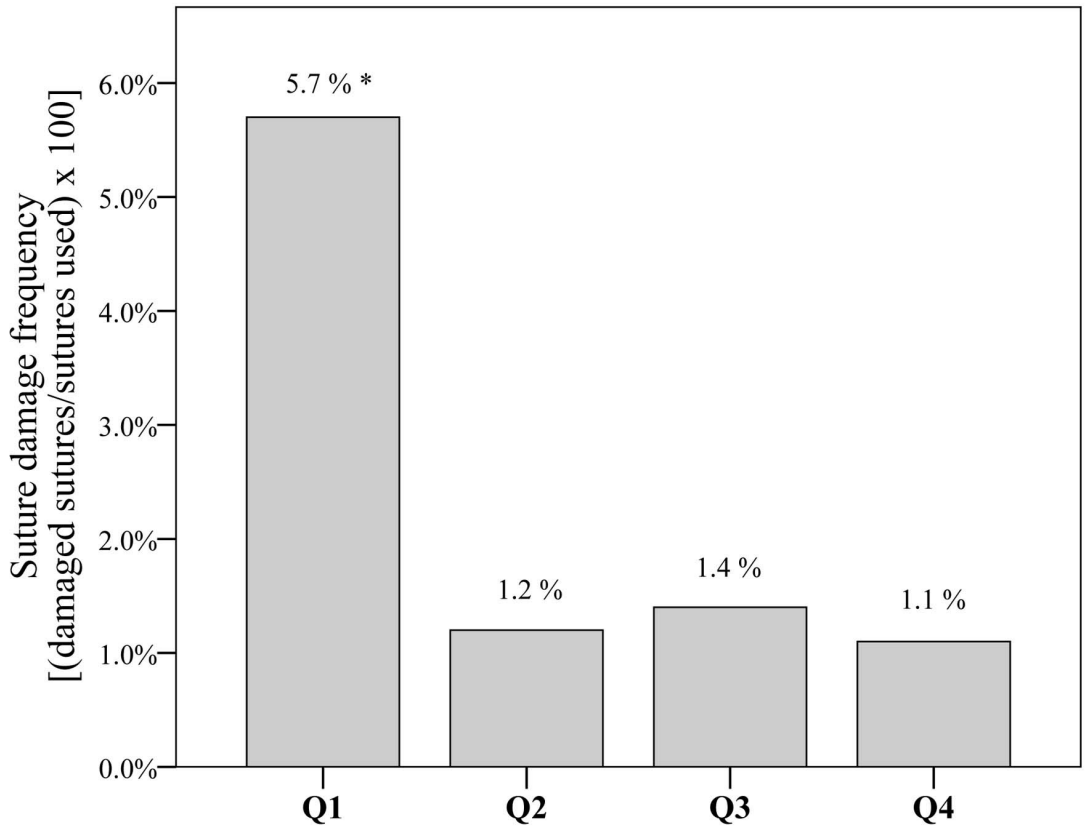


Figure 6.3 Suture damage frequencies amongst quartile periods of surgeon experience (n = 13 cases in each group). * Significant differences in suture damage frequency were observed between Q1 versus Q2 - Q4 (χ^2, $P < 0.001$) and also Q2, Q3, and Q4 (Fisher's Exact, P = 0.002, 0.005, 0.009 respectively). No significant differences were detected between Q2, Q3 and Q4 periods.

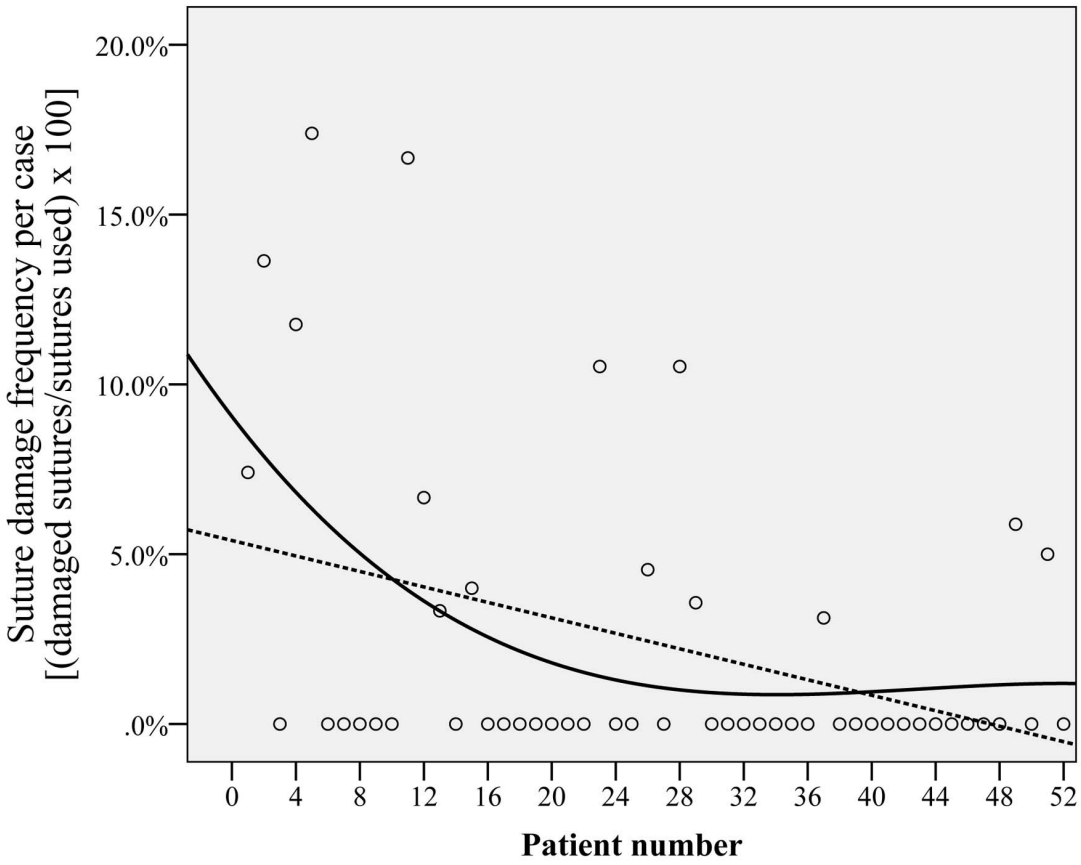


Figure 6.4 Suture damage frequencies for all individual cases in the study cohort (n = 52). Dotted and solid lines represent linear trend lines and cubic curvilinear regression lines respectively.

6.1.3.3 Intra-operative events

Five events of inadvertent tissue damage occurred that were attributed to haptic feedback loss. Two of these events were graded as major and three as minor. All involved injury to exposed edges of renal pelvis (the site of primary anastomosis that frequently requires handling); with major events necessitating trimming of serrated damaged tissue for completion of anastomosis. The relevant anatomy was acutely inflamed in three of the five cases in which these events occurred. There was no significant difference in inadvertent tissue damage between quartile periods. No other intra-operative complications were encountered and no cases required conversion.

6.1.3.4 Clinical outcomes

The mean length of post-operative hospital stay was 1.6 days. There were two post-operative complications; one post-operative ileus that resolved with conservative management and one

recurrence of obstructive symptoms. The latter patient demonstrated radiological features of recurrent PUJO and underwent an uneventful and successful second robot-assisted laparoscopic pyeloplasty six-months after the initial procedure.

6.1.4 Discussion

The complex and multi-faceted organic interpretation of haptic feedback may be classified within a framework of two primary sensory channels – *kinesthetic force* and *cutaneous tactility* [213]. Kinesthetic perception comprises sensations of force, torque, velocities, proprioception, constraints and inertia [213]. Fine tactile discrimination is provided by sensory perception of cutaneous stimuli pertaining to pressure, stretch, vibration, geometry, texture and slippage, among others [213] . Disconnected transmission status between master (surgeon) and slave (robot) for the above sensory input states generates understandable clinical concern. This issue is compounded by consideration that the large and powerful slave components of the da Vinci® are often used for delicate reconstructive procedures. While these concerns may seem valid, it is interesting to note that they remain unsubstantiated by clinical data despite over 1 million robot-assisted MIS procedures being performed worldwide to date. The true clinical impact of haptic feedback loss is therefore unclear, as is the influence of compensatory mechanisms that develop with surgeon experience.

This chapter uses suture damage as an *in vivo* measure of haptic loss related error. Handling of suture thread is inevitable, repetitive and frequent in reconstructive MIS despite a traditional '*no-touch*' principle that applies in open surgery [208, 209, 214]. *Ex vivo* studies have previously demonstrated that handling of suture thread with conventional laparoscopic and robotic instruments is damaging to thread integrity [208, 209, 211, 214]. Risk of complete or incomplete suture damage is felt to be due to uncontrolled and disproportionate applied force due to a lack of direct haptic feedback. Results of this chapter demonstrate that with experience, less damaging handling of suture thread is afforded in robot-assisted MIS.

6.1.4.1 Experience-related adaptive factors in non-haptic sensory perception

Humans possess an innate cognitive plasticity that can compensate for deficiencies in sensory input states by enhancing the perceptual awareness of non-affected sensory modalities. For example, this phenomenon is clearly evident in the context of congenital or acquired deafness and visual impairment [205]. The observation in Chapter 5 that experienced or expert robotic surgeons perceive *haptic feedback loss* as a less of a limitation than non-experts is explained

only by anecdotal and qualitative evidence [207]. Results of this chapter provide objective and quantitative evidence to strengthen support for the hypothesis that similarly acquired compensatory sensory mechanisms might occur in surgeons undertaking robot-assisted surgery.

Awareness and attention to visual cues are described as the most important contributors to non-tactile perception of haptic feedback [207, 212, 215, 216]. Tissue discoloration (e.g. blanching), deformation (e.g. compression), moving shadows and other subtle visual changes within the operative environment permit the surgeon to perceive tool-tissue interaction [2, 207]. Likewise, the magnitude of force applied to suture material may be appreciated by visual signs of tensile stress, knot tautness and deformation of relevant surrounding tissue [2, 206, 207, 217]. High-definition stereoscopic optics provided by da Vinci® systems is felt to enhance recognition of visual cues as well as enable improved depth perception [206, 207]. Specific to suturing using the da Vinci®, Badani *et al* demonstrated that viewing the operative field in stereoscopic display compared to monoscopic display improved suturing performance and reduced error for both novices and experts [218].

Conscious or subconscious sentience of visual cues is either dependently linked to, or greatly complemented by a good internal model of innate tissue and suture characteristics and behavior . Surgeons' knowledge of permissible force, torque and tension for tool-tissue interaction is likely transferrable between open surgery, conventional MIS and robot-assisted MIS. Expert laparoscopic surgeons should therefore benefit from applying existing adaptive skills in non-tactile haptic perception when they first undertake robot-assisted MIS. The process of acquiring skills in visual cue awareness and linking these skills with internal models of tissue (and suture) is driven by experience and has been likened to a form of neuronal or cortical conditioning [207]. It is beyond the scope of this chapter to attempt to deduce the intricate and relatively unmapped brain activation and neural network patterns involved in this learning pathway. However, the field of neuroergonomics is an interesting and growing area of multi-disciplinary research that is expected to unlock greater understanding of human-robot interaction through techniques such as functional near-infrared spectroscopy, as well as explore new horizons through the exciting concept of perceptual docking [219-222].

6.1.4.2 Suture material, size and closure technique

Sutures were observed to mostly break during the process of securing the knot, although this was not formally measured. It is suspected that integrity weaknesses at manipulation point damage sites would have predisposed to suture breakage, or uncontrolled opposing grasp forces overcame the maximum inherent tensile strength of undamaged suture thread.

There is a lack of consensus regarding which suture material should be favoured in conventional or robot-assisted laparoscopic reconstructive surgery. Strength of braided absorbable suture (POLYSORB™, Covidien, Mansfield MA) has been shown to be less diminished by repetitive manipulation with robotic needle driver instruments compared to monofilament absorbable suture (BioSyn™, Covidien, MA) [211]. In the *ex vivo* controlled laboratory experiment by Ricchuiti *et al*, it was also demonstrated that strength of both these suture materials is significantly impaired compared to un-tampered monofilament suture thread (3% versus 35% reduction in suture strength for braided and monofilament respectively) [211]. A woven polytetrafluoroethylene suture material, 'ePTFE' (Gore-Tex, Flagstaff, AZ) has been shown to be more invulnerable to mechanical damage from robotic instrument manipulation compared to monofilament and braided suture [208]. This suture material is unique in that it tolerates compressive grasp forces well through an air-cushioning characteristic.

Tensile strength of suture material is inversely related to suture size [214]. Fine sutures are preferred for many delicate reconstructive procedures, particularly in paediatric patients. Interestingly, Diks *et al* found no significant difference amongst 3/0, 4/0 and 5/0 suture sizes for robotic instrument manipulation point breakage when maximal tensile strength was applied in an *ex vivo* setting [208]. In this chapter, larger gauge 4/0 suture material was found to be damaged more frequently than 5/0 sutures, although this is likely confounded by the fact that this size suture was used for continuous suture lines that required more thread handling.

As the surgeon subjectively felt more adapted to haptic loss towards the end of this study period, more continuous suture lines were used with smaller size 5/0 suture. This has permitted more economic suture packet usage per case (Figure 6.2, Table 6.2) and is believed to expedite anastomosis times. Corresponding increase in suture damage frequency has not been noted.

6.1.4.3 Robotic instruments

Higher suture damage frequency was observed when a needle driver and forceps instrument were paired together, in comparison with paired needle driver instruments. This is in contrast with findings reported in the existing literature that is limited to several *ex vivo* laboratory based studies only. Mucksavage *et al* demonstrated that needle driver instruments exert grasping force that is almost two-fold greater than Cadiere or DeBakey forceps (7.95 versus 11.38 versus 21.64 newtons respectively) [223]. When needle driver instruments repeatedly grasped suture thread three times at the same manipulation point, Hirano *et al* observed a significantly greater loss of suture tensile strength compared with suture similarly manipulated with Cadiere and DeBakey forceps [209]. Interestingly, Mucksavage *et al* also showed that grip force was greater with both new instruments compared to used training instruments, and also instruments used with the da Vinci Standard® compared to the da Vinci Si® Surgical System [223].

Results in this chapter might be explained by differences in suture manipulation forces that occur *in vivo*. In the *in vivo* setting, forces of varying magnitude are applied in a multitude of torque directions, with instrument grip at assorted degrees of angulation to the suture thread, and many different manipulation sites located along thread length. This differs greatly from controlled open-grasp-close forces that are typically employed in *ex* studies with instruments perfectly perpendicular to the suture. Forceps instruments also have a larger overall grip surface area, and deeper-pitched serrated grip surface pattern which might produce a cutting and/or '*sawing*' effect (Figure 6.5). The milled '*cross-hatched'* grip surface pattern on needle holder instruments provides greater grip security over a smaller instrument tip surface area, possibly limiting slippage and any '*sawing*' when counter-traction is applied on suture thread. A simple and low-cost solution involving a soft-silicone coated robotic needle driver instrument has been proposed by Ishikawa *et al* [210]. Promising preliminary *ex vivo* results are reported but interference with instrument functionality remains a concern [210].

6.1.4.4 Implications for clinical practice

The lack of haptic feedback in robot-assisted MIS generates concern for untoward surgical errors or adverse events that may be observed in clinical practice as inadvertent tissue injury or suture damage. The integrity of suture material plays an important role in the quality and durability of any anastomotic repair [211]. No post-operative clinical features of pyeloplasty anastomosis compromise (i.e. urine leak) were observed that might be attributable to haptic

feedback loss related suture damage. Additionally, despite the potential for uncontrolled forceful tool-tissue interaction in robot-assisted MIS, the incidences of intra-operative unintended tissue injury, bleeding and post-operative complications (related or unrelated to suture damage) in this study was minimal. Before assuming that the clinical impact of absent haptic feedback might therefore be overestimated, these results should be interpreted in the context of an expert laparoscopic surgeon who had already performed 39 robot-assisted cases. Further studies are needed to investigate how haptic feedback loss might impact tool-tissue interaction for novice robotic surgeons with or without background experience in conventional laparoscopy. It also must be acknowledged that different anatomical structures are more susceptible to mechanical stress injury from tool-tissue interaction. The ureter is recognised as a more resilient tissue due to high connective tissue and muscle content, unlike small bowel, vascular structures or solid-organs which might be more vulnerable to inadvertent injury during robot-assisted surgery [224].

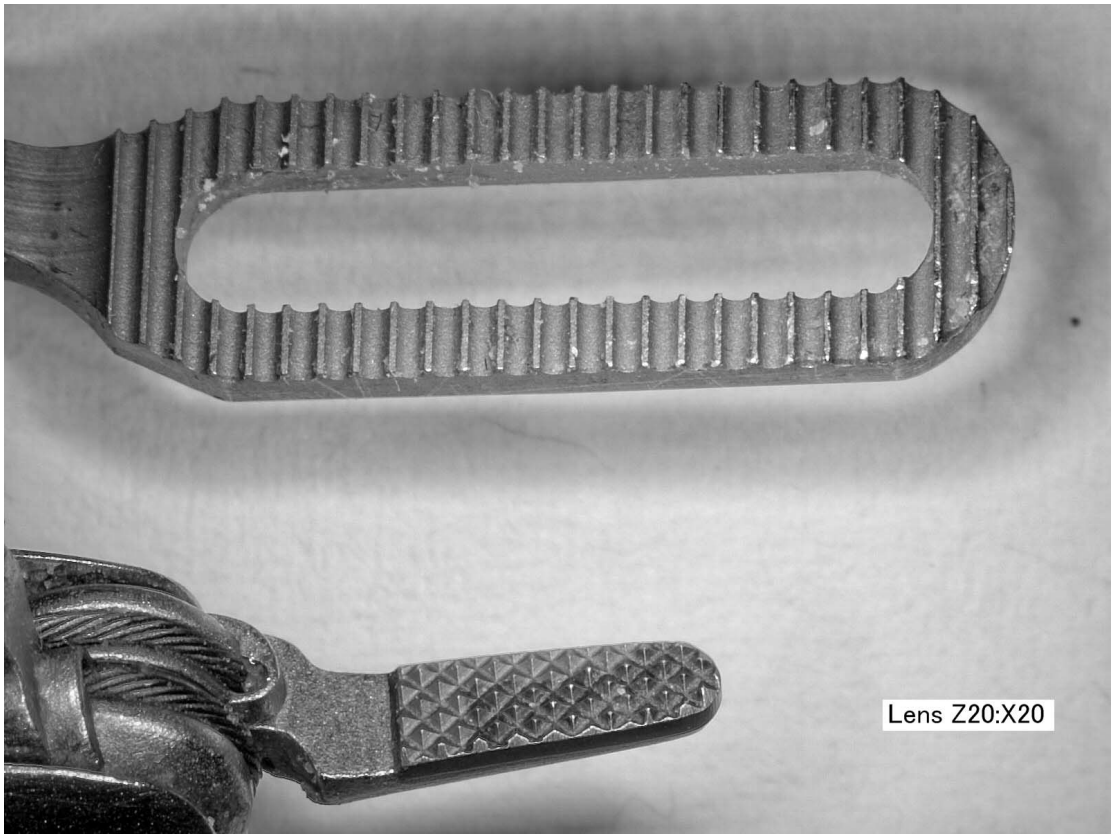


Figure 6.5 End-effector grip surfaces of Cadiere forceps (top) and large needle driver (bottom) instruments viewed at 20x magnification (VHX-2000 Series Digital Microscope).

Given that suture damage frequency and operating time were both found to be similarly strong predictors of surgeon experience, suture damage frequency might be considered as a worthwhile independent or combined metric of overall proficiency or status of haptic compensatory skills. Suture damage is an easily measurable, objective and reproducible event that equally applies in *ex vivo* and *in vivo* settings.

6.1.4.5 Limitations

This chapter presents data from a single surgeon's experience, captured from a period that was beyond the steep early learning curve period. In this regard, it is possible that experience related effect is underestimated and subject to a degree of type II error. Additionally, there was some inter-patient heterogeneity in suture quantity, technique, size and instruments used. This is felt to be reflective of refinement in surgical technique during a familiarisation period with new technology, and also inevitable variation in patient characteristics. Results of sub-group analysis of these variations justify further investigation into different suture materials, sizes, and closure techniques, as well as robotic instruments used for suture handling.

6.1.4.6 Future directions

Integrated technology that transmits sensitive real-time haptic information to the surgeon is a challenging goal that is being actively pursued for next-generation robotic surgical platforms [225, 226]. Force feedback systems are regarded as a more tangible and relevant objective for clinical translation in contrast to tactile feedback counterparts. To date there are no haptic devices or systems that are commercially available for clinical use with bimanual robotic surgical systems, although the VerroTouch system developed by Kuchenbecker *et al* seems imminent [226, 227]. Indirect haptic feedback technologies currently reported in the pre-clinical literature include auditory or visual graphic display systems [216, 217, 225, 228]. More '*organic*' and transparent systems under development include sensorized instrument shafts or end-effectors that directly transmit haptic information to the master control interface [227, 229-233].

In examining the effect of visual force feedback (via graphical colour coded display) on robot-assisted suturing amongst novices and experts in an *ex vivo* setting, Reiley *et al* found that this sensory substitute benefited novices only, resulting in less suture breakage, lower peak applied force, and decreased force inconsistencies [228]. These results implied that expert surgeons possessed experience-related compensatory skills that were not improved by an artificial haptic substitute. Given these findings, and realising the persisting technical barriers

in the field of haptics for robot-assisted surgery, more attention might be invested towards the role of experience related compensatory skills. These human factors are independent from technology barriers and are likely to be attainable in the early or intermediate stage of the learning curve period. Hagen *et al* have reported that following an initial 45 to 60 minute dry-lab simulation and training session on a da Vinci®, 50% of novices acknowledged some perception of haptic feedback [207]. Laboratory-based simulation and training presents an ideal environment for acquisition of compensatory skills such that potential impact of haptic loss is minimised in the clinical setting and operative performance is maximised. As such, this is investigated further in Chapter 6.2.

In conclusion, these results provide empirical evidence to support the safety of robot-assisted minimally invasive surgery in that very few inadvertent tissue injury events were observed that could be attributed to lack of haptic feedback. This prospective *in vivo* data also demonstrates significantly lower frequency of suture damage with increasing surgeon experience. Suture damage therefore may be a useful and sensitive measure to determine acquisition status of experience related skills that compensate for haptic loss. Importantly, this is easily reproducible in the simulation laboratory setting and could be tangibly integrated as a component of pre-clinical training curricula that are under development. Strategies for minimising suture damage in the early learning phase of robot-assisted reconstructive MIS could include selection of larger suture size, braided suture material, preferential use of interrupted sutures and paired needle driver instruments.

6.2 A Force Sensing Enhanced Simulation Environment (ForSense) for Laparoscopic Surgery Training and Assessment

6.2.1 Introduction

Tissue handling with appropriate application of force is an essential skill for safe practice in surgery. As with the vast majority of technical features that constitute surgical expertise, this skill element is positively influenced by experience [234]. The pre-eminent surgeon Lord Moynihan of Leeds aptly described, "*…in surgery, the hand of the beginner is heavy*" [235-237]. Novices may either be unnecessarily rough, or timid in their engagement of tool-tissue interaction. In contrast, experts are observed to demonstrate more judicious, purposeful and consistent force behaviour. A historical recollection of the mastery in surgical technique attained by the aforementioned Lord Moynihan describes that "*he handled the tissues with the utmost gentleness; there was no tugging of organs in order to visualize them…"*.

There is a *relative* loss of haptic feedback in conventional laparoscopic surgery and *absolute* loss of haptic feedback in robot-assisted laparoscopic surgery. Compared to a surgeon's gloved finger in use during traditional open surgery, the sensitivity of palmar sensory stimuli in conventional laparoscopic surgery is estimated to be diminished between 8- and 20-fold [206]. Familiarising and adapting to these altered sensory circumstances involves a learning process. It is not surprising therefore that excessive or inappropriate force is a major contributor to operative errors enacted by trainees during laparoscopic surgery [234]. The teaching of safe and effective skills in tissue handling is challenging, particularly as the teaching surgeon is often "*hands-off*" as either scrubbed camera assistant or un-scrubbed supervisor.

Simulation-based training and assessment (SBTA) comprises an increasingly established role in modern surgical curricula. Structured use of box trainer or virtual reality simulators has been well demonstrated to improve surgical trainee performance in the operating theatre [238-244]. The McGill Inanimate System for the Training and Evaluation of Laparoscopic Skills (MISTELS) is the most popular platform for SBTA in laparoscopic surgery. Initially promoted as a training tool, its purpose has expanded to become the default global curriculum for assessment of core laparoscopic skills. Endorsed by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and American College of Surgeons, the MISTELS represents the psychomotor component of the Fundamentals of Laparoscopic Surgery (FLS) curriculum [244]. Satisfactory completion of this curriculum is a board

certification requirement for graduating general surgeons in the United States. Recognising the unique differences in training needs for laparoscopic surgery in children, a size appropriate Pediatric Laparoscopic Surgery (PLS) simulator has recently been developed and validated based on the MISTELS [245].

Key performance measures for the majority of commercially available SBTA platforms, including the FLS and PLS, concentrate almost exclusively on time efficiency and accuracy. While these measures are extensively studied and well established in terms of validity and reliability [244, 246, 247], they lack sensitivity as objective indicators of skill *quality*. Force offers potential as a valuable discriminator of skill *quality and safety* in tissue interaction, with particular appeal due to obvious clinical relevance. Direct measurement of instrument or '*tissue*' force is lacking however in SBTA platforms, especially in box trainers. This chapter therefore aims to 1) develop a force sensing unit that is easily and unobtrusively retrofitted with existing box-trainer simulators, 2) utilise this Force Sensing Enhanced Simulation Environment (ForSense) to investigate and validate multiple force variables as objective measurements of laparoscopic skill, and 3) to determine concurrent validity of a force error integrated scoring metric against the validated standard metric. The motivation to develop a validated force sensing simulation environment is to address unmet need for an *accessible* resources that may be used to accelerate and assess the acquisition of haptic compensatory skills in both conventional and robot-assisted paediatric laparoscopic surgery.

6.2.2 Materials and Methods

6.2.2.1 Hardware development

A number of modifications were made to the existing PLS simulator. Firstly, a replacement base was manufactured using a 3D-printer (Figure 6.6a). This base incorporated a 55mm x 32mm cutout space at the site in which simulation task items would normally be positioned. A separate 53mm x 30mm x 6mm rectangular plate was 3D printed to fit within this empty space, allowing a 2mm margin. The plate was sensitized by three-point screw mounting to a calibrated Nano17 6-axis force-torque (F/T) transducer (ATI Industrial Automation, NC, United States). Four supporting columns were included in the design of the replacement base to accommodate the F/T transducer underneath the PLS box, and also to securely position both the box and F/T transducer mount to a main stabilising board. The pegboard supplied with the PLS simulator was drilled with two countersunk holes for attachment to the base plate using screws (6.6b). The penrose drains supplied with the PLS simulator were interchangeably affixed to the base plate using 3M™ Atraumatic Command™ adhesive

patches (3M™, MN, United States) (Figure 6.6d). When in place, the location and orientation of both the pegboard and penrose drain were identical to the standard PLS simulator.

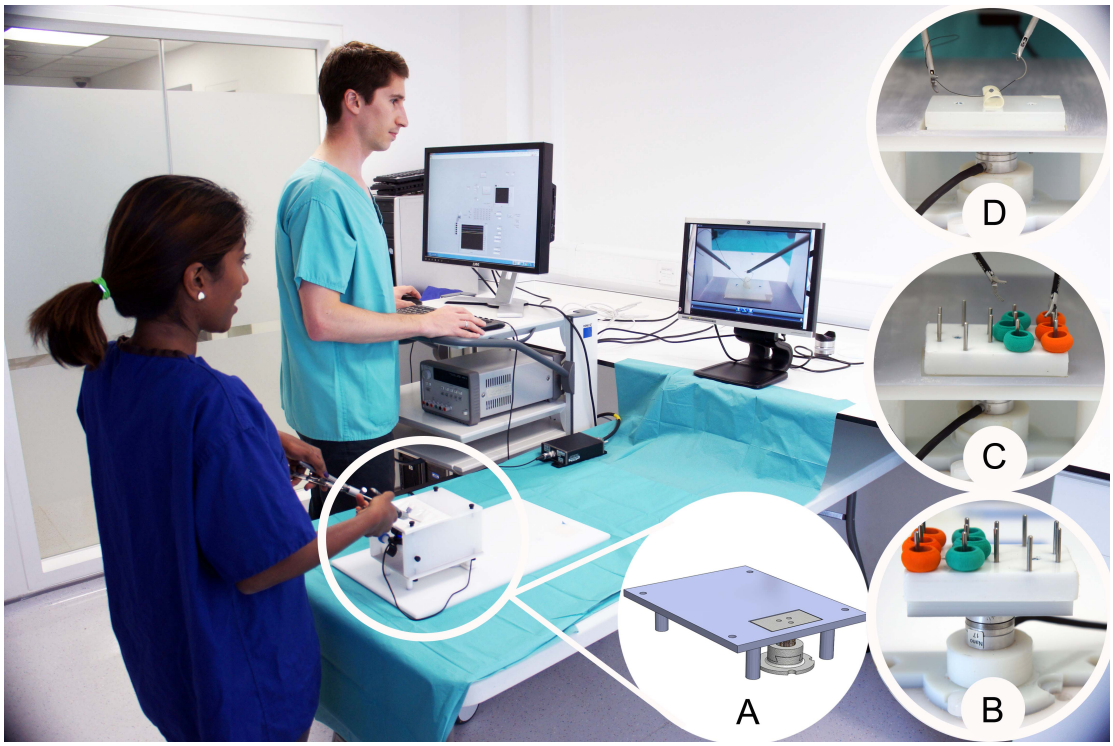


Figure 6.6 Overview of the ForSense and experimental set-up, showing the replacement base and sensitized plate (a), attachment of existing peg board (b), and reverse angle views of the peg transfer and suture tasks (c and d).

6.2.2.2 Software development and system integration

The F/T transducer was tethered to the same computer used for the video input and display. Synchronisation of force data and video feed was provided by custom software operated in C++, using UDP communication through LabVIEW (National Instruments Cooperation, TX, United States) for reading force data and the OpenCV (Open Source Computer Vision) library for recording video feed. The F/T transducer transmits data at a frequency of 25 Hz, and is able to detect forces to a resolution of 3.5 mN. The 3 axes of measured force were aggregated to a single force modulus output. A dual monitor display was configured such that participants viewed only the video feed and were blinded to real-time force feedback that was displayed as a live trace on the other monitor (Figure 6.6).

6.2.2.3 Participant testing

The MISTELS based FLS and PLS curricula consist of 5 inanimate abstract tasks. Participants were recruited to perform 5 repetitions each of 2 PLS curriculum tasks; the peg transfer and suturing with intra-corporeal knot tying. These two tasks are respectively regarded as the easiest and hardest components of the manual skills curricula. As previously described, participants were stratified into novice, intermediate and expert surgeon groups based on recent clinical experience involving < 10, 10 – 50 or > 50 laparoscopic procedures respectively [245]. Following informed consent, participants were shown a short pre-recorded instructional video and allowed one minute to familiarise with the task set up.

Scores were calculated for each peg transfer and suture task performance in accordance with standard metrics [245]. Raw task scores were not normalised (i.e. divided by a target score) to receive equivalent range of scores amongst tasks and weighting towards a composite score [244, 246]. A maximum allowable peak force of 1.5 N was assigned for both tasks, and the number of times this threshold was breached in each task repetition was regarded as the force error. This value was based on data reported by Rodrigues *et al*, who determined that macroscopic tissue damage was visible when >1.5 N tractive force was applied to suture through fresh porcine intestine [248]. Modified scoring metrics (fPLS) were calculated post-hoc that imposed additional penalties based on force error. The fPLS metrics for the peg transfer and suture tasks were, "PLS score – (force error x 10)" and "PLS score – (force error x 2)" respectively.

6.2.2.4 Data collection and analysis

Raw force data was exported as text files for post processing. The data was pre-processed to isolate and condense force measurement output to time points in which laparoscopic instruments were actively engaged with the task objects. This was achieved by zeroing at the value of minimum recorded force, and then eliminating force data points that were < 0.2 N. This process essentially removed interference from baseline noise and restricted data to that which represented '*tool-tissue*' interaction only. Mean relative non-zero force (henceforth referred to as '*mean*' force), maximum force and overall magnitude of force exerted over time (henceforth referred to as '*force magnitude*') was determined for each task repetition as well as force error. Force magnitude was calculated in Newton/seconds (N/s), where 1 N/s represents 1 Newton force exerted for 1 second.

Synchronised video files were analysed to confirm scoring using standard metrics, explore force signature patterns for individual task components, and assist segmentation of data into four sequential suture subtasks. The subtasks represented needle drive, double throw knot, first single throw knot and second single throw knot phases.

Statistical analysis was undertaken using SPSS version 19.0 (IBM Corp, NY, United States). One-way analysis of variance (ANOVA) was used for comparison of age between groups of experience level and Chi-square tests to determine differences in gender distribution. Outcomes for time, error and force data were evaluated on a task-by-task basis, rather than selecting a representative best performance task for each participant, or generating central tendency values for all task repetitions performed by each participant. Construct validity was assessed using the Kruskal-Wallis test to compare force variables between groups of experience level. Mann-Whitney U tests were used to further investigate significant differences between two groups of experience level, with the Bonferroni correction. Relationships between experience level, task completion time and force variables were evaluated using two-tailed Pearson's correlation tests. Linear regression models were used to assess predictive strength of PLS and fPLS scoring metrics for level of experience.

6.2.3 Results

6.2.3.1 Participant demographics

Demographic information for participants is summarised in Table 6.4. Age was found to differ significantly between groups ($P < 0.001$). There was no significant difference in gender distribution between groups ($P = 0.11$).

	Novices	Intermediates	Experts
n	6	6	6
Age (mean ± SD)	23.2 ± 1.6	31.7 ± 2.9	36.0 ± 3.3
Gender (M:F)	3:3	5:1	6:0

Table 6.4 Demographic characteristics of the study cohort.

6.2.3.2 Force

Force measurements and level of experience were inversely related in all circumstances with experts found to exert the lowest forces for both tasks, and novices the highest (Table 6.5). Mean, maximum and overall magnitude of force, as well as force error, were significantly different amongst levels of experience for both tasks (Table 6.5). Examples of force signatures for different levels of experience are illustrated in Figure 6.7. The force variables with strongest correlation to level of experience were force magnitude and force error (Table 2).

		Novices ***Mean ± SD*** ***N vs I P value****	**Intermediate** ***Mean ± SD*** ***I vs E P value****	**Experts** ***Mean ± SD*** ***E vs N P value****	***r*** ***P*** **
Peg Transfer	**Time (seconds)**	158.9 ± 34.8 < 0.001	126.0 ± 23.8 0.034	113.1 ± 22.7 < 0.001	-0.56 < 0.001
	Mean force (N)	0.61 ± 0.36 NS	0.51 ± 0.31 NS	0.46 ± 0.25 0.005	-0.40 0.006
	Maximum force (N)	2.7 ± 1.6 NS	2.3 ± 1.2 0.043	1.7 ± 0.9 0.008	-0.31 0.020
	Force magnitude (N/s)	21.8 ± 22.0 NS	13.5 ± 9.3 0.004	7.3 ± 4.6 0.001	-0.39 0.001
	PLS penalty score	11.7 ± 18.6 0.015	3.9 ± 11.3 NS	3.3 ± 8.1 0.022	-0.25 0.022
	Force errors	3.7 ± 3.7 NS	2.7 ± 2.9 0.028	1.3 ± 1.8 0.002	-0.33 < 0.001
Suture	**Time (seconds)**	324.7 ± 100.5 < 0.001	200.1 ± 59.4 0.001	146.6 ± 56.8 < 0.001	-0.69 <0.001
	Mean force (N)	0.81 ± 0.20 NS	0.73 ± 0.23 NS	0.67 ± 0.12 0.003	-0.31 0.018
	Maximum force (N)	3.9 ± 1.6 NS	3.2 ± 1.3 NS	3.0 ± 1.0 0.012	-0.28 0.033
	Force magnitude (N/s)	89.1 ± 44.1 <0.001	40.8 ± 13.7 <0.001	26.0 ± 10.7 < 0.001	-0.68 < 0.001
	PLS penalty score	4.8 ± 2.3 NS	4.7 ± 1.5 < 0.001	3.2 ± 0.95 < 0.001	-0.35 < 0.001
	Force errors	20.7 ± 14.9 NS	9.3 ± 6.5 NS	6.4 ± 4.2 < 0.001	-0.52 < 0.001

Table 6.5 Time, force, and score metric outcomes amongst levels of experience for the peg transfer and suture tasks. N = Newtons, N/s = Newton/seconds, NS = not statistically significant, *r* = Pearson correlation coefficient, *P* = p value, * Mann-Whitney U test, ** Kruskall-Wallis test.

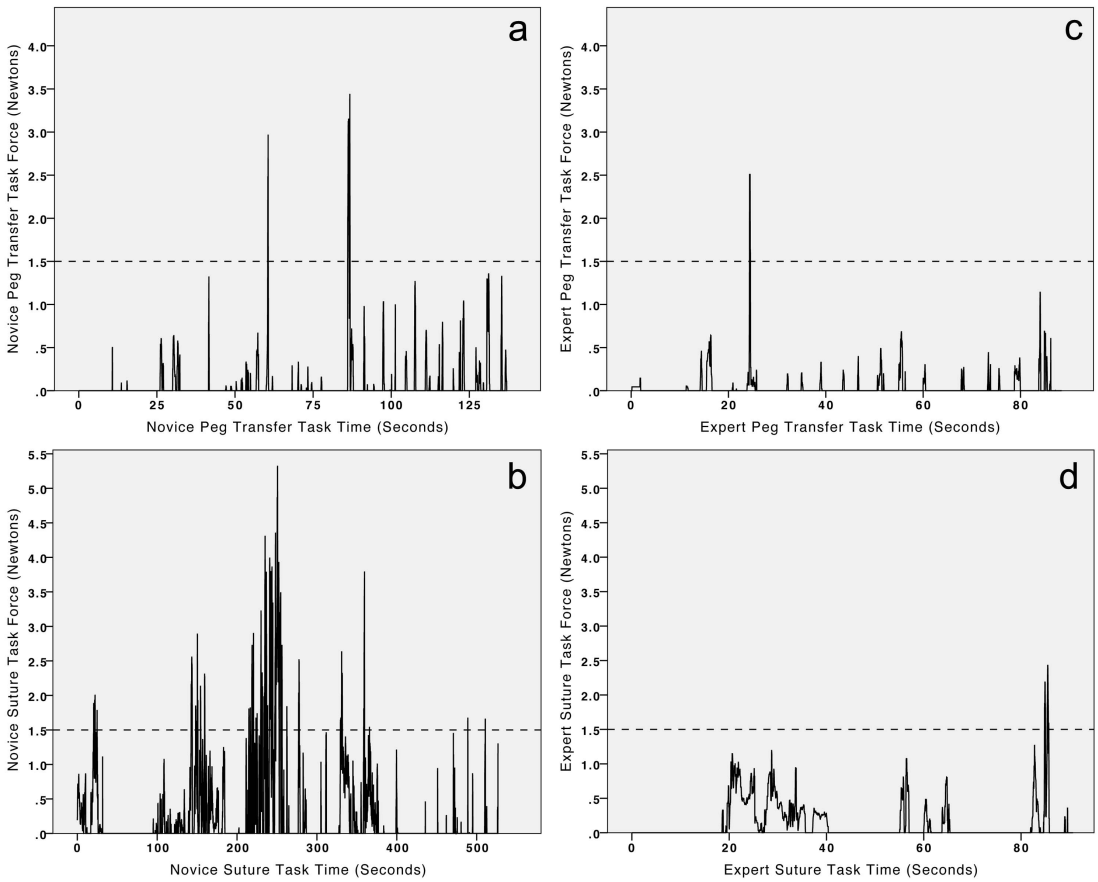


Figure 6.7 Force signatures of low scoring peg transfer and suture task repetitions by a novice (Figures 6.7a and 6.7b respectively) and high scoring peg transfer and suture task repetitions by an expert (Figures 6.7c and 6.7d respectively). The dotted horizontal line represents the threshold for force error (1.5 N).

6.2.3.3 Correlation with task completion time

Peg transfer and suture task completion times were both significantly different amongst levels of experience ($P < 0.001$). Amongst all force measurements, force magnitude was the most highly correlated with task completion time ($r = 0.65$ and $r = 0.75$, for peg transfer and suture tasks respectively, Figure 6.8).

6.2.3.4 Scoring metrics

PLS and fPLS score outcomes are summarised in Table 6.6. Standard penalty scores were less strongly correlated with level of experience than the force error in both tasks (Table 6.6). Predictive strength of the PLS and fPLS scores were similar for both tasks (Table 6.6). This is explained by high degrees of collinearity between the two scoring metric outputs ($r >$

0.85), which were also not statistically different from one another (P = 0.48, Kruskall-Wallis).

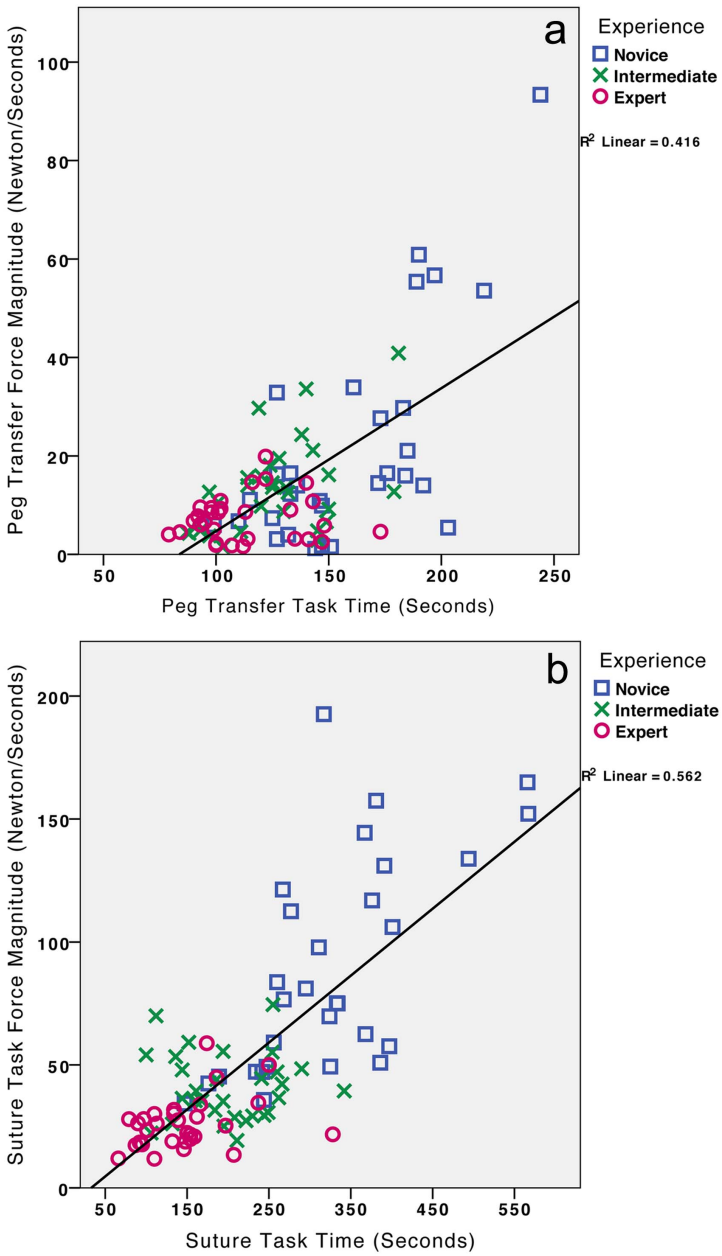


Figure 6.8 Correlations between task completion time and force magnitude, with least-squares linear regression lines.

		PLS *Mean ± SD*	fPLS *Mean ± SD*
Peg transfer	**Novice**	129 ± 43	92 ± 58
	Intermediate	170 ± 27	143 ± 43
	Expert	184 ± 27	171 ± 30
	R^2 value (β, *P* value)	0.31 (0.011, < 0.001)	0.33 (0.009, < 0.001)
Suture	**Novice**	271 ± 100	229 ± 117
	Intermediate	395 ± 59	377 ± 59
	Expert	450 ± 57	437 ± 58
	R^2 value (β, *P* value)	0.49 (0.005, < 0.001)	0.51 (0.005, < 0.001)

Table 6.6 PLS and fPLS scores amongst groups of experience level. For each scoring metric, comparisons between all combinations of two experience level groups were statistically significant ($P < 0.001$ - 0.038, Mann-Whitney U). β = unstandardised regression coefficient.

6.2.3.5 Video analysis

Correlation of recorded video feed with force signatures allowed characteristic force events to be appreciated in context of individual task components. Peaks in force for the peg transfer task invariably occurred when instruments made contact with the pegs. This was significantly more frequent and more forceful in novices compared to experts, and intermediates compared to experts (Table 6.5). For the suture task, force error threshold breaches typically occurred when excessive torque was applied to the drain in the following circumstances; 1) poor needle drive technique that lacked supination movement to guide the curve of the needle through its insertion point, 2) pulling the drain (tissue) towards the prepared knot rather than laying down the knots onto the passive drain, 3) over-tensioning knots with unbalanced force applied on loose thread ends (particularly the double throw knot). Examples of these events are presented in Figure 6.9.

Segmentation of the suture task into sequential phases revealed significant differences for time and force magnitude only (Table 6.7). The longest time taken was for the double throw knot, and highest force magnitude for the needle drive maneuver. Values for all parameters investigated amongst all suture phases were highest for novices and lowest for experts, although this was statistically significant for time and force magnitude only (Table 6.7).

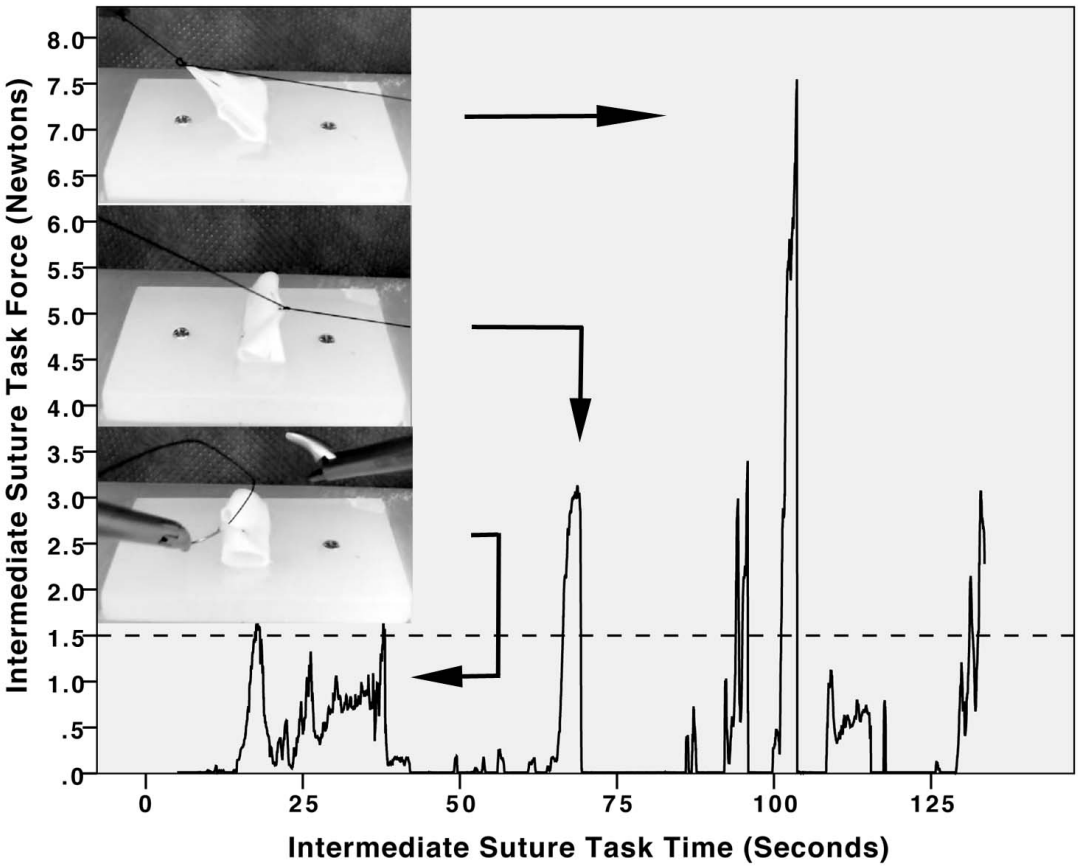


Figure 6.9 Force signature for an intermediate level participant undertaking a suture task. Events corresponding to various force peaks are illustrated.

		Needle drive	Double throw knot	Single throw knot 1	Single throw knot 2	*P*
N	**Time**	65.8 ± 35.1	93.0 ± 40.9	82.7 ± 38.7	83.2 ± 59.9	0.05
	Mean force	0.81 ± 0.49	0.75 ± 0.52	0.79 ± 0.50	0.72 ± 0.48	0.34
	Maximum force	4.94	8.24	5.53	7.55	0.41
	Force magnitude	42.16	17.77	17.87	11.38	< 0.001
I	**Time**	45.0 ± 28.0	67.2 ± 38.2	43.3 ± 20.3	44.6 ± 25.8	0.005
	Mean force	0.71 ± 0.42	0.63 ± 0.38	0.78 ± 0.51	0.67 ± 0.35	0.16
	Maximum force	5.52	4.18	7.55	4.35	0.32
	Force magnitude	34.88	13.73	19.30	3.80	< 0.001
E	**Time**	40.4 ± 25.1	46.6 ± 30.3	33.2 ± 21.9	26.4 ± 11.0	0.01
	Mean force	0.66 ± 0.36	0.64 ± 0.40	0.70 ± 0.45	0.64 ± 0.39	0.25
	Maximum force	4.05	5.54	3.90	5.39	0.23
	Force magnitude	30.29	6.05	17.38	4.37	< 0.001
P	**Time**	0.004	< 0.001	< 0.001	< 0.001	
	Mean force	0.018	0.13	0.47	0.45	
	Maximum force	0.10	0.16	0.50	0.10	
	Force magnitude	< 0.001	< 0.001	< 0.001	0.002	

Table 6.7 Time and force results for suture subtasks. All values represent mean or mean ± SD for time (seconds) and force (Newtons or Newton/seconds) variables. N = novices, I = intermediates, E = experts, *P* = *P value*.

6.2.4 Discussion

The era of SBTA has involved a generational shift in relocating the teaching and credentialing of core psychomotor laparoscopic skills outside of the operating theatre environment and into skills laboratories [249]. Building upon the important volume of early formative research in this field that focused on processes of development and validation, current direction is more targeted towards optimising the effectiveness and delivery method of SBTA. This chapter demonstrates that existing widespread box-trainer simulators can be subtly adapted to enhance their effectiveness potential and broaden the objective data that can be obtained. The results obtained confirm the role of force measurement at the tool-tissue interface as a feasible, reliable and valid measure of skill assessment [250].

6.2.4.1 Objective measures of laparoscopic skill in a simulation setting

In reflecting on what defines the end-outcome of SBTA, the question of *'can you do it quickly?'* and *'can you do it well?'* are importantly different. The validity of task completion time has been thoroughly demonstrated and remains highly popular [249]. Its almost ubiquitous presence as a skill assessment outcome measure is undoubtedly related to ease of measurement and transparency. Time is however, a crude and indirect measurement of skill *quality* for any given simulation or clinical task [251-253]. The ideal pre-clinical training platform will maximally expedite the acquisition of necessary skill proficiency before transfer to the clinical setting. With this in mind, the exact skills that are desired need to be carefully considered in order to define proficiency and optimise the efficiency of SBTA.

Inappropriately forceful tissue handling, or the inverse, presents genuine threat to patient safety through inadvertent tissue injury or damage. As an outcome measure in surgical simulation, it is therefore suggested that measurement of force at the tool-tissue interface is more clinically relevant and important compared to other popular variables such as task completion time and motion analysis. Results of this chapter indicate that force variables are independently competitive alongside time efficiency and accuracy measures (Table 6.5).

In isolation, individual parameters are heavily vulnerable to misinterpretation and inaccuracy. For example, many subjects seeking to achieve proficiency standards in the time and accuracy based FLS or PLS curricula focus on rushing through the assessment tasks with less consideration towards appropriate force and economy of motion. This approach to skills training certainly does not reflect the expected approach to transfer of skill in the operating theatre, where mastery in all possible skill areas should be the ultimate goal. Improvements

and refinement of sensitivity in skill assessment within the simulation setting will come through assimilation of multiple modalities (i.e. time, accuracy, motion tracking and force analysis) into composite scores. Using this approach the effectiveness of training will be enhanced, as trainees or test candidates are less able to sacrifice or compensate parameters to achieve higher scores.

6.2.4.2 Force as a determinant of skill

Based on the data derived from the tasks evaluated in this chapter, it seems clear that the force output characteristics are uniquely task dependent.

The '*flawless*' force profile for a peg transfer task would detect near zero sum force. This would involve lifting, transferring and placing the rings without touching the peg spikes. Due to the very low weight of the rings, placement of the rings should not register as reactive force. The higher frequency and scale of force in novices and intermediate level surgeons for this task suggests naïve skill development status in areas of depth perception, visual-spatial orientation, psychomotor coordination and bimanual dexterity translates to excessive force measurements. Extrapolating these results to the potential clinical setting, one would anticipate that trainees might unintentionally apply frequent undue force to neighbouring anatomy.

For the suture task, existing FLS and PLS box trainers possess a rudimentary binary strategy to indicate whether excessive force is applied or not. This depends on whether the penrose drain is avulsed from the velcro adhesive block. To avulse the drain in the PLS box trainer, a direct and sudden upwards vertical force of 5.2 N is required. The alternate method of drain fixation used in this chapter was purposefully designed such that a negligible interface between the drain and sensitised base plate ensured all tool-tissue force was detected as signal. As such, the ForSense permits measurement of force as a continuous variable for detailed force signature patterns to be determined across the entire duration of any task (Figures 6.7 and 6.9).

Force has unique plurality as a measurement. Consensus regarding the preferential selection of available force variables remains unclear. While literature is generally scarce in this field, the Delft University of Technology group shows a tendency to favour mean absolute non-zero force [254, 255]. In comparing multiple force variables, it was found in this chapter that the difference in mean force amongst experience groups was less significant than other variables

investigated. It is hypothesised that this is due to bias introduced by increased time that non-experts spend in the "*idle*" state that brings down any central tendency value. Force threshold breaches ("*force error"*) are attractive as a preferred variable due to empirical clinical relevance.

As discussed in Chapter 6.1, experts are likely to have learned skills that compensate for sensory deficits in minimally invasive surgery, and assimilate this with acquired knowledge of permissive forces that are tolerable by various anatomical structures relevant to their laparoscopy practice. It is also proposed that experts exhibit greater force consistency in repeated tasks due to a status of seemingly effortless automaticity [256]. Although this was not statistically determined in this chapter, it is supported by smaller standard deviations in all force variables measured, indicating that experts apply precise and controlled force with lower variability (Table 6.5, Figure 6.7).

6.2.4.3 Role for a hybrid class of laparoscopy simulators

Comparative effectiveness of box trainer (BT) versus virtual reality (VR) simulators is contentious. Recent evidence indicates that BT simulators are at least as effective VR simulators for training [249, 257-260]. Both modalities have respective merits and drawbacks, generating argument that training curricula should involve exposure to each such that the best features of all available resources are exploited [260]. BTs are inexpensive, more portable, widely implemented for credentialing, and use real instruments that produce a more realistic ergonomic interface while also being easily interchangeable. VR simulators on the other hand utilise benefits of computer graphics and processing to deliver high-fidelity procedure specific simulation scenarios and ability for instantaneous multi-dimensional objective performance feedback.

The ForSense seeks to bridge this dichotomy in training platform attributes, offering a relatively low-cost box trainer that is enhanced with computer-generated objective outcomes provided by force sensing. The advantage of this hybrid style approach is that the existing box trainer is retrofitted such that user experience with the box is not altered, thereby avoiding interference with previously well-validated tasks. The sensitised base plate of the ForSense can be restored to the original base plate within minutes and without the need for any special equipment.

6.2.4.4 Limitations and future directions

The ForSense generates almost 2,000 F/T data items for 1 minute of uninterrupted task time. In this chapter, F/T data was manually processed and this played a limiting role in sample size capacity. Future iterations will integrate software for automated data processing, permitting near instantaneous feedback summaries of force data and scoring metrics.

An inherent issue with generating a force modulus using a multi-axis F/T sensor is that forces in perfectly equal and opposite directions will cancel each other out and register as zero force. Given the sensitivity of the F/T sensor and highly infrequent expected frequency of this occurrence, this is not considered a major concern. Indeed, good suturing technique for a properly cinched square surgeon's knot involves preparation and tensioning of loose thread ends in equal and opposite directions, and this would be rewarded by lower force readings on the ForSense.

The ForSense set-up requires task objects to be firmly fixed to the sensitized base plate. This is practical as it allows different task items to be interchangeably mounted; however this means that the 'tissue' itself is not innately sensitised. There are some potential drawbacks to this approach. Firstly, the fixity of the penrose drain is higher than the physiologic mobility of a similar sized tubular anatomical structure. Secondly, the ForSense is unable to measure direct grip (or "*pinch*") force. Several groups have described development of sensitised laparoscopic instruments that measure grip and/or instrument shaft force, however this is subject to considerable trocar interference and instrument force can occur without tool-tissue interaction [261-264].

The value of haptic feedback in VR simulators is debatable. Latest pooled evidence indicates that its utility in training is over-estimated [206, 249]. The ForSense is not a haptic feedback platform, as it confers no sensory substitution or augmented sensory output to the user. Rather than developing the capabilities of the ForSense towards distractive real-time tactile or visual haptic feedback, utilisation of force output summaries and force signatures with concurrent video analysis may be more effective alternatives for both formative and summative feedback. Benchmarking expert force patterns and signatures would allow novices to goal direct their training, and also provide a quantitative approach for expert trainers to communicate expected skill requirements [263].

It would not be unreasonable to expect novices or trainees to demonstrate consistent laparoscopic task performance with safe and appropriate tool-tissue force before transferring

to the clinical setting. This would be more of a rational expectation in robot-assisted laparoscopic surgery as potential for adverse events due to absent haptic feedback is greater. In further evaluating the role of the ForSense as a training tool as well as assessment platform, agendas for future work should focus on understanding the learning curves of force in tool-tissue interaction, and efficient methods for accelerating progress along these curves such that the potential for trainees to encounter force-related adverse intra-operative events are attenuated.

In conclusion, current popular box trainer simulators can be retrofitted for enhanced objective measurements of skill, while preserving all original features. This chapter outlines development of a force sensing enhanced simulation environment (ForSense) and demonstrates construct validity for numerous force variables, as well as concurrent validity of a force error integrated scoring metric.

CHAPTER 7 INSTRUMENTATION FOR SMALL OPERATIVE WORKSPACES

Content from this chapter was submitted as:

TP Cundy, HJ Marcus, A Hughes-Hallett, T MacKinnon, AS Najmaldin, GZ Yang, A Darzi. Robotic versus non-robotic instruments in spatially constrained operative workspaces – a pre-clinical randomized crossover study. British Journal of Urology International. [accepted with revisions]

Content from this chapter was presented as:

TP Cundy, HJ Marcus, A Hughes-Hallett, T MacKinnon, AS Najmaldin, GZ Yang, A Darzi. Robotic versus non-robotic instruments for minimally invasive surgery in spatially constrained operative workspaces. 7th Hamlyn Symposium on Medical Robotics, London, UK. July, 2014.

7.1 Robotic versus Non-Robotic Instruments in Spatially Constrained Operative Workspaces – A Pre-Clinical Randomised Crossover Study

7.1.1 Introduction

As endoscopic instruments act as extensions of surgeons' hands, instrument characteristics critically impact the capability and quality of surgical task performance. Paediatric minimally invasive surgery is characterised by small and challenging operative workspaces. Instinctively, smaller instruments are better suited for these environments. However, balance exists in minimisation potential of instruments, with smaller calibre instruments risking compromise in structural rigidity, durability and concentration of force over tip surface area. As scalability limits are reached, focus shifts to design and control mechanism solutions for optimising performance capabilities. These technical goals are most tangibly achieved with robotic technology.

There is strong anecdotal opinion that robot-assisted surgery has niche roles for complex surgical tasks in diminutive workspaces [5, 265], however this remains unsupported by scientific evidence. In Chapter 5, both expert and non-expert paediatric surgeon groups identified wristed instruments as the highest rating beneficial feature of robot-assisted minimally invasive surgery in children. The aim of this chapter is to compare wristed 7 DOF robotic instruments with conventional 4 DOF non-robotic instruments for intra-corporeal suturing, and to investigate the influence of both workspace size and instrument characteristics on task performance.

7.1.2 Methods

7.1.2.1 Participants and study settings

Participants completed single intra-corporeal interrupted suture tasks in various different sized workspaces with various robotic and non-robotic instruments. The selected task was a validated component of the Pediatric Laparoscopic Surgery (PLS) simulator model described in Chapter 6 [244, 245, 247]. Intra-corporeal suturing was specifically chosen, as it is an essential bimanual technical skill for many endoscopic procedures across numerous specialty fields. This task consists of driving the suture needle through pre-marked entry and exit points on a

2/8 inch (0.635cm) size penrose drain and then tying a secure surgeon's knot (2:1:1 knot configuration).

The task was assembled within a modified PLS simulator such that it could be interchanged between three different ascendingly sized cylindrical workspaces (Figure 7.1). The 3 workspace dimensions had a constant height of 4cm and diameters of 4cm, 6cm and 8cm respectively. As such, workspace volumes were $50cm^3$, $113cm^3$ and $201cm^3$. The task was positioned at the cylinder base and the cylinder was aligned in parallel line of sight to the camera or scope such that the optical axis-to-target angle was perpendicular. The cylinders were formed by wire frame mesh that was coated with elastic foam medical tape (Microfoam™ , 3M™ , MN). The composition of the cylinders was compliant and with shape memory that was more anatomically representative than a rigid and solid structure. The instrument manipulation angle was 35 degrees and distance from the port sites to task position site was 16cm. The suture material used was a 4/0 monofilament thread that was pre-cut to 80mm.

Three pairs of needle driver instruments were compared; 3mm non-robotic instruments (Karl Storz, Tuttlingen, Germany), 5mm robotic instruments and 8mm robotic instruments (Intuitive Surgical, CA) (Figure 7.2). Port positioning was kept constant and configured according to the PLS manual [245].

To test the hypothesis that wristed robotic instruments are superior for less ergonomic vertical orientation suturing orientation, participants were asked to perform an additional vertical (sagittal plane) suture in the 8mm workspace size only. This was arranged by rotating the penrose drain 180 degrees from the default axis.

To standardise the visual quality for robotic and non-robotic study arms, all tasks were undertaken with 2-D standard definition optics. A 5mm zero degree laparoscope (Karl Storz, Tuttlingen, Germany) with all-in-one camera system (TELE PACK, Karl Storz, Tuttingen, Germany) was used for non-robotic tasks repetitions. To avoid distractions of a camera assistant, the laparoscope was mounted to a fixed Martin's Arm retractor clamp. A standard da Vinci® 12mm zero degree scope was used for robotic task repetitions. The field of view was also standardised and set such that the proximal rim of the 10mm cylinder formed the peripheral image boundary. The motion scaling setting on the robotic system was set to "fine" for all tasks.

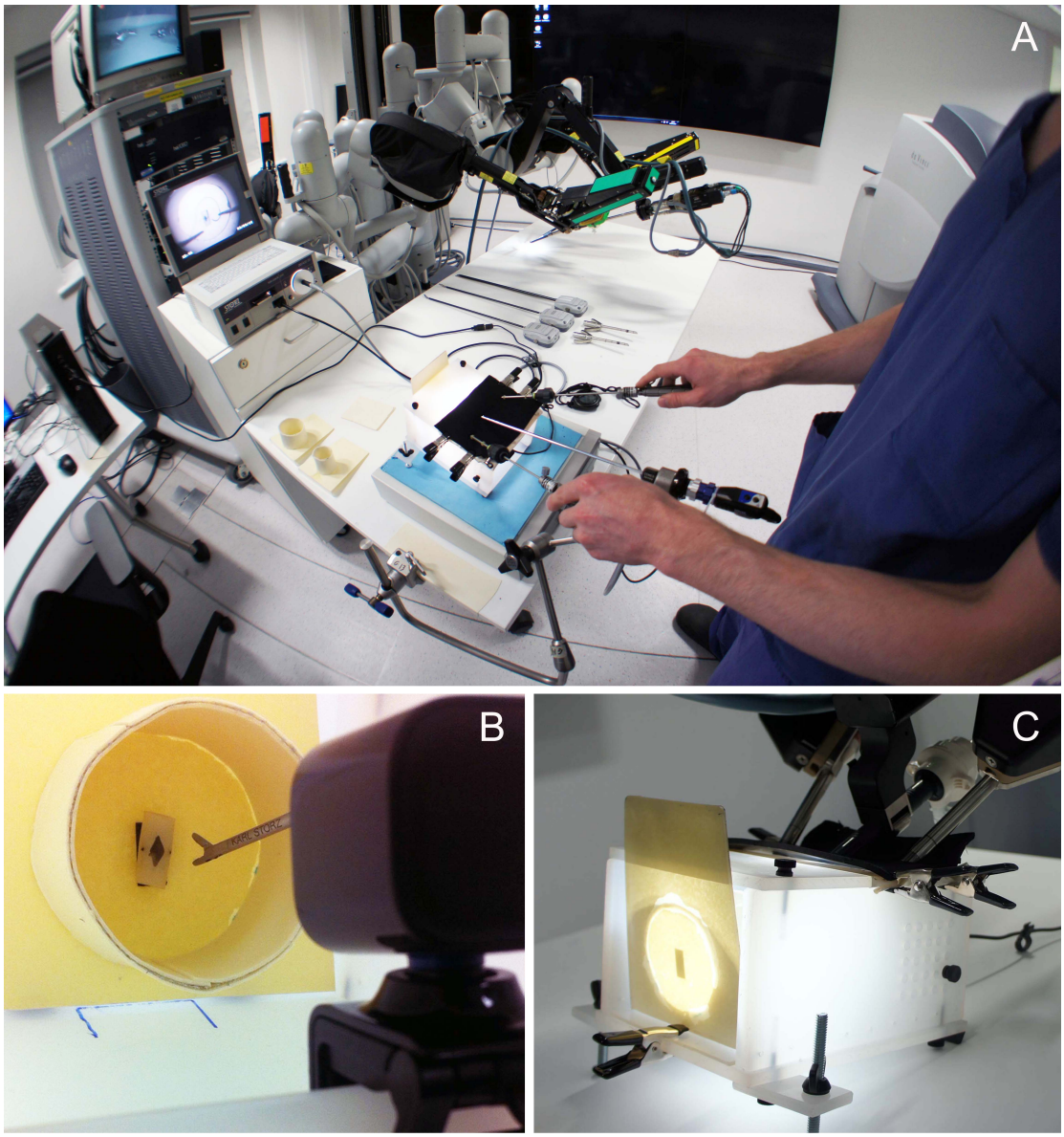


Figure 7.1 Overview of the experimental set-up demonstrating a participant engaged with the non-robotic instrument task (A), interior view of the task assembled within the PLS box trainer (B), and reverse angle view of the robot docked to the modified PLS box trainer (C).

7.1.2.2 Trial design

All participants were surgeons or surgeons-in-training recruited from one university hospital trust. A minimum proficiency standard was set for participants to be eligible for study inclusion. The eligibility criterion was successful completion of consecutive intra-corporeal suture tasks in the PLS simulator within a time cut-off of 200 seconds [245]. This was required to be satisfied with both robotic and non-robotic instruments. As this eligibility assessment process exposed participants to the experimental set-up, no further training sessions were offered for further familiarisation. Informed consent was obtained from all participants.

A randomised double-crossover design was implemented. Three randomisation sequences were run for each participant; firstly to determine order of robot or non-robotic instruments, secondly to determine order of robotic instruments, and thirdly to determine order of workspace sizes. Due to the time taken to dock and un-dock the robot, the sequence of instrument use was arranged in robotic and non-robotic blocks. A sealed opaque envelope method was used for the first 2 randomisation sequences. Envelopes were opened immediately following the eligibility screening process described above. The order of workspace sizes was randomised using an electronic allocation tool (www.random.org).

Participants performed intra-corporeal sutures with each of the 3 pairs of instruments within each of the 3 workspace sizes. With 3 additional vertical direction sutures in the largest workspace size, each participant therefore performed a total of 12 sutures.

7.1.2.3 Outcomes

Participants were instructed to complete each task repetition to the best of their ability and were blinded to the outcome measures being assessed. If the task was abandoned or unable to be completed then a maximum time of 600 seconds was recorded.

Primary outcomes were objective task scores and instrument workspace breaches. Task scores were calculated based on the validated PLS metric, incorporating task completion times and error penalties. Raw scores were not normalised. Workspace breaches were regarded as the number of times that the instrument made contact with the internal surface of the cylinder, and this was assessed post-hoc by analysing video recordings captured using a high-definition webcam (Microsoft, WA). Penalty scores were graded according to the PLS curricula that focuses on accuracy and knot security [245].

Secondary outcomes included task scores for suture orientation (vertical or horizontal), assessment of perceived task workload using the validated National Aeronautics and Space Administration Task Load Index (NASA-TLX) and post-test subjective opinions of the preferred instrument pair that a participant would choose for a laparoscopic procedure involving intra-corporeal suturing. The NASA-TLX incorporates self-reported evaluations of performance, effort, frustration, as well as mental, physical and temporal demands of the task in order to generate an aggregated workload rating.

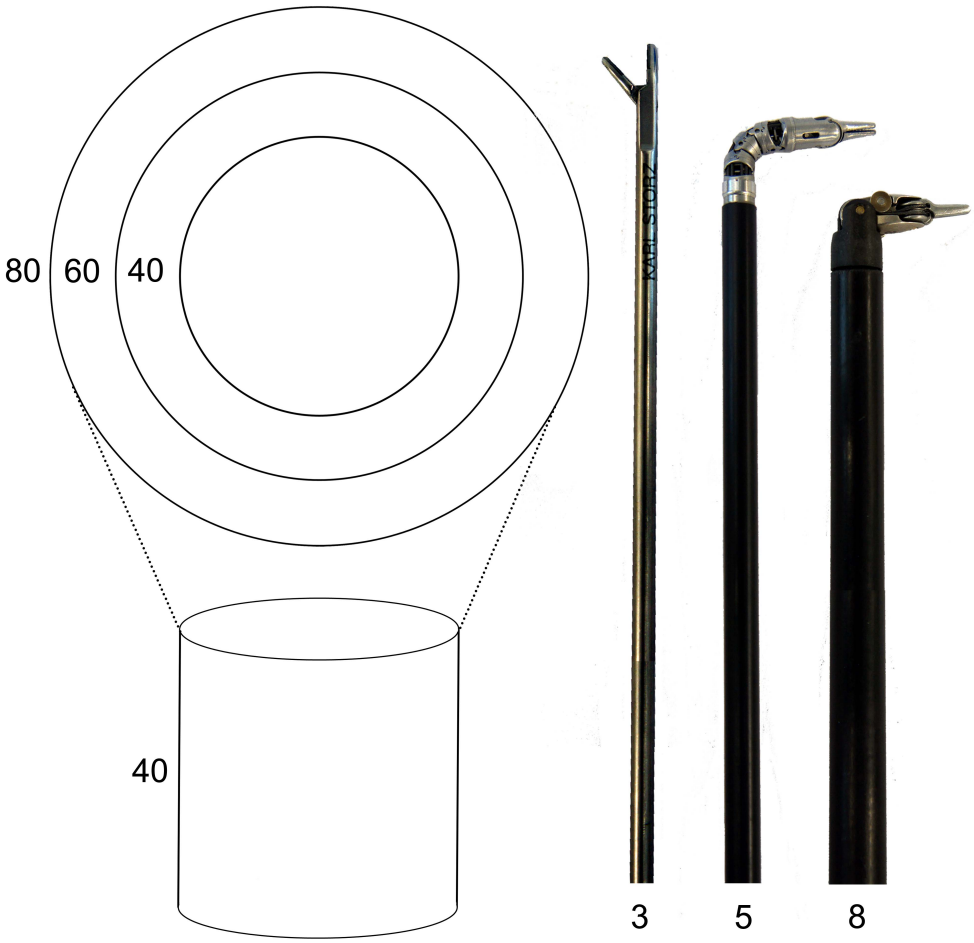


Figure 7.2 Illustrative depiction of the 3 cylindrical workspace sizes (constant height of 40mm and diameters of 40mm, 60mm and 80mm) drawn to scale alongside singular items of the 3 instrument pairs investigated (3mm non-robotic, 5mm robotic and 8mm robotic) that are each in maximum positions of distal angulation. All measurement values in millimetres.

7.1.2.4 Statistical analysis

A sample size calculation was conducted *a priori* based on experience with the PLS in Chapter 6 that determined time for intermediate-level surgeons to complete the suture task to be 200.1 ± 59.4 seconds (mean ± SD). It was estimated that to detect a 25% difference in task completion time between groups, with a two-sided 5% significance level and power of 80%, a sample size of 23 participants was required.

Median and interquartile range values were calculated for all outcome measures. Kruskal-Wallis one-way analysis of variance was used to compare outcomes between instruments and workspace sizes. If significant differences were determined, then the Mann-Whitney test was

used to further compare outcomes between 2 groups (i.e. 5mm versus 8mm robotic instruments) with the Bonferroni correction. Comparison between robotic and non-robotic instruments for suturing direction was also evaluated using the Mann-Whitney test.

Statistical significance was regarded as $P < 0.05$. Statistical analysis was undertaken using SPSS version 21.0 (IBM Corp, NY).

7.1.3 Results

A total of 23 participants performed 276 suture task repetitions. All tasks were completed successfully. Participant demographic information is summarised in Table 7.1.

Median age (IQR)	32 (4)	
Median postgraduate year (IQR)	7 (2.5)	
Gender (male:female)	19:4	
Number of laparoscopic procedures performed as primary surgeon	0 – 100 100 – 200 > 200	12 7 4
Estimated number of hours of simulation-based training involving intra-corporeal suturing	0 – 20 20 – 50 >50	14 4 5

Table 7.1 Participant demographic information (n = 23).

7.1.3.1 Primary outcomes

Overall median task performance scores for 3mm, 5mm and 8mm instruments were 421, 398 and 402 respectively (P = 0.12). Task scores were highest (best) for 3mm non-robotic instruments in all workspace sizes that were evaluated (Figure 7.3a). Scores were significantly lower when spatial constraints were imposed by smaller workspace sizes, with median task performance scores for 4cm, 6cm and 8cm workspaces being 388, 415 and 420 respectively ($P = 0.026$). Score disparity between instrument groups became most apparent in the 4mm diameter workspace size. In this smallest workspace, median scores for 5mm and 8mm instruments were 6.8% and 14.5% lower than the median 3mm instrument score, although these differences were not statistically significant ($P = 0.186$). Scores were significantly different only for tasks performed with 8mm robotic instruments across workspace sizes ($P = 0.014$, Table 7.2).

Median and interquartile range values for workspace boundary breaches are summarised in Table 7.3. For each instrument pair evaluated, significant indirect relationships were seen between boundary breaches and workspace size ($P < 0.001$, Figure 7.3b). There were also significant differences in breach counts when comparing instrument pairs for each workspace size ($P < 0.001 – 0.006$, Table 7.3). A higher number of breaches occurred with robotic instruments compared to non-robotic instruments, and these were significant when comparing 3mm versus 5mm instruments in all workspace sizes ($P <0.001 – 0.004$) and when comparing 3mm versus 8mm instruments in the smallest workspace size ($P = 0.004$).

	3 mm non-robotic instrument Median (IQR)	**5 mm robotic instrument Median (IQR)**	**8 mm robotic instrument Median (IQR)**	***P***
8 cm ∅	431 (90)	407 (77)	424 (54.5)	0.619
6 cm ∅	421 (69.5)	414 (84)	412 (81.5)	0.409
4 cm ∅	414 (126)	386 (100.5)	354 (107.5)	0.186
P	0.631	0.434	0.014	

Table 7.2 PLS task scores (higher score = superior performance) for non-robotic and robotic instruments in various workspace sizes. IQR = interquartile range, ∅ = diameter

7.1.3.2 Secondary outcomes

Vertical orientation sutures were performed with higher task scores using robotic instruments compared to non-robotic instruments, however this did not reach statistical significance (Table 7.4).

Higher perceived task workload ratings were observed for smaller workspace sizes (Figure 7.3c). NASA-TLX ratings were significantly different for 8mm robotic instruments only, with median values of 57, 61 and 73 for 8cm, 6cm and 4cm workspace sizes respectively ($P = 0.038$). Ratings between instrument pairs were not significantly different amongst each workspace size.

When asked to select one instrument pair for preferred clinical use, 3mm non-robotic (10/23, 43.5%) and 8mm robotic instruments (10/23, 43.5%) were equally favoured, whereas the 5mm instruments were the least favoured (3/23, 13%).

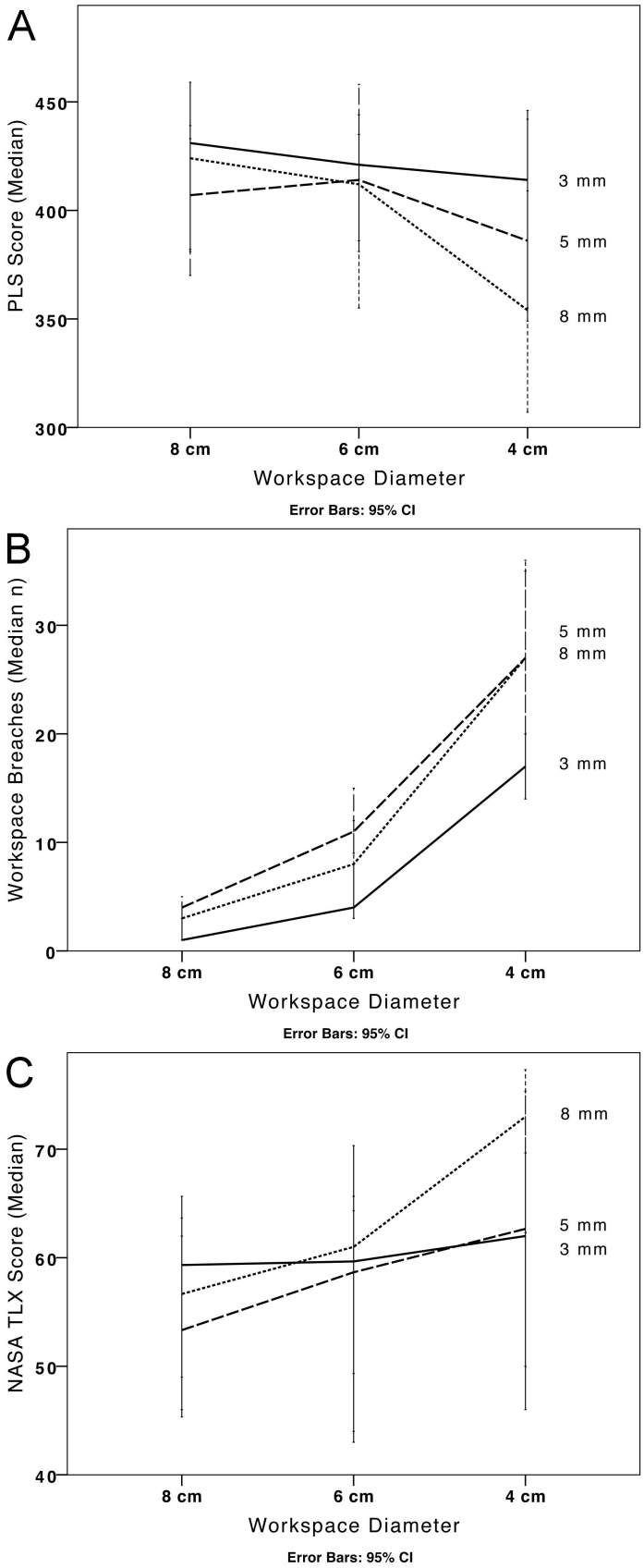


Figure 7.3 Objective task scores (higher score = superior performance) (A), workspace breach counts (B), and perceived task workload scores (higher NASA TLX score = higher workload) (C) for instrument pairs amongst the workspace sizes investigated.

	3 mm non-robotic instrument Median (IQR)	5 mm robotic instrument Median (IQR)	8 mm robotic instrument Median (IQR)	*P*
8 cm ∅	1 (2)	4 (2)	3 (2)	0.006
6 cm ∅	4 (5)	11 (6.5)	8 (9)	<0.001
4 cm ∅	17 (8)	27 (18.5)	27 (17.5)	0.003
P	<0.001	<0.001	<0.001	

Table 7.3 Workspace boundary breaches for non-robotic and robotic instruments in various workspace sizes. IQR = interquartile range, ∅ = diameter

	Non-robotic instruments Median (IQR)	Robotic instruments Median (IQR)	*P*
Horizontal suturing	431 (90)	418.5 (62.75)	0.383
Vertical suturing	395 (124.5)	421.5 (57.75)	0.633
P	0.553	0.827	

Table 7.4 PLS task scores (higher score = superior performance) for horizontal and vertical suture directions performed with non-robotic and robotic instruments. IQR = interquartile range.

7.1.4 Discussion

Conceptually, there are numerous features of robotic surgical systems that *should* facilitate enhanced operative performance in small workspaces. These technological attributes include tremor elimination, motion scaling, increased dexterity, comfortable ergonomics, improved visuomotor coordination, stereoscopic vision and optical magnification. However, the larger diameter, articulating design and bulkier form of commercially available robotic instruments pose dimensional limitations for which they can be physically accommodated in a safe and effective manner.

These findings indicate that the influence of spatial constraints negatively impacts performance capabilities for both non-robotic and robotic instruments. The degree to which performance is restricted is proportional to instrument size, with larger instruments being most impaired and vice-versa for smaller instruments. In spatially constrained workspaces ≤200cm^3, 5mm and 8mm robotic instruments do not confer an objective or subjective advantage over 3mm non-robotic instruments for an advanced bimanual task. At more

extreme workspaces sizes of 50cm^3, inferiority of 5mm and 8mm robotic instruments became evident compared to 3mm non-robotic instruments.

The spatial dimensions investigated are clinically relevant for a variety of anatomical locations in which feasibility of robotic surgery is currently being marketed towards and clinically assessed; such as the deep pelvis, oropharynx, transanal approach to the rectum, mediastinum, retroperitoneoscopic space, anterior neck for endoscopic thyroid surgery, and the infant thorax and abdomen. In many of these relevant fields, various age, weight, and anthropomorphic measurement cut-offs have been described to guide eligibility of robot-assisted approaches for specific procedures. These are based on reports of early clinical experiences in which major challenges were encountered due to principal issues of lack of operative domain despite mitigating measures such as strategic port site placement, patient positioning and retraction or decompression of neighbouring anatomical structures. In paediatric surgery, Meehan *et al* have described a patient weight threshold of 3kg for robot-assisted laparoscopic procedures and 4kg for robot-assisted thoracoscopic procedures [7]. Marchini *et al* have suggested that candidates for robot-assisted laparoscopic intravesical procedures require bladder capacity greater than 200mL [266].

Intracorporeal suturing was chosen as the task for this chapter as it is a well-validated simulation curriculum component that is clinically relevant. The ability to suture a quality visceral or vascular anastomosis is one of the most advanced skills to master in endoscopic surgery. It is this somewhat prohibitive technical step that is felt to limit many relevant procedures from being undertaken via a minimally invasive approach in circumstances when semi-automated tissue approximation devices are not appropriate. Improved process (e.g. time, error) and outcome-based (e.g. anastomosis integrity) results for robot-assisted suturing compared to conventional laparoscopic suturing have consistently been reported in a diverse range of laboratory and *in vivo* studies [178, 267-271]. Only a small number of studies have specifically examined suturing in spatially constrained settings. Thakre *et al* observed that suture task performance times and scores significantly improved with larger cube-shaped workspace sizes (125cm^3, 216cm^3, 343cm^3, 512cm^3 and 3,375cm^3 range) using 8mm robotic instruments [11]. Interestingly, workspace size did not influence performance for three different basic tasks such as a pick and place drill [11].

7.1.4.1 Instrument size

This study highlights the importance of both instrument size and design for use in small operative workspaces. Based on results from this chapter, instrument size should be regarded as the priority consideration. This is logical as millimetres are a luxury in extreme workspace constraints; larger instruments not only obscure the field of view but also compromise an already limited volume of manoeuvreable space. Lee *et al* have previously demonstrated intracorporeal knot tying to be significantly faster using 3.5mm non-robotic instruments compared to 5mm non-robotic laparoscopic instruments in a neonatal box simulator with 40mm diameter endoscopic field of view [272].

Selection of instruments for comparative assessment in this study included the smallest available robotic and non-robotic laparoscopic needle holders. Until recently, 2mm non-robotic instruments were commercially available. These mini-laparoscopy instruments were fragile and prone to breakage during routine use. There were also concerns regarding adequate shaft stiffness tissue manipulation requirements and concentration of force at fine distal ends. Likely contributed by these fundamental technical drawbacks, 2mm instruments have been made obsolete from manufacturing. The da Vinci® instrument range is limited to 5mm and 8mm ranges and as indicated in the survey study in Chapter 4, this is far from ideal for paediatric patient use. The 5mm range was released in 2004 and is more expensive than 8mm instrument counterparts.

7.1.4.2 Instrument design

Distances from the instrument tip to the proximal articulation axis are 28mm and 18.5mm for the 5mm and 8mm robotic needle holder instruments respectively. These differences in articulating segment length mean that the '*gooseneck*' 5mm instruments need more room to manoeuvre and are paradoxically less well suited for smaller operative workspaces. This explains the unpopular subjective impressions that these instruments received in this study and reasons for critical opinion in the clinical literature [10, 273]. The longer curve radius of the 5mm robotic instrument continuum wrist design undoubtedly accounts for the higher workspace boundary breach counts that were observed compared to 8mm robotic instruments that possess a compact proprietary EndoWrist® (Figure 7.2).

In this chapter, workspace breaches were considered as a proxy safety measure. Controlled or uncontrolled instrument clashes with structures in the periphery of the operative field have

the potential for unintended tissue injury. Theoretically this is more of a concern with robotic instruments due to complete absence of haptic feedback. Additionally, it could be expected that collisions with semi-fixed boundaries in the experimental set-up would be represented *in vivo* as instruments being momentarily lost from the field of view, and this also poses safety concerns.

7.1.4.3 Future needs for robotic instruments

There is now empirical evidence to justify a degree of clinical caution when contemplating robot-assisted minimally invasive surgery that involves intracorporeal suturing (or similarly advanced bimanual tasks) within endoscopically accessed anatomical regions less than 200cm^3. Future challenges for enhancing robotic instrument design to bridge this technical gap will require efforts towards miniaturisation, shortening articulating segment curve radius length, limiting degree-of-freedom redundancy, and optimising extracorporeal arm configurations to diminish external collision. Several non-robotic and robotic tools are emerging such as the Endo Stitch™ devices (Covidien, Dublin, Ireland) and Smart Tissue Anastomosis Robot (STAR) [274]. Many of these developments offer promising solutions to expand minimally invasive surgery to indications that currently lack enabling technology. Some of the most restrictive workspace sizes that this applies to include procedures such as congenital diaphragmatic hernia and oesophageal atresia repair in infants where the endoscopic operative field is estimated to be as small as 27cm^3 [3, 147].

7.1.4.4 Limitations

There are countless possible variations in equipment and ergonomic configuration for the experimental set-up that was used in this chapter. Although set-up arrangements were felt to be representative of optimal conditions [275], adjustments in factors such as port positioning, distance to target site, suture needle/thread selection and robot docking might yield differences in outcomes [275]. The port positions and remote centres of motion (RCM) remained constant for all tasks so that this factor did not act as a confounding variable. Generalising the context of this laboratory experiment to the clinical environment would involve appropriate port re-location for varying operative workspaces. In investigating this, Thakre *et al* found that proportionally scaling port separation distance with sequentially down-sized workspaces resulted in major external robotic arm collisions that prevented use of the robot in workspace sizes ≤125cm^3 [11].

The default stereoscopic optics on the da Vinci® were disabled for this study in order to standardise the visual quality across each instrument group evaluated. This may have disadvantaged performance of tasks undertaken with the robot as 3-D vision might have a synergistic effect on overall functionality of the robotic system [79, 270, 276]. Moorthy *et al* have previously demonstrated that 3-D vision improves economy of hand movement by 10 – 15% in robotic suturing tasks [270]. This same study however also reported superior task performance time and error outcomes for both 2-D and 3-D robotic suturing compared to conventional laparoscopic suturing in an adult sized box trainer [270]. If optical set-up was standardised to 3-D in this study, it would be fair to assume that many of the same advantages of 3-D vision would be applicable to outcomes in both robotic and non-robotic instrument groups.

Background experience in conventional and robot-assisted laparoscopic surgery was not universally homogenous in the study cohort. This is reflective of the spectrum of mixed experience that broadly exists for technology adoption in clinical practice. While it would be ideal for study participants to have parallel abilities with robotic and non-robotic minimally invasive techniques, few surgeons, if any, would be equally facile in both. Study eligibility criterion was based on previous construct validity data for the PLS simulator that meant all participants demonstrated baseline proficiency prior to enrolment.

Lastly, suturing is one discrete aspect of an overall surgical procedure, just as instrument characteristics are one component of an overall robotic system. These factors must be acknowledged when interpreting the generalisability of the findings of this chapter.

In conclusion, the influence of smaller workspaces limits performance of robotic and non-robotic instruments. In spatially constrained operative workspaces less than 200cm^3, 3mm non-robotic instruments are better suited for advanced bimanual operative tasks such as suturing in comparison to larger diameter 5mm and 8mm robotic instruments. Future robotic instruments need further size and design characteristic optimisation if this technology is to be uniquely advantageous for clinical roles that involve endoscopic access to workspace restricted anatomical areas that correspond to dimensions investigated in this chapter.

CHAPTER 8 POSITION STATEMENT & NEXT-GENERATION SURGICAL ROBOTS

Intellectual property related to this chapter was filed as:

Title:	CYCLOPS: A Smart Versatile Robotic Tool for Single-Port Access and Natural Orifice Endoscopic Surgery
Inventors:	G Mylonas, **TP Cundy**, GZ Yang, AW Darzi
Applicant:	Imperial College Innovations Ltd
Patent number:	1316333.2
Filed:	13th September, 2013

Content from this chapter was published or submitted as:

V Vitiello, SL Lee, **TP Cundy**, GZ Yang. Emerging robotic platforms for minimally invasive surgery. IEEE Reviews in Biomedical Engineering. 2013;6:111–126.

G Mylonas, V Vitiello, **TP Cundy**, A Darzi, GZ Yang. CYCLOPS: a versatile robotic tool for bimanual single-access and natural-orifice endoscopic surgery. Proceedings of the 2014 IEEE International Conference on Robotics and Automation.

Content from this chapter was presented as:

TP Cundy, NK Patel, J Shang, CA Seneci, CJ Payne, V Vitiello, J Clark, JP Teare, AW Darzi, GZ Yang. Per-oral endoscopic cardiomyotomy and pyloromyotomy using a flexible snake robot – proof of concept with a porcine model. 6th Hamlyn Symposium on Medical Robotics, London, UK. June, 2013.

V Vitiello, **TP Cundy**, A Darzi, GZ Yang, GP Mylonas. Augmented instrument control for the CYCLOPS robotic system. 7th Hamlyn Symposium on Medical Robotics, London, UK. July, 2014.

8.1 Robotic Surgery in Children – Adopt Now, Await, or Dismiss?

8.1.1 Introduction

The diffusion path of innovative technologies in surgery is dynamic and intriguing in its unpredictability. Robotic systems for minimally invasive surgery have arguably been the most dominant technology item to be introduced to paediatric surgery in recent years. It remains uncertain what direction the diffusion trajectory of robotic surgery will follow in years to come and what its eventual fate might evolve towards. Numerous stakeholders weigh in to the debate regarding robotic surgery. These include clinicians, hospital administrators, healthcare economists and policy makers, industry, patients, parents, and others. Often these groups have competing interests and this contributes to a mixture of partisan voices that have unequal exposure to respective audiences. This chapter aims to distil the confusing argument about the role of robot-assistance in paediatric surgery into a decision-making taxonomy; to adopt this technology 1) *now*, 2) *later*, or 3) *not at all*. As scientific evidence is the great arbitrator of modern clinical practice, an evidence-based approach is used to address each of these in turn before committing to a position statement.

8.1.2 Adopt Now

Trends in the literature and from national inpatient databases indicate that paediatric robot-assisted minimally invasive surgery is continuing to grow in global adoption [89, 90, 277, 278]. Findings in Chapter 2 indicate that the pattern of uptake appears to be progressing along the early phase of the characteristic S-shaped diffusion of innovation curve [89, 194] (Figure 8.1). Numerous case reports, case series and comparative studies have unequivocally demonstrated that robotic surgery in children is *safe*. Initial concerns regarding potential danger relating to electronic equipment malfunction and system instability have been conciliated, with no known reports of patient harm due to these factors [89].

Fundoplication and pyeloplasty are the standout applications at present [89]. Collectively, these procedures comprise an estimated 46% proportion of overall volume of robotic procedures performed in children [89]. In Chapter 3, meta-analyses of comparative effectiveness literature for these 2 procedures has identified that clinical outcomes are mostly either comparable or marginally superior to alternative techniques [279, 280].

The spectrum of pathology encountered in paediatric surgery is epitomised by incredible variety of infrequently encountered operative indications. As a consequence of this, it is unlikely that quality comparative effectiveness evidence will ever emerge for many lower volume procedures that robot-assistance is promoted towards, such as Mitrofannof appendicovesicostomy and excision of choledochal cyst. When unexpectedly faced with a rare and complex reconstructive procedure, it would be fair to offer surgeons the best technology that is available to enhance their operative abilities and aid them to achieve the best possible patient outcomes.

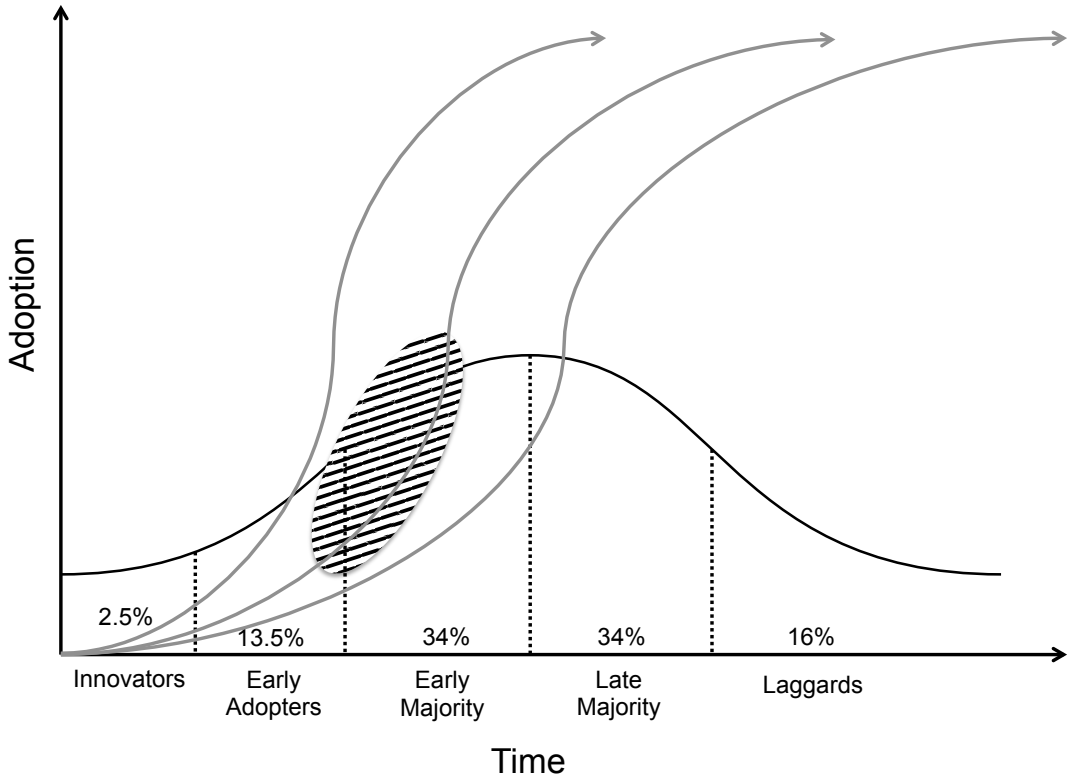


Figure 8.1 The theoretical S-shaped diffusion of innovation curve that is based on the seminal work of Everett Rogers (grey sigmoid curved line) [194]. A 'tipping point' region of the curve is shaded that typically represents a point of rapid and irrevocable adoption, often triggered when 15-20% overall adoption is reached [22].

One of the most persuasive arguments in support of the role of robot-assisted surgery is that it more broadly enables a minimally invasive approach in circumstances when it otherwise might not be offered [23]. This is supposedly due to various technological enhancements lowering the degree of difficulty for a specific procedure. Clearly there are some experts that have mastered conventional laparoscopic or thoracoscopic techniques and do not find added benefit from robot-assistance, however these advanced skills are not universally shared.

Several large North American national coding database studies have shown increasing rates of paediatric minimally invasive pyeloplasty in recent years that is attributed to the growing uptake of the robot-assisted technique [90, 277, 278]. For the argument that robot-assisted surgery may "*democratise*" minimally invasive surgery, it should be regarded as an *adjunct* to support propagation of laparoscopy and thoracoscopy in settings where its uptake has barriers using non-robotic technology.

The ergonomic set-up of the robotic system master console is unique and offers unrivalled comfort for the surgeon. This reduces physical fatigue, discomfort and risk of musculoskeletal injury for the surgeon that in turn may possibly lead to improved patient outcomes by means of a less physically inhibited surgeon [107, 281]. Particularly in an ageing workforce, long-term physical health benefits for the surgeon offers an incentive for use [107].

Finally, it is hard to imagine a major item of technology that has diffused as far as robotic surgery only to later be abandoned. Institutions currently practicing paediatric robot-assisted surgery have vested reason to persist with their robotic surgery service in order to seek return on their considerable capital investment. Hospitals around the world are continuing to purchase new da Vinci® Surgical Systems despite the major cost deterrent, suggesting that robotic surgery is here to stay.

8.1.3 Dismiss

The da Vinci® Surgical System is a generic platform that was fundamentally designed with the adult patient in mind. Intuitive Surgical initially targeted its use towards cardiac surgery, specifically the coronary artery bypass graft procedure. Approximately 90% of its global clinical application usage is now in urology and gynaecology for assorted organectomies [282]. In general, the approach for the da Vinci® Surgical System has been to find a clinical need for a multi-purpose technology, rather than to specifically design a technology for a targeted clinical need. More so for paediatric surgery than any other specialty, it has been a technology and industry led *"push"* instead of a clinical need driven *"pull"*. The technology isn't suited for small paediatric patients in its current form, and there are few signs of optimism that Intuitive Surgical will deliver a technological remedy to this anytime soon. Paediatric surgery is described as an "*orphan*" field for commercial scale innovation due to unappealingly small gross market capacity for which to seek profit through purposefully designed products [283]. Even amongst some adult specialties for which the technology is size appropriate, there has been a recent movement of diminished enthusiasm and even

dissonance [136, 284, 285]. One might interpret this disposition to be consistent with a post-peak phase of the Hype Cycle curve (Figure 8.2).

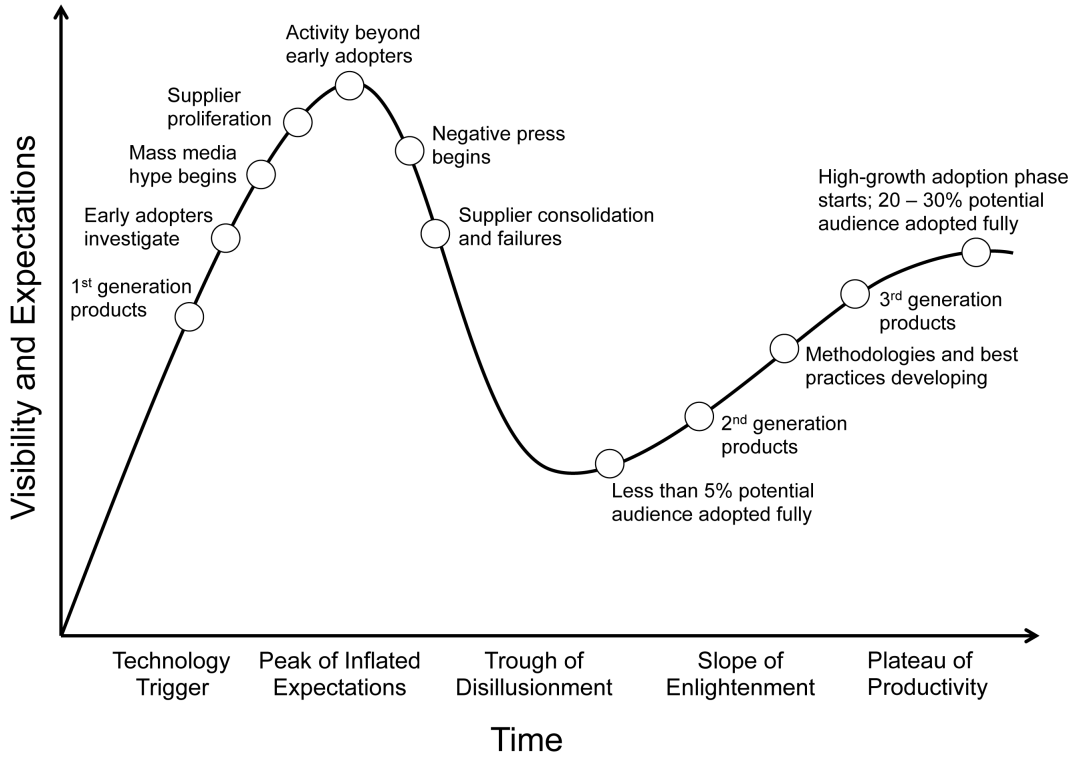


Figure 8.2 The Gartner Hype Cycle curve is a graphical tool that represents the maturity, adoption and social application of specific technologies (Gartner Inc., CT). It categories the predicted evolution of a technology into 5 key life cycle phases.

Healthcare spending is under intense pressure of budget restraints and prioritised distribution of resources. Medical care has arguably never been more expensive. Any new technology in a modern healthcare system must prove cost-effectiveness to be considered viable. The cost-benefit ratio for first-generation robotic surgical systems is heavily skewed towards cost. Even if costs were neutral between robot-assisted surgery and existing alternatives, the clinical relevance of outcome benefits are questionable, even if statistically significant. Underneath the illusion of marketing hype, this new technology is not necessarily better for the patient and lacks strong evidence to justify added costs.

For an individual surgeon, surgical department or institution to commit to investing in establishing a hospital programme, the technology must be *accessible*. Herein lies the major obstacle. Costs associated with the da Vinci® Surgical System are enormous. For all but a small number of well-financed tertiary institutions in the developed world, robotic surgery is financially inaccessible. The two da Vinci® Surgical Systems in use for paediatric surgery in

the United Kingdom were funded through long processes of charity fundraising and generous philanthropic donations. Maintenance and consumables costing remain a challenge in addition to the fact that every da Vinci® Surgical System becomes outdated every 5 – 10 years as new models are released and old models become unsupported by the manufacturer.

Opportunity cost and cost inaccessibility generates important ethical debate [286]. Should something that so drastically widens healthcare inequality be endorsed [286]? An underestimate of the capital outlay for a latest model da Vinci® Surgical System would be £2,000,000. For a fraction of the same amount of money a range of *non-robotic* equipment can be purchased to provide some of the more popular features of robotic systems, such as a state-of-the-art 3D HD laparoscopic stack [287-289], manually articulated instruments [290] and devices to facilitate intra-corporeal suturing [291]. One could also propose that expenditure of this money might better invested in a resource *unlimited* training strategy for *non-robotic* minimally invasive surgery, that might include funding for a modern multi-modal simulation laboratories and travel to recognised centres of excellence for intensive one-on-one proctorship. The rationale for this is that highly skilled laparoscopic or thoracoscopic surgeons find little added benefit with robot-assistance, and there does not seem to be any procedure that is accomplishable *only* with robot-assistance. Overall, this approach of investment in *human training* rather than *technology acquisition* would have more lasting permanency and broader return. Technology ages and eventually expires, whereas in the right environment, human skill develops further with experience and also may be transferred on to colleagues in order to produce perpetuating longevity.

The procedural breakdown and case volume of paediatric urology and general surgery differs to adult counterpart specialties. For example, prostatectomy, cystectomy and partial nephrectomy make up a considerable portion of the overall case distribution and volume for an adult urologist. So much so, that the clinical practice of some urologists is geared to solely perform robot-assisted prostatectomies in concentrated high volume. Probably the leading example of this approach is Dr Vipul Patel of the Global Robotics Institute in Florida who has a personal series of over 6,000 robot-assisted prostatectomies. The most recent analysis of cost and hospital volume for robot-assisted prostatectomy was undertaken by Barco *et al* in Victoria, Australia. They found that a per hospital case volume quota of at least 140 procedures was required each year for cost to return a net positive for the public healthcare system. There are few, if any, paediatric robot-assisted procedures that could be classified as high volume and reach > 140 cases per hospital per annum. For the current direct and indirect financial costs of robotic surgery, necessary case volumes are not sufficient for its use to be

economically sustainable in paediatric surgery, especially in centres for which da Vinci® Surgical Systems are not shared with other specialties.

8.1.4 Await

As aptly described by Professor Craig Peters, "*similar to children, new technologies do not spring forth in mature form but, rather, require time for development and refinement*" [292]. First-generation robotic systems are immature for ideal paediatric use [160, 293]. Early adopters and enthusiasts of robotic surgery no doubt see the future potential [160]. Their early buy-in contributes to a process of active engagement with the field such that various iterations can be evaluated in context, relative strengths and weaknesses can be exposed, and ongoing development can be guided towards meeting the needs of their clinical practice.

The nature of digital age technology is that of rapid advancement. Moore's Law dictates that the processing power of computers doubles every year based on the number of transistors per inch on integrated circuit boards. The earliest computers were a similar size to current da Vinci® Surgical Systems, and over the years have evolved to become smaller, cheaper, more accessible, and remarkably more intelligent (Figures 8.3 and 8.4). Progress of software for robotic surgical systems seems to have outpaced the progress of hardware components. Hardware design and material barriers limit miniaturisation of instruments. Time is needed for new micro-motors or superior tendon biomaterials to be developed and integrated into sub-5mm sized instruments.

On the horizon are ultimate goals of micro- or even nano-bots that may wirelessly enter and exit the body in a silent but pervasive manner to accomplish surgical tasks [294]. This would represent entirely new paradigms of surgery such as the "*swallowable surgeon*" [294]. In the more imminent years ahead, we can expect to see an array of sophisticated cooperatively controlled hand-held robotic tools that serve to aid both open and minimally invasive surgery. Features of these hand-held tools would include tremor suppression for microsurgery, haptic feedback sensing capabilities, mechatronic articulation, and force control for cellular level "*optical biopsy*" using probe-based confocal laser endomicroscopy [295]. Perhaps the most exciting potentials of robot-assisted surgery lie in the embedment of complex computers directly within the operating environment. The possibilities facilitated by this are subject to highly active areas of research that are yet to be fully exploited and clinically translated. Concepts being explored include active constraints (i.e. invisible "*no-fly zone*" boundaries set within the operative field so that instruments can safely be prohibited

from entering areas of critical anatomy), semi-automated task performance (i.e. programming a suture line to be performed with the precision and control expected of an automated industrial sewing machine), and augmented reality (i.e. simultaneously superimposing or aligning registered pre-operative or intra-operative imaging onto the operative field of view to provide surgeons with "*x-ray vision*") [3, 201, 296]. To reject and abandon first-generation rigid multi-arm robotic systems would cause serious detriment to the motivation of academic institutions and R&D groups pursuing more advanced and better-suited robotic technologies for future clinical use.



Figure 8.3 IBM launched the 305 RAMAC in September 1956. This was the first computer with a hard disk drive. To demonstrate its impressive portability at the time, this 5 MB computer weighing over 1000kg is captured being loaded into a Pan-American Airways plane. Portable hand-held 1,000,000 MB (1 TB) USB flash drives are now commonly available and affordable for everyday community use.

Some are waiting for more evidence to accumulate to make more informed decisions on whether to reject or accept robotic surgery. The speed of technical progress has generally exceeded the speed of scientific evaluation. Comparative effectiveness studies comprise only 14% of the paediatric robotic surgery literature base, however more of these informative studies are becoming available [89]. Others feel that it is not yet reasonable to compare

outcomes between new *versus* established techniques due to disparate positions of most surgeons along respective learning curves (Figure 8.5). In this regard, more favourable evidence might be expected to appear with time, although it would be prudent to remain wary of Buxton's Law that reminds us that "*it is always too early until, unfortunately, it's suddenly too late*" [191].

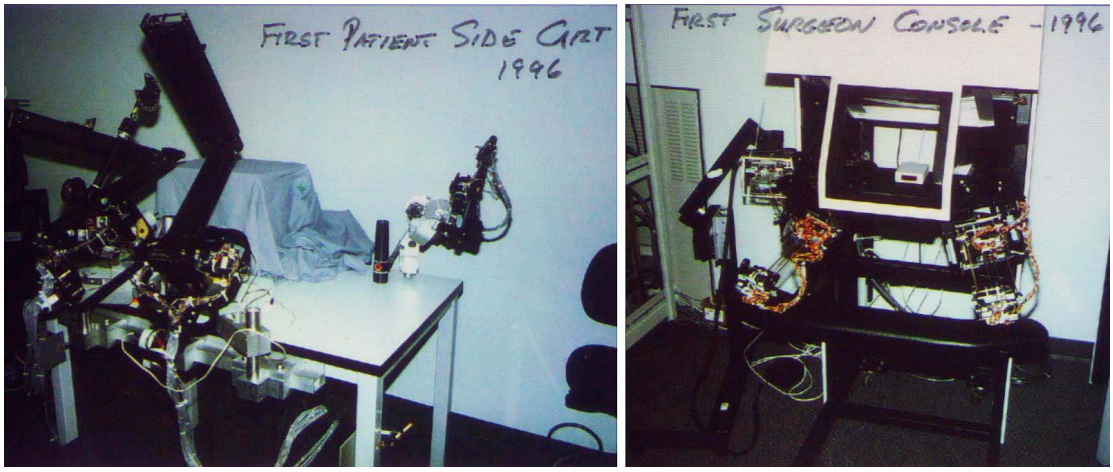


Figure 8.4 First prototype master console and slave component for the da Vinci® Surgical System, pictured in 1996.

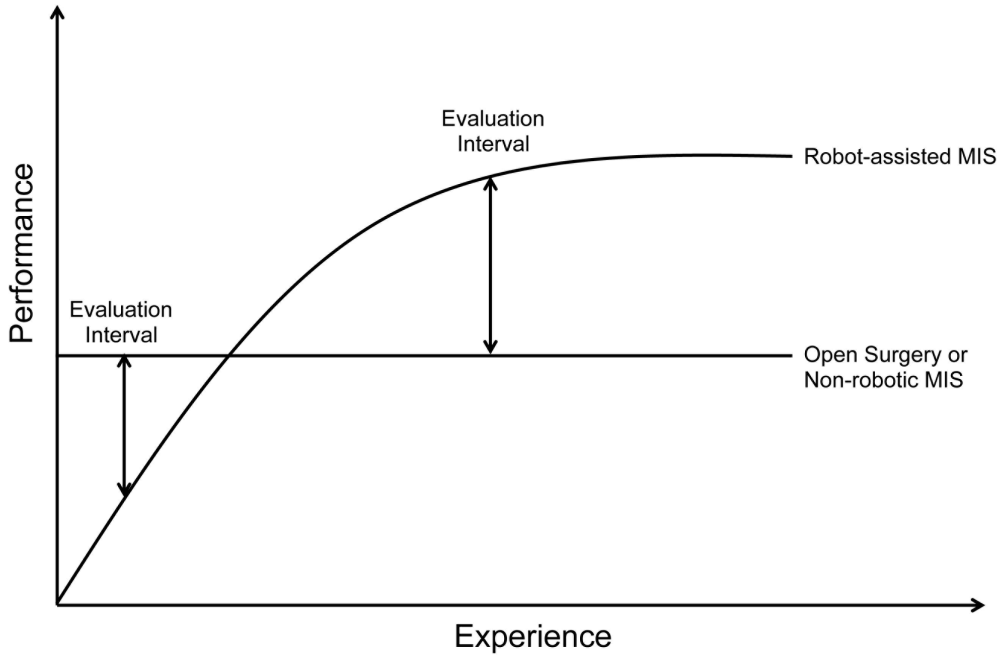


Figure 8.5 Schematic diagram illustrating the speculative effect of different evaluation intervals on comparative outcomes when established techniques of plateaued learning curve status are compared with new techniques that require further experience to overcome the learning curve. Adapted from Ramsay *et al* [191].

If cost was removed from the innovation-decision process then the argument for robot-assisted surgery suddenly becomes less debatable. Healthy market competition is needed to stimulate impetus for price trajectory reversal. The history of CT scanners is an excellent example of how market competition can stimulate dramatic cost reductions and propelled technology adoption. There are at least 20 different robotic surgical system prototypes that are being developed around the world by various academic and industry groups [193]. Each of these is in different stages of being driven forward through pre-clinical testing phases. One system that is close to clinical translation is the SPORT™ (Single Port Orifice Robotic Surgery) Surgical System that is being developed by Titan Medical (Titan Medical Inc., Toronto, Canada). Advertisement on the company web page announces that this system is expected to be commercially available in late 2015 (www.titanmedicalinc.com). Almost simultaneously, Intuitive Surgical will be launching its own new single-port system, the da Vinci® Sp™ (Figure 8.6). At the time of writing, final specifications for the Sp™ system are yet to be publically available, however the estimated port size diameter is approximately 25mm with a required insertion length of approximately 75mm for instrument deployment [297].



Figure 8.6 The da Vinci® Sp™ System that is due to be commercially available in 2015.

Encouragingly, several prototype paediatric-specific robotic platforms and devices have also recently been reported. The KidsArm project based at The Hospital for Sick Children in Toronto has secured substantial funding to develop a compact single-port image-guided robotic arm for automated suture anastomosis. *Ex vivo* validation data for this platform has

recently been presented [298]. The Smart Tissue Anastomosis Robot (STAR) is under development at the Sheikh Zayed Institute for Pediatric Surgical Innovation at Children's National Medical Centre in Washington DC. This surgical robot is intended to improve the quality, consistency, accuracy and efficiency of paediatric laparoscopic suturing [274]. Core system components include an actuated suturing tool mounted on a lightweight robotic arm with an on-board force-sensor and monoscopic camera. Both manual and automatic modes may be used [274]. In automatic mode, the surgeon visually outlines the contour of the planned suture line (linear and non-linear) and the STAR then proceeds to place sutures at specified intervals using a visual tracking algorithm. Data from preliminary experiments on silicone phantom models indicates that in either mode the STAR is up to 4 time more consistent and 5 times faster than surgeons using the da Vinci®, and 9 times faster than surgeons using conventional laparoscopic instruments [274]. A stapling tool based on the STAR concept is supposedly also under development [274].

Procedure-specific robotic technology for paediatric surgery is emerging. A customised Smart Surgical Robot (SSR) for oesophageal atresia and tracheo-oesophageal fistula repair has been designed and assembled by Liu *et al* at Kyushu University Hospital in Japan [299]. This robotic system is intended to be used for open surgery to improve manual dexterity and visualisation within the small confines of the infant hemithorax. It is configured to work within a $27cm^3$ workspace. Early pilot experiment results demonstrate proof-of-concept on dry-lab simulation tasks [299]. The Pediatric Cardiac Bioengineering Lab led by Pierre Dupont at Boston Children's Hospital are investigating the role of a robotic implant for gradual controlled apposition in long-gap oesophageal atresia [300]. The proposed device is a small lightweight motorized implant that is surgically fixed to both the proximal and distal oesophageal pouches via rigid suture rings and then remains *in situ* 'floating' within the right mediastinum [300]. *Ex vivo* work on fresh porcine oesophagus specimens has investigated tractional force responses with a functional prototype [300]. The prototype is currently sized for a 2-year old child. Ongoing work will focus on challenges of miniaturisation, as well as wireless powering and defining exact force requirements.

8.1.5 Position Statement

The most compelling of the 3 arguments presented is to *await* ongoing and future developments in the field and as such, this is the position statement of this thesis. The practice of surgery remains one of the few fields of profession that has not yet fully embraced computer technology. The world is becoming more digital and fast approaching the

ubiquitous computing paradigm. As remarked by Berlinger, "*surgery is going digital…it is no longer about blood and guts but bits and bytes*" [5]. Today's first-generation robotic surgery systems are designed to replicate existing minimally invasive procedures. Second-generation robotic surgery systems that are *awaited* will offer technology to enable *new* procedures that are more minimally invasive than procedures currently performed. While it is notoriously unreliable to forecast too far forward, it could be expected that third-generation robotic surgery systems will enter a *personalised* healthcare era where robotic instruments, sensors, implants, transplant organs, tissue scaffolds, targeted pharmaceuticals and integrated imaging are all individualised for each patient. While this may seem far-fetched, exciting related concepts such as in-the-home 3D printers are only several years away from general community availability. Earlier this year, Rankin *et al* reported their experience of 3D printing surgical instruments using a commercially available computer software package and printer [301]. In 90 minutes they were able to print a surgical retractor that met all sterility and functional requirements to be ready for immediate clinical use. The cost of raw material was USD $0.46 and estimated overall cost was approximately 1/10th of a regular stainless steel instrument. Progress in robot-assisted minimally invasive surgery will undergo dramatic and rapid changes in years to come. These advancements have much to offer paediatric surgery and will be worth *waiting* for. As a prelude to what might be anticipated with second-generation robotic surgery systems, Chapters 8.2 and 8.3 will introduce two novel single-shaft flexible robotic system prototypes under development at Imperial College London.

8.2 Per-Oral Endoscopic Cardiomyotomy and Pyloromyotomy using a Flexible Snake Robot – Proof of Concept with a Porcine Model

8.2.1 Introduction

Surgical innovators are pursuing a second renaissance period in minimally invasive surgery. The first period was defined by a revolutionary shift from traditional large open surgical incisions to multiple small '*key-hole*' incisions. This transition inferred many patient benefits, contributing to acceptance of minimally invasive surgery as standard surgical care in many settings. Today, there is growing momentum towards further minimising access trauma such that many procedures may be essentially '*scarless*' when performed via single-port laparoscopic surgery (SPLS), natural orifice endoluminal surgery (NOES) and natural orifice translumenal endoscopic surgery (NOTES) techniques (Figure 8.7).

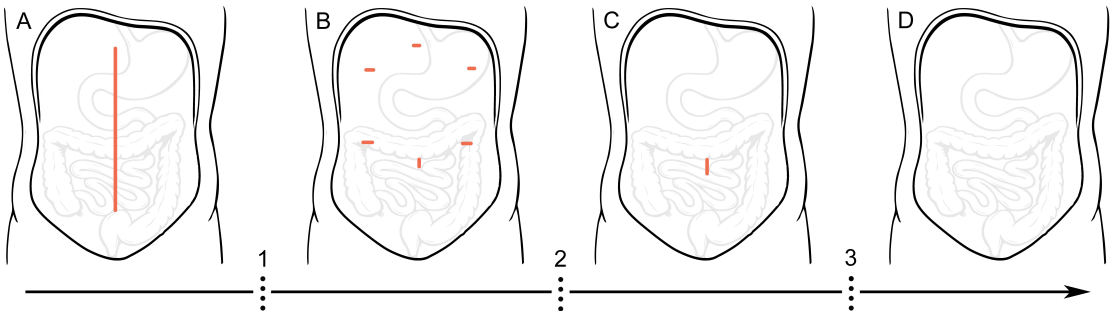


Figure 8.7 Schematic representation of the progression of minimally invasive surgery, transitioning from A) laparotomy, B) multi-port laparoscopy, C) single-port laparoscopy, and to D) 'incisionless' natural orifice endoscopic surgery. Crucial technological innovation intervals are numbered 1 to 3.

While it seems logical and naturally progressive to refine, or re-define, surgical techniques to be *more* minimally invasive, the reality of these ambitions is that they are inextricably reliant upon enabling technology. Potentially disruptive novel techniques need tools that are purpose designed to fulfil these clinical needs. Such technology inevitably involves fundamentally bespoke features, ranging from entirely unique platform design to radical modification of existing market items. With the exception of improved image quality and minor adjustments in scalability, the laparoscope and flexible endoscope are items of surgical technology that remain essentially *undisturbed* over past decades. These instruments are currently the default platforms for SPLS, NOES and NOTES. It is perhaps unsurprising therefore, that these novel

techniques have achieved little progression beyond the experimental phase, despite nearly 10 years of committed effort at exploration and early assessment.

Natural orifice surgery is an attractive operative approach due to reduced surgical trauma, '*scarless*' cosmesis and often a more direct route to the target operative site. Ongoing concern regarding the safety of transluminal access has prompted a shift of attention towards more tangible natural orifice *endoluminal* techniques. The most successful and translated NOES or NOTES procedure worldwide has been the peroral endoscopic myotomy (POEM) for oesophageal achalasia. There are variations to the procedure technique but the core steps involve utilising a flexible endoscope to create and navigate a submucosal tunnel before making a longitudinal selective myotomy of the circular muscle fibres only using an endoscopic hook diathermy tool. The length of the mytotomy usually commences 10 – 15cm proximal to the gastro-oesophageal junction and continues 2cm into the cardia of the stomach. This technique is an alternative to the laparoscopic Heller's cardiomyotomy, or endoscopic balloon dilatation. It was first performed in 2008 by Inoue in Yokohama, Japan [302]. Over 1,000 cases have now been performed worldwide [302, 303]. The first United Kingdom clinical case was performed in December 2013 at King's College Hospital, London.

A comparative study was recently undertaken by Bhayani *et al* comparing laparoscopic Heller's cardiomyotomy with anterior fundoplication versus POEM in adult patients [304]. Results of this non-randomised trial of 101 patients (64 Heller's cardiomyotomy, 37 POEM) indicated significantly shorter operating time (29%) and length of hospital stay (50%) with POEM. Swallowing function at 1 month with significantly better following POEM using Eckardt score assessment, and both groups has similarly sustained swallow function at 6 months [304].

Evidence for POEM in children is currently limited to case reports and small case series. The first POEM case in child was reported in 2012 by Inoue's group for a 3-year old child with Down's syndrome following failed balloon dilation [305]. At 1 year follow this patient was asymptomatic and was of normal weight for her age after previously being on the 3rd weight centile. Since this initial report, a total of 26 further paediatric POEM cases have been reported, with patient ages ranging from 3 to 17 years of age [306]. The overall success rate for paediatric POEM is 96.3% (26/27).

Similar to the principles underlying POEM, several groups have been investigating the concept of peroral endoscopy pyloromyotomy (POEP) for infantile hypertrophic pyloric

stenosis (IHPS). In fact, the first in-human POEP procedures were reported in 2005, preceding the first in-human POEM procedures [307]. Human series of POEP for IHPS is comprised of two studies only, reporting a total of 19 cases [307, 308]. All reported cases were performed under conscious procedural sedation. Ibarguen-Secchia from Texas published a series of 10 consecutive infants [307]. A 8.4mm diameter gastroscope was used to make 2 selective myotomies on the antimesenteric border of the pylorus (antrum to duodenal bulb). A submucosal tunnel was not made. Instead, a longitudinal mucosotomy was made to access the muscle fibres. An electrosurgical needle knife was initially used, but the technique was later refined to use an endoscopic sphincterotome together with an argon plasma coagulation probe. All infants fed within 1 hour post-operatively. There were no intra-operative or post-operative complications. The second series is reported by Zhang *et al* from Guangzhou, China who performed POEP procedures on 9 consecutive infants using a 5.9mm gastroscope [308]. Anterior and posterior mucosotomies and myotomies were made similar to the technique described by Ibarguen-Seccia. All infants were fed 2 – 10 hours post-operatively. One infant had persisting vomiting 1 month post-operatively and underwent a successful re-do POEP. More recently, *in vivo* porcine survival model studies by Kawai *et al* and Chaves *et al* have sought to consolidate the POEP technique and empirically investigate functional outcomes [309, 310]. Unlike the technique reported in human series, these animal model studies successfully demonstrated that a submucosal tunnelled approach to the pyloric ring is possible for POEP. Kawai *et al* examined pyloric resting pressures using a manometric catheter. Median pyloric pressures were reduced from 16.5mmHg to 6.1 mmHg and 8.4mmHg for pre-operative, immediate post-operative and 2 weeks post-operative measurements respectively [310].

Surgical platforms currently available for POEM and POEP are limited to conventional flexible endoscopes of varying external diameter size. Flexible endoscopes are known to be problematic due to a lack of adequate stability, precision and navigational control. They are principally *diagnostic* tools that lack many required features for more complex *interventional* use. This purpose of this study is to explore the potential of a flexible snake robot to overcome existing technological limitations in order to make *endoluminal surgery* a more realisable paradigm for the emerging clinical applications of POEM and POEP.

8.2.2 Methods

Proof-of-concept for these targeted surgical approaches was investigated using a flexible snake robot, the i-Snake®, that is being developed by Yang *et al* at Imperial College London [193, 311]. The rationale for utilising a snake robot is that, compared to a conventional flexible endoscope, it is believed to offer improved stability, precision and control for which to

perform interventional procedures. The i-Snake® is a hyper-redundant master-slave robot. The prototype model used in this study consisted of 3 segments; 1) a rigid proximal shaft, 2) a semi-flexible middle shaft manually actuated via a ratchet control mechanism similar to a conventional flexible endoscope, and 3) a modular joint based robotic distal shaft (Figure 8.8). Overall, the system delivers ten degrees of freedom (DOF). The four actuated joints deliver a combined 8 DOF. A further 2 DOF is provided via the adjustable semi-rigid mid-shaft and linear translation of the rigid shaft. A novel hybrid micromotor and tendon design for the joints allows independent joint actuation and space for multiple parallel internal channels [193]. In addition to an optical channel, two internal channels of 3.0mm and 2.4mm diameter are available for interchangeable focused energy devices and air insufflation respectively. Optics is provided by a custom camera and light source unit that features a display and control unit. Visual resolution of the monoscopic standard definition video feed is 160,000x pixels. External diameter of the prototype is 13mm. To avoid contamination of the motor components during the study, the actuated portion of the robot was housed in a thin latex sheath. Control of the robot was via a one-handed joystick interface so that the unoccupied hand could control linear translation of the back shaft, and interchangeable deployment of flexible devices through the internal channels.

8.2.2.1 Ex vivo experimental set-up

A cadaveric porcine upper gastrointestinal tract specimen was used, consisting of oesophagus, stomach and proximal duodenum. Size of the specimen corresponded to adult human sized anatomy. The pyloric anatomy of the pig is different to human due to a prominent submucosal bulge in the gastric side of the pylorus named the pyloric ring or *torus pyloricus* [310]. This effectively acts as a ball valve mechanism. The muscle thickness of the pyloric ring was approximately 10mm (Figure 8.9). Diagnostic criteria for infantile hypertrophic pyloric stenosis on ultrasound is generally considered to be pylorus muscle thickness ≥ 4mm. The specimen was assembled within a validated EASIE-R™ Simulator for Interventional Endoscopy and Laparoscopy (ENDOSIM, MA). An overview of the experimental set-up is shown in Figure 8.10. A 12mm trocar was inserted and fixed to the proximal oesophagus end. The distal duodenum end was clamped in order to prevent air leak. The i-Snake® was inserted directly into oesophagus via the trocar. In addition to free navigation within the insufflated specimen, feasibility of five essential procedural steps for both POEM and POEP were assessed (Figure 8.11). The HybridKnife T-type multi-function probe (ERBE Elektromedizin, Tubingen, Germany) and HookKnife Electrosurgical Knife (Olympus Corporation, Tokyo) were both used. The HybridKnife is a high-pressure water-jet dissection

probe that can also be used for monopolar electrocautery. It was used with the ERBEJET™ 2 water pump console to make the initial mucosal incision and then develop a submucosal dissection plane (Figure 8.10). The HookKnife was used with the ERBE VIO® 2 Electrosurgical Generator to perform the pyloromyotomy. For this experiment, no attempt was made to close the mucosal incision although there are a variety of endoscopic clip devices that are used in clinical practice for this procedural step in POEM such as the Resolution™ clip (Boston Scientific, MA).

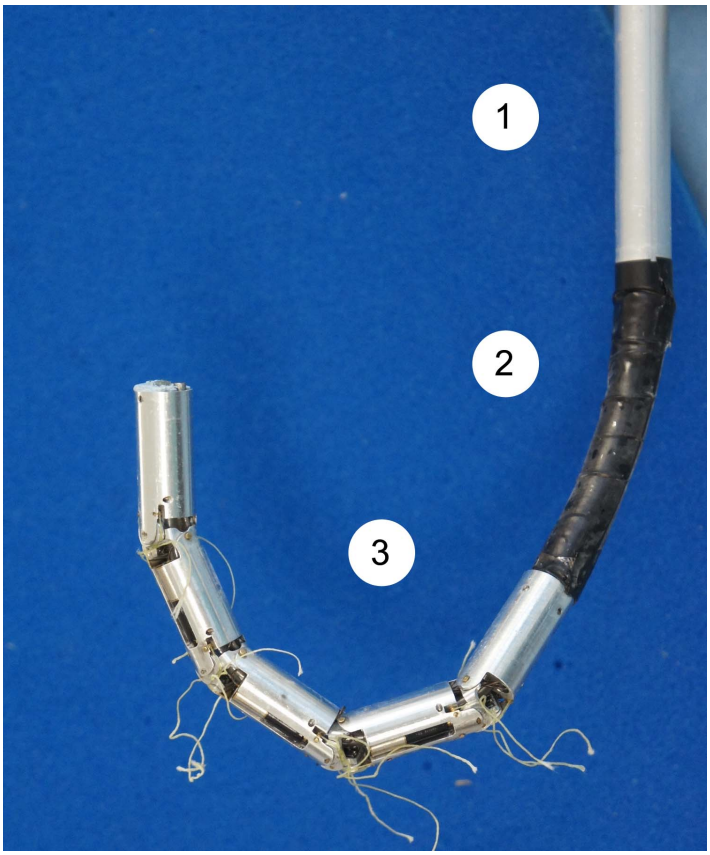


Figure 8.8 The i-Snake® prototype used for the experiment, featuring 1) proximal rigid shaft, 2) semi-flexible mid-shaft, and 3) modular joint based robotic distal shaft.

8.2.2.2 In vivo experimental set-up

Using the same technique described above, submucosal dissection of the distal third of the oesophagus using the i-Snake® was trialled in a live 65kg female *Large White* pig. The trial was undertaken with full ethical approval according to the animals for scientific procedures act (1986), with UK Home Office approved license number PPL 80/2297.

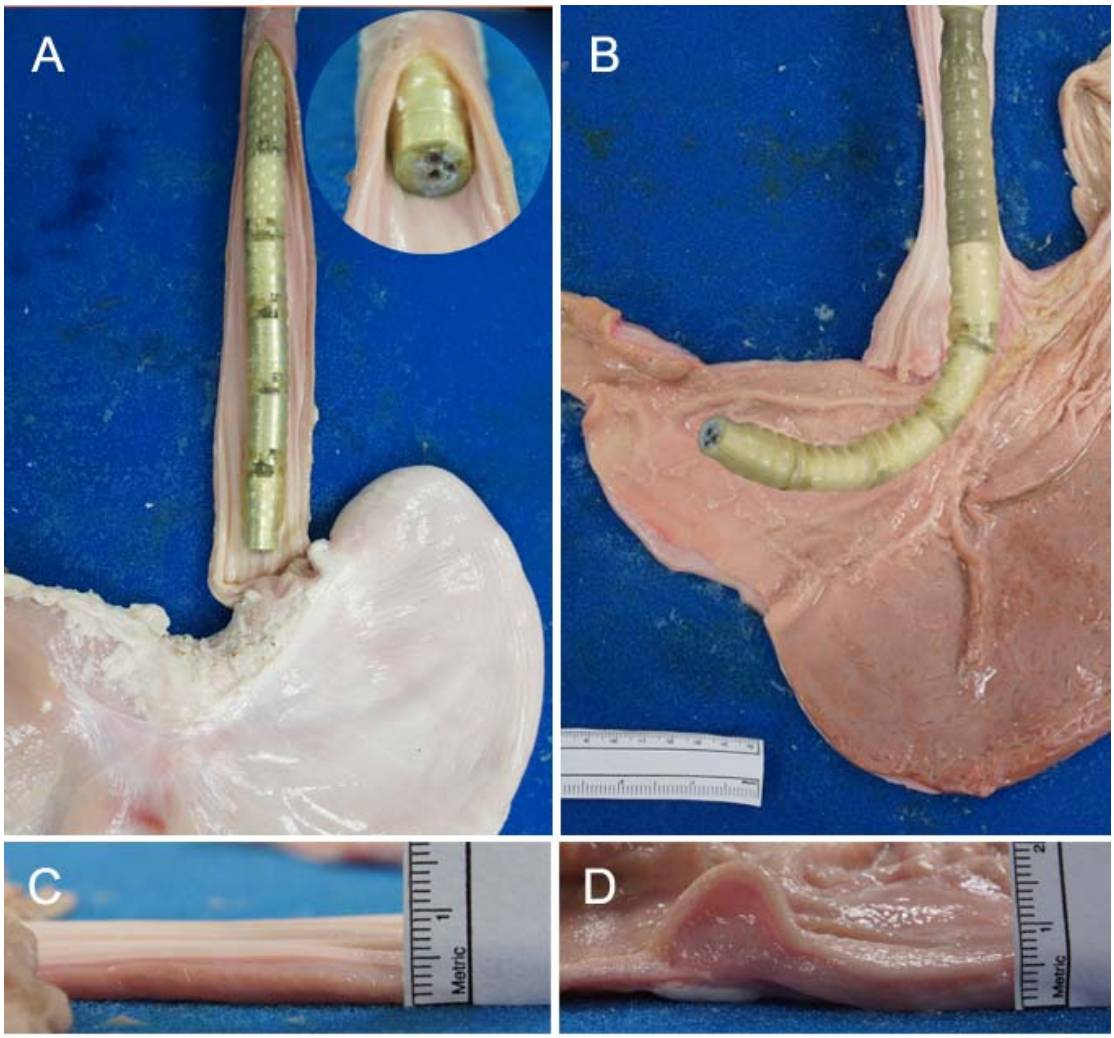


Figure 8.9 Ex-vivo porcine upper gastro-intestinal specimens with a) oesophagus detubularised and b) stomach transected in mid-coronal plane, demonstrating procedural configurations of the i-Snake® for POEM and POEP respectively. Thickness of luminal muscle layers were 3mm, 4mm and 10mm for the c) oesophagus, d) stomach and pylorus respectively.

Under general anaesthesia with endotracheal intubation, a rigid overtube was inserted from the incisors to the upper third of the oesophagus. This was done in order to straighten the acute angle of the oropharynx for insertion of rigid proximal segment of the i-Snake® prototype. The HybridKnife electrocautery function was used to make a small mucosal incision and then water-jet assisted dissection was used to develop a submucosal tunnel. The i-Snake® was then navigated into the submucosal tunnel for further dissection distally towards the gastro-oesophageal junction. At the proximal end, the i-Snake® actuation pack and cabling was supported by an actuated assistive arm (Figure 8.12). This robotic arm prototype device has 6 DOF and supports an approximate 1.5kg payload. An actuation clutch

button is used for re-positioning of the arm. For this prototype, the button was positioned at one of the proximal joints. When the clutch button is not engaged, the arm maintains rigidity and stiffness. A separate linear drive function was integrated to the robotic assistive arm to allow robotic control of linear translation (forwards and backdriveable movement along the axis of the i-Snake® shaft). This was controlled by a separate joystick. The linear translation range was estimated as approximately 20mm.

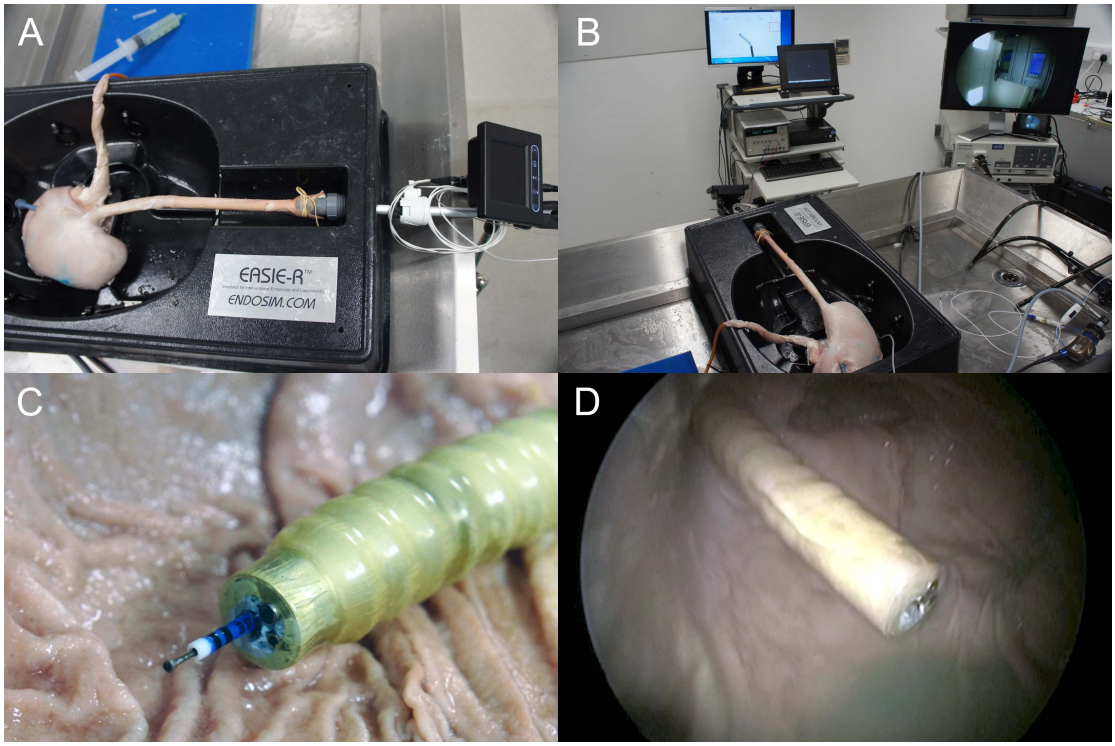


Figure 8.10 Overview of the *ex vivo* experimental set-up including a) specimen assembled within the EASIE-R™ simulator with docked i-Snake®, b) view of the control system cart for the i-Snake®, c) i-Snake® positioned on gastric mucosa with HybridKnife multi-function probe extending from the larger 3mm internal channel, and d) intra-gastric view of the i-Snake® entering through the gastro-oesophageal junction into the cardia of the stomach.

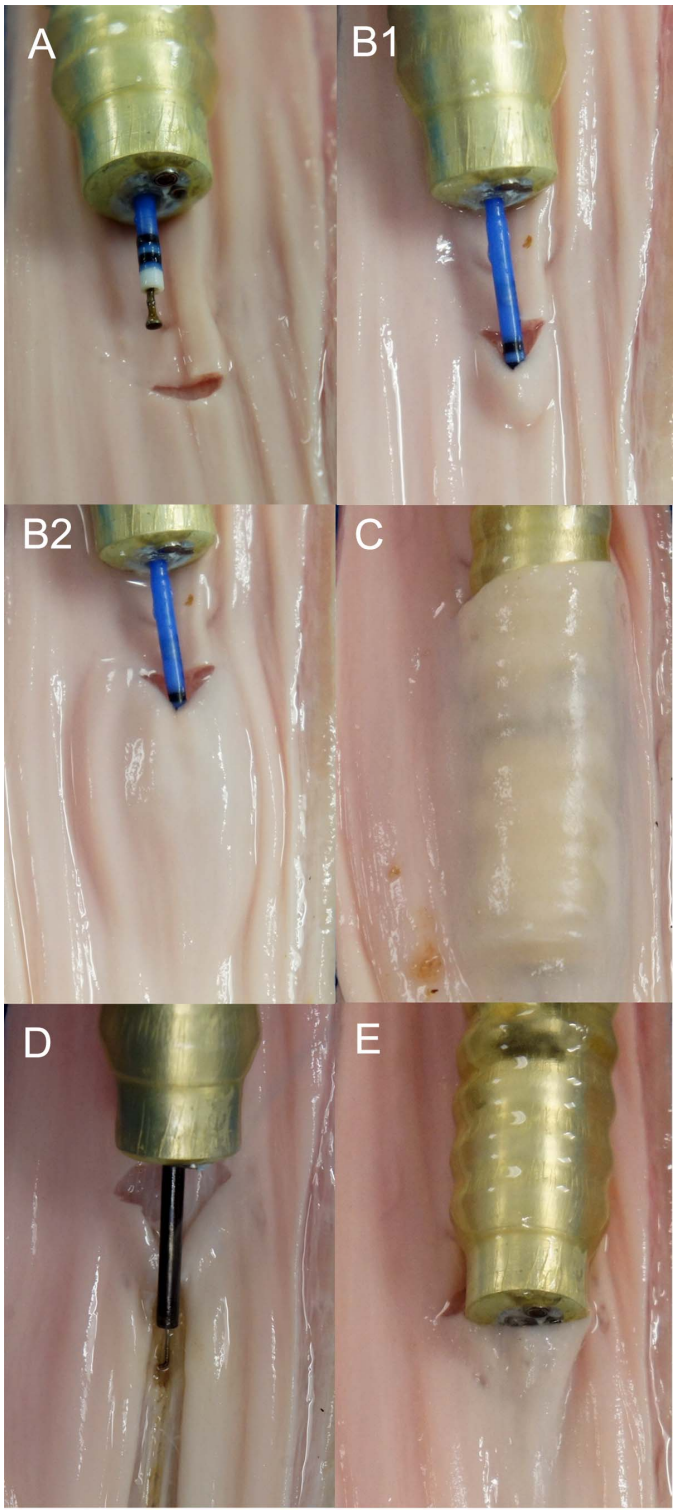


Figure 8.11 Five essential procedural steps for POEM and POEP were undertaken, defined by a) creation of a 15 – 20mm transverse mucosal incision, b1) & b2) submucosal tunneling using the HybridKnife, c) intubation of submucosal tunnel, d) myotomy using the HookKnife (Olympus Corporation, Tokyo) (mucosal tunnel opened for illustrative purpose only), and e) extubation of submucosal tunnel in preparation for mucosal closure (i.e. with endoclip).



Figure 8.12 The mechanically actuated assistive arm robot supporting the i-Snake® shaft, actuation pack and cabling weight during the *in vivo* trial. For sterility reasons, a clear protective drape is covering the robotic arm. The linear drive controller is visible as the red joystick.

8.2.3 Results

8.2.3.1 Ex vivo

Controlled and targeted actuation within the constrained workspace of the foregut was attainable in this setting (Figure 8.10). The i-Snake® was able to reach almost all mucosal surfaces of the stomach. Each procedural step was achieved for both POEM and POEP. Submucosal tunnel and myotomy lengths of 60 – 80mm were repeatedly performed.

Submucosal tunnel intubation and navigation was identified as the most challenging procedural step due to limited visualisation and shear forces exerted at the mucosal incision site. The HybridKnife performed well at rapidly developing and expanding the submucosal space. Mucosal or transmural perforation was not encountered, however the specimens were subjectively felt to be more resilient than *in vivo* human tissue. Although performed in staged intervals, estimated time for total procedural completion is 30 – 45 minutes.

Some backlash was encountered when the water-jet was activated and the i-Snake® was in a flexed position. This is presumably due to the force of the water jet being propelled along the HybridKnife acting to find a path of least resistance and generating a linear direction of force that was counter-acting against the curved position of the i-Snake®. After examining the HybridKnife probe afterwards it was additionally noted that diathermy char had formed at the probe tip. This may have caused occlusion of the water-jet exit site, resulting in higher pressure and exacerbation of backlash.

8.2.3.2 In vivo

Deployment of the i-Snake® into the both the porcine oesophagus and stomach was achieved, and confirmed with fluoroscopy imaging (Figure 8.13). Similar to the results of the *ex vivo* experiment, a small transverse mucosal incision was made in the oesophagus and water-jet assisted dissection was used to develop a submucosal tunnel (Figure 8.14). At times, the i-Snake® camera view was impaired by fogging and organic debris (i.e. blood, splash from water-jet).The i-Snake® was navigated approximately 5cm into the submucosal tunnel before mucosal tearing was encountered at the initial mucosal incision site. The POEM procedure attempt was subsequently abandoned. It was not possible to attempt a POEP procedure due to a large amount of partially digested straw feed that was found in the unprepared stomach of the animal.

For this particular trial, a joint position feedback graphic interface display was also tested (Figure 8.14). This was made possible by integrating miniature potentiometers at each joint. The graphic display allowed the operator to see the exact orientation of the robot in real-time. Particularly in retroflexed positions where disorientation is common, this was highly helpful and aided spatial awareness. During moments of joint locking or latency between the master and slave components, the graphic joint position feedback interface also proved useful from a system error recognition perspective.

The assistive arm robot was easily mounted to the operating table side rail and considerably improved ergonomics during the trial by obviating the need for a bed-side assistant to support the i-Snake® platform body. In this trial the assistive arm was mounted to the i-Snake® laterally, although in future it may also be mounted the back-end of the actuation pack. It was noted that the weight of the platform exceeded the payload during the trial; requiring use of a mechanical clamp offset the weight by supporting cabling weight.

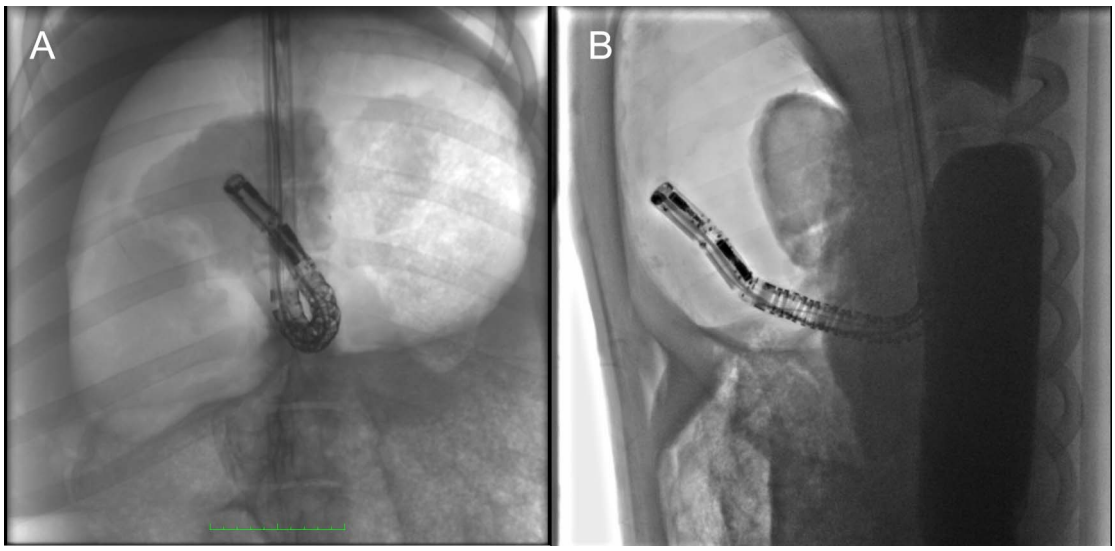


Figure 8.13 Attempted retroflexion of the i-Snake® as confirmed on a) antero-posterior and, b) lateral fluoroscopy imaging.

8.2.4 Discussion

This preliminary assessment provides proof-of-concept results for a flexible snake robot to perform two natural orifice endoluminal surgery clinical applications. The motivation for targeting these two applications is to seek new advances in clinical outcome improvement through less invasive operative approaches that are effectively *incisionless*. Avoidance of skin incisions eliminates post-operative abdominal wall related sequelae such as pain, wound infection, incisional herniae and visible scarring. Furthermore, there is the possibility of these procedures being undertaken under conscious procedural sedation rather than general anaesthesia, making these alternative approaches more amenable to the prospect of being offered as day surgery cases.

It is presumed that technological barriers are a key limiting reason for these approaches remaining relatively unexplored. Enabling features of a flexible snake robot are felt to include improved stability, precision, control, and navigational awareness – all contributing

to a lower degree of technical difficulty for advanced interventional endoluminal surgery. Of course, these putative benefits require more detailed quantification through further *ex vivo* and *in vivo* feasibility testing as well as comparative assessment against existing platforms – principally the standard flexible endoscope.

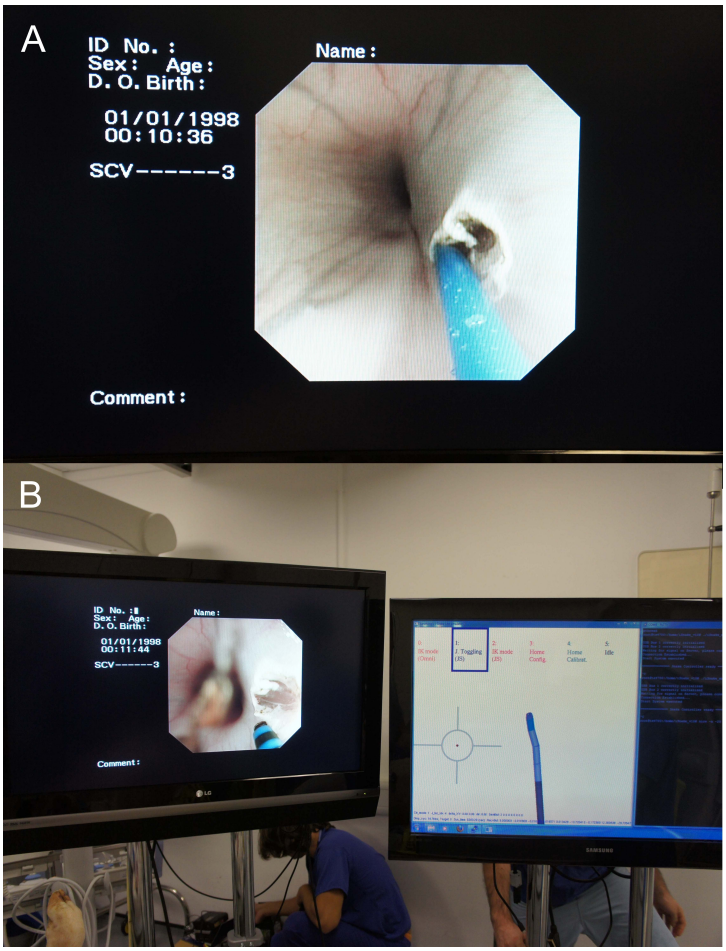


Figure 8.14 The HybridKnife entering the oesophageal submucosal space with views from the a) on-board camera, and b) separate graphic interface screen proving joint position feedback.

8.2.4.1 POEM

Oesophageal achalasia is a rare condition in children with an incidence of approximately 0.02 – 0.18 per 100,000 [306]. The pathology usually presents in adult life between the ages of 25 to 40 years, with less than 5% of cases occurring in children. A challenge with the laparoscopic or open cardiomyotomy technique is achieving adequate proximal myotomy length above the level of the oesophageal hiatus. The POEM technique allows unrestricted access to the entire length of the oesophagus and cardia.

Gastric fundoplication is frequently performed in conjunction with a Heller's cardiomyotomy for surgical prophylaxis against an increased risk of gastro-oesophageal reflux secondary to disruption of gastro-oesophageal sphincter integrity. POEM series reported in the literature to date have not described concomitant fundoplications, although endoluminal antireflux techniques are feasible in both adults and children [312]. Preserving the longitudinal muscle layer in POEM would probably result in less compromise of the gastro-oesophageal sphincter. Long-term follow up data suggests that despite this, mild reflux symptoms occur in up to 46% of patients following POEM [302]. From the same institution, this compares with 33% reflux in patients following laparoscopic Heller's cardiomyotomy with Toupet fundoplication [302].

There are obvious and serious concerns about the risk of transmural perforation and mediastinitis. Amongst the larger adult series the perforation rate is 2 – 5% [302] and these events are almost always repaired endoscopically using mucosal endoclips, over-the-scope full thickness clips or full-thickness closure devices such as T-tags (Cook Endoscopy, NC), and the Brace-Bar (Olympus Medical Systems, Toyko, Japan). The submucosal tunnel is protective in itself as it forms a flap-valve to seal any site of perforation. There is also a possible risk of submucosal abscess formation but this complication remains unreported.

8.2.4.2 POEP

In contrast to the low case volume of oesophageal achalasia, hypertrophic pyloric stenosis is one of the most common indications for surgery in infants. The incidence of infantile hypertrophic pyloric stenosis is 1 – 4 per 1000 children. Pyloromyotomy, in all its various guises is an excellent surgical procedure that is relatively simple, highly effective and with low complication rates. The open technique may be performed via right upper quadrant or supraumbilical approach. The laparoscopic technique is gaining popularity. It is usually performed using a 3-port technique but a single-port approach is also reported. Level 1 evidence indicates shorter time to commence full feeds and shorter length of hospital stay for the laparoscopic approach [313]. In a recent meta-analysis by Oomen *et al*, rates of major complications (mucosal perforation, incomplete myotomy and re-operation) were found to be 4.9% for laparoscopic pyloromyotomy versus 2.0% for open pyloromyotomy, however this difference was not statistically significant [314].

Per-oral endoscopic pyloromyotomy challenges the notion of whether an excellent existing operation can be made better, and if so, what clinical gains might warrant pursuit of such an

endeavor. It would be reasonable to expect that an incisionless approach would lead to a further expedited and less painful recovery as well as cosmetic advantage. The endoluminal approach permits unique freedom to make singular, multiple or even radial myotomies at any circumferential location. Division of muscle fibres can be undertaken selectively as demonstrated by Kawai *et al* and Chaves *et al* who performed myotomies of the inner circular muscle layer only, preserving the longitudinal muscle layer that usually is spared from hypertrophic changes. Together, these theoretical advantages offer tangible potential for meaningful improvements clinical and functional outcomes.

Risk of translumenal perforation and submucosal abscess formation are similar for POEP as they are for POEP. Neither of these potentially devastating events are reported in the limited human series available.

8.2.4.3 Technological refinement and optimisation

These initial proof-of-concept experiments have identified strengths and weaknesses for the i-Snake® for clinical roles in paediatric upper gastrointestinal endoluminal surgery. Several further stages of iterative prototype refinement are needed to move closer to a stage of readiness for clinical translation. Miniaturisation of the robot and making the entire shift flexible are clearly essential requirements. A target external diameter of 6mm would be appropriate for use in the infant upper gastrointestinal tract. This represents a 54% down-sizing from the 13mm diameter of the prototype used in this experiment. Micromotors are not yet small enough to support this degree of scalability and smaller motors considerably impair both the force capabilities and robustness of the platform. Non-robotic ultrathin flexible endoscopes are commercially available on the market now through no less than four separate manufacturers [315]. The term 'ultrathin' is used as a reference term for scopes that are sub-6mm diameter [315]. Non-robotic scopes are tendon driven. This manual actuation mechanism means that a a maximum of 2 DOF is usually achievable at the distal tip (i.e. left-right and up-down movement). Many ultrathin scopes offer only 1 DOF (i.e. left-right movement) as the decrease in external diameter size is made possible through a decrease in tendon number and therefore DOF. It may be that *"roboticising"* an ultrathin flexible endoscope is a more practical and realistic solution for clinical translation. This would involve motorizing tendons at the proximal end of the scope. The scenario of external diameter *versus* added DOF tradeoff requires further work to determine the optimal number of DOF for advanced upper gastrointestinal endoluminal surgery and how much DOF can be conceded to reach adequate miniaturisation dimensions.

While attempting retroflexion within the stomach to visualise the fundus and gastro-oesophageal junction, it was revealed that the arc length of the i-Snake® prototype was insufficient. The difference in arc length and maximal retroflexion angulation between the i-Snake® prototype and a single-channel gastroscope is highlighted in Figure 8.15. Target arc length would need to be 5 - 10cm. The retroflexion arc length of the prototype is approximately 18cm. One solution for improving the arc length of the i-Snake® would be to shorten the length of each modular component.

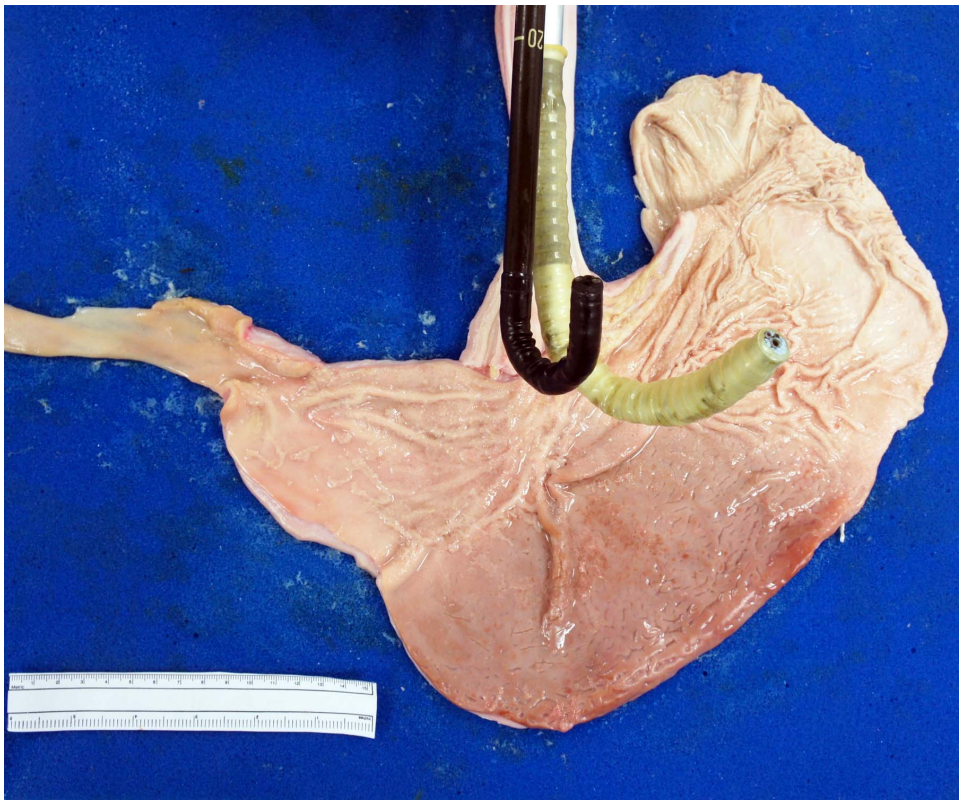


Figure 8.15 Positions of maximal retroflexion for a 12mm gastroscope and the 13mm i-Snake® prototype used in this study (NB: flexible mid-shaft segment not articulated).

It was observed that the proximal 2 joints of the i-Snake® prototype were used more for gross positioning and the distal 2 joints were used for fine articulation at the target operative site. A motion scaling differential between the proximal and distal joints could therefore be advantageous. This could be achieved by using different gear ratios for motors depending on their joint location.

Additional problems or shortcomings that were identified are summarised in Table 8.2 along with proposed solutions.

Problem	Proposed Solution
Submucosal dissection	Blunt beveled distal end. Defining water-jet pressure settings for safe dissection.
Visualisation within submucosal tunnel	Transparent distal caps to offset camera tip from the operative site. Micro-channel for air or water-irrigation camera lens cleaning.
Tearing at mucosal incision site	Low friction sheath designs without ridging. Programming remote-centre of motion at mucosal incision site.
Myotomy	Alternative flexible focused energy devices. Endoscopic ultrasound probes for image-guided myotomy depth estimation.

Table 8.1 Identified problems and proposed solutions for i-Snake®-assisted POEM and POEP procedures.

8.2.4.4 Related or additional clinical applications

Wall *et al* have proposed POEM for lengthening the upper oesophageal pouch in long-gap oesophageal atresia [316]. They investigated this in an *in vivo* porcine non-survival model study that compared percentage oesophageal elongation for 4 different study groups; 1) bilateral submucosal lengthening endoscopic selective myotomies, 2) open approach full thickness circumferential myotomies, 3) open approach full thickness spiral myotomies, and 4) a non-intervention control. The 8cm resected oesophagus specimens that had bilateral submucosal myotomies were lengthened by a mean of 41.7% under 100g tensile testing force, compared to 28.5% elongation for the control group [316]. Percentage elongation was significantly higher in the circular and spiral myotomies performed via a thoracotomy. It was postulated that compared to full thickness myotomies, selective division of the circular muscle fibres would help to preserve perfusion to the oesophago-oesophagostomy anastomosis, maintain physiological oesophageal function and protect against long-term dilatation.

Rather than intervention use, the i-Snake® might be used as a diagnostic tool to aid delivery of *in situ in vivo* tissue characterisation through advanced probe-based high-resolution imaging. This new concept of intra-operative real-time cellular level imaging has been colloquially termed '*optical biopsy*'. Hand-held robotic tools are important in this field as computer-assisted precision and control is needed to maintain steady probe contact force, especially for mosaicking of larger tissue surfaces [317]. An example of enhanced imaging in paediatric surgery is reported by Frykman *et al* who successfully demonstrated the utility of a Sagnac-based spectral imaging system on a mouse model of Hirschprung's disease [318]. High levels of discrimination between aganglionic and ganglionic bowel segments were shown, with sensitivity of 97%, specificity of 94%, positive predictive value of 92% and negative

predictive value of 98% [318]. One of the main complications and challenges in surgical management of Hirschprung's disease is re-operation for residual aganglionosis or transition zone bowel at the distal pull through segment. Children with Hirschprung's disease typically undergo one or more rectal biopies pre-operatively and then frozen section biopsies intra-operatively. These biopsies could be avoided with use of intra-operative *in situ in vivo* imaging. Outcomes could also be improved by an ability to map the pathological transition zone in real-time, thereby ensuring complete excision of the diseased colon. The interferometer used in this study by Frykman *et al* was large, rigid and seemingly intentioned for clinical use as an *exoscope* to image bowel from the serosal surface during endoanal pullthrough. An attractive alternate strategy might be to acquire cellular-level imaging endoluminally from the mucosal surface. This would require a probe-based catheter and a flexible robotic platform to deliver the device. The i-Snake® seems well suited and has already proven to be reliable for laparoscopic *in situ in vivo optical biopsy* using probe-based confocal laser endomicroscopy (pCLE) [311]. Future work is needed to explore this specific clinical role.

8.3 Evaluation of Pressure Effect Settings in Water-Jet Assisted Oesophago-Gastric Submucosal Dissection

8.3.1 Introduction

Per-oral endoscopic cardiomyotomy and pyloromyotomy rely on creation of a submucosal tunnel working space. Submucosal dissection is predominantly achieved using time-consuming and technically difficult methods of blunt dissection, electrocautery, carbon dioxide insufflation, and water irrigation [319]. Flexible probe water-jet devices deliver a high-pressure water jet for rapid development and expansion of anatomical planes such as the submucosal space. Preliminary i-Snake® proof-of-concepts experiments have shown that water-jet assisted dissection of the submucosal space is effective. Higher pressure settings for the water jet might result in unintended transmural perforation and lower pressure settings might result in water-sodden tissue that is not dissected. There is no guidance from the literature or manufacturer regarding pressure effect settings for this clinical use. To further explore application of this new focused energy delivery device for peroral endoluminal surgery, the following objectives were investigated; 1) to assess the effect of different water-jet pressure settings for submucosal dissection and 2) to evaluate the risk of inadvertent perforation.

8.3.2 Methods

Water-jet assisted submucosal dissection was performed on eight porcine *ex vivo* upper gastrointestinal specimens using the ERBEJET™2 console (ERBE Elektromedizin, Tubingen, Germany) with the T-type HybridKnife (ERBE Elektromedizin, Tubingen, Germany) multi-function probe (Figure 8.16). Pressure effect settings were increased in increments of 5 across a range of 20 – 60 (1 effect setting = ~100kpa). Maximum pressure effect setting is 80. The submucosal space was accessed from pre-prepared 10mm mucosal incisions in the posterior oesophagus located 10 cm proximal to the gastro-oesophageal junction. The water-jet was deployed from a static position for 10 seconds at zero degrees of angulation using methylene blue stained normal saline. Length and width of submucosal elevation, as well as inadvertent perforations were assessed for each effect setting (Figure 8.17).

8.3.3 Results

Submucosal elevation was achieved at each pressure effect setting. A linear relationship was observed between pressure effect setting and submucosal tunnel length (Figure 8.18). Direction of tunneling was uniformly straight, with no spiraling effect seen. Submucosal elevation width remained relatively constant across the range of water-jet effect settings used. No instances of mucosal or transmural perforations were encountered.

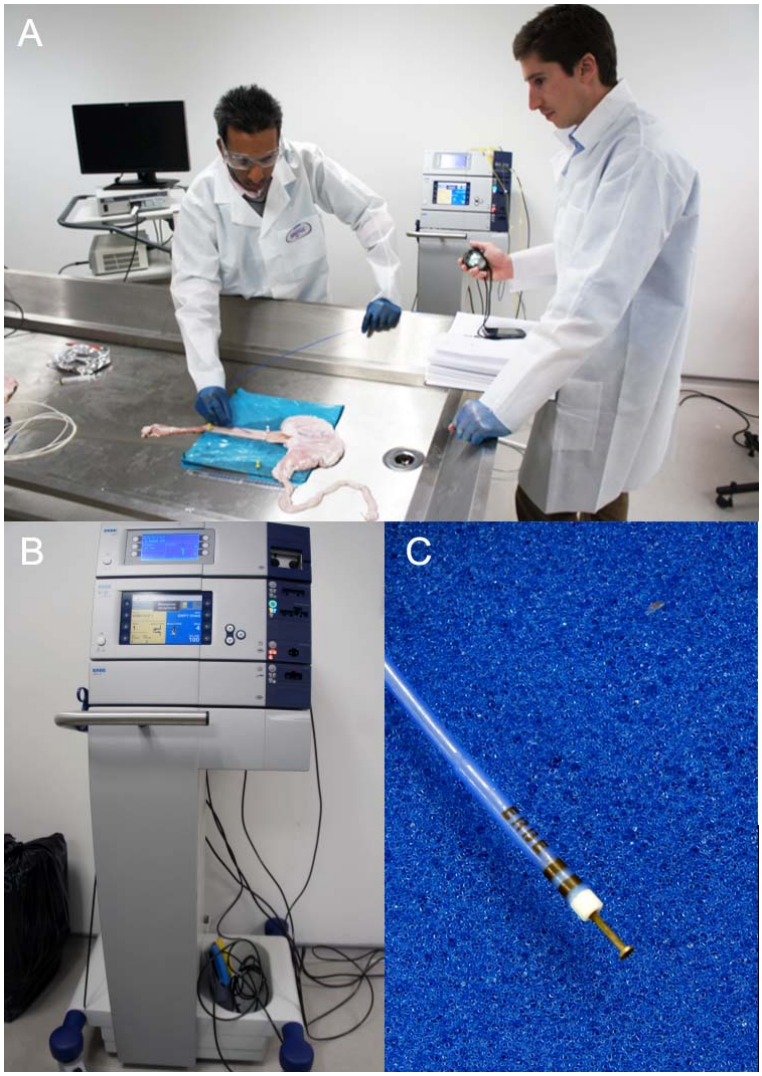


Figure 8.16 Overview of the experimental set-up involving a) cadaveric porcine upper gastrointestinal tract specimen, 2) ERBE VIO® 2 Electrosurgical Generator and ERBEJET™ 2 water pump console unit, and 3) HybridKnife T-type multi-function probe.

8.3.4 Discussion

This *ex vivo* feasibility study provides encouraging results that support a role for water-jet assisted submucosal dissection to facilitate an essential and technically challenging aspect of natural orifice peroral endoluminal surgery. The water-jet effect settings explored appear to be safe, however translation to *in vivo* tissue is needed. Further research is required to define optimum effect settings for efficient plane preserving dissection. It is reassuring that higher water jet pressures did not result in lateral expansion of submucosal elevation. If this was the case then there would valid concern for long-segment circumferential stripping of mucosa and risk of devascularisation if sufficient collateral blood supply was not present. Taking a conservative value, a pressure effect setting of 35 would be recommended for initial *in vivo* use.

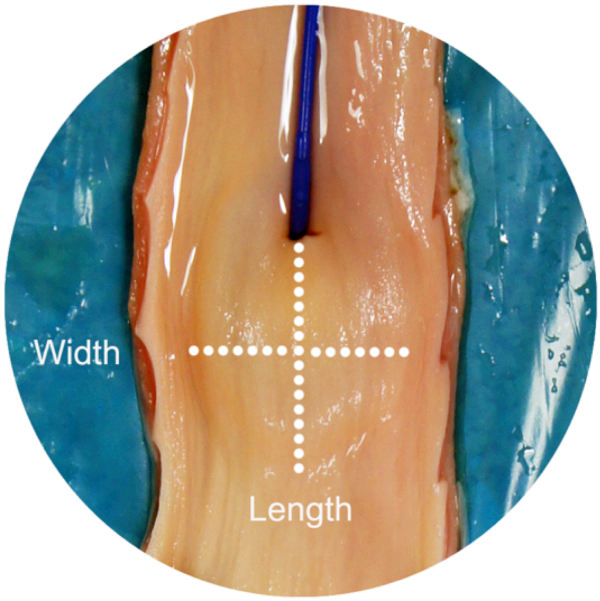


Figure 8.17 Detubularised esophagus with water-jet probe tip in situ demonstrating submucosal elevation length and width at effect setting 20.

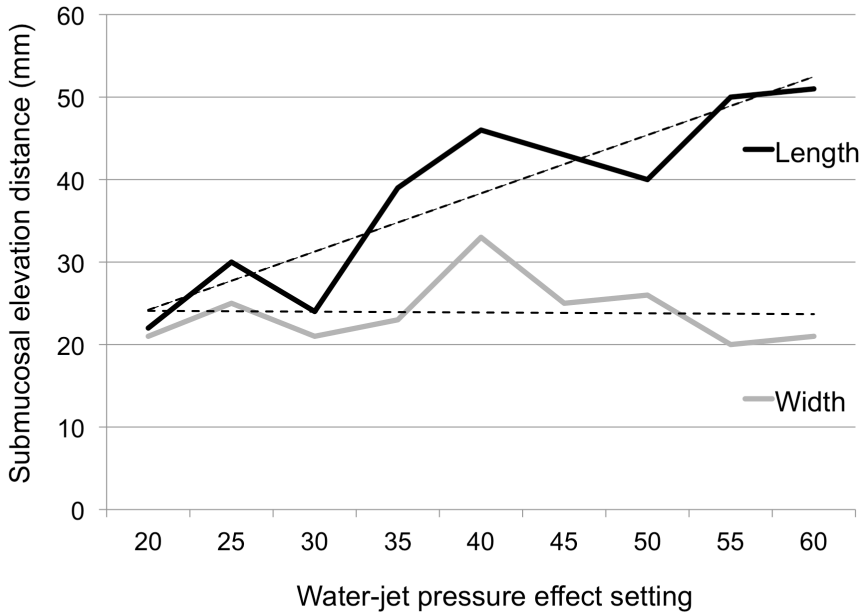


Figure 8.18 The effect of water-jet pressure effect settings on submucosal elevation.

8.4 Cyclops v1 Prototype Evaluation for Use in Paediatric Laparoscopy

8.4.1 Introduction

One of the key limitations identified during prototype experiments in Chapter 8.2 was that the i-Snake® platform is fundamentally a *single-armed* device. Without a second arm for *bimanual* tissue manipulation, eligible clinical roles are restricted to diagnostic procedures and simple reconstructive or ablative procedures even with the addition of a second internal channel. The vast majority of bimanual single-shaft prototype platforms being developed worldwide for SPLS, NOES and NOTES face considerable resistance to transition beyond the pre-clinical phase due to demanding *technical* needs and *non-technical* barriers. These challenges are universally shared and are summarised in Table 8.3 [193]. Capability of any one prototype to breakthrough to clinical translation and wide uptake is critically dependent on these requirements being met without compromise.

The CYCLOPS platform developed by Mylonas *et al* at Imperial College London is a proposed solution. It is a low-barrier entry technology that seeks to address bimanual instrument triangulation and force-delivery via a unique and highly original concept design that is adaptive to the existing laparoscope or flexible endoscope [320]. As an advanced adaptive design, stability and navigational control of these existing scopes are preserved. It is intended to re-purpose the flexible endoscope or laparoscope for new and enhanced use as therapeutic tools (Figure 8.20). By easily integrating with current practice setting infrastructure in an affordable way, the CYCLOPS would be anticipated to follow an accelerated clinical translation pathway



Figure 8.19 Digitally enhanced concept image of the CYCLOPS system mounted on a flexible endoscope.

Technical needs and non-technical barriers
Adequate triangulation for bimanual tissue traction-countertraction, destruction and reconstruction.
Sufficient delivery of force > 10 Newtons at the tool tissue interface.
Platform stability to meet both safety and robustness needs in the operating theatre.
Intuitive and reliable control for precise, ergonomic and consistent operative performance.
Easily portable and mountable technology for on-demand use
Small technology footprint is needed to minimise disruption to operating theatre surgical workflow.
Reluctance amongst service providers to incorporate major equipment items that are entirely incompatible with existing equipment.
Affordable capital outlay and overall cost-effectiveness are necessary priorities in modern healthcare systems.

Table 8.2 Technical needs and non-technical barriers that are required to be addressed for successful single-shaft bimanual surgical platforms.

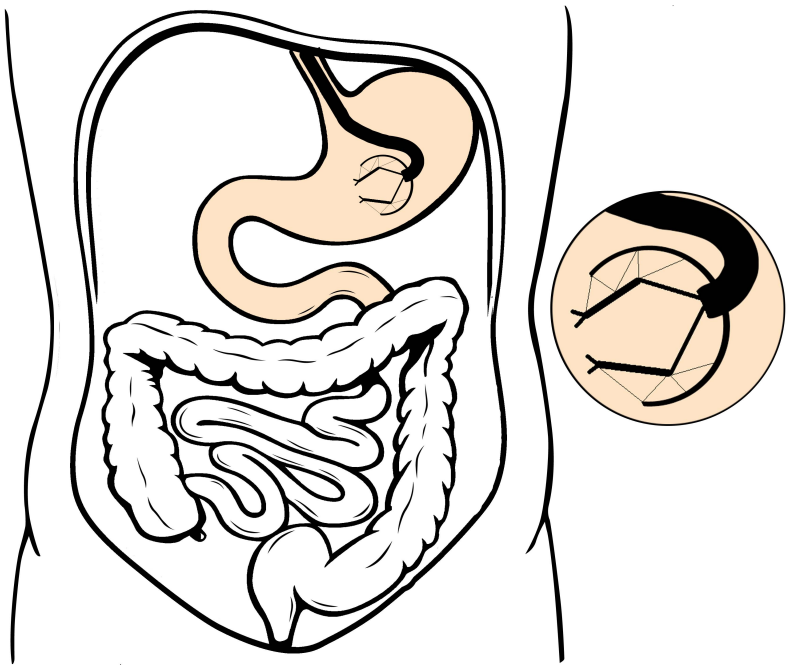


Figure 8.20 Schematic of the CYCLOPS deployed within the stomach cavity for natural orifice endoluminal surgery.

8.4.2 Materials and Methods

To assess the ability of the CYCLOPS to perform a simple bimanual task in a paediatric sized workspace, a modified prototype was used to perform a peg transfer task in the Pediatric Laparosopic Surgery (PLS) box trainer simulator [245].

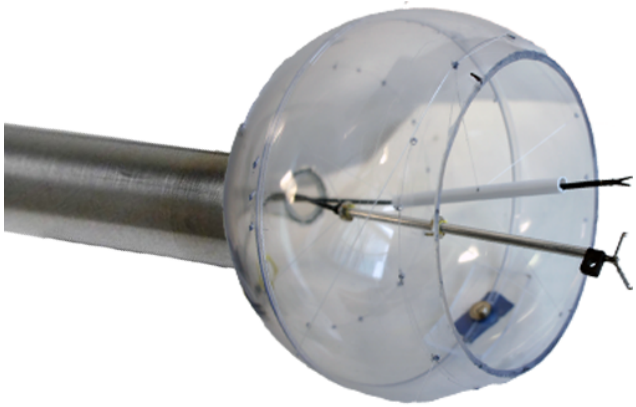


Figure 8.21 Digitally enhanced concept image of the CYCLOPS system mounted on a laparoscope.

8.4.2.1 CYCLOPS system

A core component of the CYCLOPS is a deployable peripheral scaffold resembling an open-ended cylinder or bulb. This structure is attached at the distal end of a conventional laparoscope or flexible endoscope in a '*clip-lock*' fashion (Figures 8.19 and 8.21). The peripheral scaffold is designed to be low profile and un-obtrusive to the functionality of the main scope as it manoeuvres to the target operative anatomy. In its collapsed state it may be integrated at the distal end of the scope in several possible ways; a scope over-sheath, through internal channel, or pre-affixed distal scope cap attachment. Once appropriately located at the operative site, the scaffold is deployed to form an expanded semi-rigid structure that is covered with a soft sheet-like biomaterial (Figure 8.22). Size of the peripheral scaffold is intended to be scalable to suit patient-specific or procedural needs. The scaffold is collapsible for extraction or extubation of the main instruments.

The primary role of the peripheral scaffold is to support a network of tendons that form a tendon-driven parallel robotic telemanipulator (Figure 8.22). Tendons are attached at a pre-defined distances along the length of rigid hollow over-tubes through which interchangeable off-shelf flexible endoscopic instruments are docked. From their most distal aspect, the tendons are networked through fulcrum points around the lateral body of the scaffold via low-friction eyelets, and then congregate at the '*neck*' of the peripheral scaffold where they are bundled through a number of small diameter flexible conduits (e.g. Bowden cables). Eyelets are positioned such that each tendon pair exerts an antagonistic actuation force on the rigid over-tubes along different planes of motion. A motorized driving unit at the proximal end of the scope provides computer-assisted actuation of the tendons.

A total of 6 tendons attach to each rigid over-tube, providing 5 DOF for each instrument (XYZ axis, pitch and yaw). Including actuation of each grasping forcep and linear translation of the scope, the CYCLOPS delivers 13 DOF overall. Master control is provided by two Geomagic® Touch™ haptic devices (3D Systems, SC).

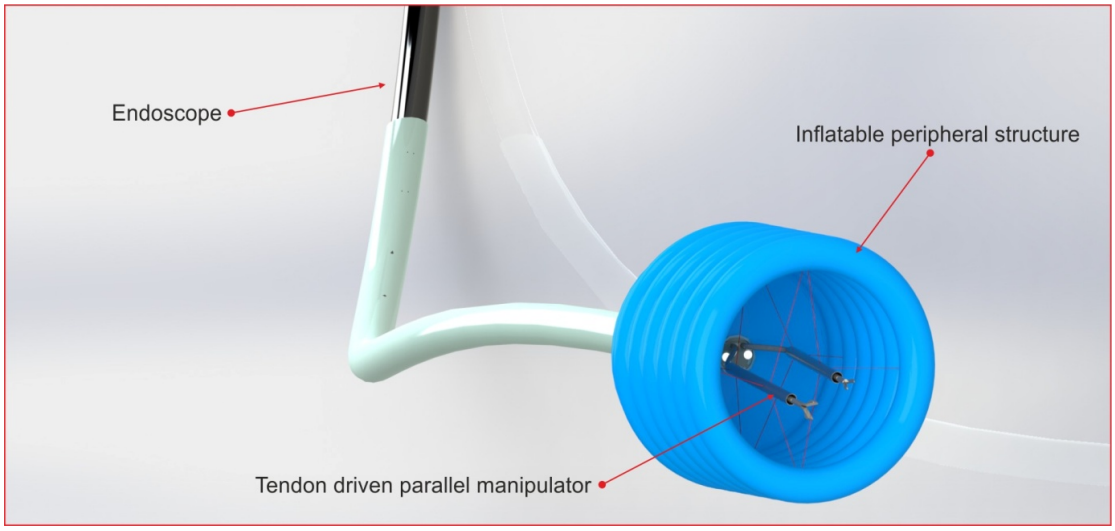


Figure 8.22 Stylistic impression of the CYCLOPS attached to a flexible endoscope, featuring a flexible over-sheath, inflated peripheral structure and tendon-driven manipulated instruments. (Image courtesy of Dr George Mylonas)

An overview of the experimental set-up is shown in Figure 8.23. For this experiment, the CYCLOPS prototype was mounted to a zero-degree 3D HD VisionSense III neuroendoscopy system (VisionSense, Petach Tikva, Israel). This endoscope is 4mm diameter, 18cm in length and provides image resolution of 1920 x 1200 pixels. Images were displayed using a 24 inch stereoscopic flat-screen monitor and viewed with low-cost passive glasses with opposing 3D polarisation filters. A small 4.5mm diameter x 5.0mm height (79.5cm^3) open-ended cylindrical peripheral scaffold was made of rigid transparent plastic. The CYCLOPS was therefore considered to be in a ready-deployed state. Positioning of the eyelets on the peripheral scaffold allowed the instruments to achieve a maximum of 26 degrees triangulation. Re-usable rat-tooth 2.8mm flexible grasping forceps (Olympus Medical Systems, Tokyo, Japan) were inserted through and docked to the rigid hollow over-tubes.

The customised CYCLOPS prototype was attached to a table mounted Martins Arm clamp (Karl Storz Endoskope, Tuttlingen, Germany). As the peripheral structure was formed by a rigid component, the PLS box was de-roofed so that the CYCLOPS could be positioned at an

appropriate distance from the peg transfer task block without needing to pass through an access port (Figure 8.24).

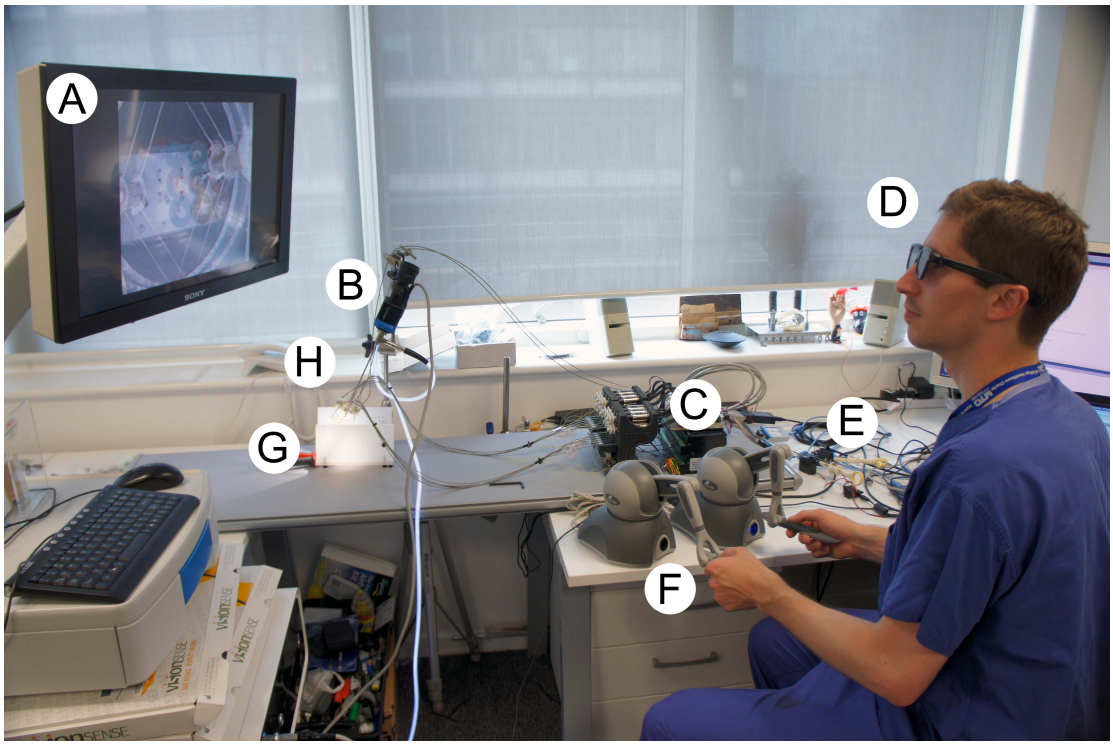


Figure 8.23 Overview of the experimental set-up demonstrating the a) stereoscopic monitor, b) VisionSense III scope camera, c) CYCLOPS tendon driving unit, d) passive 3D glasses, e) motorised actuation mechanisms for endoscopic forceps, f) Geomagic® Touch™ haptic devices, g) Pediatric Laparoscopic Surgery (PLS) box trainer, and h) CYCLOPS peripheral scaffold attached to the VisionSense scope.

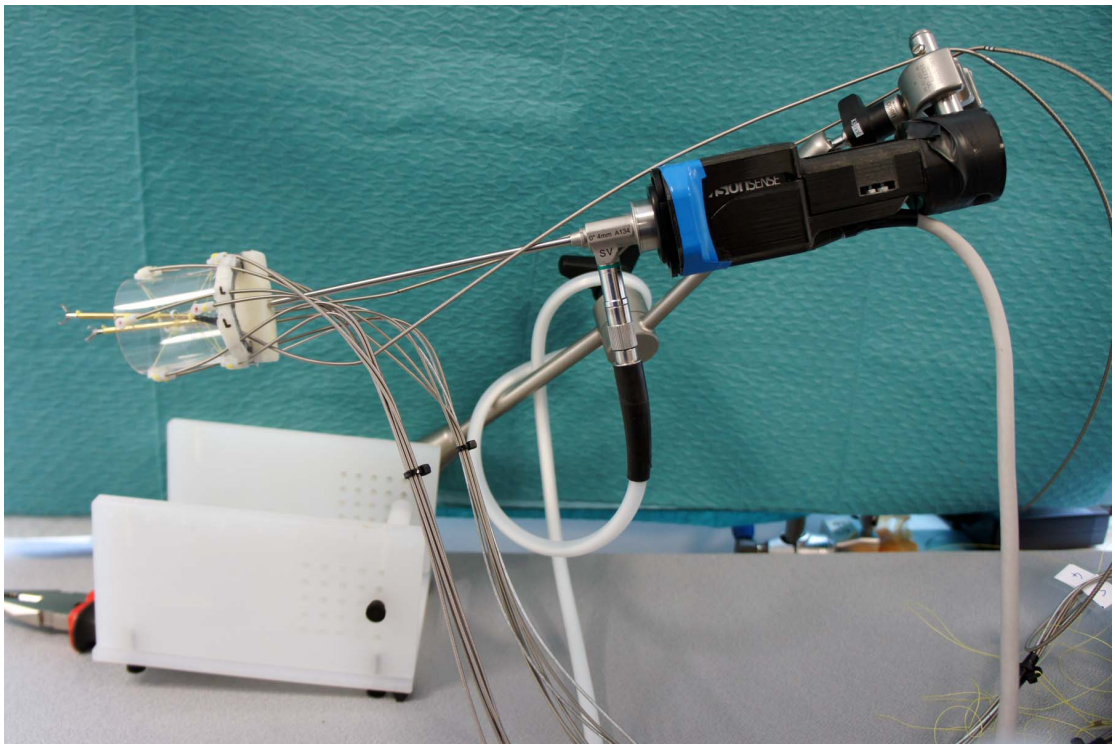


Figure 8.24 Assembled paediatric sized CYCLOPS prototype positioned above an open-roof PLS box trainer.

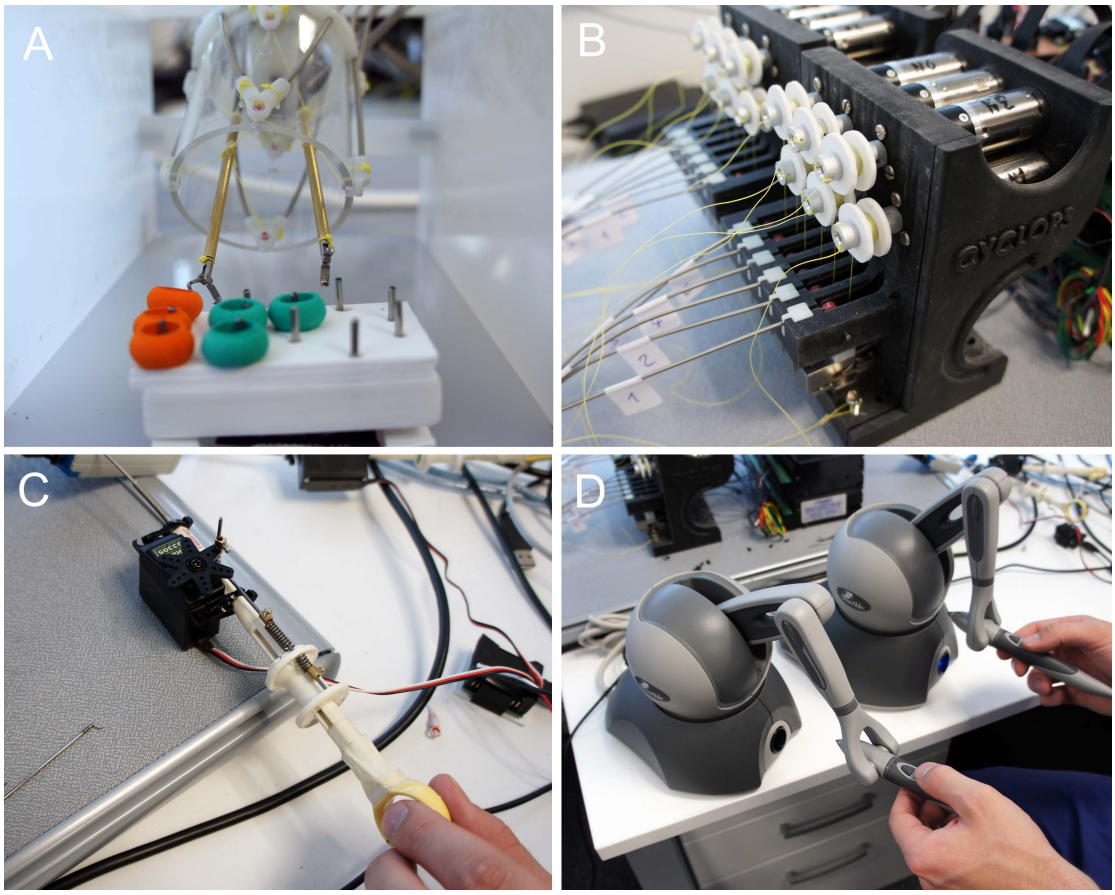


Figure 8.25 Individual components of the CYCLOPS prototype system demonstrating a) reverse angle view of the CYCLOPS end-effectors performing the peg transfer task, b) the CYCLOPS tendon driving unit with tendons (yellow) and 1.9mm Bowden cables (silver) attached to each of the 12 motors, c) motorised control mechanism for one of the two endoscopic forceps, and d) the master control interface provided by Geomagic® Touch™ haptic devices.

8.4.3 Results

The PLS peg transfer task was able to be completed in its entirety without interruption (Figure 8.26). Instrument control was sufficiently dexterous, responsive and precise. The fastest task completion time was 169 seconds and this task repetition involved only 1 dropped peg. Coordination between instruments for bimanual transfer of the peg ring was intuitive, especially as instruments were able to cross into the contralateral hemisphere of the peripheral structure. There was no noticeable time lag between the master and slave components.

For the position that the scope was fixed, the reachable workspace for the instrument tips included all aspects of the peg board. As the rigid over-tubes were at times parallel with the line of sight for the scope, stereoscopic vision greatly aided depth perception of the instrument tip location and general functionality of the system. The presence of visible tendons in the field of view did not interfere with task performance, although it was acknowledged that transparent tendons (rather than opaque yellow) might be a consideration in future prototype iterations (Figure 8.27). There was no cross-tendon clashing or entanglement. One tendon snapped towards the end of the feasibility assessment. This was felt to be have been contributed by higher tendon tension and friction at the eyelet site resulting from more acute tension insertion angles in the smaller paediatric sized peripheral structure. Long and slim eyelets were used for this experiment that had a relatively sharp rim. Replacement with shorter rounded-rim eyelets would help to alleviate tendon friction.

Force exertion was not recognised as an issue. Indeed, previous experimental work involving the CYCLOPS has demonstrated capability of the tendon design to exert forces up to 65 Newtons. Force requirements for most surgical tasks require 5 – 10 Newtons [320]. When pegs were accidentally dropped, this was invariably due to poor initial grasp bite of the peg ring.

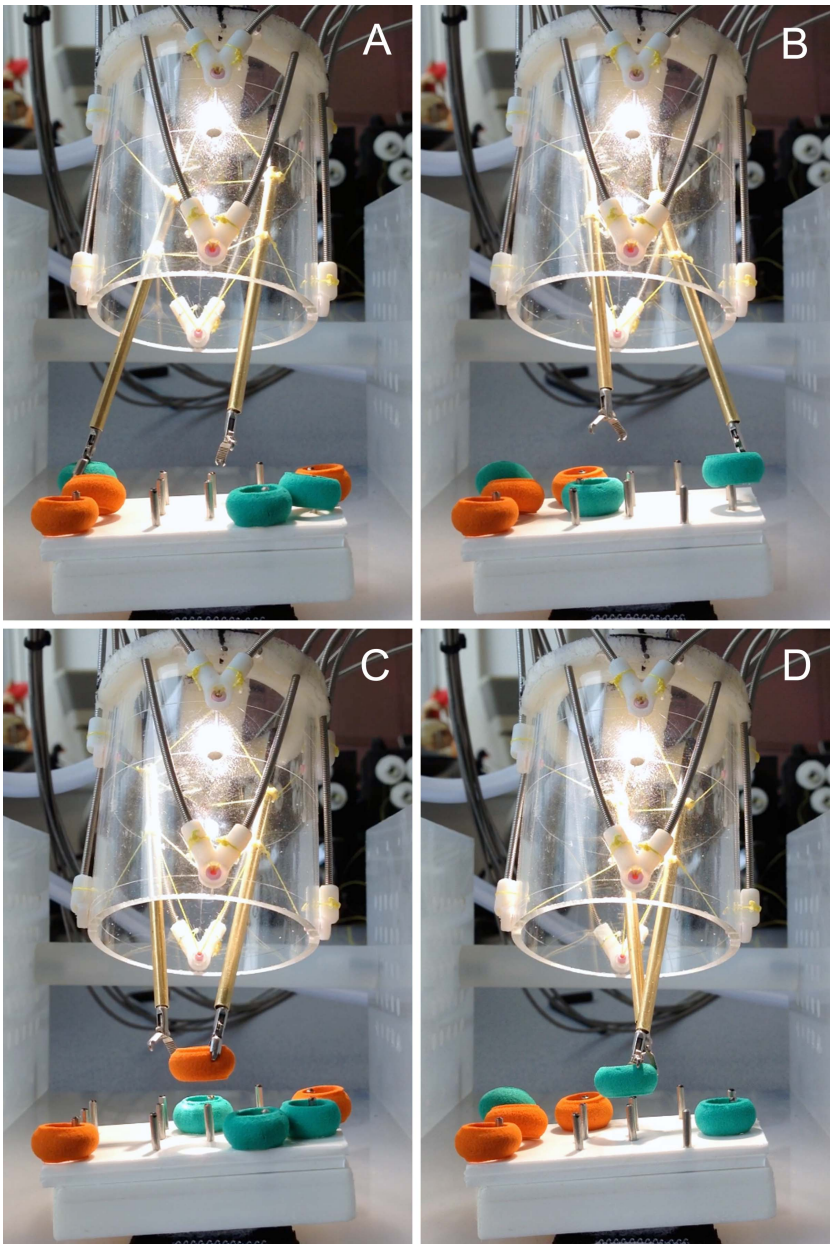


Figure 8.26 Sequence of the CYCLOPS performing the peg transfer task demonstrating a) far right lateral reach, b) far left lateral reach, c) coordinated instrument triangulation and bimanual control to exchange the peg ring, and d) crossover of instruments into the contralateral workspace hemisphere of the peripheral scaffold.

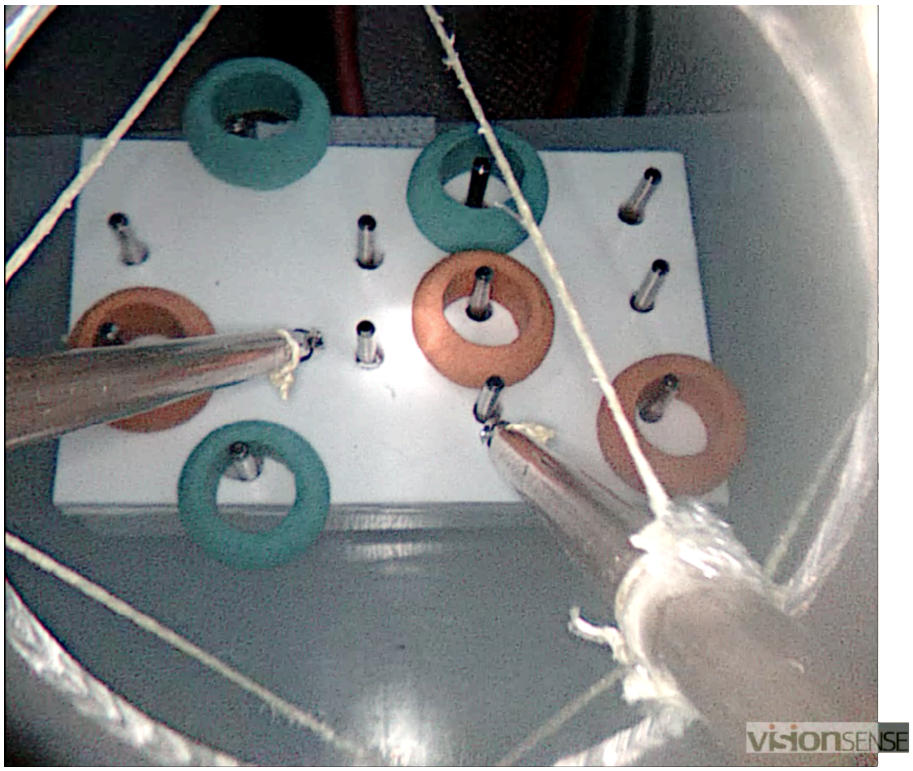


Figure 8.27 CYCLOPS on-board camera view during the peg transfer task.

8.4.4 Discussion

This initial pre-clinical evaluation of the CYCLOPS for use in paediatric laparoscopy involved customising the core peripheral scaffold component to a small size. The prototype used in this study is a low-cost early iteration and the 79.5cm^3 volume cylindrical scaffold was the smallest peripheral component to have been tested with the CYCLOPS system to date. As a first trial, the scaled prototype performed well and demonstrated that a simple bimanual task could be completed successfully and with promising potential for testing with more complex tasks. Constrained dimensions for the tendon-driven parallel robot design revealed several specific technical problems to be addressed. Firstly, each peripheral structure size requires its own optimised tendon network configuration. Tendon configuration for smaller peripheral scaffold needs to be more geometrically exact for optimum performance. Minor misplacements in the positioning of tendon fulcrum points (eyelets) and tendon attachment sites on the rigid over-tubes can result in major variations in tendon tension, tendon friction, controllability, reachable workspace and force-exertion. Such errors have an almost unnoticeable impact on system performance for larger peripheral scaffolds (i.e. > 200cm^3). Secondly, it was appreciated that the circumference of the open end of the peripheral scaffold is proportional to the X- and Y-axis thresholds for the reachable

workspace of the instruments. This might have little clinical relevance as the size of the selected peripheral scaffold to be attached to a laparoscope or flexible endoscope would generally be expected to correspond with a similarly small operative workspace.

8.4.4.1 Future work

Short- and medium-term goals for future development of the CYCLOPS will broadly involve biomaterial selection and deployable design structure for the peripheral scaffold, rationalising tendon configuration and control, force-based control implementation, exploring the compatible range of commercially available flexible endoscopic instruments, and integration with flexible endoscopes.

Rationalisation of tendons will involve replacing the supportive Bowden cables with lower profile tendon channels. The added diameter of the Bowden cables at the moment takes the overall external diameter of the system to 11.6mm once they are concentrically bundled around the 4mm scope. Given that the tendons themselves are <0.5mm, there is ample room to downsize the Bowden cables (or similar structures) from 1.9mm to 0.5mm, thereby bringing the overall diameter of the system closer to 6mm – a size appropriate for many paediatric indications.

With some adjustments to tendon configuration, the CYCLOPS concept could be modified to accommodate and 3rd or 4th working instrument arm. Instruments would operate within independent quadrants but as shown in Figure 8.26 they will be able to cross into adjacent quadrants. Additional arms could be used for retraction, suction, irrigation or focused energy delivery.

It is planned to proceed with further functionality testing using this stable functional prototype. This will include more complex tasks on inanimate models and procedure specific cadaveric tissue models. For more complex tasks such as suturing, an additional axial rotational DOF is needed (i.e. pronation-supination). Preliminary work has demonstrated that a 'pseudo' 6th DOF is possible using a novel strategy that doesn't interfere with the existing tendon arrangement [321]. This is achieved by intertwining opposed tendon pairs around the shaft of the rigid over-tubes [321]. Motorised actuation of a tendon pair generates controlled clockwise or counter-clockwise torque [321]. Another feature that must be addressed for more sophisticated prototype testing is a control mechanism for actuating the end-effector in a non-binary fashion. This might be accomplished by incorporating a gear mechanism to the motor

unit on the flexible endoscopic instrument and replacing the Geomagic® Touch™ haptic devices with omega.7 or sigma.7 haptic devices that have passive graspers (Force Dimension, Nyon, Switzerland).

8.4.4.2 Clinical roles

Paediatric applications for the CYCLOPS assembled with a *laparoscope* would include a single-port approach for almost all laparoscopic procedures performed as multi-port procedures today. The CYCLOPS design directly addresses all the existing shortcomings of single-port laparoscopy, principally triangulation and ergonomic comfort. The technology would be affordable, with capital outlay cost projections for the CYCLOPS being £10,000 - £15,000 and consumables expenses on par with single use items for single-port laparoscopy on the market today (i.e. £80 - £200 per item).

Single-port laparoscopy can probably only offer small incremental clinical gains. The opportunity for the CYCLOPS to have greatest clinical impact in paediatric surgery is felt to be for applications that involve mounting the system to a *flexible endoscope*. These include natural orifice endoluminal and translumenal procedures within hollow viscera such as the stomach, bladder, colon and uterus. These capacious anatomical structures would accommodate larger scaffold dimensions for the CYCLOPS. Existing interventional endoluminal approaches to these organs are made difficult by an operative environment that is dynamic, mobile and constantly collapsing on itself. The ability of the deployable scaffold to uniformly retract the viscus from its luminal surface would provide a stable and un-obstructed surgical field. Dexterous high degree-of-freedom bimanual control, instrument triangulation, and adequate delivery of force at the tool-tissue interface would then enable essentially unrestricted ability for a wide variety of ablative and reconstructive procedures to be performed. The scaffold also offers advantages beyond improved triangulation, force delivery, large workspace, stability and control. Creation and maintenance of a submucosal space or tunnel for NOES procedures is laborious and risky. Using the scaffold to mechanically expose and confidently maintain this working space presents a practical solution. Alternatively, the scaffold may also be used to suction or invaginate tissue for resection as well as protecting it for safe specimen extraction. Finally, there are numerous imaging opportunities of the scaffold design ranging from multiple mobile camera positioning, improved illumination of the operative field and real time in-situ image-guided dissection using the bulb as a wide radial-array ultrasound probe.

Eligible clinical roles for the CYCLOPS in paediatric *NOES* might include POEM, POEP, per-oral endoluminal bariatric surgery (gastroplication) for morbidly obese adolescents, transurethral intravesical ureteral reimplantation, and transurethral intravesical bladder diverticulectomy. Possible clinical roles for the CYCLOPS in paediatric *NOTES* might include transoesophageal oesophageal atresia repair with ligation of trachea-oesophageal fistula and transanal endorectal pull through for long-segment Hirschprung's disease. For both these radical NOTES concepts, early experimental studies in animals and humans have been reported however with ill-suited technology [322-327].

In conclusion, the motivation for the CYCLOPS concept is to deliver *affordable*, *accessible and novel technology* that enables *new less invasive techniques* for higher quality surgical outcomes. Preliminary testing of early CYCLOPS prototypes shows promise that this ambitious goal is realisable.

CHAPTER 9 CONCLUSIONS & FUTURE WORK

9.1 Achievements of this Thesis

At the commencement of this thesis, the role of robot-assisted surgery in children could be judged only on conflicting anecdotal opinion, industry-led marketing hype and low level of evidence literature (≤ Level III). This thesis generates and consolidates strengthened evidence to form a more explicit and comprehensive critical appraisal. The thesis also ventures beyond the confines of the present and seeks to address empirically identified shortcomings of existing technology by undertaking preliminary work on next-generation robot prototypes for targeted use in paediatric surgery.

The systematic reviews in Chapter 2 form the most extensive summations of the literature that have been undertaken to date. The exercise of quantitatively mapping the adoption chronology and procedure-based clinical application breakdown is unprecedented and examines paediatric robot-assisted surgery from a broad overarching perspective. The reviews affirm that application of robot-assisted surgery in children is uniquely different from other surgical specialties. The key factor in this difference is there is a negligible role and volume for oncological organectomies in children, with focus instead on reconstructive surgery for congenital or acquired functional pathologies. The meta-analyses in Chapter 3 represent the first and only available efforts at data synthesis of comparative effectiveness data. These studies are fundamental to understanding the value of robot-assistance in comparison to existing standards and whether its use is justified in terms of clinical outcome benefit.

Education and training are essential for safe introduction of new technology. The workshop reported in Chapter 4 actively sought to provide an educational resource that was lacking in the European region. Its popularity and success indicates that there is an unmet training needs that it serves. It is hoped that this workshop is maintained as an ongoing annual event, although issues with sustainability of such events are candidly discussed within the chapter. Knowledge of learning curve shapes, transition points and durations are necessary to inform expectation requirements of training and educational goals. Chapter 4 also challenges and exposes methodological deficiencies in learning curve analysis. The cumulative summation technique for learning curve analysis is reported in only a handful of studies in paediatric surgery, and none that examine learning curves of operative techniques. Its advantages are

highlighted through studies that define multi-dimensional learning curves for paediatric robot-assisted laparoscopic pyeloplasty and fundoplication. As such, it is proposed that the under-utilised cumulative summation technique be re-considered as a preferential statistical approach for learning curve analysis.

The social science theory orientated survey study in Chapter 5 captures the attitudes of a representative international group of early adopters in paediatric robotic surgery. This approach of structured direct enquiry yielded informative responses that demystify what really is influencing, or not influencing, the early adoption of robotic surgery amongst paediatric surgeons. It also clearly defines the agenda for future progress in the field by outlining specific needs of this technology end-user community.

Findings of the survey study prompted the concept of haptic feedback loss to be studied in more detail. In particular, the hypothesis that experts acquire adaptive non-tactile skills that compensate for this sensory deficit. In Chapter 6, analysis of suture damage frequency provided supportive evidence to allow the null hypothesis to be rejected and for it to be quantitatively verified for the first time using *in vivo* data that experience related factors do compensate for haptic feedback loss. Along with the observation that minimal inadvertent tissue injury occurs as a result of haptic feedback loss, these findings lend support to the argument that more focus should be spent on pre-clinical training to acquire compensatory skills rather than investing in sophisticated technological solutions such as instrument mounted micro-sensors for real-time transmission of tactile haptic information. Practical suggestions for preferential use of braided suture material, robotic needle holder instruments instead of forceps and interrupted sutures instead of continuous suture lines are offered to avoid inconvenience or clinical implications of haptic feedback loss related suture damage during the learning phase of robot-assisted surgery.

To explore the concept of haptic compensatory skills being acquirable in the pre-clinical setting, a force sensing enhanced paediatric laparoscopy simulator was developed and validated. Through this process, it was demonstrated that tool-tissue interaction force is a reliable and sensitive discriminator of skill level that may be used to improve the effectiveness of simulation-based education and training. The ForSense was designed to be easily integrated with a low-cost and well-validated existing paediatric laparoscopy box trainer simulator. In doing this, a new category of hybrid simulators is realised that unites the endearing low-cost low-barrier features of box trainer simulators with data rich computer-generated objective outcomes that are associated with virtual reality simulators.

Chapter 7 investigated the feature of robot-assisted surgery that paediatric surgeons identify as most advantageous - articulated wristed instruments. Appeal for this speculative benefit lacked scientific support and for this reason a randomised cross-over study was designed to compare robotic versus non-robotic instruments for use in various spatially constrained operative workspaces that were clinically relevant to paediatric minimally invasive surgery. It was found that the influence of spatial constraints negatively impacts performance capabilities for both non-robotic and robotic instruments. The degree to which performance is restricted is proportional to instrument size. Larger diameter, articulating design and bulkier form of robotic instruments were found to pose dimensional limitations for which they can be physically accommodated in a safe and effective manner. In spatially constrained workspaces $\leq 200cm^3$, 5mm and 8mm robotic instruments do not confer an objective or subjective advantage over 3mm non-robotic instruments for an advanced bimanual task. These findings unequivocally prove for the first time that existing robot instruments are too large and bulky to be well suited for use in paediatric surgery. Miniaturisation must be a priority for next-generation robotic systems. Results from the survey study reveal that the most preferred diameter for robotic instruments is 3mm.

Perhaps the most exciting achievement of this thesis is the early evaluation of novel single shaft second-generation robotic surgery system prototypes for use in paediatric surgery. Preliminary results of prototype testing demonstrate the potential for cost attainable robots to enable new procedural approaches that are less invasive. This is the direction that robot-assisted surgery must strive towards if disruptive progression in clinical outcome benefit is to be achieved rather than small incremental gains.

9.2 Future Work

Directions for future work and limitations of each chapter are discussed in detail within relevant aspects of the text.

9.2.1 Ongoing monitoring and assessment

Paediatric robot-assisted minimally invasive surgery is an evolving entity. As global adoption continues to grow, more evidence will accumulate that will allow higher-powered critical assessment. The process of ongoing monitoring will require vigilance through periodical re-assessment. It remains unclear what selected procedures are appropriate for a robot-assisted approach, and what procedures are extravagant use of expensive technology. Fundoplication

and pyeloplasty were evaluated in detail in this thesis as they are the highest volume procedures, however there are at least 50 other procedures for which robot-assistance has been reported as safe and feasible. Moreover, the role of robot-assisted surgery in selected cases of fundoplication and pyeloplasty are yet to be studied in isolation (i.e. more complicated re-do procedures). Further comparative effectiveness evidence is needed to define the case-mix for which robot-assisted surgery is indicated, however this will be limited by low volume for many indications.

Just as clinicians have a responsibility to reject pro-innovation bias and formerly evaluate the safety and effectiveness of robotic surgery, it is equally important to prospectively monitor its diffusion on local, regional, national and international levels so that processes of adoption can be understood and studied. The idea of mandatory or voluntary registries for robot-assisted surgery have been entertained however there are major obstacles associated with the establishment and governance of such endeavours. The technique of evaluation of published literature data that was used in Chapter 2 is a tangible and sufficiently sensitive measure of adoption trends.

Funding models for robot-assisted surgery are fragmented amongst individual practice settings. Large high-volume tertiary institutions that share use of the robot amongst multiple specialty groups are more likely to be able to absorb higher associated costs. In this sense there is a legitimate argument for centralising first-generation robotic surgery systems. This thesis does not include formal cost-effectiveness analyses and this remains an under-addressed objective for future research in the field.

Lastly, it must be realised only two technical aspects of robot-assisted surgery were studied in detail in this thesis; haptic feedback loss and wristed instruments. There are many more technical aspects that require formal evaluation to investigate their relative advantage or disadvantage in paediatric minimally invasive surgery. Such factors include cognitive and musculoskeletal ergonomy, tremor filtration for microsurgery, motion scaling and stereoscopic vision for example.

9.2.2 Education and training in paediatric robotic surgery

Educational resources and training curricula are poorly provided for in paediatric robot-assisted surgery. This is contributed by a state of uncertainty for where responsibility should be assigned for ensuring these important needs are satisfied. Some feel that substantial

proportion of responsibility should lie with the manufacturer, while others feel that responsibility should be shared amongst specialty accreditation bodies or societies (i.e. various Colleges, SAGES etc.), hospitals and individual surgeons. The workshop described in Chapter 4 represents an initial step in providing an organised pre-clinical event for paediatric surgeons to gain exposure and familiarisation with the robot while learning basic principles from experienced faculty. Resources that cater for training needs beyond this are absent. Considerable future attention is needed to both implement and evaluate more advanced education and training resources in line with the framework outlined in Figure 4.1.

As described in Chapter 4, comparative assessment of learning curves for robot-assisted versus conventional laparoscopic or open surgery remain uninvestigated and this is needed to justify the widespread claims that robot-assistance permits more accelerated and steep learning curves.

Lastly, the ForSense simulator platform presented in Chapter 5 requires further work to validate it for adaptive haptic skills training in robot-assisted surgery. A pilot experimental set-up has been assembled to test the utility of photometric signal feedback to train naïve users to more easily recognise non-tactile cues and integrate perceptions of these sensory mechanisms to compensate for a haptic deprived state. The set-up involves the addition of several rows of small coloured light-emitting diodes (LEDS) within the ForSense. The LEDs are programmed to illuminate when pre-defined force thresholds are breached. This will signal the ambient light to change colour to reflect a warning alert of high tolerable tool-tissue interaction force (i.e. yellow or amber light) and then an alarm when an intolerable force is registered (i.e. red light).

9.2.3 Next-generation robotic systems

The examples provided in Chapter 8 verify that second-generation robotic systems are on the imminent horizon and that this next phase of technology will be better suited for paediatric surgery. It is greatly encouraging that research groups are already designing robotic tools and devices that are exclusive for paediatric patients in general or specific paediatric procedures. Historically, investment funding for paediatric themed technology is difficult to secure due to low volume markets and therefore small capacity for capital return. The FDA Office for Orphan Products Development provides incentives for sponsors or investors to develop products for diseases that affect <200,000 people in the United States. Through this government body, a Pediatric Device Consortia Grant Program has recently been launched that provides an annual budget of USD $2,000,000 to support non-profit groups to develop

paediatric medical devices. These initiatives are well timed to attract interest of academic and industry R&D groups to concentrate on paediatric themed technologies during the inevitable and imminent transition period between first- and second-generation robotic surgery systems.

The i-Snake® and CYCLOPS prototypes will continue to progress through the iterative phases of medical device development. The convoluted innovation process is well described by Gertner [197]. Next steps for future work are summarised within Chapter 8 and will include prototype refinement and more comprehensive testing using *ex vivo* and *in vivo* animal models.

9.3 Conclusion

For the surgeon, the advent of first-generation innovation in robotic surgery has been an impressive engineering achievement that changes the dynamic of an operating room and provides improved physical comfort while operating. In an unprecedented way, the surgeon and patient are distanced from one another but closely linked via a master-slave telerobotic system. In effect, this allows the power of modern computing science to positively influence the relationship between the surgeon and patient. The result is an ability to augment the operative environment with features that overcome limitations of non-robotic minimally invasive surgery, and empower the surgeon with abilities that restore those appreciated in open surgery and even transcend physical and cognitive limits.

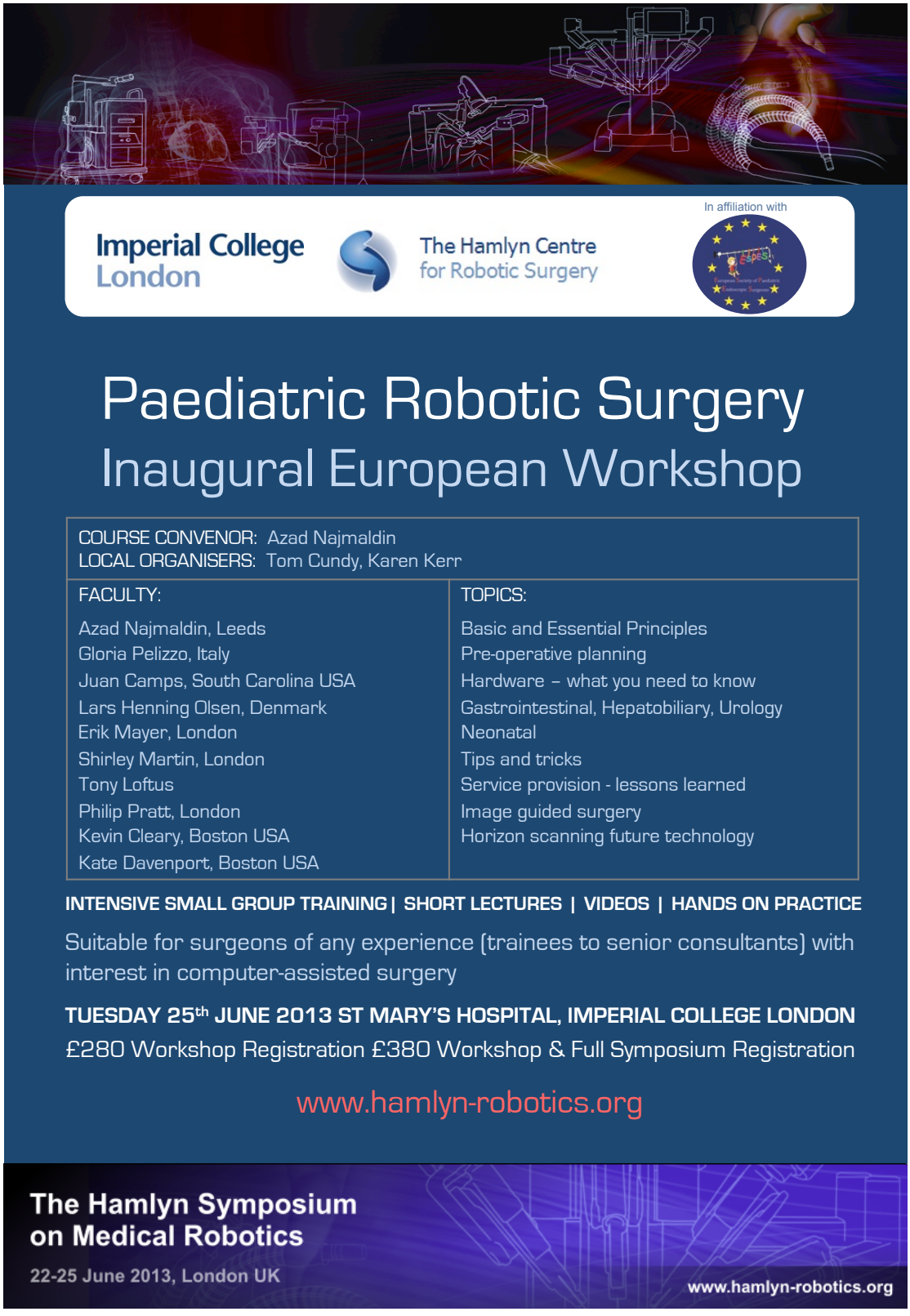
For the paediatric patient, the impact of robot-assisted surgery is quite unremarkable and underwhelming from an innovation perspective. Compared to conventional laparoscopic and thoracoscopic procedures that they might undergo, a robot-assisted minimally invasive procedure will replicate the same surgical steps. At the tool-tissue interface, their internal anatomy will essentially be handled and manipulated in the same fashion. Their skin incisions will be indifferent, or more likely slightly larger. Their outcomes will be more or less comparable. It must be recognised however that robot-assisted surgery may allow some children to undergo minimally invasive surgery when this approach might otherwise not be considered.

For hospitals and health systems, the expense of first-generation robotic surgery systems makes this technology either inaccessible or challenging to sustain financially. The physical footprint occupies considerable space in operating theatres. Unlike laparoscopic stacks, it is both impractical and impossible for hospitals to accommodate multiple robotic systems for

simultaneous use in more than one operating theatre. Combined effects of these factors mean it is unrealistic that first-generation robotic systems will replace conventional laparoscopic surgery infrastructure in even the most modern and well-financed health systems.

It seems unlikely that we should expect compelling patient benefits when it is only the *mode* of minimally invasive surgery that differs, and the surgical approach and procedural steps remain indistinguishable from pre-existing operative alternatives. In this regard, rigid multi-arm robotic platforms on the market today represent more of a minimally invasive *evolution* than a surgical *revolution*. Like the automobile industry equivalent of the Ford Model T car, the legacy of first-generation surgical robots will be to have contributed to society as pioneering gateway technology that inspired generations of ongoing future development and primed stakeholder groups. There is enormous potential in the capacity of surgical robotics to breakthrough and achieve exciting new less invasive ways to better treat childhood surgical disease that are not possible today. The challenge for next-generation robotic technologies will be to target direct opportunities for clinical benefit and to exploit modern technology to enable these innovative endeavors. This will demand technology that is customised to selected patient populations or procedures. Prototype examples of such technology are presented in Chapter 8. Importantly, financial affordability must be a high priority to ensure accessibility for clinical use. Much of tomorrow's translatable innovation is being conceived and incubated in laboratories today. To accelerate this process, an attitude of active interest and involvement (both critical and supportive) by the surgical end-user community will be immensely more impactful than that of being passive end-product recipients. The paediatric surgical community should remain engaged and patiently optimistic regarding the great potential that robotic technology has to offer for enabling improved delivery of surgical care in children.

Appendices



Appendix 1. Flyer for the Paediatric Robotic Surgery Inaugural European Workshop.



Appendix 2. Flyer for the Paediatric Robotic Surgery 2nd Annual European Workshop.

The Hamlyn Centre for Robotic Surgery

Imperial College London

International Attitudes toward Current and Future Robotic Technology for Paediatric MIS

Page 1/4

1. In what country is your current clinical practice?

Country:

2. How many paediatric robot-assisted MIS cases have you performed as primary SURGEON?

- <10
- 10 - 30
- 30 - 50
- >50

3. How many paediatric robot-assisted MIS cases have you been involved with as ASSISTANT?

- <10
- 10 - 30
- 30 - 50
- >50

4. How much SIMULATION and TRAINING have you received in robotic surgery?

- < 5 hours
- 5 - 10 hours
- 10 - 15 hours
- 15 - 20 hours
- > 20 hours

International Attitudes toward Current and Future Robotic Technology for Paediatric MIS

Page 2/4

5. What are your attitudes toward the following features of robot-assistance that are perceived as BENEFITS in paediatric MIS?

	Strongly Agree	Agree	Neither	Disagree	Strongly Disagree	*(Don't Understand)
Stereoscopic (3D) vision						
Shorter learning curve						
Tremor filtration						
Hand-eye coordination						
Magnified view						
Wristed instruments						
Instrument re-indexing						
Motion scaling						
Surgeon controlled camera movement						
Operator comfort						

Other (please specify)

International Attitudes toward Current and Future Robotic Technology for Paediatric MIS

Page 3/4

6. What are your attitudes toward the following features of robot-assistance that are perceived as LIMITATIONS in paediatric MIS?

	Strongly Agree	Agree	Neither	Disagree	Strongly Disagree	*(Don't Understand)
Emergency access to the patient	○	○	○	○	○	○
Instrument range	○	○	○	○	○	○
Capital outlay expense	○	○	○	○	○	○
Re-positioning for multi-quadrant surgery	○	○	○	○	○	○
Set-up and docking time	○	○	○	○	○	○
Instrument size	○	○	○	○	○	○
Haptic feedback (tactile) loss	○	○	○	○	○	○
Maintenance expense	○	○	○	○	○	○
Consumables expense	○	○	○	○	○	○
System instability (i.e. software or hardware failure)	○	○	○	○	○	○
Access to simulation and training	○	○	○	○	○	○
Unclear supportive evidence	○	○	○	○	○	○
System size in the operating theatre	○	○	○	○	○	○

Other (please specify)

International Attitudes toward Current and Future Robotic Technology for Paediatric MIS

Page 4/4

7. Is there a future role for robot-assisted MIS in children?

- ○ Definitely
- ○ Probably
- ○ Unsure
- ○ Probably Not
- ○ Definitely Not

8. What are your attitudes toward the following next-generation robotic technologies

	Very Interested	Interested	Neutral	Not Very Interested	Not At All Interested	*(Don't Understand)
Flexible snake robots for NOTES or SILS	○	○	○	○	○	○
Image guidance (i.e. augmented reality)	○	○	○	○	○	○
Micro-bots	○	○	○	○	○	○
Remote-access telesurgery	○	○	○	○	○	○
da Vinci Single-Site	○	○	○	○	○	○
Hand-held bedside operated robotic instruments	○	○	○	○	○	○

Other (please specify)

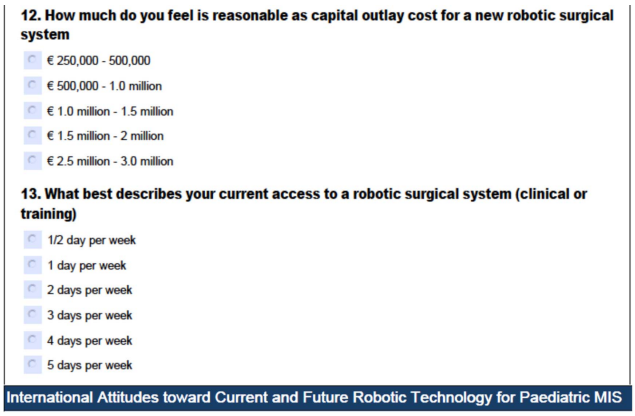
9. What are the priorities for future robotic platforms in paediatric MIS?

10. What is the preferred scope diameter for paediatric robot-assisted MIS?

- ○ 3mm
- ○ 5mm
- ○ 8mm
- ○ 10mm
- ○ 12mm

11. What is the preferred instrument size for paediatric robot-assisted MIS?

- ○ 2mm
- ○ 3mm
- ○ 3.5mm
- ○ 5mm
- ○ 8mm



Appendix 3. Example copy of the electronic survey that was generated via SurveyMonkey®, a subscription-based online survey software and questionnaire tool.

List of References

1. Moran ME. The da Vinci robot. *J Endourol* 2006; 20(12):986-90.
2. Chandra V, Dutta S, Albanese CT. Surgical robotics and image guided therapy in pediatric surgery: emerging and converging minimal access technologies. *Semin Pediatr Surg* 2006; 15(4):267-75.
3. Kant AJ, Klein MD, Langenburg SE. Robotics in pediatric surgery: perspectives for imaging. *Pediatr Radiology* 2004; 34(6):454-61.
4. van Haasteren G, Levine S, Hayes W. Pediatric robotic surgery: early assessment. *Pediatrics* 2009; 124(6):1642-9.
5. Berlinger NT. Robotic surgery--squeezing into tight places. *N Engl J Med* 2006; 354(20):2099-101.
6. Drasin T, Gracia C, Atkinson J. Pediatric Applications of Robotic Surgery. *Pediatric Endosurgery & Innovative Techniques* 2003; 7(4):377 - 384.
7. Meehan JJ. Robotic surgery in small children: is there room for this? *J Laparoendosc Adv Surg Tech A* 2009; 19(5):707-12.
8. Meehan JJ. Robotic repair of congenital duodenal atresia: a case report. *J Pediatr Surg* 2007; 42(7):E31-3.
9. Najmaldin A. Paediatric telerobotic surgery: where do we stand. *Int J Med Robot* 2007; 3(3):183-6.
10. Orvieto MA, Large M, Gundeti MS. Robotic paediatric urology. *BJU Int* 2012; 110(1):2-13.
11. Thakre AA, Bailly Y, Sun LW, et al. Is smaller workspace a limitation for robot performance in laparoscopy? *J Urol* 2008; 179(3):1138-42.
12. Luebbe BN, Woo R, Wolf SA, et al. Robotically assisted minimally invasive surgery in a pediatric population: initial experience, technical considerations, and description of the da Vinci surgical system. *Pediatric Endosurgery & Innovative Techniques* 2003; 7(4):385 - 403.
13. Okada S, Y T, Yamauchi H, et al. Single-surgeon thoracoscopic surgery with a voice-controlled robot. *Lancet* 1998; 351(9111):1249.
14. Partin A, Adams J, Moore R, et al. Complete robot-assisted laparoscopic urologic surgery: a preliminary report. *J Am Coll Surg* 1995; 181(6):552-7.
15. Meininger DD, Byhahn C, Heller K, et al. Totally endoscopic Nissen fundoplication with a robotic system in a child. *Surg Endosc* 2001; 15(11):1360.
16. Gutt CN, Markus B, Kim ZG, et al. Early experiences of robotic surgery in children. *Surg Endosc* 2002; 16(7):1083-6.
17. Heller K, Gutt C, Schaeff B, et al. Use of the robot system Da Vinci for laparoscopic repair of gastro-oesophageal reflux in children. *Eur J Pediatr Surg* 2002; 12(4):239-42.
18. Lee RS, Borer JG. Robotic surgery for ureteropelvic junction obstruction. *Curr Opin Urol* 2006; 16(4):291-4.
19. Peters CA. Robotically assisted paediatric pyeloplasty: cutting edge or expensive toy? *BJU Int* 2004; 94(9):1214-5.
20. Barkun JS, Aronson JK, Feldman LS, et al. Evaluation and stages of surgical innovations. *Lancet* 2009; 374(9695):1089-96.
21. Bax NM. Karl Storz Lecture. Ten years of maturation of endoscopic surgery in children. Is the wine good? *J Pediatr Surg* 2004; 39(2):146-51.
22. Wilson CB. Adoption of new surgical technology. *BMJ* 2006; 332(7533):112-4.
23. Meehan JJ, Sandler A. Pediatric robotic surgery: A single-institutional review of the first 100 consecutive cases. *Surg Endosc* 2008; 22(1):177-82.
24. Jones VS, Cohen RC. Two decades of minimally invasive pediatric surgery-taking stock. *J Pediatr Surg* 2008; 43(9):1653-9.

25. Adikibi BT, Mackinlay GA, Clark MC, et al. The risks of minimal access surgery in children: an aid to consent. *J Pediatr Surg* 2012; 47(3):601-5.
26. Alqahtani A, Albassam A, Zamakhshary M, et al. Robot-assisted pediatric surgery: how far can we go? *World J Surg* 2010; 34(5):975-8.
27. Camps JI. The use of robotics in pediatric surgery: my initial experience. *Pediatric Surg Int* 2011; 27(9):991-6.
28. Kasturi S, Sehgal SS, Christman MS, et al. Prospective long-term analysis of nerve-sparing extravesical robotic-assisted laparoscopic ureteral reimplantation. *Urology* 2012; 79(3):680-3.
29. Minnillo BJ, Cruz JA, Sayao RH, et al. Long-term experience and outcomes of robotic assisted laparoscopic pyeloplasty in children and young adults. *J Urol* 2011; 185(4):1455-60.
30. Lindgren BW, Hagerty J, Meyer T, et al. Robot-assisted laparoscopic surgery in children: does it apply to all levels of the ureter? Presented at the 22nd *Annual Congress of the International Pediatric Endosurgery Group,* San Diego, CA, June 17-22, 2012.
31. Gattas N, Smith C, Alizai NK, et al. Short and long term complications of robotic abdominal surgery in children. Presented at the 5th *Hamlyn Symposium on Medical Robotics*, London, United Kingdom, July 1-2, 2012.
32. Meehan JJ. Pediatric Robotic Surgery: the ultimate diversity. *6th Annual Minimally Invasic Robotic Surgery Congress* 2011; Athens, Greece.
33. Alqahtani A. Single port laparoscopic and robotic nissen fundoplication in children. Presented at the 22nd *Annual Congress of the International Pediatric Endosurgery Group,* San Diego, CA, June 17-22, 2012.
34. Frader JE, Flanagan-Klygis E. Innovation and research in pediatric surgery. *Semin Pediatr Surg* 2001; 10(4):198-203.
35. Moss RL, Henry MC, Dimmitt RA, et al. The role of prospective randomized clinical trials in pediatric surgery: state of the art? *J Pediatr Surg* 2001; 36(8):1182-6.
36. Ergina PL, Cook JA, Blazeby JM, et al. Challenges in evaluating surgical innovation. *Lancet* 2009; 374(9695):1097-104.
37. Curry JI, Reeves B, Stringer MD. Randomized controlled trials in pediatric surgery: could we do better? *J Pediatr Surg* 2003; 38(4):556-9.
38. Rangel SJ, Henry MC, Brindle M, et al. Small evidence for small incisions: pediatric laparoscopy and the need for more rigorous evaluation of novel surgical therapies. *J Pediatr Surg* 2003; 38(10):1429-33.
39. Riskin DJ, Longaker MT, Krummel TM. The ethics of innovation in pediatric surgery. *Semin Pediatr Surg* 2006; 15(4):319-23.
40. Ostlie DJ, St Peter SD. The current state of evidence-based pediatric surgery. *J Pediatr Surg* 2010; 45(10):1940-6.
41. Rangel SJ, Kelsey J, Henry MC, et al. Critical analysis of clinical research reporting in pediatric surgery: justifying the need for a new standard. *J Pediatr Surg* 2003; 38(12):1739-43.
42. Shamberger RC. Cooperative group trials in pediatric oncology: The surgeon's role. *J Pediatr Surg* 2013; 48(1):1-13.
43. Holcomb GW, 3rd, Tomita SS, Haase GM, et al. Minimally invasive surgery in children with cancer. *Cancer* 1995; 76(1):121-8.
44. Blucher D, Lobe TE. Minimal access surgery in children: the state of the art. *Int Surg* 1994; 79(4):317-21.
45. Guys J, Delarue A, H. LH-A, et al. Videosurgery in oncological pediatrics. *Pediatr Surg Int* 1995; 10:371-373.
46. Malek MM, Mollen KP, Kane TD, et al. Thoracic neuroblastoma: a retrospective review of our institutional experience with comparison of the thoracoscopic and open approaches to resection. *J Pediatr Surg* 2010; 45(8):1622-6.

47. Iwanaka T, Arai M, Kawashima H, et al. Endosurgical procedures for pediatric solid tumors. *Pediatr Surg Int* 2004; 20(1):39-42.
48. Warmann S, Fuchs J, Jesch NK, et al. A prospective study of minimally invasive techniques in pediatric surgical oncology: preliminary report. *Med Pediatr Oncol* 2003; 40(3):155-7.
49. Kim T, Kim DY, Cho MJ, et al. Use of laparoscopic surgical resection for pediatric malignant solid tumors: a case series. *Surg Endosc* 2011; 25(5):1484-8.
50. Saenz NC, Conlon KC, Aronson DC, et al. The application of minimal access procedures in infants, children, and young adults with pediatric malignancies. *J Laparoendosc Adv Surg Tech A* 1997; 7(5):289-94.
51. Duarte RJ, Denes FT, Cristofani LM, et al. Laparoscopic nephrectomy for Wilms' tumor. *Expert Rev Anticancer Ther* 2009; 9(6):753-61.
52. Schmidt AI, Reismann M, Kubler JF, et al. Exposure to carbon dioxide and helium reduces in vitro proliferation of pediatric tumor cells. *Pediatr Surg Int* 2006; 22(1):72-7.
53. Holcomb GW, 3rd. Minimally invasive surgery for solid tumors. *Semin Surg Oncol* 1999; 16(2):184-92.
54. Metzelder ML, Kuebler JF, Shimotakahara A, et al. Role of diagnostic and ablative minimally invasive surgery for pediatric malignancies. *Cancer* 2007; 109(11):2343-8.
55. Spurbeck WW, Davidoff AM, Lobe TE, et al. Minimally invasive surgery in pediatric cancer patients. *Ann Surg Oncol* 2004; 11(3):340-3.
56. de Lijster MS, Bergevoet RM, van Dalen EC, et al. Minimally invasive surgery versus open surgery for the treatment of solid abdominal and thoracic neoplasms in children. *Cochrane Database Syst Rev* 2012; 1:CD008403.
57. Chan KW, Lee KH, Tam YH, et al. Minimal invasive surgery in pediatric solid tumors. *J Laparoendosc Adv Surg Tech A* 2007; 17(6):817-20.
58. Anderberg M, Backman T, Annerstedt M. Robot-assisted radical cystoprostatectomy in a small child with rhabdomyosarcoma: a case report. *J Robot Surg* 2008; 2:101-103.
59. Duarte RJ, Denes FT, Cristofani LM, et al. Further experience with laparoscopic nephrectomy for Wilms' tumour after chemotherapy. *BJU Int* 2006; 98(1):155-9.
60. Meehan JJ, Sandler AD. Robotic resection of mediastinal masses in children. *J Laparoendosc Adv Surg Tech A* 2008; 18(1):114-9.
61. Meehan JJ, Phearman L, Sandler A. Robotic pulmonary resections in children: series report and introduction of a new robotic instrument. *J Laparoendosc Adv Surg Tech A* 2008; 18(2):293-5.
62. Cost NG, Geller JI, DeFoor WR, Jr., et al. A robotic-assisted laparoscopic approach for pediatric renal cell carcinoma allows for both nephron-sparing surgery and extended lymph node dissection. *J Pediatr Surg* 2012; 47(10):1946-50.
63. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *Open Med* 2009; 3(3):e123-30.
64. Volkin D, Yerram N, Ahmed F, et al. Partial adrenalectomy minimizes the need for long-term hormone replacement in pediatric patients with pheochromocytoma and von Hippel-Lindau syndrome. *J Pediatr Surg* 2012; 47(11):2077-82.
65. Backes FJ, Seamon LG, Fowler JM. Robotic radical hysterectomy and pelvic lymphadenectomy for uterine rhabdomyosarcoma. *J Robot Surg* 2008; 2:197–200.
66. Cost NG, Dajusta DG, Granberg CF, et al. Robot-Assisted Laparoscopic Retroperitoneal Lymph Node Dissection in an Adolescent Population. *J Endourol* 2012.
67. Sodergren MH, Darzi A. Robotic cancer surgery. *Br J Surg* 2013; 100(1):3-4.
68. DeUgarte DA, Teitelbaum D, Hirschl RB, et al. Robotic extirpation of complex massive esophageal leiomyoma. *J Laparoendosc Adv Surg Tech A* 2008; 18(2):286-9.

69. Choy B, Gordetsky J, Varghese M, et al. Mixed epithelial and stromal tumor of the kidney in a 14-year-old boy. *Urol Int* 2012; 88(2):247-8.
70. Rogers CG, Blatt AM, Miles GE, et al. Concurrent robotic partial adrenalectomy and extra-adrenal pheochromocytoma resection in a pediatric patient with von Hippel-Lindau disease. *J Endourol* 2008; 22(7):1501-3.
71. St Julien J, Ball D, Schulick R. Robot-assisted cortical-sparing adrenalectomy in a patient with Von Hippel-Lindau disease and bilateral pheochromocytomas separated by 9 years. *J Laparoendosc Adv Surg Tech A* 2006; 16(5):473-7.
72. Hassan M, Smith JM. Robotic assisted excision of a left ventricular myxoma. *Interact Cardiovasc Thorac Surg* 2012; 14(1):113-4.
73. Lee J, Kang SW, Jung JJ, et al. Multicenter study of robotic thyroidectomy: short-term postoperative outcomes and surgeon ergonomic considerations. *Ann Surg Oncol* 2011; 18(9):2538-47.
74. Lee KE, Koo do H, Kim SJ, et al. Outcomes of 109 patients with papillary thyroid carcinoma who underwent robotic total thyroidectomy with central node dissection via the bilateral axillo-breast approach. *Surgery* 2010; 148(6):1207-13.
75. Akar ME, Leezer KH, Yalcinkaya TM. Robot-assisted laparoscopic management of a case with juvenile cystic adenomyoma. *Fertil Steril* 2010; 94(3):e55-6; author reply e57.
76. Nakib G, Calcaterra V, Scorletti F, et al. Robotic assisted surgery in pediatric gynecology: promising innovation in mini invasive surgical procedures. *J Pediatr Adolesc Gynecol* 2013; 26(1):e5-7.
77. Stephenson J, Gow KW, Meehan J, et al. Ewing sarcoma/primitive neuroectodermal tumor arising from the adrenal gland in an adolescent. *Pediatr Blood Cancer* 2011; 57(4):691-2.
78. Lee RS, Sethi AS, Passerotti CC, et al. Robot-assisted laparoscopic nephrectomy and contralateral ureteral reimplantation in children. *J Endourol* 2010; 24(1):123-8.
79. Jourdan IC, Dutson E, Garcia A, et al. Stereoscopic vision provides a significant advantage for precision robotic laparoscopy. *Br J Surg* 2004; 91(7):879-85.
80. Gunther P, Troger J, Holland-Cunz S, et al. Surgical complications in abdominal tumor surgery in children. Experiences at a single oncological center. *Eur J Pediatr Surg* 2009; 19(5):297-303.
81. Mariano ER, Furukawa L, Woo RK, et al. Anesthetic concerns for robot-assisted laparoscopy in an infant. *Anesth Analg* 2004; 99(6):1665-7, table of contents.
82. Anderberg M, Kockum CC, Arnbjornsson E. Paediatric robotic surgery in clinical practice: a cost analysis. *Eur J Pediatr Surg* 2009; 19(5):311-5.
83. Rowe CK, Pierce MW, Tecci KC, et al. A Comparative Direct Cost Analysis of Pediatric Urologic Robot-Assisted Laparoscopic Surgery Versus Open Surgery: Could Robot-Assisted Surgery Be Less Expensive? *J Endourol* 2012.
84. Gumus E, Boylu U, Turan T, et al. The learning curve of robot-assisted radical prostatectomy. *J Endourol* 2011; 25(10):1633-7.
85. Sammon J, Perry A, Beaule L, et al. Robot-assisted radical prostatectomy: learning rate analysis as an objective measure of the acquisition of surgical skill. *BJU Int* 2010; 106(6):855-60.
86. Najmaldin A, Antao B. Early experience of tele-robotic surgery in children. *Int J Med Robot* 2007; 3(3):199-202.
87. O'Brien ST, Shukla AR. Transition from open to robotic-assisted pediatric pyeloplasty: a feasibility and outcome study. *J Pediatr Urol* 2012; 8(3):276-81.
88. Ehrlich PF, Newman KD, Haase GM, et al. Lessons learned from a failed multi-institutional randomized controlled study. *J Pediatr Surg* 2002; 37(3):431-6.
89. Cundy TP, Shetty K, Clark J, et al. The first decade of robotic surgery in children. *J Pediatr Surg* 2013; 48(4):858-65.
90. Monn MF, Bahler CD, Schneider EB, et al. Trends in robot-assisted laparoscopic pyeloplasty in pediatric patients. *Urology* 2013; 81(6):1336-41.

91. Hirst A, Agha RA, Rosin D, et al. How can we improve surgical research and innovation?: The IDEAL framework for action. *Int J Surg* 2013; 11(10):1038-42.
92. Athanasiou T, Al-Ruzzeh S, Kumar P, et al. Off-pump myocardial revascularization is associated with less incidence of stroke in elderly patients. *Ann Thorac Surg* 2004; 77(2):745-53.
93. Barbosa JA, Kowal A, Onal B, et al. Comparative evaluation of the resolution of hydronephrosis in children who underwent open and robotic-assisted laparoscopic pyeloplasty. *J Pediatr Urol* 2013; 9(2):199-205.
94. Behan JW, Kim SS, Dorey F, et al. Human capital gains associated with robotic assisted laparoscopic pyeloplasty in children compared to open pyeloplasty. *J Urol* 2011; 186(4 Suppl):1663-7.
95. Franco I, Dyer LL, Zelkovic P. Laparoscopic pyeloplasty in the pediatric patient: hand sewn anastomosis versus robotic assisted anastomosis--is there a difference? *J Urol* 2007; 178(4 Pt 1):1483-6.
96. Kim S, Canter D, Leone N, et al. A comparative study between laparoscopic and robotically assisted pyeloplasty in the *J Urol* 2008; 179 Supplement(4):357.
97. Lee RS, Retik AB, Borer JG, et al. Pediatric robot assisted laparoscopic dismembered pyeloplasty: comparison with a cohort of open surgery. *J Urol* 2006; 175(2):683-7.
98. Riachy E, Cost NG, Defoor WR, et al. Pediatric standard and robot-assisted laparoscopic pyeloplasty: a comparative single institution study. *J Urol* 2013; 189(1):283-7.
99. Sorensen MD, Delostrinos C, Johnson MH, et al. Comparison of the learning curve and outcomes of robotic assisted pediatric pyeloplasty. *J Urol* 2011; 185(6 Suppl):2517-22.
100. Subotic U, Rohard I, Weber DM, et al. A minimal invasive surgical approach for children of all ages with ureteropelvic junction obstruction. *J Pediatr Urol* 2012; 8(4):354-8.
101. Swana HS, Rodriguez AR, Weber TA, et al. Pediatric robotic pyeloplasty: the learning curve and comparison with a cohort of open pyeloplasty. *Int J Med Robot* 2011; 7(S1):25.
102. Yee DS, Shanberg AM, Duel BP, et al. Initial comparison of robotic-assisted laparoscopic versus open pyeloplasty in children. *Urology* 2006; 67(3):599-602.
103. Casella DP, Fox JA, Schneck FX, et al. Cost analysis of pediatric robot-assisted and laparoscopic pyeloplasty. *J Urol* 2013; 189(3):1083-6.
104. Dangle PP, Kearns J, Anderson B, et al. Outcomes of infants undergoing robot-assisted laparoscopic pyeloplasty compared to open repair. *J Urol* 2013; 190(6):2221-7.
105. Freilich DA, Penna FJ, Nelson CP, et al. Parental satisfaction after open versus robot assisted laparoscopic pyeloplasty: results from modified Glasgow Children's Benefit Inventory Survey. *J Urol* 2010; 183(2):704-8.
106. Marcus HJ, Hughes-Hallett A, Cundy TP, et al. Not everything that counts can be easily counted. *BMJ* 2013; 346:f2461.
107. Esposito C, El Ghoneimi A, Yamataka A, et al. Work-related upper limb musculoskeletal disorders in paediatric laparoscopic surgery. A multicenter survey. *J Pediatr Surg* 2013; 48(8):1750-6.
108. Cook JA, McCulloch P, Blazeby JM, et al. IDEAL framework for surgical innovation 3: randomised controlled trials in the assessment stage and evaluations in the long term study stage. *BMJ* 2013; 346:f2820.
109. Paul S, McCulloch P, Sedrakyan A. Robotic surgery: revisiting "no innovation without evaluation". *BMJ* 2013; 346:f1573.
110. Autorino R, Eden C, El-Ghoneimi A, et al. Robot-assisted and Laparoscopic Repair of Ureteropelvic Junction Obstruction: A Systematic Review and Meta-analysis. *Eur Urol* 2014; 65(2):430-52.

111. Braga LH, Pace K, DeMaria J, et al. Systematic review and meta-analysis of robotic-assisted versus conventional laparoscopic pyeloplasty for patients with ureteropelvic junction obstruction: effect on operative time, length of hospital stay, postoperative complications, and success rate. *Eur Urol* 2009; 56(5):848-57.
112. Al-Shanafey S, Habib Z. Feasibility and safety of laparoscopic adrenalectomy in children: special emphasis on neoplastic lesions. *J Laparoendosc Adv Surg Tech A* 2008; 18(2):306-9.
113. Peters CA. Pediatric robot-assisted pyeloplasty. *J Endourol* 2011; 25(2):179-85.
114. Olsen LH, Rawashdeh YF, Jorgensen TM. Pediatric robot assisted retroperitoneoscopic pyeloplasty: a 5-year experience. *J Urol* 2007; 178(5):2137-41.
115. Rodriguez AR, Rich MA, Swana HS. Stentless pediatric robotic pyeloplasty. *Ther Adv Urol* 2012; 4(2):57-60.
116. Kane TD, Brown MF, Chen MK. Position paper on laparoscopic antireflux operations in infants and children for gastroesophageal reflux disease. American Pediatric Surgery Association. *J Pediatr Surg* 2009; 44(5):1034-40.
117. Georgeson KE. Laparoscopic gastrostomy and fundoplication. *Pediatr Ann* 1993; 22(11):675-7.
118. Lobe TE. Laparoscopic fundoplication. *Semin Pediatr Surg* 1993; 2(3):178-81.
119. Kleinman L, Nelson S, Kothari-Talwar S, et al. Development and psychometric evaluation of 2 age-stratified versions of the Pediatric GERD Symptom and Quality of Life Questionnaire. *J Pediatr Gastroenterol Nutr* 2011; 52(5):514-22.
120. Mauritz FA, van Herwaarden-Lindeboom MY, Zwaveling S, et al. Laparoscopic Thal Fundoplication in Children: A Prospective 10- to 15-Year Follow-up Study. *Ann Surg* 2014; 259(2):388-93.
121. Albassam AA, Mallick MS, Gado A, et al. Nissen fundoplication, robotic-assisted versus laparoscopic procedure: a comparative study in children. *Eur J Pediatr Surg* 2009; 19(5):316-9.
122. Copeland DR, Boneti C, Kokoska ER, et al. Evaluation of initial experience and comparison of the da Vinci surgical system with established laparoscopic and open pediatric Nissen fundoplication surgery. *J Soc Laparoendoscopic Surg* 2008; 12(3):238-40.
123. Lehnert M, Richter B, Beyer PA, et al. A prospective study comparing operative time in conventional laparoscopic and robotically assisted Thal semifundoplication in children. *J Pediatr Surg* 2006; 41(8):1392-6.
124. Antao B, Merrigan T, Nemechek C, et al. Comparison of robotic and laparoscopic Nissen fundoplication in children. Presented at the 19th Annual Congress of the International Pediatric Endosurgery Group, Waikolao, HI, June 8-12, 2010.
125. Ivascu FA, Geirger JG, Dongrowski R, et al. Experience with robotic laparoscopic Nissen fundoplication in children at a single institution. Presented at the 13th Annual Congress of the International Pediatric Endosurgery Group, Maui, HI, May 5-8, 2004.
126. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; 240(2):205-13.
127. Diaz DM, Gibbons TE, Heiss K, et al. Antireflux surgery outcomes in pediatric gastroesophageal reflux disease. *Am J Gastroenterol* 2005; 100(8):1844-52.
128. Maeso S, Reza M, Mayol JA, et al. Efficacy of the Da Vinci surgical system in abdominal surgery compared with that of laparoscopy: a systematic review and meta-analysis. *Ann Surg* 2010; 252(2):254-62.
129. Markar SR, Karthikesalingam AP, Hagen ME, et al. Robotic vs. laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease: systematic review and meta-analysis. *Int J Med Robot* 2010; 6(2):125-31.

130. Mi J, Kang Y, Chen X, et al. Whether robot-assisted laparoscopic fundoplication is better for gastroesophageal reflux disease in adults: a systematic review and meta-analysis. *Surg Endosc* 2010; 24(8):1803-14.
131. Wang Z, Zheng Q, Jin Z. Meta-analysis of robot-assisted versus conventional laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease. *ANZ J Surg* 2012; 82(3):112-7.
132. McHoney M, Wade AM, Eaton S, et al. Clinical outcome of a randomized controlled blinded trial of open versus laparoscopic Nissen fundoplication in infants and children. *Ann Surg* 2011; 254(2):209-16.
133. Siddiqui MR, Abdulaal Y, Nisar A, et al. A meta-analysis of outcomes after open and laparoscopic Nissen's fundoplication for gastro-oesophageal reflux disease in children. *Pediatr Surg Int* 2011; 27(4):359-66.
134. Margaron FC, Oiticica C, Lanning DA. Robotic-assisted laparoscopic Nissen fundoplication with gastrostomy preservation in neurologically impaired children. *J Laparoendosc Adv Surg Tech A* 2010; 20(5):489-92.
135. Meehan JJ, Meehan TD, Sandler A. Robotic fundoplication in children: resident teaching and a single institutional review of our first 50 patients. *J Pediatr Surg* 2007; 42(12):2022-5.
136. Weissman JS, Zinner M. Comparative effectiveness research on robotic surgery. *JAMA* 2013; 309(7):721-2.
137. Smith JA. Surgeon responsibility. *J Urol* 2013; 190(2):379-80.
138. Schwartz JAT. Innovation in pediatric surgery: the surgical innovation continuum and the ETHICAL model. *J Pediatr Surg* 2014; 49(4):639-45.
139. Lendvay TS, Hannaford B, Satava RM. Future of robotic surgery. *Cancer J* 2013; 19(2):109-19.
140. Buchs NC, Pugin F, Volonte F, et al. Learning tools and simulation in robotic surgery: state of the art. *World J Surg* 2013; 37(12):2812-9.
141. Olsen LH. Robotics in paediatric urology. *J Pediatr Urol* 2006; 2(1):40-5.
142. Buffi N, Van Der Poel H, Guazzoni G, et al. Methods and priorities of robotic surgery training program. *Eur Urol* 2014; 65(1):1-2.
143. Lee JY, Mucksavage P, Sundaram CP, et al. Best practices for robotic surgery training and credentialing. *J Urol* 2011; 185(4):1191-7.
144. Chitwood WR, Jr., Nifong LW, Chapman WH, et al. Robotic surgical training in an academic institution. *Ann Surg* 2001; 234(4):475-84.
145. Lucas SM, Gilley DA, Joshi SS, et al. Robotics training program: evaluation of the satisfaction and the factors that influence success of skills training in a resident robotics curriculum. *J Endourol* 2011; 25(10):1669-74.
146. de Lambert G, Fourcade L, Centi J, et al. How to successfully implement a robotic pediatric surgery program: lessons learned after 96 procedures. *Surg Endosc* 2013; 27(6):2137-44.
147. Klein MD, Langenburg SE, Kabeer M, et al. Pediatric robotic surgery: lessons from a clinical experience. *J Laparoendosc Adv Surg Tech A* 2007; 17(2):265-71.
148. Herron DM, Marohn M. A consensus document on robotic surgery. *Surg Endosc* 2008; 22(2):313-25; discussion 311-2.
149. Lendvay TS. Surgical simulation in pediatric urologic education. *Curr Urol Rep* 2011; 12(2):137-43.
150. Najmaldin A. Karl Storz Lecture. Skills training in pediatric minimal access surgery. *J Pediatr Surg* 2007; 42(2):284-9.
151. Smith R, Patel V, Satava R. Fundamentals of robotic surgery: a course of basic robotic surgery skills based upon a 14-society consensus template of outcomes measures and curriculum development. *Int J Med Robot* 2013 Nov 26. doi 10.1002/rcs.1559. [Epub ahead of print]
152. Wang MH, Chen B, Kern D, et al. Pediatric urology fellowship training: are we teaching what they need to learn? *J Pediatr Urol* 2013; 9(3):318-21.

153. Sorensen MD, Johnson MH, Delostrinos C, et al. Initiation of a pediatric robotic surgery program: institutional challenges and realistic outcomes. *Surg Endosc* 2010; 24(11):2803-8.
154. Abboudi H, Khan MS, Aboumarzouk O, et al. Current status of validation for robotic surgery simulators - a systematic review. *BJU Int* 2013; 111(2):194-205.
155. Hung AJ, Jayaratna IS, Teruya K, et al. Comparative assessment of three standardized robotic surgery training methods. *BJU Int* 2013; 112(6):864-71.
156. Khan N, Abboudi H, Khan MS, et al. Measuring the surgical 'learning curve': methods, variables and competency. *BJU Int* 2014; 113(3):504-8.
157. Ramsay CR, Wallace SA, Garthwaite PH, et al. Assessing the learning curve effect in health technologies. Lessons from the nonclinical literature. *Int J Technol Assess Health Care* 2002; 18(1):1-10.
158. Vemulakonda VM, Cowan CA, Lendvay TS, et al. Surgical management of congenital ureteropelvic junction obstruction: a Pediatric Health Information System database study. *J Urol* 2008; 180(4 Suppl):1689-92.
159. Ficarra V, Iannetti A, Vianello F, et al. Different Pyeloplasty Approaches, Similar Excellent Results. *Eur Urol* 2014; 65(2):453-4.
160. Cundy TP, Marcus HJ, Hughes-Hallett A, et al. International attitudes of early adopters to current and future robotic technologies in pediatric surgery. *J Pediatr Surg* 2014 Jul 11. doi 10.1016/j.pedsurg.2014.05.017. [Epub ahead of print]
161. Maguire T, Mayne CJ, Terry T, et al. Analysis of the surgical learning curve using the cumulative sum (CUSUM) method. *Neurourol Urodyn* 2013; 32(7):964-7.
162. Tekkis PP, Senagore AJ, Delaney CP, et al. Evaluation of the learning curve in laparoscopic colorectal surgery: comparison of right-sided and left-sided resections. *Ann Surg* 2005; 242(1):83-91.
163. Chaput de Saintonge DM, Vere DW. Why don't doctors use cusums? *Lancet* 1974; 1(7848):120-1.
164. Wohl H. The cusum plot: its utility in the analysis of clinical data. *N Engl J Med* 1977; 296(18):1044-5.
165. Biau DJ, Resche-Rigon M, Godiris-Petit G, et al. Quality control of surgical and interventional procedures: a review of the CUSUM. *Qual Saf Health Care* 2007; 16(3):203-7.
166. Noyez L. Control charts, Cusum techniques and funnel plots. A review of methods for monitoring performance in healthcare. *Interact Cardiovasc Thorac Surg* 2009; 9(3):494-9.
167. Van Rij AM, McDonald JR, Pettigrew RA, et al. Cusum as an aid to early assessment of the surgical trainee. *Br J Surg* 1995; 82(11):1500-3.
168. Abboudi H, Khan MS, Guru KA, et al. Learning curves for urological procedures: a systematic review. *BJU Int* 2013.
169. Parikh AM, Park AM, Sumfest J. Cumulative summation (CUSUM) charts in the monitoring of hypospadias outcomes: A tool for quality improvement initiative. *J Pediatr Urol* 2013; 10(2):306-11.
170. Link RE, Bhayani SB, Kavoussi LR. A prospective comparison of robotic and laparoscopic pyeloplasty. *Ann Surg* 2006; 243(4):486-91.
171. de la Rosette JJ, Opondo D, Daels FP, et al. Categorisation of complications and validation of the Clavien score for percutaneous nephrolithotomy. *Eur Urol* 2012; 62(2):246-55.
172. Mamoulakis C, Efthimiou I, Kazoulis S, et al. The modified Clavien classification system: a standardized platform for reporting complications in transurethral resection of the prostate. *World J Urol* 2011; 29(2):205-10.
173. Bokhari MB, Patel CB, Ramos-Valadez DI, et al. Learning curve for robotic-assisted laparoscopic colorectal surgery. *Surg Endosc* 2011; 25(3):855-60.
174. Buchs NC, Pugin F, Bucher P, et al. Learning curve for robot-assisted Roux-en-Y gastric bypass. *Surg Endosc* 2012; 26(4):1116-21.

175. Sng KK, Hara M, Shin JW, et al. The multiphasic learning curve for robot-assisted rectal surgery. *Surg Endosc* 2013; 27(9):3297-307.
176. Montgomery DC. Introduction to Statistical Quality Control. 6th ed: John Wiley & Sons, Inc., 2001.
177. Mackenzie H, Miskovic D, Ni M, et al. Clinical and educational proficiency gain of supervised laparoscopic colorectal surgical trainees. *Surg Endosc* 2013; 27(8):2704-11.
178. Passerotti CC, Passerotti AM, Dall'Oglio MF, et al. Comparing the quality of the suture anastomosis and the learning curves associated with performing open, freehand, and robotic-assisted laparoscopic pyeloplasty in a swine animal model. *J Am Coll Surg* 2009; 208(4):576-86.
179. Tasian GE, Wiebe DJ, Casale P. Learning Curve of Robotic Assisted Pyeloplasty for Pediatric Urology Fellows. *J Urol* 2013; 190(4 Suppl):1622-6.
180. Williams AK, Chalasani V, Martinez CH, et al. Cumulative summation graphs are a useful tool for monitoring positive surgical margin rates in robot-assisted radical prostatectomy. *BJU Int* 2011; 107(10):1648-52.
181. Biau DJ, Williams SM, Schlup MM, et al. Quantitative and individualized assessment of the learning curve using LC-CUSUM. *Br J Surg* 2008; 95(7):925-9.
182. Sibanda N, Lewsey JD, van der Meulen JH, et al. Continuous monitoring tools for pediatric surgical outcomes: an example using biliary atresia. *J Pediatr Surg* 2007; 42(11):1919-25.
183. Salowi MA, Choong YF, Goh PP, et al. CUSUM: a dynamic tool for monitoring competency in cataract surgery performance. *Br J Ophthalmol* 2010; 94(4):445-9.
184. Benway BM, Wang AJ, Cabello JM, et al. Robotic partial nephrectomy with sliding-clip renorrhaphy: technique and outcomes. *Eur Urol* 2009; 55(3):592-9.
185. Jimenez-Rodriguez RM, Diaz-Pavon JM, de la Portilla de Juan F, et al. Learning curve for robotic-assisted laparoscopic rectal cancer surgery. *Int J Colorectal Dis* 2013; 28(6):815-21.
186. Steinberg PL, Merguerian PA, Bihrle W, 3rd, et al. The cost of learning robotic-assisted prostatectomy. *Urology* 2008; 72(5):1068-72.
187. Rothenberg SS. Experience with 220 consecutive laparoscopic Nissen fundoplications in infants and children. *J Pediatr Surg* 1998; 33(2):274-8.
188. Anderberg M, Kockum CC, Arnbjornsson E. Robotic fundoplication in children. *Pediatr Surg Int* 2007; 23(2):123-7.
189. Meehan JJ, Georgeson KE. The learning curve associated with laparoscopic antireflux surgery in infants and children. *J Pediatr Surg* 1997; 32(3):426-9.
190. Lebeau T, Roupret M, Ferhi K, et al. The role of a well-trained team on the early learning curve of robot-assisted laparoscopic procedures: the example of radical prostatectomy. *Int J Med Robot* 2011 Oct 7. doi: 10.1002/rcs.435. [Epub ahead of print]
191. Ramsay CR, Grant AM, Wallace SA, et al. Statistical assessment of the learning curves of health technologies. *Health Technol Assess* 2001; 5(12):1-79.
192. Rogers CA, Ganesh JS, Banner NR, et al. Cumulative risk adjusted monitoring of 30-day mortality after cardiothoracic transplantation: UK experience. *Eur J Cardiothorac Surg* 2005; 27(6):1022-9.
193. Vitiello V, Lee SL, Cundy TP, et al. Emerging robotic platforms for minimally invasive surgery. *IEEE Rev Biomed Eng* 2013; 6:111-26.
194. Rogers EM. Diffusion of Innovations. 5th edition ed. New York: Free Press, 2003.
195. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *J Med Internet Res* 2004; 6(3):e34.
196. Schimpf DK, Powers CJ, Kirker EW, et al. Minimally invasive and robotic surgery techniques in the future of pediatric surgery: a national survey of pediatric surgery fellows. Presented at the 12th Annual Congress of the International Pediatric Endosurgery Group, Los Angeles, CA, March 10-13, 2003.

197. Gertner M. You have an idea, now what? *Semin Pediatr Surg* 2006; 15(4):302-8.
198. Dutta S, Woo R, Albanese CT. Minimal access portoenterostomy: advantages and disadvantages of standard laparoscopic and robotic techniques. *J Laparoendosc Surg Adv Tech A* 2007; 17(2):258-64.
199. Peters CA. Robotically assisted surgery in pediatric urology. *Urol Clin North Am* 2004; 31(4):743-52.
200. Ziegler MM. The innovation of success: the pediatric surgery and APSA response to "disruptive technologies". *J Pediatr Surg* 2009; 44(1):1-12.
201. Marcus H, Nandi D, Darzi A, et al. Surgical robotics through a keyhole: from today's translational barriers to tomorrow's "disappearing" robots. *IEEE Trans Biomed Eng* 2013; 60(3):674-81.
202. Duchene DA, Moinzadeh A, Gill IS, et al. Survey of residency training in laparoscopic and robotic surgery. *J Urol* 2006; 176(5):2158-66.
203. McCulloch P, Kaul A, Wagstaff GF, et al. Tolerance of uncertainty, extroversion, neuroticism and attitudes to randomized controlled trials among surgeons and physicians. *Br J Surg* 2005; 92(10):1293-7.
204. Shaligram A, Meyer A, Simorov A, et al. Survey of minimally invasive general surgery fellows training in robotic surgery. *J Robot Surg* 2012; 7(2):131- 36.
205. Robles-De-La-Torre G. The importance of the sense of touch in virtual and real environments. *MultiMedia, IEEE* 2006; 13(3):24 - 30.
206. van der Meijden OA, Schijven MP. The value of haptic feedback in conventional and robot-assisted minimal invasive surgery and virtual reality training: a current review. *Surg Endosc* 2009; 23(6):1180-90.
207. Hagen ME, Meehan JJ, Inan I, et al. Visual clues act as a substitute for haptic feedback in robotic surgery. *Surg Endosc* 2008; 22(6):1505-8.
208. Diks J, Nio D, Linsen MA, et al. Suture damage during robot-assisted vascular surgery: is it an issue? *Surg Laparosc Endosc Percutan Tech* 2007; 17(6):524-7.
209. Hirano Y, Ishikawa N, Watanabe G. Suture damage after grasping with EndoWrist of the da Vinci Surgical System. *Minim Invasive Ther Allied Technol* 2010; 19(4):203-6.
210. Ishikawa N, Watanabe G, Hirano Y, et al. The effect of a silicone-coated robotic needle holder. *J Robot Surg* 2013; 7:153-55.
211. Ricchiuti D, Cerone J, Shie S, et al. Diminished suture strength after robotic needle driver manipulation. *J Endourol* 2010; 24(9):1509-13.
212. Ballantyne GH. Robotic surgery, telerobotic surgery, telepresence, and telementoring. Review of early clinical results. *Surg Endosc* 2002; 16(10):1389-402.
213. Lee SL, Lerotic M, Vitiello V, et al. From medical images to minimally invasive intervention: Computer assistance for robotic surgery. *Comput Med Imaging Graph* 2010; 34(1):33-45.
214. Bariol SV, Stewart GD, Tolley DA. Laparoscopic suturing: effect of instrument handling on suture strength. *J Endourol* 2005; 19(9):1127-33.
215. Abdullah F, Ortega G, Islam S, et al. Outcomes research in pediatric surgery. Part 1: overview and resources. *J Pediatr Surg* 2011; 46(1):221-5.
216. Kitagawa M, Dokko D, Okamura AM, et al. Effect of sensory substitution on suture-manipulation forces for robotic surgical systems. *J Thorac Cardiovasc Surg* 2005; 129(1):151-8.
217. Bethea BT, Okamura AM, Kitagawa M, et al. Application of haptic feedback to robotic surgery. *J Laparoendosc Adv Surg Tech A* 2004; 14(3):191-5.
218. Badani KK, Bhandari A, Tewari A, et al. Comparison of two-dimensional and three-dimensional suturing: is there a difference in a robotic surgery setting? *J Endourol* 2005; 19(10):1212-5.
219. Yang GZ, Mylonas GP, Kwok KW, et al. Perceptual docking for robotic control. *Medical Imaging and Augmented Reality* 2008; 5128:21 - 30.

220. James DR, Orihuela-Espina F, Leff DR, et al. Cognitive burden estimation for visuomotor learning with fNIRS. *Med Image Comput Comput Assist Interv* 2010; 13(Pt 3):319-26.
221. Leff DR, Orihuela-Espina F, Elwell CE, et al. Assessment of the cerebral cortex during motor task behaviours in adults: a systematic review of functional near infrared spectroscopy (fNIRS) studies. *Neuroimage* 2011; 54(4):2922-36.
222. Leff DR, James DR, Orihuela-Espina F, et al. The frontal cortex is activated during learning of endoscopic procedures (Ohuchida et al., Surgical Endoscopy, January 2009). *Surg Endosc* 2010; 24(4):968-9.
223. Mucksavage P, Kerbl DC, Pick DL, et al. Differences in grip forces among various robotic instruments and da Vinci surgical platforms. *J Endourol* 2011; 25(3):523-8.
224. De S, Rosen J, Dagan A, et al. Assessment of tissue damage due to mechanical stresses. *Int J Robot Res* 2007; 26(11 - 12):1159 - 1171.
225. Okamura AM. Haptic feedback in robot-assisted minimally invasive surgery. *Curr Opin Urol* 2009; 19(1):102-7.
226. Wedmid A, Llukani E, Lee DI. Future perspectives in robotic surgery. *BJU Int* 2011; 108(6 Pt 2):1028-36.
227. Bark K, McMahan W, Remington A, et al. In vivo validation of a system for haptic feedback of tool vibrations in robotic surgery. *Surg Endosc* 2013; 27(2):656-64.
228. Reiley CE, Akinbiyi T, Burschka D, et al. Effects of visual force feedback on robot-assisted surgical task performance. *J Thorac Cardiovasc Surg* 2008; 135(1):196-202.
229. Franco ML, King CH, Culjat MO, et al. An integrated pneumatic tactile feedback actuator array for robotic surgery. *Int J Med Robot* 2009; 5(1):13-9.
230. Moradi Dalvand M, Shirinzadeh B, Shamdani AH, et al. An actuated force feedback-enabled laparoscopic instrument for robotic-assisted surgery. *Int J Med Robot* 2014; 10(1): 11-21.
231. Rizun P, Gunn D, Cox B, et al. Mechatronic design of haptic forceps for robotic surgery. *Int J Med Robot* 2006; 2(4):341-9.
232. Tavakoli M, Patel RV, Moallem M. Haptic interaction in robot-assisted endoscopic surgery: a sensorized end-effector. *Int J Med Robot* 2005; 1(2):53-63.
233. Zbyszewski D, Challacombe B, Liu H, et al. Air-cushion force-sensitive probe for soft tissue investigation during minimally invasive surgery. *J Endourol* 2009; 23(9):1421-4.
234. Tang B, Hanna GB, Cuschieri A. Analysis of errors enacted by surgical trainees during skills training courses. *Surgery* 2005; 138(1):14-20.
235. Moynihan SB. Addresses on surgical subjects: WB Saunders Company, Philidelphia, 1928.
236. Schrock TR. The endosurgery evolution: no place for sacred cows. *Surg Endosc* 1992; 6(4):163-8.
237. Thomas WE. Teaching and assessing surgical competence. *Ann R Coll Surg Engl* 2006; 88(5):429-32.
238. Hamilton EC, Scott DJ, Fleming JB, et al. Comparison of video trainer and virtual reality training systems on acquisition of laparoscopic skills. *Surg Endosc* 2002; 16(3):406-11.
239. McCluney AL, Vassiliou MC, Kaneva PA, et al. FLS simulator performance predicts intraoperative laparoscopic skill. *Surg Endosc* 2007; 21(11):1991-5.
240. Scott DJ, Bergen PC, Rege RV, et al. Laparoscopic training on bench models: better and more cost effective than operating room experience? *J Am Coll Surg* 2000; 191(3):272-83.
241. Gallagher AG, Seymour NE, Jordan-Black JA, et al. Prospective, randomized assessment of transfer of training (ToT) and transfer effectiveness ratio (TER) of virtual reality simulation training for laparoscopic skill acquisition. *Ann Surg* 2013; 257(6):1025-31.

242. Seymour NE, Gallagher AG, Roman SA, et al. Virtual reality training improves operating room performance: results of a randomized, double-blinded study. *Ann Surg* 2002; 236(4):458-63.
243. Aggarwal R, Ward J, Balasundaram I, et al. Proving the effectiveness of virtual reality simulation for training in laparoscopic surgery. *Ann Surg* 2007; 246(5):771-9.
244. Fried GM, Feldman LS, Vassiliou MC, et al. Proving the value of simulation in laparoscopic surgery. *Ann Surg* 2004; 240(3):518-25.
245. Azzie G, Gerstle JT, Nasr A, et al. Development and validation of a pediatric laparoscopic surgery simulator. *J Pediatr Surg* 2011; 46(5):897-903.
246. Fraser SA, Klassen DR, Feldman LS, et al. Evaluating laparoscopic skills: setting the pass/fail score for the MISTELS system. *Surg Endosc* 2003; 17(6):964-7.
247. Derossis AM, Fried GM, Abrahamowicz M, et al. Development of a model for training and evaluation of laparoscopic skills. *Am J Surg* 1998; 175(6):482-7.
248. Rodrigues SP, Horeman T, Dankelman J, et al. Suturing intraabdominal organs: when do we cause tissue damage? *Surg Endosc* 2012; 26(4):1005-9.
249. Zendejas B, Brydges R, Hamstra SJ, et al. State of the evidence on simulation-based training for laparoscopic surgery: a systematic review. *Ann Surg* 2013; 257(4):586-93.
250. van Hove PD, Tuijthof GJ, Verdaasdonk EG, et al. Objective assessment of technical surgical skills. *Br J Surg* 2010; 97(7):972-87.
251. Ritter EM, Scott DJ. Design of a proficiency-based skills training curriculum for the fundamentals of laparoscopic surgery. *Surg Innov* 2007; 14(2):107-12.
252. Aggarwal R, Moorthy K, Darzi A. Laparoscopic skills training and assessment. *Br J Surg* 2004; 91(12):1549-58.
253. Moorthy K, Munz Y, Sarker SK, et al. Objective assessment of technical skills in surgery. *BMJ* 2003; 327(7422):1032-7.
254. Horeman T, Rodrigues SP, Jansen FW, et al. Force parameters for skills assessment in laparoscopy. *IEEE Transactions on Haptics* 2012; 5(4):312-322.
255. Heijnsdijk EA, Pasdeloup A, van der Pijl AJ, et al. The influence of force feedback and visual feedback in grasping tissue laparoscopically. *Surg Endosc* 2004; 18(6):980-5.
256. Gallagher AG, Satava RM, Shorten GD. Measuring surgical skill: a rapidly evolving scientific methodology. *Surg Endosc* 2013; 27(5):1451-5.
257. Marlow N, Altree M, Babidge W, et al. Laparoscopic skills acquisition: a study of simulation and traditional training. *ANZ J Surg* 2013.
258. Munz Y, Kumar BD, Moorthy K, et al. Laparoscopic virtual reality and box trainers: is one superior to the other? *Surg Endosc* 2004; 18(3):485-94.
259. Tan SC, Marlow N, Field J, et al. A randomized crossover trial examining low- versus high-fidelity simulation in basic laparoscopic skills training. *Surg Endosc* 2012; 26(11):3207-14.
260. Tanoue K, Ieiri S, Konishi K, et al. Effectiveness of endoscopic surgery training for medical students using a virtual reality simulator versus a box trainer: a randomized controlled trial. *Surg Endosc* 2008; 22(4):985-90.
261. Hanna GB, Drew T, Arnold G, et al. Development of force measurement system for clinical use in minimal access surgery. *Surg Endosc* 2008; 22(2):467-71.
262. Jayaraman S, Trejos AL, Naish MD, et al. Toward construct validity for a novel sensorized instrument-based minimally invasive surgery simulation system. *Surg Endosc* 2011; 25(5):1439-45.
263. Yoshida K, Kinoshita H, Kuroda Y, et al. Analysis of laparoscopic dissection skill by instrument tip force measurement. *Surg Endosc* 2013; 27(6):2193-200.
264. Wottawa CR, Cohen JR, Fan RE, et al. The role of tactile feedback in grip force during laparoscopic training tasks. *Surg Endosc* 2013; 27(4):1111-8.
265. Chang L, Satava RM, Pellegrini CA, et al. Robotic surgery: identifying the learning curve through objective measurement of skill. *Surg Endosc* 2003; 17(11):1744-8.

266. Marchini GS, Hong YK, Minnillo BJ, et al. Robotic assisted laparoscopic ureteral reimplantation in children: case matched comparative study with open surgical approach. *J Urol* 2011; 185(5):1870-5.
267. Chandra V, Nehra D, Parent R, et al. A comparison of laparoscopic and robotic assisted suturing performance by experts and novices. *Surgery* 2010; 147(6):830-9.
268. Gettman MT, Peschel R, Neururer R, et al. A comparison of laparoscopic pyeloplasty performed with the daVinci robotic system versus standard laparoscopic techniques: initial clinical results. *Eur Urol* 2002; 42(5):453-7.
269. Kenngott HG, Muller-Stich BP, Reiter MA, et al. Robotic suturing: technique and benefit in advanced laparoscopic surgery. *Minim Invasive Ther Allied Technol* 2008; 17(3):160-7.
270. Moorthy K, Munz Y, Dosis A, et al. Dexterity enhancement with robotic surgery. *Surg Endosc* 2004; 18(5):790-5.
271. Stefanidis D, Wang F, Korndorffer JR, Jr., et al. Robotic assistance improves intracorporeal suturing performance and safety in the operating room while decreasing operator workload. *Surg Endosc* 2010; 24(2):377-82.
272. Lee AC, Haddad MJ, Hanna GB. Influence of instrument size on endoscopic task performance in pediatric intracorporeal knot tying: smaller instruments are better in infants. *Surg Endosc* 2007; 21(11):2086-90.
273. Anderberg M, Kockum CC, Arnbjornsson E. Paediatric computer-assisted retroperitoneoscopic nephrectomy compared with open surgery. *Pediatr Surg Int*2011; 27(7):761-7.
274. Leonard S, Wu KL, Kim Y, et al. Smart tissue anastomosis robot (STAR): a vision-guided robotics system for laparoscopic suturing. *IEEE Trans Biomed Eng* 2014; 61(4):1305-17.
275. Hanna GB, Shimi S, Cuschieri A. Influence of direction of view, target-to-endoscope distance and manipulation angle on endoscopic knot tying. *Br J Surg* 1997; 84(10):1460-4.
276. Blavier A, Gaudissart Q, Cadiere GB, et al. Comparison of learning curves and skill transfer between classical and robotic laparoscopy according to the viewing conditions: implications for training. *Am J Surg* 2007; 194(1):115-21.
277. Sukumar S, Roghmann F, Sood A, et al. Correction of ureteropelvic junction obstruction in children: national trends and comparative effectiveness in operative outcomes. *J Endourol* 2014; 28(5):592-8.
278. Varda BK, Johnson EK, Clark C, et al. National trends of perioperative outcomes and costs for open, laparoscopic and robotic pediatric pyeloplasty. *J Urol* 2014; 191(4):1090-5.
279. Cundy TP, Harling L, Hughes-Hallett A, et al. Meta analysis of robot-assisted versus conventional laparoscopic and open pyeloplasty in children. *BJU Int* 2014 Jul 27. doi 10.1111/bju.12683. [Epub ahead of print]
280. Cundy TP, Harling L, Marcus HJ, et al. Meta analysis of robot-assisted versus conventional laparoscopic fundoplication in children. *J Pediatr Surg* 2014; 49(4):646-52.
281. Hubert N, Gilles M, Desbrosses K, et al. Ergonomic assessment of the surgeon's physical workload during standard and robotic assisted laparoscopic procedures. *Int J Med Robot* 2013; 9(2):142-7.
282. Brody F, Richards NG. Review of robotic versus conventional laparoscopic surgery. *Surg Endosc* 2014; 28(5):1413-24.
283. Krummel TM. What is surgery? *Seminars in Pediatric Surgery* 2006; 15(4):237-41.
284. Heemskerk J, Bouvy ND, Baeten CG. The end of robot-assisted laparoscopy? A critical appraisal of scientific evidence on the use of robot-assisted laparoscopic surgery. *Surg Endosc* 2014; 28(4):1388-98.
285. Yoo J. The robot has no role in elective colon surgery. *JAMA Surg* 2014; 149(2):184.

286. Winter DC. The cost of laparoscopic surgery is the price of progress. *Br J Surg* 2009; 96(4):327-8.
287. Buchs NC, Volonte F, Pugin F, et al. Three-dimensional laparoscopy: a step toward advanced surgical navigation. *Surg Endosc* 2013; 27(2):692-3.
288. Kunert W, Storz P, Kirschniak A. For 3D laparoscopy: a step toward advanced surgical navigation: how to get maximum benefit from 3D vision. *Surg Endosc* 2013; 27(2):696-9.
289. Storz P, Buess GF, Kunert W, et al. 3D HD versus 2D HD: surgical task efficiency in standardised phantom tasks. *Surg Endosc* 2012; 26(5):1454-60.
290. Frede T, Hammady A, Klein J, et al. The radius surgical system - a new device for complex minimally invasive procedures in urology? *Eur Urol* 2007; 51(4):1015-22; discussion 1022.
291. Lukish J, Rasmussen S, Garrett D, et al. Utilization of a novel unidirectional knotless suture during minimal access procedures in pediatric surgery. *J Pediatr Surg* 2013; 48(6):1445-9.
292. Peters CA. Pediatric robotic-assisted surgery: too early an assessment? *Pediatrics* 2009; 124(6):1680-1.
293. Meininger D, Byhahn C, Mierdl S, et al. Hemodynamic and respiratory effects of robot-assisted laparoscopic fundoplication in children. *World J Surg* 2005; 29(5):615-9; discussion 620.
294. Bergeles C, Yang GZ. From passive tool holders to microsurgeons: safer, smaller, smarter surgical robots. *IEEE Trans Biomed Eng* 2014; 61(5):1565-76.
295. Payne CJ, Yang GZ. Hand-held medical robots. *Ann Biomed Eng* 2014; 42(8):1594-605.
296. Hughes-Hallett A, Mayer EK, Marcus HJ, et al. Augmented reality partial nephrectomy: examining the current status and future perspectives. *Urology* 2014; 83(2):266-73.
297. Kaouk JH, Haber GP, Autorino R, et al. A Novel Robotic System for Single-port Urologic Surgery: First Clinical Investigation. *Eur Urol* 2014 Jul 17. doi: §0.§016.j.eururo.2014.06.039. [Epub ahead of print]
298. Looi T, Yeung B, Umasthan M, et al. KidsArm – an image-guided pediatric anastomosis robot. Presented at the IEEE/RSJ International Conference on Intelligent Robots and Systems, Tokyo, Japan, Nov 3-8, 2013.
299. Liu Q, Kobayashi Y, Zhang B, et al. Development of a smart surgical robot with bended forceps for infant congenital esophageal atresia surgery. Presented at the IEEE International Conference on Robotics and Automation, Hong Kong, China, May 31 - June 7, 2014.
300. Damian D, Arabagi S, Fabozzo A, et al. Robotic implant to apply tissue traction forces in the treatment of esophageal atresia. Presented at the IEEE International Conference on Robotics and Automation, Hong Kong, China, May 31 - June 7, 2014.
301. Rankin TM, Giovinco NA, Cucher DJ, et al. Three-dimensional printing surgical instruments: are we there yet? *J Surg Res* 2014; 189(2):193-7.
302. Swanstrom LL, Kurian A, Dunst CM, et al. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. *Ann Surg* 2012; 256(4):659-67.
303. Stavropoulos SN, Desilets DJ, Fuchs KH, et al. Per-oral endoscopic myotomy white paper summary. *Surg Endosc* 2014; 28(7):2005-19.
304. Bhayani NH, Kurian AA, Dunst CM, et al. A comparative study on comprehensive, objective outcomes of laparoscopic Heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. *Ann Surg* 2014; 259(6):1098-103.
305. Maselli R, Inoue H, Misawa M, et al. Peroral endoscopic myotomy (POEM) in a 3-year-old girl with severe growth retardation, achalasia, and Down syndrome. *Endoscopy* 2012; 44 Suppl 2 UCTN:E285-7.
306. Chao S, Russo M, Wright R, et al. Introduction of the per-oral endoscopic myotomy technique to pediatric surgical practice. *J Ped Surg Case Reports* 2014; 2:313 - 315.

307. Ibarguen-Secchia E. Endoscopic pyloromyotomy for congenital pyloric stenosis. *Gastrointest Endosc* 2005; 61(4):598-600.
308. Zhang YX, Nie YQ, Xiao X, et al. Treatment of congenital hypertrophic pyloric stenosis with endoscopic pyloromyotomy. *Zhonghua Er Ke Za Zhi* 2008; 46(4):247-51.
309. Chaves DM, Gusmon CC, Mestieri LH, et al. A new technique for performing endoscopic pyloromyotomy by gastric submucosal tunnel dissection. *Surg Laparosc Endosc Percutan Tech* 2014; 24(3):e92-4.
310. Kawai M, Peretta S, Burckhardt O, et al. Endoscopic pyloromyotomy: a new concept of minimally invasive surgery for pyloric stenosis. *Endoscopy* 2012; 44(2):169-73.
311. Newton RC, Noonan DP, Vitiello V, et al. Robot-assisted transvaginal peritoneoscopy using confocal endomicroscopy: a feasibility study in a porcine model. *Surg Endosc* 2012; 26(9):2532-40.
312. Chen S, Jarboe MD, Teitelbaum DH. Effectiveness of a transluminal endoscopic fundoplication for the treatment of pediatric gastroesophageal reflux disease. *Pediatr Surg Int* 2012; 28(3):229-34.
313. Ure B. Enthusiasm, evidence and ethics: The triple E of minimally invasive pediatric surgery. *J Pediatr Surg* 2013; 48(1):27-33.
314. Oomen MW, Hoekstra LT, Bakx R, et al. Open versus laparoscopic pyloromyotomy for hypertrophic pyloric stenosis: a systematic review and meta-analysis focusing on major complications. *Surg Endosc* 2012; 26(8):2104-10.
315. Rodriguez SA, Banerjee S, Desilets D, et al. Ultrathin endoscopes. *Gastrointest Endosc* 2010; 71(6):893-8.
316. Wall J, Perretta S, Diana M, et al. Submucosal endoscopic myotomies for esophageal lengthening: a novel minimally invasive technique with feasibility study. *Eur J Pediatr Surg* 2012; 22(3):217-21.
317. Latt WT, Newton RC, Visentini-Scarzanella M, et al. A hand-held instrument to maintain steady tissue contact during probe-based confocal laser endomicroscopy. *IEEE Trans Biomed Eng* 2011; 58(9):2694-703.
318. Frykman PK, Lindsley EH, Gaon M, et al. Spectral imaging for precise surgical intervention in Hirschsprung's disease. *J Biophotonics* 2008; 1(2):97-103.
319. Swanstrom LL, Rieder E, Dunst CM. A stepwise approach and early clinical experience in peroral endoscopic myotomy for the treatment of achalasia and esophageal motility disorders. *J Am Coll Surg* 2011; 213(6):751-6.
320. Mylonas GP, Vitiello V, Cundy TP, et al. CYCLOPS: a versatile robotic tool for bimanual single-access and natural-orifice endoscopic surgery. Presented at the IEEE International Conference on Robotics and Automation, Hong Kong, China, May 31 - June 7, 2014.
321. Vitiello V, Cundy TP, Darzi A, et al. Augmented instrument control for the CYCLOPS robotic system. Presented at the 7th Hamlyn Symposium on Medical Robotics, London, United Kingdom, July 12-15, 2014.
322. Ishimaru T, Hatanaka A, Takazawa S, et al. Development of new devices for translumenal endoscopic esophageal anastomosis. *J Laparoendosc Adv Surg Tech A* 2014; 24(4):268-73.
323. Ishimaru T, Iwanaka T, Hatanaka A, et al. Translumenal esophageal anastomosis for natural orifice translumenal endoscopic surgery: an ex vivo feasibility study. *J Laparoendosc Adv Surg Tech A* 2012; 22(7):724-9.
324. Lamas-Pinheiro R, Henriques-Coelho T, Carvalho JL, et al. Duhamel pull-through assisted by transrectal port: a hybrid natural orifice transluminal endoscopic surgery approach. *J Pediatr Surg* 2012; 47(10):1962-5.
325. Li N, Zhang W, Yu D, et al. NOTES for surgical treatment of long-segment hirschsprung's disease: report of three cases. *J Laparoendosc Adv Surg Tech A* 2013; 23(12):1020-3.

326. Velhote MC, Velhote CE. A NOTES modification of the transanal pull-through. *J Laparoendosc Adv Surg Tech A* 2009; 19(2):255-7.
327. Zaritzky M, Ben R, Johnston K. Magnetic gastrointestinal anastomosis in pediatric patients. *J Pediatr Surg* 2014; 49(7):1131-7.