



Clinical Considerations for Flexible Access Surgery

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Declaration of Originality

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For my son; Thomas James Clark, Born 27th September 2010,

“You are bounded only by the limits of your imagination and the ferocity of your determination, so strive for the unimaginable”

With Love
Dad; 27th Sept 2012

Abstract

The expectation of excellence in health care in modern times continues to be challenged. Government and patients alike continue to demand superior health care with excellent treatment outcomes at minimal expense to their time and convenience. Although surgery is the most definitive treatment option in modern medicine, it can be the most demanding both physically and psychologically. The less invasive the procedure offered the more acceptable it has been shown to be to the patient more often with fewer complications attributed and a faster return to health (1).

The positive impact of the minimally invasive concept on the healthcare system has been unfathomable. The domino effect created by the early results from laparoscopic surgery was felt not only across the surgical community but also the medical. Across different specialties, alternative novel therapeutic techniques were devised to overcome problems relating to the large operative procedures which struggled to cross over to the laparoscopic approach. The best example of this is in cardiovascular surgery, where image guided endovascular techniques have overcome the need for many of the once extensive operative procedures including the abdominal aortic aneurysm repair and the coronary bypass procedure. The risks and complications from these operative interventions remain significant and are still performed, though far less frequently than in the past. Selective aneurysms as well as primary coronary events are managed routinely through the endovascular technique with surgery being retained for the complex cases or the non-responders. It seems obvious in hindsight that given the choice of a small 5mm groin incision over a large 30cm open chest or abdominal incision which the public would choose, even with the greater long term benefits sometimes favoring the open approaches.

Gastrointestinal endoscopy has the potential to move in the same direction. The use of the endoscope as a surgical tool rather than simply an investigative device has only recently been recognized, promoted through the concept of Natural Orifice Translumenal Endoscopic Surgery (NOTES). The technique aims to provide a cosmetic enhancement to routine surgical procedures by creating the access incision within a natural orifice. The endoscope provides the vision and the biopsy channels in-built are able to guide operative instruments to the target site to enable a therapeutic procedure to be undertaken. However, it would be naïve to

believe that in the current state NOTES is anything but a fashionable research technique and far from routine clinical use. However, it's most superior element, which has the potential to extend the boundaries of surgery aside from all else, is the flexibility of the platform.

This thesis provides a detailed investigation into the use of the flexible endoscope as a surgical platform. It defines Flexible Access Surgery (FAS) as an all encompassing surgical technique which utilizes flexible platforms at its heart, describes some novel applications representative as exemplars of the technique and explores the significant challenges which would hinder clinical translation. These challenges are described and integrated into two novel enhanced mechatronic flexible access surgical platforms which are further validated and trialed within the pre-clinical *in-vivo* setting as the future of flexible surgery.

The major original contributions of this thesis include the description and definition of the flexible access technique with novel clinical applications. The design, construction and validation of a flexible access box simulator for describing flexible endoscopic navigation within a spatial environment highlighting the challenge this encompasses for many clinicians. The instrumental requirements are explored through the evaluation of the force requirements within the preclinical setting and the instrument refinement both in design and practice that can be adopted to optimize the force delivery particularly when relating to novel flexible platform designs. Finally, the thesis describes the integrated clinical design and validation of two enhanced mechatronic flexible access platforms and describes their clinically driven construction through a series of pre-clinical live *in-vivo* trials. The evolution of each device is described with performance evaluation and clinical exemplars undertaken.

The impact of the results presented within this thesis and the potential for further high impact research is centered on the design and integration of future flexible robotic platforms for minimally invasive surgery. The clinical and mechanical requirements essential for optimal clinical performance will enable designs to be more clinically relevant and ultimately more clinically translatable in the future. Defining these requirements has entailed the use of mapping and sensing the relevant tools which has in turn exposed future potential research avenues to be opened into the perhaps more relevant real time evaluation of the surgical workflow, enabling clinical skills to be more reliably quantified during laparoscopic and endoscopic procedures.

Acknowledgments

"We are like dwarfs sitting on the shoulders of giants. We see more, and things that are more distant, than they did, not because our sight is superior or because we are taller than they, but because they raise us up, and by their great stature add to ours."

12th century Theologian and author John of Salisbury; Metalogicon 1159ad.

This phrase is no less true today than it was 900 years ago and indeed no more pertinent than when considered in respect to this thesis. This experience, through the countless minds I have met, has enabled me to peep above the scientific parapet and experience, for perhaps what may be only a brief moment in my time, what it is like to be on the frontier of medical science and it is nothing less than wondrously intoxicating.

First and foremost I need to thank and acknowledge my supervisors Lord Professor Ara Darzi and Professor Guang-Zhong Yang. I can only hope that I have, at some point along the way, learnt some of the visionary attributes and business acumen that both display towards their respective sciences. I am grateful for all the opportunities that they have given me and I hope that I can stand tall in respect to the way I have faced each of them.

This thesis has only been achieved through collaboration with what can only be described as some of the brightest and inspirational individuals that I have had the pleasure of working alongside from across a range of disciplines including mechanical engineering, computer software engineering as well as the clinical scientists.

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I would also like to acknowledge the work of the Biomedical engineers who played a significant role in a number of areas of this project, most evidently in the design and integration of the robots trialed and tested in this thesis; Dr David Noonan (Robotics - Electronics), Dr Jianzhong Shang (Robotics - Mechanics), Mr Christopher Payne (Robotics –

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Chapter 1

Introduction

1.1. Prologue

From the birth of minimal access surgery in 1985, surgery has strived towards developing ever less invasive procedures without compromising on treatment outcomes. This expansion has explored the possibilities of transumbilical single incision surgery with some moderate success but in April 2007 this evolution took another conceptual shift, with a move of the single port to a natural orifice. A 30 year old lady underwent a radically new surgical procedure for the treatment of symptomatic cholelithiasis. She had undergone the first ever operation leaving no visible abdominal scars having experienced the world's first endoscopically performed transluminal cholecystectomy. Natural Orifice Transluminal Endoscopic Surgery (NOTES) had moved into the human arena; a radical new direction for surgery, one requiring no abdominal wall incision.

The technique involves the passage of a flexible endoscope through a natural orifice. The endoscope is passed within the lumen of the gastrointestinal tract to a point which is closest to the target operative site. The lumen wall is breached and the appropriate bodily cavity, peritoneum or thoracic cavity entered. The endoscope is navigated to the operative site within the cavity from where the operation can be carried out. Using tools passed through biopsy channels within the endoscopes, dissection can be undertaken. Once the operation is completed the endoscope and specimen are removed and the luminal breach closed behind. The idea of using a flexible endoscope or articulated device to undertake surgery was unique and although the NOTES flag is flailing, the concept of an articulated device for surgery whether via a natural orifice or transcutaneously is potentially not.

Flexible access surgery promotes the concept that a target operative point can be reached from any incision point distant or otherwise. This distant point enables the access site to be chosen by the patient and through a single incision the flexibility of the platform will enable the target to be reached even if it is out of the line of sight from the external incision.

As with some of the clinical NOTES trials it is evident that the technique is clumsy and requires more surgeons and assistants to successfully carry out a straight forward surgical procedure than when undertaken laparoscopically. Invariably with many of the problems directed towards the inadequacy of the equipment rather than the technique. Current endoscopic equipment is adapted for, rather than designed for surgical use. The endoscopes are rudimentary, based on instruments designed in the 1960s for intraluminal investigation and although specialist tools are under development and now becoming specifically designed for NOTES, no matter how these evolve, the technique still requires a flexible instrument to operate within a space, be it peritoneum or thoracic cavity, without the usual constraints of the endoluminal environment to support. The major technical challenges associated with the flexible endoscope as a surgical platform include:

1. ***Controlled endoscopic navigation***; predominantly an ergonomic issue as a result of the inability to control the endoscope other than the lead 10cm.
2. ***Disorientation***; as a result of the 2-dimensional (2D) camera being placed at the end effector of a poorly controlled flexible platform.
3. ***Spatial Awareness***; the lack of consideration as to the position of the tail of the endoscope.
4. ***Surgical platform instability***; the inability to introduce force for tissue manipulation due to the instrument and the platform continual uncontrollable motion.
5. ***Instrument control***; control requires the instruments to be manipulated through two channels whilst attempting to control endoscope position. Additional assistance required.
6. ***Instrument triangulation***; the current inability to provide tension on the tissues with one instrument whilst dissecting with the other is lack as currently each exteriorize parallel to one another and not at an optimal triangulating angle.

Over recent years adjunctive surgical technologies have entered the surgical arena. Robotic surgery has been developed over the past twenty years but it has only been over the last seven where such dramatic changes to the utilization of robots in surgery and their adaptation to laparoscopic surgery have been seen. The introduction of the four arm master-slave DaVinci Si robot™ from Intuitive labs, California, USA is the most current and the one which has had the most impact on surgery, in particular Urology and the radical prostatectomy. The use of

the robot offers superior optics allowing for clear 3-dimensional (3D) visualization of the operative site, seven degrees of freedom about which to perform more complex tasks efficiently such as suturing and the dampening of physiological tremors to allow for a more accurate and precise dissection. This in effect translates to a far more superior operation with outcomes which should exceed those from standard open and laparoscopic surgical procedures particularly when reviewing Urological operations.

Combining the minimal invasiveness of the flexible access technique with the technological advantages of robotics would offer a superior surgical treatment option. An operator-assisted robotic endoscope with motorized flexibility, forward drive and superior optics will allow the user to navigate safely through the body cavities to investigate, diagnose and even prepare for operative procedures. The flexibility will allow for precise navigation to even the most inaccessible parts of the body to then become rigid and allow for a magnified, robotically assisted procedure to be undertaken. However, this is only achievable once the safety and technical challenges facing the flexible access technique are studied and the problems addressed.

1.2. Aims of the research

This work is placed to bridge the gap created by the clinical reality of single incision surgery and the conceptual leap to natural orifice surgery. The dogma surrounding the challenges of access associated with NOTES are bypassed with the focus more aptly placed on the introduction of flexible operating surgical platforms to clinical practice.

The aim of the research is to define the concept of Flexible Access Surgery, evaluate some of the main challenges facing the technique and explore the potential of how technology could be used to translate it into a true clinical reality. This will be achieved through;

- Highlighting the advantages of the technique and the challenges facing its widespread adoption within the clinical setting.
- To define the ergonomics of the investigative flexible endoscope as a surgical platform to determine if any potential alterations made to the device could offer a

more effective tool for the undertaking of surgical tasks or merely an ill-considered adaptation.

- To trial and formulate the clinical requirements for a prototype single incision robot for the purpose of flexible access surgery and ascertain the clinical requirements essential for the robotic device to be clinically effective *in-vivo*.

In essence the research not only hopes to offer a sound basis and understanding of the ergonomic challenges facing the use of the endoscope as a surgical platform but also to explore technological enhancements which may expand the possibilities enabling flexible access surgery to become a safer and more ergonomic technique to perform, with the hope of promoting wider dissemination.

1.3. Thesis Overview

Hypotheses upon which each of the chapters are based:

- **Chapter 3.** *The challenge of accurately navigating a flexible endoscope within a spatial environment requires significant endoscopic experience.*
- **Chapter 4.** *Navigation and Instrumentation are progressive limitations of the technique.*
- **Chapter 5.** *The forces required to manipulate tissue for clinical application are measurable and the level can be optimised through appropriate tool-tissue placement.*
- **Chapter 6.** *A clinically relevant hyper-redundant robotic endoscope can be engineered to reliably and repeatedly be used to access a target within the in-vivo environment from two separate single incision sites one of which includes using a natural orifice.*
- **Chapter 7.** *The flexible access platforms can be validated to confirm translatable clinical applications.*

The opening review chapter explores the shift in surgical practice from the birth of minimally invasive surgery to the exposure in this thesis of the flexible access surgical technique. A

concept of utilising the benefit of an articulated platform to offer not only better access to difficult organs once intra-cavity but also flexible in the point of access externally; a concept which could conceivably promote personalised surgery; surgery tailored to the individual. As a form of flexible access surgery, the use of the flexible endoscope through a natural orifice for clinical application was reviewed. Furthermore, outcomes of an original survey presented to the public are presented. This explored the public's reaction to choosing their incision site and their preferences as to the site of their incision for some more clinically relevant procedures. The chapter further explores the potential of introducing robotic application to flexible access surgery to enhance clinical uptake, with a detailed review of the role of robotic technology in current surgical practice. This chapter has inset passages from referenced journal publications undertaken by the lead author (2, 3). A proportion of this chapter was also incorporated as part of a Masters in Science (MSc) degree project for the second author; Mr Kunal Shetty MRCS MSc.

Chapter three aims to undertake a series of trials within a custom made flexible access simulator phantom model. The design and validation of the model for flexible endoscopic navigation is described together with an exploration of the ergonomics of the instrument whilst a subject is undertaking a given navigation task. The body motion of the clinician is monitored using a video motion tracker, capable of determining the position of all pre-defined points on the endoscope and subject to expose those particular points worthy of further investigation due to their motion affects. The outcomes aim to determine the level of experience required to undertake the navigational task efficiently to confirm the hypothesis. This chapter has inset passages from referenced journal publications undertaken by the lead author (4, 5).

Chapter four aims to define flexible access surgery in depth with novel examples drawn from *in-vivo* animal trials, cadaveric models and clinical trials. The desire by the general public to be offered these techniques is evident in this chapter with the benefits and more specifically the challenges of using a flexible endoscope highlighted using these examples. These challenges, directed predominantly towards the flexible endoscope, are discussed with the subsequent chapters exploring these in greater depth. This chapter has inset passages from referenced journal publications undertaken by the lead author (6, 7).

Chapter five examines the forces required to be met within the abdominal cavity as an exemplar to describing the clinical need for any future flexible access platform to meet. This chapter describes the design and integration of a novel laparoscopic instrument integrated with force measuring sensors capable of measuring the forces it imparts on the tissue bed in a two dimensional plane. The force requirements are mapped as well as the most optimal angle of triangulation to minimise tissue force for the design of future bimanual instrument designs.

Chapter six describes the early design and *in-vivo* testing of a prototype robotic flexible access device. The challenges of trialling such articulated devices *in-vivo*, the pitfalls and methods of overcoming them through design and innovation are described with early results. This chapter has inset passages from referenced journal publications undertaken by the lead author (8)

Chapter seven evaluates these mechanised flexible access platforms within the *ex-vivo* as well as *in-vivo* setting with clinical applications determined and explored. Quantification of suitability of the articulated robotic platforms for clinical use was undertaken with *in-vivo* and *ex-vivo* user trials to demonstrate both the ease of control, as well as detailed analysis of the main capabilities of each of the designs for clinically relevant procedures; including workspace analysis of the articulating platform and the workspace and force capabilities of the instrument arms of the bimanual design. The outcomes derived enabled both quantitative assessment of the performance of the designs and the ascertainment of the further engineering requirements essential for formal clinical translation to be determined.

Clinical procedural validation was undertaken using a sequence of criteria defined which explores, access, the capabilities of diagnostics as well as the ability to dissect and reconstruct tissue. Potential clinical applications given the capabilities of each of the current designs are discussed with the relevance of current and existing energy delivery instruments (7).

Future development is evaluated in the final chapter which aims to highlight the potential for the devices described to be translated into a clinically marketable product. A relevant clinical procedure is essential for the translation of such a product and once in the clinical arena will highlight its beauty, simplicity and effectiveness on its own merits. The future developments of this thesis will also explore some of the potential spin out areas of research which could be pursued as a result of this work.

1.4. Original Contribution of the Thesis

The original contributions as a result of this thesis include:

1. Deriving a potential method of quantifying endoscopic performance in surgical applications.
2. Defining a generic surgical nomenclature which encompasses the utilisation of flexible platforms for surgical application.
3. Defining a unique method of accessing distant surgical sites through the utilisation of the pre-fascial anatomical planes.
4. Determining the level of force required to manipulate tissue within the pre-clinical setting as a benchmark model for engineering future flexible access surgical tools.
5. Deriving a potential quantitative measure of surgical skill in surgical trainees through the evaluation of tool-tissue interaction.
6. The introduction of a clinically relevant hyper-redundant flexible mechanised platform, capable of full robotic transform, presenting a benchmark for future robotic assisted flexible access platforms.
7. Describing the methods of overcoming the challenges of introducing novel flexible surgical robots into the *in-vivo* setting.
8. The relevance of constrained workspace analysis in evaluating and validating the performance of flexible robotic platforms for clinical application.

The main publications associated with this thesis include:

1. Clark J, Sodergren MH, Purkayastha S, Mayer EK, James D, Athanasiou T, et al. The role of robotic assisted laparoscopy for oesophagogastric oncological resection; an appraisal of the literature. *Dis Esophagus*. 2011;24(4):240-50. Epub 2010/11/16.
2. Clark J, Sodergren M, Correia-Pinto J, Zacharakis E, Teare J, Yang GZ, et al. Natural orifice transluminal thoracoscopic surgery: does the slow progress and the associated risks affect feasibility and potential clinical applications? *Surg Innov*. 2009;16(1):9-15.
3. Clark J, Shetty K, Sodergren M, James DRC, Purkayastha S, Athanasiou T, et al. Robotic-assisted Total Mesorectal Excision; should it be the technique of choice in the management of rectal cancer? *Journal of Robotic Surgery*. 2012; 6(2): 99-114.

4. Clark J, Sodergren M, Noonan D, Darzi A, Yang GZ. The natural orifice simulated surgical environment (NOSsE): exploring the challenges of NOTES without the animal model. *J Laparoendosc Adv Surg Tech A*. 2009;19(2):211-4.
5. Clark J, Orihuela-Espina F, Sodergren M, James D, Karimyan V, Teare J, et al. A quantitative scale to define the quality of endoscopic torque control during Natural orifice transluminal endoscopic surgery. *Minimally Invasive Therapy and Allied Technologies*. *Minim Invasive Ther Allied Technol*. 2012 Jun 4. [Epub ahead of print].
6. Clark J, Leff D, Sodergren MH, Newton R, Noonan D, Goldin R, et al. Single Incision Transumbilical Levels 1 and 2 Axillary Lymph Node Dissection using a Flexible Endoscope in Human Cadaveric Models. *Surgical Endoscopy*. *Surg Endosc*. 2012 Aug 31. [Epub ahead of print]
7. Clark J, Noonan D, Sodergren M, Vitiello V, Shang J, Payne C, et al. Robotic assisted transvaginal tubal ligation; focused clinical application for a novel flexible hyper-redundant surgical robot. *Surgical Endoscopy*. April 2012;Accepted for publication.

Chapter 2

From Minimally Invasive Surgical Techniques to Flexible Access Surgery.

2.1. Surgical Evolution; Challenging the Conventions of Surgery

Surgery has always evolved from the earliest skull trepanning of 6500BC to the post-anaesthetic, post-antibiotic era of the modern surgical age. Surgery continues to refine its effectiveness and capabilities motivated by benefits, both in terms of operative and now more than ever; economic outcomes, creating a treatment option which is even more enhanced than ever before.

Surgery has always been seen as a traumatic form of medicine. The risks of which are still considered too high for many of the population to consider and where the risks and benefits of any procedure is always weighed up for each individual prior to any procedure. The open surgical approach, still essential to undertake for many operative procedures; elective and emergency, exposes the patient to a significant incision and excessive tissue handling, with the consequential increased risks of wound infection, chronic pain and a greater risk of exposure to adhesions and their sequelae. The overall consequence of which is a slower recovery and potentially long term problems as a result of the surgery alone.

Laparoscopic Surgery

The advent of laparoscopic surgery in the mid 1980's heralded a new era for surgery and surgical technology. The small, muscle splitting incisions of 5mm to 12mm associated with the laparoscopic procedures reduced the impact of surgery on patients significantly with clear benefits in terms of a faster recovery, earlier hospital discharges and a faster return to work demonstrated. The impact of such a technique was revolutionary and enabled previously common open procedures, such as the Sub-Costal Kocher's Cholecystectomy to become obsolete, a technique which often kept the patient in hospital for over one week in turn now being undertaken across the field by the laparoscopic technique; which invariably is able to send the patient home within one day. However the technique was challenging to learn with

the use of long rigid instruments whose hand-tool manipulation was reversed with the fulcrum effect of the port site through the skin coupled with the disorientation effects of attempting to visualise this 3 dimensional environment and instrument movement through a 2 dimensional camera. For the surgeons, it has taken a generational shift for its introduction to become mainstay. Initially the outcomes for laparoscopic surgery were significantly higher than open but after the proficiency curve had been met a new benchmark for the risks of surgery had been set enabling a far greater number of patients to be exposed to its therapeutic value.

Single Incision Surgery (SILS)

The dynamic nature of surgery and the drive of the surgeons who practice it, has continued to move the field further forward with the introduction of ever less invasive surgical techniques such as Single incision laparoscopic surgery (SILS). Drawing on the further reduction in the number of incisions required to undertake a particular procedure many have adopted the single incision approach. This requires the use of existing laparoscopic instruments, or be it with some slight modification, to undertake a surgical procedure with two instruments and a camera inserted through either one larger port of approximately 16 - 25mm to three 5mm incisions made deep to a single standard incision in the skin. In either case the benefits are slight, when compared to the laparoscopic technique, with the significant benefits being cosmetic (9) with no supportive evidence of improvement in postoperative pain (10). However, the challenges of the technique are even greater than that of laparoscopy. The instruments are closely approximated which not only creates tool interference but also reduces tool tip triangulation at the tissue bed; essential for the traction required to safely undertake dissection and prolonged anaesthetic times (10). This has, coupled with the same challenges as laparoscopic surgery, limited its use to selective patients only performed within selective high volume laparoscopic centres. However, innovative ways of overcoming a number of these challenges have been explored with alternative retraction techniques, such as puppetry of the tissue (11), however this is difficult to perform and take a significant level of experience to master safely. The technique is limited by its ergonomic challenges.

Mini-laparoscopic surgery (MiniLap)

The drive for the benefits of improved surgical cosmesis without the challenges of the lack of instrument triangulation and the juggling of alternative retractile techniques has exposed a

potentially new possibility. Though currently under-represented in the surgical community, it is a field which uses needle sized 2.5mm calibre instruments to undertake and perform the procedure using the standard triangulating format used with the conventional laparoscopic technique with only a single 5-10mm camera port alone used for both visualisation and removal of the specimen. Although, this overcomes those triangulation challenges faced with SILS, the inability, with current mini-laparoscopic designs, to change instruments at will, or indeed introduce other affiliated devices such as endoloops or even endoscopic clips limits its capacity. However, some small series are being published to demonstrate their capabilities for selective surgical applications such as the appendicectomy or cholecystectomy with the use of a 10mm port and a 5mm camera (12). With this setup the endoloops, endoshears or 5mm clip applicators can be introduced in parallel to the 5mm camera and complete the procedure. This demonstrates the capacity of the instruments as an effective adjunctive tool and their potential to maintain cosmesis but also enable procedures such as single incision and natural orifice surgery to be safe and effective. However, some concerns regarding tissue injury caused as a result of these instruments has limited their use.

Natural Orifice Transluminal Endoscopic Surgery (NOTES)

NOTES is a revolutionary new concept in surgery though within the UK remains strictly within the research arena with clinical trials undertaken only under ethical guidance. The concept of the technique aims to enhance the cosmetic benefits of surgery as highlighted by the single incision technique through moving the single incision to a natural orifice, promoting what is in essence surgery without the scars.

There is no doubt that NOTES is challenging to undertake yet the possibilities of what can be achieved when the endoscope is visualised as a therapeutic device rather than a diagnostic tool is overwhelming both within the endoluminal as well as transluminal environment.

Heralded as the next step in the evolution of minimally invasive surgery, Natural Orifice Transluminal Endoscopic Surgery (NOTES) has attracted significant interest since its introduction. As the numbers of those that support the continual efforts to explore the approach grows, however, so do the number of those opposing it (13, 14).

Using the body's natural orifices to gain access to the thoracic or abdominal cavity explores a surgical technique that struggles against all conventional teaching; however, since the first

published human NOTES procedure in April 2007 (15), the technique has gained extensive interest worldwide.

Performed using a flexible, dual lumen gastroscope, the endoscope is past, via the mouth to the stomach. A gastrotomy allows the endoscope access to the peritoneal cavity within which a surgical procedure can be performed using instruments passed down the biopsy channels of the endoscope (16, 17). This has become the firm basis for the exploration of the technique with numerous animal and human studies, using a multitude of different approaches, being undertaken within the abdominal environment (18-28).

The potential benefits

There is certainly disenchantment amongst some clinicians in the acceptance of this technique as it seems to go against the conventional surgical teachings with a purposeful perforation made in the bowel wall to access the appropriate cavity, however, there are certainly theoretical advantages which make exploring this technique so important which can be considered as intraoperative and postoperative benefits.

Potential Intraoperative advantages:

- Introduction of instruments parallel rather than perpendicular to major blood vessels
- Lower CO₂ pressure for pneumoperitoneum.
- Possibility of using instruments larger than in Laparoscopy.

Potential Postoperative advantages:

- Lower risk for herniation
- No risk for eventration
- Lower risk for wound infection
- Lower risk for adhesions

Since no abdominal wound incision is required the need to undergo a full general anaesthetic may be unnecessary. The analgaesic requirements may therefore be satisfied with conscious sedation alone, allowing for the procedure to be performed outside the confines of the operating theatre. In practical terms this has already expanded the use of NOTES to the

Intensive care unit where it has been successfully used to attach electrodes to the diaphragm for diaphragmatic pacing, an aid to weaning patients off mechanical ventilation (29).

There is of course that final advantage of the NOTES technique; the improved cosmetic result. Certainly an important but by no means the sole drive to research NOTES. However, in a world where scarring is not only cosmetically unattractive but also a sign of ill health the choice to undergo a purely “no scar” operation with all the added benefits of minimal access surgery would be a greatly preferred option in the mind of any potential patient. Despite the critics this will be the most significant drive for the adoption of this technique within surgical practice. Already newspaper headlines internationally have publicized the technique with the cosmesis as its key focus (30, 31). In same way that patient preference drove the exponential expansion of the laparoscopic technique so, when clinically accepted, will it drive NOTES.

2.2. Potential Therapeutic Applications for the Use of the Flexible Endoscope; Transthoracic NOTES.

The original concept of the Natural orifice Transthoracic Endoscopic Surgery was modelled around its development within the abdomen as part of the NOTES evaluation. The introduction of the technique to the thoracic cavity has, however, been met with more apprehension or perhaps caution. This may in part be due to the lack of experience that the thoracic and cardiac surgeons have in the handling of the flexible endoscopes but more likely it is associated with the risks of thoracic cavity contamination. This stems either from an inadequate closure of the viscerotomy entry site, which is probably the most concerning or the introduction of a non sterile instrument into a sterile environment. With the mortality associated with empyema being as high as 50% in some series and morbidity associated even higher (32); the risk is considered by many to be too high to even consider exploring the technique in humans. Only a few studies have therefore been conducted within this environment but with so few studies undertaken, neither the benefits nor indeed the risks of the technique can truly be elicited.

This article aims to systematically review all the studies to date that have used the Natural orifice endoscopic technique to perform procedures specifically related to the cardiothoracic

specialty highlighting some of the benefits and also the shortfalls that this approach could bring.

2.2.1. Method

A systematic review of the current literature was performed using Pubmed, a search tool of the national library of medicine and the national institute of library of databases including Medline. An additional search was performed within the Cochrane library for related articles. The keywords used for the search included: natural orifice transluminal endoscopic thoracic surgery, natural orifice surgery and natural orifice thoracic surgery. The search was broadened using the “related articles” function. The bibliographies of all publications were manually searched for any relevant references. The Cochrane database was also searched for further related trials or pilot trials.

Endpoints.

The search was undertaken to systematically review the extent and outcomes of all thoracic cases undertaken using the natural orifice endoscopic technique. The endpoints were: (1) the preoperative preparation and postoperative care, (2) the approach and techniques adopted for each operation, and (3) the procedure and related complications.

Inclusion & exclusion criteria and definition of procedures.

Inclusion criteria included all articles which related to the use of the natural orifice transluminal endoscopic approach to the thoracic cavity including the mediastinum. All trial types and case reports up until August 2008 were considered for the review. All articles were independently reviewed as to whether they fulfilled the criteria (*Figure 2.1*)

2.2.2. Results

A total of 37 cases from seven studies were highlighted to have used the NOTES technique to undertake a thoracic related procedure (29, 33-38). All studies were performed in porcine models as no human cases have yet to be identified from the literature. From the cases identified five series were survival studies; survival time post operatively ranging from 7 to 42 days (mean 16) (*Table 2.1*).

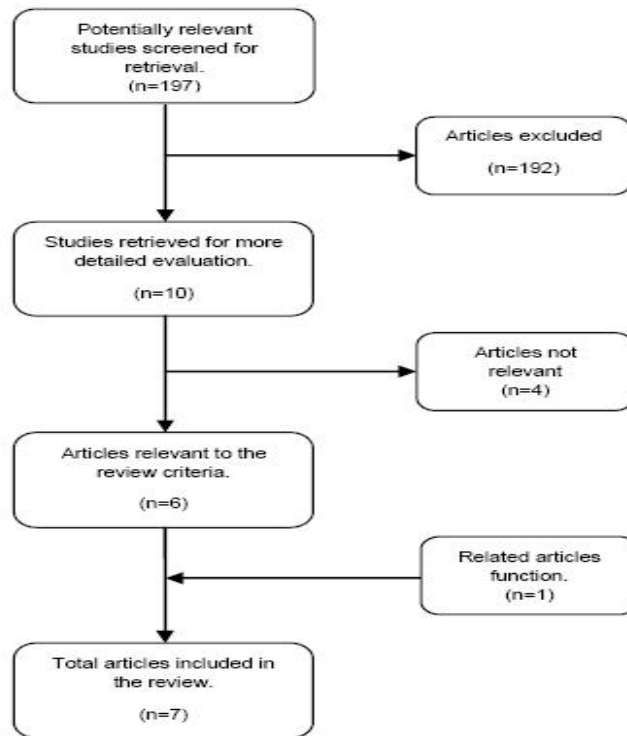


Figure 2.1; A diagrammatical representation of the inclusion methods used for the review.

Table 2.1; Highlights all the thoracic related studies undertaken using the Natural Orifice Transluminal Endoscopic technique.

Sudy	Year	Animal Model	Survival Sudy (Yes/No)	Number of cases performed	Intervention	Access to Thoracic Cavity	Survival Length (days)
⁽³³⁾ Sumiyama	2007	Porcine	Y	4	Post. Mediastinoscopy	TO	14
⁽³⁴⁾ Lima	2007	Porcine	Y	6	Thoracoscopy and lung biopsy	TV/TD	15
⁽³⁵⁾ Fritscher-Ravens	2007	Porcine	Y n=7 N n=2*	9	Lymph node retrieval n=2 Pericardial fenestration n=5 * Myocardial Saline inject n=4	TO	14 (n=3) 28 (n=2) 42 (n=2)
⁽²⁹⁾ Onders	2007	Porcine	N	4	Diaphragmatic pacing wire placement	TG	-
⁽³⁶⁾ Willingham	2008	Porcine	N	5	Lymph node resection and pleural biopsy	TO	-
⁽³⁷⁾ Sumiyama	2008	Porcine	Y	5	Epicardial coagulation	TO	7
⁽³⁸⁾ Gee	2008	Porcine	Y	4	Mediastinoscopy and thoracoscopy (n=4) + Pleural biopsy (n=3)	TO	8 (n=2) 12 (n=2)

(TO - Transoesophageal, TG – Transgastric, TV - Transvesical, TD – Transdiaphragmatic)

(indicate s the non-survival study intervention in this series)*

All studies were performed to assess the feasibility of performing a safe Natural Orifice Endoscopic technique for a thoracic problem. Six of the studies were conducted to review the general feasibility of performing intrathoracic procedures: mediastinoscopy, thoracoscopy, lung or pleural biopsies, lymph node retrievals and epicardial coagulation, whilst one series reviewed the feasibility of using the NOTES technique for the placement of diaphragmatic pacing wires on the peritoneal side; a novel method of weaning patients from mechanical ventilators either in the Intensive care setting or after high cervical cord damage.

Pre-operative preparation and post operative care

A variety of preparation techniques were used with little consistency between the studies. All the animals were kept nil by mouth (NBM) from various time periods preoperatively ranging from 6 hours to 24 hours with a variety of regimens of feed used prior to that period. In three series, the animals were prepared with an endoscopically delivered lavage of sterilized water and 60mls of 10% Povidine Iodine.

Two of these cases were followed up with postoperative oral antibiotics (5-7 days of Enterofloxacin 10mg/kg once daily) and additionally a 7 day course of proton pump inhibitors (Esomeprazole 40mg twice a day). The series by Gee *et al* which also undertook the preoperative lavage did not record any further prophylactic therapy. Antibiotics however, were used postoperatively in the case series by Fischer-Ravens *et al* who although used the same post operative regimen as has been described; i.e a 7 day course of Enterofloxacin 10mg/kg once daily, did not adopt the oesophageal lavage preoperatively, instead the animals were kept NBM for a longer period preoperatively. The series by Lima *et al* from Portugal who performed the transvesical and transdiaphragmatic survival study used only intramuscular administration of Ceftriaxome upon induction of anaesthesia and no other therapeutic prophylaxis. The remaining series used no preparation or postoperative therapy prior to undertaking the operations.

Approach to the Thoracic cavity

Considering the six intrathoracic case series, access to the cavity was performed via the oesophagus in five of these and via the transvesical and transdiaphragmatic approach in one. This original approach utilised a 9.8 Fr Ureteroscope to access the bladder. Scissors and a dilator were used to perforate the anatomical dome from where the peritoneal cavity could be

accessed. The insertion of an over-tube allowed guidance of the endoscope to the upper abdomen and an incision through the muscularis part of left hemi-diaphragm was made. Access to the thoracic cavity was subsequently performed and a biopsy of the lower left lobe of the lung undertaken without complication. Decompression of the cavity and re-inflation of the lung was performed under direct vision before closure of the pleura and diaphragm.

The remaining cases describe approaches to the thoracic cavity via the oesophagus. In 4 of the series (n = 18 cases), the studies describe tunnelled approaches through the oesophagus whilst 1 series (n = 9) describes a more direct transmural dissection through the oesophagus using a needle knife and balloon dilator.

The submucosal endoscopy with mucosal flap safety valve (SEMF) is a technique of dissecting the mucosal and submucosal planes from the muscular wall of the oesophagus with the openings staggered at a distance from each other so inadequate approximation closure of one hole will be overcome by the valve effect from the adjacent layer. Described initially by Sumiyama and colleagues (Rochester, Minnesota, USA) it has been the most favoured opening technique used in the review with four of the seven series adopting it. Although two of these series which described using this approach were from Sumiyama's team, the approach had also been adapted by Gee and colleagues both for the non-survival (Wallingham et al) and survival studies.

Ascertaining access to the correct side of thoracic cavity was highlighted as a problem in all but one series. In the largest of the case series, the use of a needle knife and balloon dilator in forming the viscerotomy was accompanied by the use of Endoscopic ultrasound (EUS). The device was not only successfully used to confirm the side of the chest the breach was accessing but also determined the presence of any abutting structures to the proposed viscerotomy site prior to making the incision.

Operative feasibility

The success of the transluminal endoscopic approach will be determined not only by the safety of the approach but also whether appropriate operative procedures can be performed. All of the intrathoracic studies described currently in the literature are proof of concept rather

than trialling specific operative interventions. However, the need to perform simple thoroscopic and mediastinoscopic inspection is essential for the acceptance of the technique; if locating a lesion is impractical with the current equipment then the technique is not feasible.

A complete and regimented inspection of the posterior mediastinum with no intervention was performed in 4 cases. Thoracoscopic Inspection was performed in 17 cases with additional pleural biopsies taken in 8 and lung biopsies in 6, of which one led to a pneumothorax requiring intervention by means of a venting transthoracic incision. Lymph node retrieval from the mediastinum was successfully attempted in 9 cases but in 2 cases; Fischer-Ravens et al (35), the resection was described as being challenging but overcome.

A pericardial window was performed in 7 cases and in 4 of these; this was followed by an injection of normal saline into the right atrium. No complications from this cardiac procedure were reported by the study group in the article. Furthermore, cardiac procedures have been performed more recently; Sumiyama *et al* (37), with the formation of a pericardial window and undertaking of focused epicardial coagulation using electrocautery. Despite some transient sinus tachycardia during diathermy no arrhythmias or cardiac anomalies were detected.

The most promising intervention that NOTES may offer the respiratory specialist is the transabdominal diaphragmatic pacing wire placement. The placement of pacing wires on the diaphragm has been shown to be of proven benefit for weaning patients off mechanical ventilators but requires an abdominal procedure. The benefits will include patients who are reliant upon mechanical ventilators after cervical spinal injury leading to tetraplegia and also patients in an Intensive Care Unit (ICU) setting. In the ICU setting diagnostic endoscopy and Percutaneous Endoscopic Gastrotomy (PEG) placement is routinely performed. The use of the NOTES technique to place pacing wires on the diaphragm has strong possibilities. Onders and colleagues (Case Western Reserve University, Ohio, USA) have successfully undertaken 4 porcine model transgastric NOTES placements of these pacing wires. Using a electrode stimulating probe to detect the motor end point for the Phrenic nerve, essential if pacing is to be effective, the wires were implanted successfully. No complications occurred during the procedures. Closure of the gastrotomy was with a PEG formation and no leakage around the gastrotomy site and PEG was detected when tested.

Closure

Closure techniques have been relatively consistent amongst the individual studies predominantly using the Submucosal Flap valve in addition to mucosal clips (n=16), mucosal clips in isolation (n=9) or endoscopic suture closure (n=6). In 2 cases, however, from the series by Gee *et al* who used the SEMF opening technique, no form of additional closure method was used. Although, from that series one pig developed fluid in the mediastinum and histological changes suggestive of a subclinical leak, this pig was in fact one of the cases to have undergone a clip closure in addition to the SEMF.

For full thickness defects of the oesophagus, closure of the defect using the mucosal clips in isolation also proved successful with no evidence of contamination being described. This was notable from the series described by Fischer-Ravens *et al*, in which the resultant defects on autopsy had been completely sealed by the closure of the mucosa despite the myotomy remaining open.

Outcomes

Two animals (5%) were euthanized as a direct result of complications from the procedure. One had an inadvertent injury to the descending Aorta during the procedure and the other had a tension pneumomediastinum leading to respiratory distress. The total number of complications described from all the series, including those which required euthanasia was 9 (24%).

Only one case described the possibility of a leak (4%), however, the animal was clinically well post operatively and thrived. The evidence became clear at autopsy where the histology of a mediastinal anomaly showed bacteria and an increased number of neutrophils. The suggestion was of a subclinical leak (*Table 2.2*).

Table 2.2; Highlights the access and closure techniques of the intrathoracic case series and the documented complications.

Sudy	Case (n)	Access technique	Closure Technique	Preparation	Mortality (n)	Morbidity (n)	Complications
(33) <i>Sumiyama</i>	4	SEMF	Mucosal Clips	L / A* / P	1	1	Tension pneumo-mediastinum (n=1)
(34) <i>Lima</i>	6	S+D	Mucosal Clips	A**	none	none	none
(35) <i>Fritscher-Ravens</i>	9	NK+D	Clips (n=3) Suturing (n=6)	A*	none	1	Asymptomatic Pericardial haematoma (n=1)
(36) <i>Willingham</i>	5	SEMF	Mucosal Clips	none	none	1	Pneumothorax (venting incision required) (n=1)
(37) <i>Sumiyama</i>	5	SEMF	Mucosal Clips	L / A* / P	1	2	Uncontrolled Haemorrhage Due to injury to descending Aorta (n=1)
(38) <i>Gee</i>	4	SEMF	Clips proximal opening (n=2) None (n=2)	NR	none	5	Mild Atelectasis (n=4) Early abscess formation in mediastinum (n=1)

(SEMF – Submucosal endoscopic with mucosal flaps, S+D – scissors and dilator, NK+D –Needle Knife and dilator)

L – Oesophageal Lavage with dilute povidine-iodine, A* - Post operative Antibiotics (5-7 days of Enterofloxacin 10mg/kg once daily),

A** -Intramuscular Antibiotics on induction (Ceftriaxome), P – Post operative proton pump inhibitors (Esomeprazole 40mg twice daily).

The requirement for chest drains in those cases which underwent a pleural opening was not reported in any of the case series. Certainly when insufflating the oesophagus the risk of air entering the pleural space and causing a pneumothorax is potentially hazardous with one case in the review describing the fatal pneumomediastinum as a result of this, however, of the remaining animals, although one case did require a venting incision to re-inflate the lung, no chest drain was ever reported as being required during the post operative period in an series.

2.2.3. Conclusion

It is clear from all these cases that NOTES could be a potentially useful technique in thoracic and possibly even cardiac surgery in the future. The ability to perform diagnostic investigations within the thoracic cavity without the need for any intercostal incision is an exciting prospect and from these case series, it has been demonstrated to be possible. These animal cases describe a safe and effective method of accessing the thoracic cavity using the SEMF technique and if used in conjunction with the EUS, as described by Fischer-Ravens *et al* (39), it could offer the operator a method to accurately and safely position the myotomy

incision to suite the operative requirements whilst avoiding injuring any underlying or adjacent structures which may be abutting the wall. The SEMF approach is one which also offers the potential security of closure once the procedure is completed. The results from the 27 trans-oesophageal cases, of which 18 used this technique, 1 subclinical leak was detected. The same group have also trialled the technique on the gastric wall for peritoneoscopy, both in an *ex vivo* model and an *in-vivo* porcine model. This was a 1 week survival study using 4 domestic pigs. All animals survived 1 week. 3 animals developed a mucosal ulceration at the incision site however leak testing was negative on all stomachs (40). The results from the limited studies do suggest that this technique could offer the method of accessing and securely closing the transluminal defect for Natural Orifice thoracic surgery which has been hampering the expansion of the technique in the thoracic cavity.

Although this could still be regarded as one too many, it does suggest that the potential for a safe thoracic procedure through this route is possible and the approach should not be completely ignored as a potentially viable route of access. However, there is a clear need for further case control and randomised studies, as the limiting factor with all large animal trials is the size of the study groups. This makes the possibility of follow on large randomised trials very difficult to undertake but may nevertheless essential if thoracic NOTES surgery is ever to be extended to the human population.

2.2.4. Discussion

Would NOTES be considered a fad or the next generation of minimally invasive cardiothoracic surgery? Natural orifice surgery is attracting a global interest. This includes not only clinicians but also patients who, from questionnaire studies in the United States and Sweden, seem to be attracted to the technique over conventional approaches; willing to accept higher risks to undergo such procedures using this approach, despite the complications having yet to be fully elicited (41).

Potential advantages for the use of NOTES in the thoracic cavity have been postulated to include reduced pain with the potential to virtually eliminate post operative intercostal neuralgia, offer access to the posterior mediastinum, improve visualization of the pulmonary hilum; both for the retrieval and biopsying of lymph nodes, and finally improve cosmesis; a statement that can be said with confidence in the context of Thoracic NOTES (36, 38).

However, NOTES remains in its infancy, the instruments currently used remain the standard diagnostic endoscopes that 10 years ago were investigating the intraluminal environment for pathology and not the external. Poorly controlled, the navigation of the instrument tip to the target is challenging enough without the loss of tail awareness and of which structure this trailing portion may be abutting. The instruments are however slowly changing, adapting to the spatial environment. Devices are available which are capable of locking the flexible instrument into a set position such as the USGI Endosurgical operating system (USGI Medical). This not only aids navigation to the proposed target but also offers a stable platform from which an operation can be performed. Instruments for intracorporeal suturing using the endoscope are also currently available and improving rapidly. As the repertoire of instruments improves, so the ergonomics and technical limitations facing this technique will be overcome.

Video Assisted Thoracoscopy (VATS) has revolutionised thoracic surgery. Its minimally invasive nature of the technique makes it perfect for diagnosis and therapeutic interventions in the critically ill patient (42) whilst offering procedures previously inconceivable even using a full thoracotomy. Operations such as lung reduction surgery for emphysematous chronic restrictive airways disease, pleurectomy for recurrent pneumothoraces and diagnostic thoracoscopy with lymph node sampling for cancer staging has secured VATS as an essential tool in thoracic surgery offering some of these procedures as day cases. However, it is operations such as the excisions of neural origin brachial plexus tumours and the undertaking of thoracic sympathectomies for facial hyperhidrosis show to be markedly more effective using this approach over conventional techniques which has proved the versatility of a minimally invasive thoracic approach, expanding VATS beyond just pulmonary diseases. It is also not to be forgotten that Cardiac surgery has for some time now also adopted the minimally invasive approach with the thoroscopic coronary artery bypass procedure being performed either conventionally or now even using the Endoscopic telemanipulator devices such as the DaVinci™ (Intuitive Surgical, California, USA). All in the effort to reduce the risk of wound infection and in the case of the median sternotomy for cardiac surgery the devastating sternal dehiscence that is quoted as having a cumulative incidence of 2.5% (43). The future for Natural Orifice Thoracic surgery could potentially offer all these procedures, including coronary artery bypass surgery but with no visible scars, post operative pain and together with a safe and effective transluminal access approach, perhaps even a reduced risk

of wound infection. As the instruments and equipment for the Natural Orifice approach improves and even adopting flexible robotic devices to improve ergonomics and manipulation would offer the surgeon a unique visual opportunity with the potential of looking around and behind structures or organs without disturbing them and this advantage has particular relevance when discussing coronary surgery.

The single most significant challenge facing the NOTES approach is related to safe access and closure, an area which has gained little ground over the five years since the first human clinical case was undertaken. Many of the current clinical cases described in the literature have predominantly been undertaken through the transvaginal route; given the historical access point for gynaecologists for the transvaginal hysterectomy, with the insecurity and difficulties of closure of the transgastric and transrectal approaches limiting clinical exploration in fear of leak. This therefore restricts the technique safely to only 50% of the population; the female group. Although, much research is being directed into both these alternative access points, the inability to perform a secure closure of these is damning to the whole technique.

2.3. From NOTES to Flexible Access Surgery (FAS); Broadening the Potential.

The strength of the NOTES technique, however, may not necessarily be in the natural orifice access that the procedure describes but perhaps more relevantly in the use of the flexible endoscope as a surgical platform. Its introduction highlights that with such a flexible surgical platform, operative target sites can be accessed from distant incision points, natural orifice or otherwise. As a result the use of such flexible operating platform has the potential to offer flexibility in the point of access on the body. A site which is in essence no longer limited to the straight path required with the more rigid instruments. The technique is termed Flexible Access Surgery (FAS)

The NOTES technique has directed more attention towards the use of flexible endoscope as a surgical tool rather than simply a diagnostic device reserved for gastroenterologists and in doing so, has highlighted a significant area for technological development which can aid both

endoluminal as well as flexible access surgery. The flexibility of the endoscope is unique. It is able to target tissues and organs of interest from a site distant from it, this in effect offers the potential from any surgical target to be approached from any access point on the body, natural orifice or percutaneous. An amalgamation of the single incision and natural orifice techniques with the advantage of promoting enhanced surgical cosmesis across the general population; men and women. The proposal of Flexible Access Surgery by no means overcomes the significant challenges of NOTES access and closure, yet it maintains the significant benefit that such a flexible platform would affirm to surgery if technologically a more refined flexible platform became available; the ability to access any target organ from any incision site, distant or otherwise. Flexible in terms of the platform and flexible in terms of access sites! Some of the current emerging technologies overcome some of the technical challenges but none meet them all (*Table 2.3*).

Table 2.3; Emerging technology, potential flexible access platforms and how they compare to the flexible endoscope.

	Name of device	Instrumental Control	Controlled Navigation	Spatial awareness	Stable platform for intervention	Instrumental triangulation
	Anubis; Karl Storz	Same as endoscope	Same as endoscope	Same as endoscope	Same as endoscope	Moderate
	Endosamurai; Olympus	Improved	Same as endoscope	Same as endoscope	Same as endoscope	Improved
	Neoguide; Neoguide Systems Inc	Improved	Improved	Improved	Same as endoscope	Same as endoscope
	R-Scope; Olympus	Same as endoscope	Same as endoscope	Same as endoscope	Same as endoscope	Moderate
	Incisionless operating Platform; USGI Medical	Improved	Same as endoscope	Same as endoscope	Improved Patented shapelock	Same as endoscope
	Cobra; USGI Medical	Unknown	Same as endoscope	Same as endoscope	Improved Patented shapelock	Improved
	Direct drive endoscopic system; Boston Scientific	Improved	Same as endoscope	Same as endoscope	Same as endoscope	Improved

Whether this is something that the general population would be keen to accept if available needs to be carefully considered but from it may be argued that by giving patients the option of the position of their scar, hidden or otherwise, could be a move towards enabling patients to re-take some control of how their surgery will be undertaken. An element which perhaps we as surgeons should not be so quick to dismiss as for some patients may be very important.

As an initial preliminary assessment, the views of a sample of the general public were evaluated using a simple questionnaire to determine whether there would be an acceptance for such a technique within general surgery should it become clinically available.

2.4. Your Surgery, Your Scar, Your Choice! A Survey to Establish Public Opinion toward *Flexible Access Surgery*.

2.4.1. Introduction

Flexible access surgery (FAS) has the potential to redefine how surgeons consider surgery. The idea that the boldest surgeons are the ones which make the largest cut is well past and this motivation will continue. Natural Orifice Surgery has demonstrated that the use of a flexible endoscope as an instrumental platform has the potential to perform a surgical procedure which only 25 years ago was being performed using the open approach. This drive towards ever less invasive surgery will ultimately lead to the boldest surgeon being the one who can offer the patient the procedure they need with the incision they desire. Flexible access surgery has the potential to empower patients. At a highly vulnerable time in a patient's life, when they must give full control to a stranger, the ability to perform a surgical procedure through a desired incision point whether this is directly over the site of the pathology or not may give some level of control and therefore satisfaction back to the patient. It would be unheard of and indeed unacceptable for us to walk into shop and request an item only to be told that this is not the item we desire but an alternative, so why are we in surgery so driven to prevent the patient from choosing their site of the incision. This is undoubtedly related to the fact that the possibility for this has never been available as the instruments and desire to change has not been present. With so many different surgical approaches fast evolving, for example the transoral, transaxillary or periareolar routes for thyroid or

parathyroidectomy (44, 45), the choice currently comes down to the preference and skill of the surgeon. However, it is only a matter of time before patient choice becomes a reality.

Flexible access surgery has the potential to enable any target point in the body to be reached from a more widely available range of access sites and although it is unlikely to be suitable for all operations, there is no reason to believe that within the elective setting patient choice could not play a more significant role even in current surgical practice.

Much debate has been ongoing as to whether the general public would accept a natural orifice approach, particularly the transvaginal or transrectal approach given the choice. Questionnaires have been developed internationally to explore this question often presented by NOTES enthusiasts and more often with bias towards the NOTES or SILS techniques (46). However, the importance of the choice of scar position to individuals was explored using our own questionnaire based survey which included a review not only of the general view of the public toward greater choice but also the consideration as to whether they would consider a natural orifice route if presented.

2.4.2. Methods

A questionnaire was created to determine how important the general public felt choosing the site of their potential surgical scar was to them and where and given the choice where would they prefer to have it placed. This questionnaire was part of a larger survey of the general public which is presented later in this chapter and aims to promote an unbiased view of the preferences of the general public to the siting of their surgical scar.

This section presented the targeted population with four hypothetical procedures, a thyroidectomy, stem cell delivery to the heart, cholecystectomy and an adrenalectomy. The adrenalectomy was repeated to create a fifth procedure but for this came with additional advice which aimed to promote the transrectal primarily followed by the transvaginal routes as the routes which provided the better outcomes from the operation to determine whether these routes would ever be considered by the general should these natural orifice approaches ever become clinically mainstream. The questionnaire also asked the population how

important they felt the position of their scar was to them. This was asked through a single question and the response gauged using a Likert scale. The question was:

“If ever you need Surgery your doctor will help you make informed decisions. However, please let us know how important it is for you to have a say in the position of the surgical incision and therefore the location of the scar on your body”

A sketch image of the human body with the target organ placed in the appropriate anatomical position was presented as the question (Figure 2.2). The image was shaded over the limbs and left unshaded over the torso as a means of defining where the choices for access sites are possible. The torso was further segmented according to various potential incision sites. These included the Transoral, Transvaginal, Transurethral, Transrectal, Transaxillary, Transumbilical, Transabdominally through the umbilicus or below the bikini line.

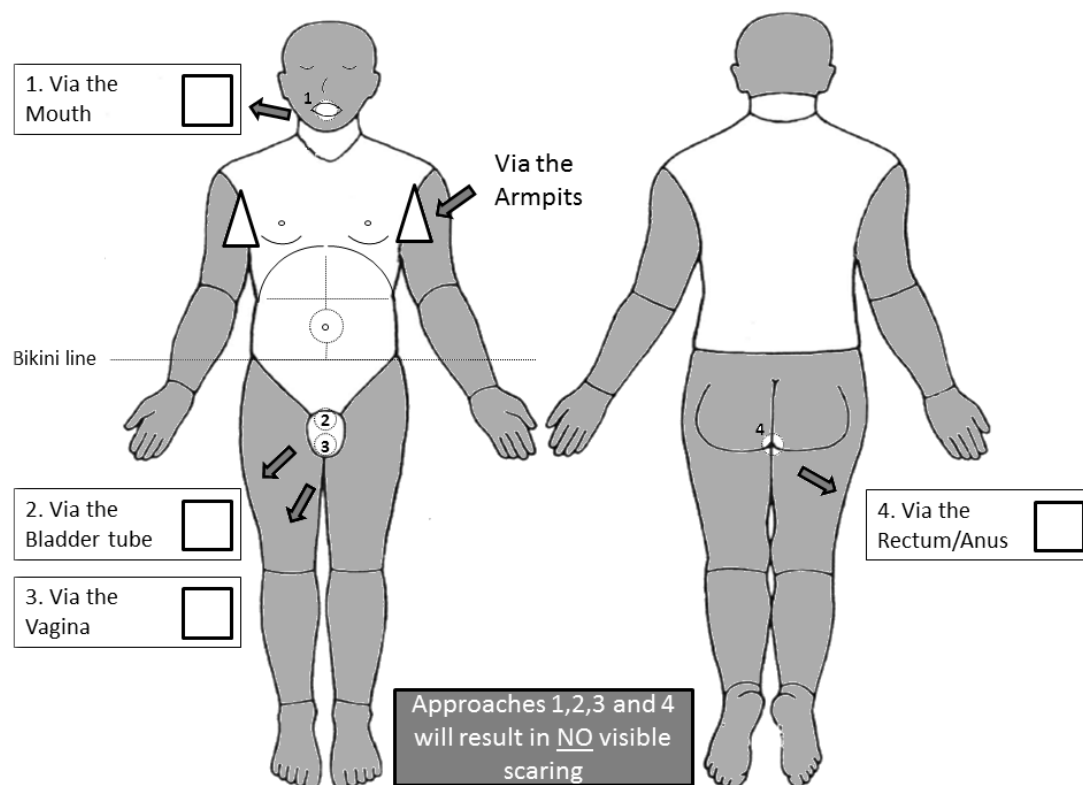


Figure 2.2; Image of the human body presented to the general public for the purposes of the survey. The shaded areas are not compatible with an incision. A cross to denote the preferred incision site can be placed anywhere on the non-shaded region. An image of the target organ in question would be placed on the body at the appropriate site.

The questionnaire advised that scars were; “to be considered to be 2cm in length and can be partially hidden if placed in the transaxillary, transumbilical, below the bikini line or in the neck crease and completely hidden if the incision is placed within a natural orifice such as the rectum, stomach, bladder or vagina.” The subjects were then asked to simply place a cross on the sketch where they would prefer to have their scar.

2.4.3. Results

114 members of the general public answered this section of the questionnaire; this included 105 women and 9 men with an average age of 41.6 (+/-12.3) years (*Table 2.4*). Only two people failed to respond fully to this section leaving the last procedure; the additional adrenalectomy procedure, unanswered. From this population the response as to how important the choice of the position of the scar was to the individual was quantified as 7.4 out of 10 as determined from the Likert scale.

In addition, the most preferred incision sites for all the operations presented in the questionnaire are the mouth and axilla, with the transurethral, transumbilical and the transabdominal approaches from *below the bikini-line* on par (*Table 2.5* and *Figure 2.3*).

Table 2.4: Demographics of the population who met the inclusion criteria for the questionnaire.

<i>Sex</i>		<i>Marital Status</i>	
Female	87	Married	52
Male	8	Single	32
		Divorced	4
		Widowed	1
		Not answered	6
<i>Age</i>		<i>Ethnicity</i>	
18-30	20	Caucasian	70
31-40	30	African	10
41-50	20	Asian	5
51-60	17	Oriental	3
61-80+	8	Middle Eastern	2
Mean Age	41.6	South American	1
		Not answered	4
<i>Surgical History</i>		<i>Religion</i>	
Previous Surgery	61	Christian	62
Previous Laparoscopy	17	No religion	24
Previous Endoscopy	20	Muslim	2
Previous Cancer	3	Budist	2
Previous Breast Cancer	3	Other	2
Previous Breast Benign	7	Sikh	1
Previous Axillary Surgery	1	Not Answered	2
<i>Education</i>			
Secondary School	11		
Sixth form college	12		
Undergraduate	28		
Postgraduate	42		
Not answered	2		

When the final adrenalectomy operation is considered with the advice that the best outcomes in terms of pain and recovery are from the transanal route, followed by the transvaginal, there is a change in the preference with a rise in the number of people choosing the transanal approach as may be expected (*Figure 2.4*). Without such advice the general choice on the position of the scar is relatively similar across the range with only moderate peaks at the transoral and transaxillary sites particularly when compared to the other operations.

2.4.4. Discussion

The widespread preferences for all the alternative approaches, aside from these two favourites, highlights the position of the scar is relevant to patients when the site of their surgical scar is discussed. The final consideration within the questionnaire related to the

approval to explore the transanal approach as a potential transluminal access route a subject which perhaps has been considered as it is felt patients would not be acceptable under any circumstance. Evidently, however, this does not appear to be absolute. If the benefits of the approach in terms of surgical outcomes are proven with the transanal approach, then it would to many, be an acceptable route for surgery and be considered. On the other hand an alternative interpretation may be that people still consider the clinicians advice over all other aspects of surgery. However, in whatever interpretation, to perform a transcolonic breach for an otherwise clean surgical procedure has the potential to expose the patient to significant morbidity beyond the conventional approach unless it can be fully assured within pre-clinical trials before being committed to any clinical trials.

It may be questioned as to why the patients would prefer different sites and perhaps the answer lies within the cultural and the fashion industry. Body image plays a significant role in current times reflected not only in the drive to stay looking younger but also in the escalation of industries such as the body tattoo. From a survey in 2010, 25% of the British public have been tattooed, with 16% of both men and women, having 2 or more (<http://www.guardian.co.uk/artanddesign/2010/jul/20/tattoos>), evidence perhaps of a more body conscious nation. It seems only reasonable to assume that if a person has a tattoo on or around their umbilicus or over their abdomen they may not wish to have this damaged by a surgical incision; well tailored or not. Although, perhaps a tenuous argument, it does however suggest that the surgery needs to continually adapt and if possible offer the general public a greater say in where and perhaps even how we perform surgery upon them. Have we reached a point in time when the old concept of informing the patient of where we will make the incision on their body does not need to apply, perhaps not quite yet but the concept of flexible access surgery moves us somewhat closer toward this ideal.

2.4.5. Conclusion

This survey highlights that there is evidently a target population within the general public who feel that choosing the position of their scar is important to them. The overwhelming preference tends toward the transoral and transaxillary approaches with surprisingly few opting for the conventional and currently mainstream transumbilical approach. This survey is

Table 2.5; The considered preferences as derived from the population surveyed.

Scar site	Proposed Operation (number of persons)				
	Thyroid	Heart	GB	Adrenal	Adrenal with advise
Over Organ - Front	8	5	9	0	0
Over Organ - Back	0	2	0	14	9
Mouth	68	42	27	22	10
Vagina	0	6	7	8	11
Rectum	0	4	6	13	54
Urethra	0	4	16	13	8
Axilla	30	38	25	18	8
Umbilicus	2	5	13	9	4
Bikini-line	4	7	9	10	6
Chest misc	1	0	0	0	0
Abdomen misc	0	1	2	5	2
Back misc	1	0	0	2	0
Total	114	114	114	114	112

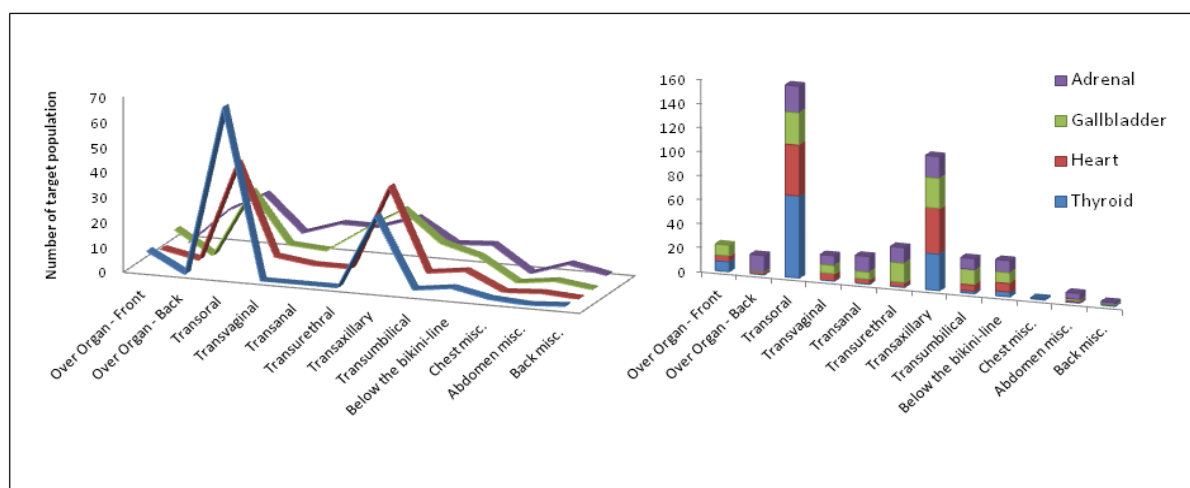


Figure 2.3; Graphical representation of the preferences from the population surveyed.

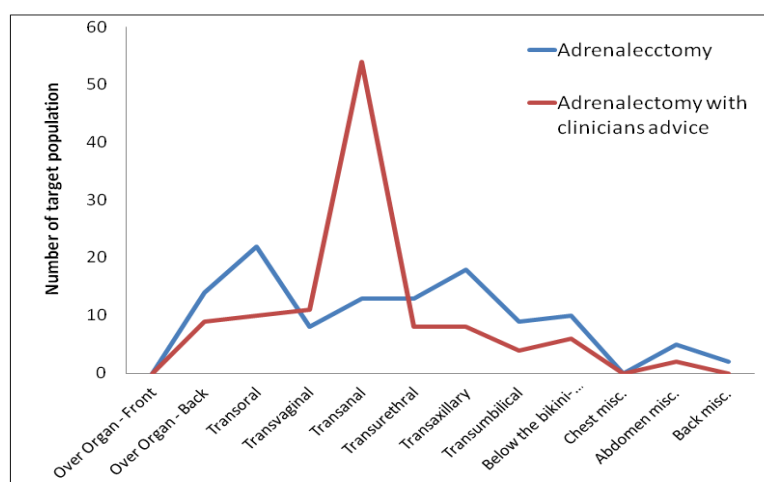


Figure 2.4; Graphical representation of the preferences of the target population for the transanal approach if it demonstrated benefits.

only a small snapshot of the views of the general population, predominantly women, and as a result can only really be taken as a guide.

2.5. The Ergonomic Challenges of Minimally Invasive Surgery.

With the every decreasing reduction in the number of ports, size of instruments or indeed the continuation of the minimally invasive surgical evolution so the challenges of operative ergonomics plays an even more substantial role. This is particularly prevalent not only in the ability to safely undertake a procedure using the less invasive techniques but also in encouraging its wider dissemination (*Figure 2.5*).

One of the very obvious challenges associated with instrumental surgery; whether laparoscopic or flexible endoscopic, is the ergonomics of manipulating instruments, tools and devices in a 3 dimensional space whilst viewing through a 2 dimensional camera. The laparoscopic era was hampered by the change in ergonomics from bygone centuries of surgery performed with the hand on tissue control over the need to manipulate instruments which move in a discordant fashion related to a fulcrum point at the port site. As such moving up externally is down internally which was in itself a significant challenge for many surgeons to grasp. This is likely to be similar, if not worse, for the introduction of flexible endoscopic or articulating devices into the surgical workflow. For their introduction, simplifying the ergonomics of the tools will no doubt make any transition from research to clinical practice far smoother and potentially safer.

Technology has already been introduced into the clinical community under the bracket of Robotic Assisted Surgery with the DaVinci™ (Intuitive Surgical, California, US) and the Zeus Robotic Surgical System™ (Computer Motion, California, United States – now disbanded) robots being first to gain the United States regulatory Food and Drug Administration (FDA) approval for human use; the United Kingdom's equivalent of the Medicines and Healthcare products Regulatory Agency (MHRA).

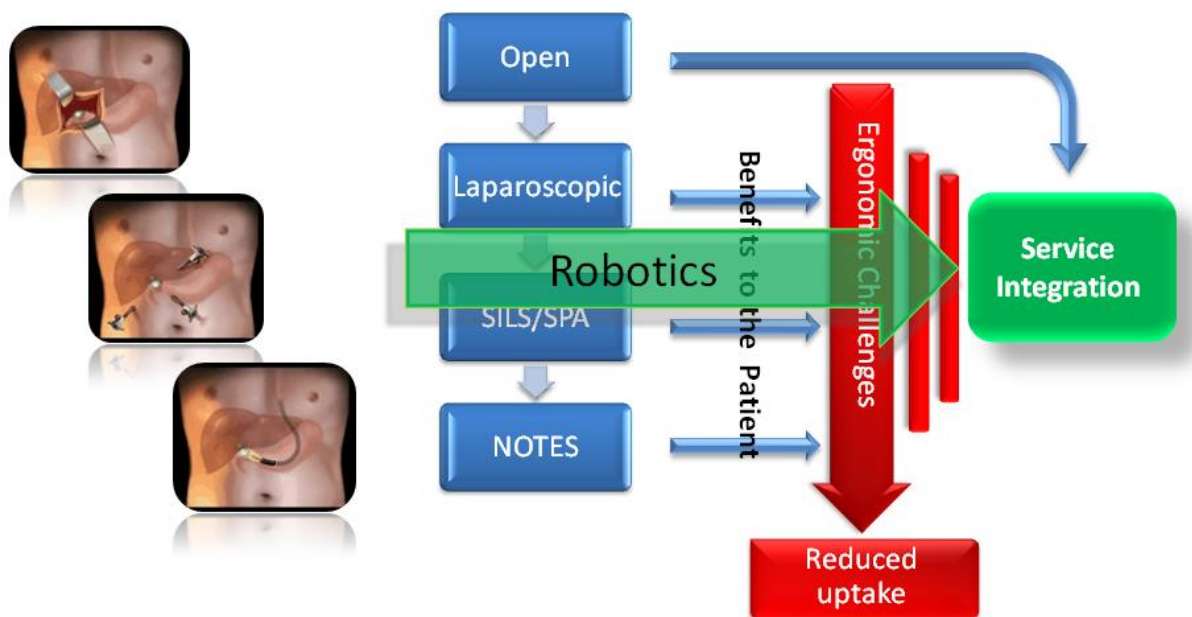


Figure 2.5; This slide schematically aims to explain how with the less invasive surgical procedure comes the increasing ergonomic challenges which ultimately reduce clinical uptake, a problem robotic assistance has the potential to overcome.

The overwhelming benefit from their introduction is the improved ergonomics of undertaking a laparoscopic procedure particularly in anatomical regions considered tight or narrow such as the pelvis. This has enabled laparoscopy to be introduced across a wider field of surgery delivering all the benefits of laparoscopic surgery to the patients in terms of faster recovery, earlier return to work and less postoperative pain when compared to the open technique.

2.6. An Evaluation of the DaVinci™ Surgical system in clinical practice.

2.6.1. Introduction

Robotic assisted surgery has generated significant global interest, with an expectation that it can overcome many of the ergonomic challenges associated with the laparoscopic approach and offer unsurpassed surgical precision. The DaVinci™ surgical system is the most globally recognised robot in current practice and offers a unique operative experience for the surgeon and exceptional precision for the patient. The feasibility of the DaVinci™ has been extensively explored across all the specialties over the past decade. As such the novelty of the

device and curiosity of what robotic surgery can do perhaps is no longer of such great interest with more of a shift towards the focused clinical applications where attributed quantifiable patient benefits can be directly measured.

Much of the current clinical evidence for the substantiation of the DaVinci™ robot within surgical practice has been generated from the radical prostatectomy; of which 70% are now undertaken robotically in the United States (Intuitive Surgical; Sunnyvale California, US; 2009). Evidence suggesting moderate improvements in urinary and sexual dysfunction post operatively as a direct result of robotic preservation of the neurovascular bundle, closely adherent to the prostate (47) is growing and has been the driving force behind such a wide dissemination of the DaVinci™ surgical system and as a result the field of robotic assisted laparoscopic surgery.

Colorectal cancer remains one of the most significant global health concerns of the 21st century. It is currently the third most prevalent form of cancer affecting an estimated 1.8 million people annually of which a third are primary rectal in origin (48, 49). The current gold standard surgical technique to optimise oncological clearance is the total mesorectal excision (TME) with autonomic nerve preservation performed either through the open or laparoscopic approach (50-53). As a result of early detection through screening, coupled with the advances in adjuvant therapy, the survival of patients with rectal cancer continues to improve. However, the morbidity associated with the radical approach remains significant with complications such as urinary and faecal incontinence, anastomotic leak, unplanned permanent stoma as well as a reduction in sexual potency impacting directly on the quality of life of the patient postoperatively (54-56).

The introduction of laparoscopic surgery revolutionised surgical practice (57). The benefits, in terms of early postoperative recovery and quality of life outcomes over the open procedure in colorectal disease are well documented (53, 58, 59), however, its wider uptake has been slow to be adopted. This in part is due to the ergonomic difficulties of operating using long rigid instruments within the confined pelvis inevitably impacting on outcomes through prolonging the learning curve for the technique and with it the fear of oncological compromise. The need to maintain mesorectal integrity to ensure complete circumferential oncological clearance is essential and in the laparoscopic TME this is challenging, ultimately resulting in elevated rates of conversion to the open approach (60, 61).

In terms of the operating constraints within the pelvis and the proximity of functionally relevant nerve bundles to the resection margin, the robotic TME demonstrates marked similarities to the robotic-assisted laparoscopic prostatectomy (RALP). It has been in relation to these very specific challenges that the RALP has demonstrated the most directly attributable improvement to patient outcomes over the conventional laparoscopic approach. Should these improvements be mirrored in the robotic-assisted TME (RTME) then it could expose an exciting new prospect in the management of rectal cancer, minimising further the impact of such radical surgery on the patient.

This article aims to review the current literature around the use of DaVinci™ robotic surgery for the management of rectal cancer and expose the potential benefits, if any, that robotic assisted TME may provide over the current conventional approaches.

2.6.2. Method

A comprehensive search strategy was used to identify relevant evidence according to the inclusion and exclusion criteria specified below using the search terms; “robotics and rectal surgery” and “robotics and anterior / abdomino-perineal resection / total mesorectal excision”, “robotics and rectal cancer”, “laparoscopic rectal surgery” and “laparoscopic and rectal cancer” to highlight relevant articles. The following electronic databases were searched: MEDLINE (Ovid); EMBASE; Google Scholar; The Cochrane Central Register of Controlled Trials Register (CENTRAL). Searches were restricted by English language publications and included all studies published prior to April 2011 (*Figure 2.6*).

Each article was screened for first author, year of publication, study population characteristics, number of subjects and study design. The level of evidence was assigned to each article by three surgeons as determined by the Oxford Centre for Evidence-based Medicine Levels of Evidence (62).

Search Methodology

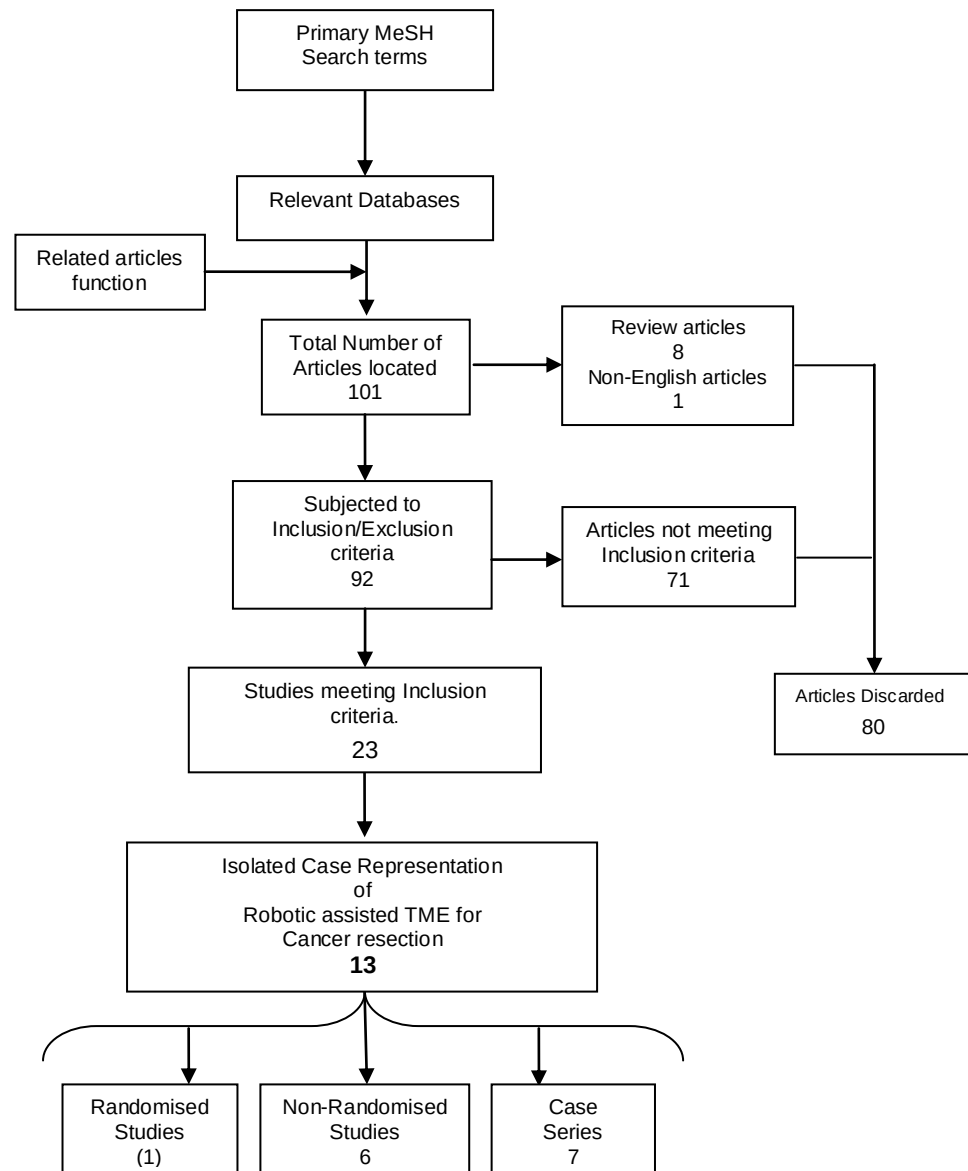


Figure 2.6: A flow diagram depicting the methodological search strategy.

(Randomised study - is in brackets as the included patients were used in the follow up non-randomised trial but given the randomisation of the evidence it has been included as separate)

The review of existing literature assessing the current evidence of robotic assisted Total Mesorectal Excision will have 2 arms:

1. A review of the literature to explore the oncological, operative and functional outcome measures for the RTME.
2. A quantification of the level of evidence which describes the current clinical effectiveness of the DaVinci™ robot in oncological surgery in terms of oncological, operative and functional outcome measures.

Outcomes

The primary outcomes of the study included the following:

1. Oncological.
2. Operative.
3. Functional/Quality of life

2.6.3. Results

23 studies across 11 institutions were deemed suitable for the review according to the inclusion criteria. Of these, 13 studies were considered to be representative of all the TMEs performed across all the institutions as outcome data was found to have been repeated or expanded upon in 10 articles. One article (*Baik et al 2007*) was a pilot non-blinded randomised control trial (Level 2b) (63), the follow up to this series abandoned the randomisation. Patients were informed of the cost of the operation before the procedure and with the expectation of the robotic technique being the most expensive, made their preferences known to the surgeon. As a result, the study was re-designed as a prospective unmatched comparison (Level 4) with evidently more advanced staged tumours in the laparoscopic arm than the robotic (64).

The remaining studies included two retrospectively matched case-controls (*Baek et al* and *Kwak et al*) with cases and controls matched from a prospectively collected database (Level 4) (65, 66), four unmatched cohorts with retrospective controls (Level 4) (64, 67-69), five case series (Level 4) (70-74) and two case reports (Level 5) (75, 76).

The Robotic-assisted Total Mesorectal Excision (R-TME)

Isolated from data repetition, a total of 452 robotic assisted laparoscopic Anterior Resections (AR) and 60 robotic-assisted laparoscopic Abdomino-Perineal Excision of the Rectum (APR) have been published since the introduction of the DaVinci™ into clinical practice. Indications for surgery included high grade dysplasia (n=24), adenocarcinoma of the rectum (n=423) and anal squamous cell carcinoma after failed primary chemoradiotherapy (n=5) (72).

Operative Setup

Patients were placed in a modified lithotomy position in a steep 30° trendelenburg with a 15° right tilt (77). Port placements varied between the studies. This is partly as a result of the lack of a universally agreed technique for the RTME but also by the variation in the model of the DaVinci™ platform used, whether it has 3 or 4 arms, or if it is the classical (Koh *et al*) or the S / Si model. However, despite the differences described in the location of the port sites between each groups, when the positions are plotted, similarities are evident and a clear prediction for the most common port positions for the technique can be inferred (*Figure 2.7*).

Early attempts at performing a complete robotic procedure using the 3 arm DaVinci™ required the robot cart to be moved two or even three times during the operation to align the arms with the splenic flexure, Inferior mesenteric vessels and the pelvis (75, 78). Advances in the robot design and optimisation of the port placement has enabled a complete single-staged total robotic procedure to be performed without requiring multiple adjustments to the cart position (73, 79).

All institutions described using the dissecting instruments in the right iliac fossa port (R1) which included either monopolar scissors or the hook diathermy, with Cadière forceps placed in the left (R2). Bipolar fenestrated graspers were used through the third robotic port (R3) to aid tissue retraction when the additional fourth robotic arm was available.

Operative Technique

A totally RTME procedure was undertaken in 247 cases (10 series) (66, 69, 71-73, 75, 76, 78-80) with the remainder employing a hybrid approach. The hybrid approach involved the

mobilisation of the descending colon and splenic flexure using conventional instruments before the robot was docked for the pelvic dissection. In all cases however, whether hybrid or totally robotic, the ligation of the inferior mesenteric vessels was undertaken with laparoscopic assistance using Endoclips, EndoGIA® (Ethicon) or Hem-o-lok® clips (Weck Closure System, Research Triangle Park, NC). Those performing a totally robotic approach skeletonised the vessels robotically prior to ligation.

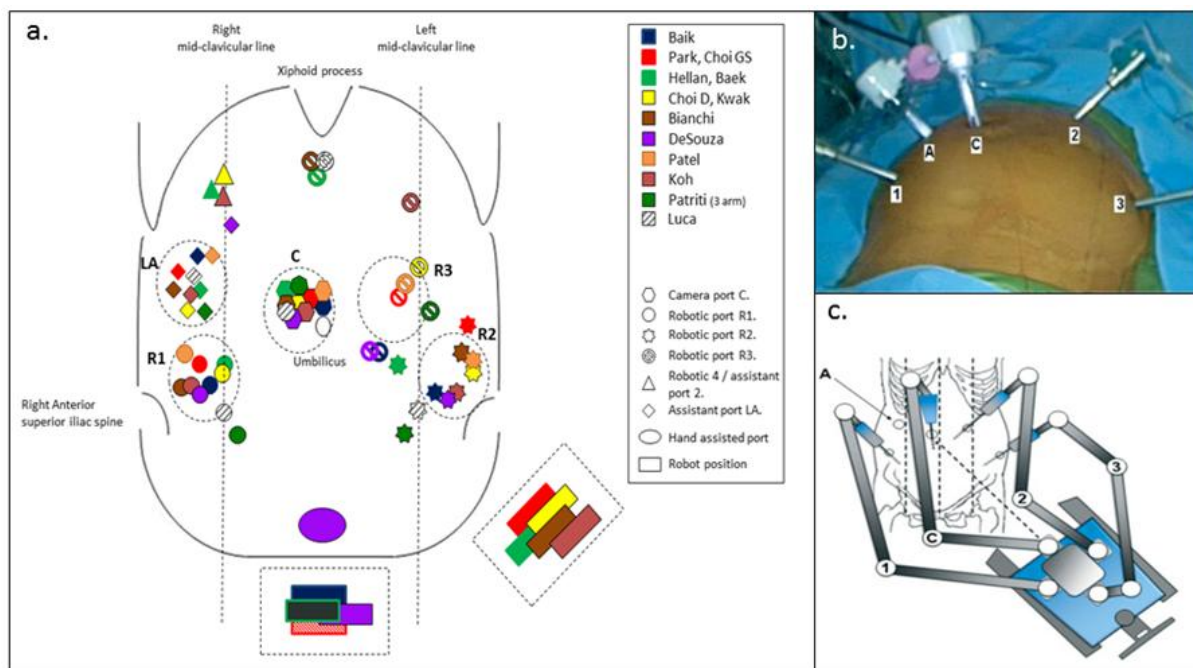


Figure 2.7; a) A schematic representation of the port positions as determined from twelve clinical robotic TME series as indicated by colour in the key.

The position of the robot in relation to the patient used for each (where mentioned) is also indicated on this schematic with the appropriate colour relating to the clinical group. b) and c) demonstrates the port position *in-vivo* and the positioning of the 4 arm Da Vinci™ model in relation to the patient.

For visual clarity, each port is represented by a specific shape and coloured according to the group(s) which defined its position. (key to right of image)

A broad estimation of the position of each port is highlighted by a dashed circle around the approximate centre of the cluster for each port.

R1 – 3 represent the 3 main robotic ports (Circle, Wheel, Star), C – camera port (Hexagon), LA– 1st laparoscopic assistant port (Diamond). R4 – Additional 4th robotic port or extra laparoscopic assistant port (Triangle).

(figures b) and c) re-published with the kind permission of John Wiley and Sons publishers from original article by Patel *et al* (72).)

The robotic pelvic dissection followed the same principles as for the laparoscopic TME (60). Once the rectum is freed from the pelvic attachments, it is divided using a mechanical stapler introduced laparoscopically. The specimen is retrieved either through a minilaparotomy (64-

66, 68, 70, 73, 75) or in the case of Choi GS *et al*, through the perineum (81). In the majority of cases, an end-to-end stapled anastomosis was performed. The anvil was placed in the proximal colon either extracorporeally once the specimen was retrieved through the minilaparotomy or after it had been inserted into the abdomen through a betadine washed rectal stump or a separate vaginal colpotomy as described by Choi GS *et al*, which was closed robotically once the anvil was retrieved (81). Hand sutured anastomosis were only described for low rectal cancers where the anastomosis could be performed transanally (63, 65, 74).

Heterogeneity between techniques which includes the methods behind the creation of the anastomosis, splenic flexure mobilisation and defunctioning stoma provision confounds the overall results (*Table 2.6*).

Primary Outcomes

Oncological Outcomes:

Endpoints: *Distal and Circumferential Margins, lymph node harvesting and local recurrence rates.*

Baik's randomised study failed to demonstrate any significant difference in the distal margin clearance between the robotic and laparoscopic groups and although the follow up comparative study did ($p=0.03$) (Level 4), the only other series which also compared the distal margins was unable to confirm the finding however, the relevant distances of the tumours from the anal verge in this later study were not clearly defined which may have impacted on the strength of the results (Baek *et al*). The circumferential margin was more widely documented. Taking the sum of all the positive margins from both the conventional and the robotic technique neither demonstrated any benefit over the other; robotic 8/251 (3.2%) compared to the laparoscopic 11/301 (3.7 %). (*Table 2.7*)

Lymph node harvesting in all cases was adequate for rectal cancer staging purposes and the numbers harvested were similar between the robotic and conventional techniques. Four comparative studies examined long term oncological outcomes. Five patients were recorded

to have developed loco-regional recurrence over a mean follow up period of 17.5 months (10 - 43) in the robotic group and 4 in the laparoscopic. No indication as to the location of the recurrence was provided in any series. Local recurrence was isolated with disease free intervals ranging from 8 months to 4 years. Patrìti *et al* briefly explored the disease-free survival over a follow up period of 34 months for the robotic TME and compared it to the laparoscopic outcomes. A definite trend towards improved disease free survival was evident in the robotic group but was not shown to be statistically significant explained in part, by the higher number of patients in the robotic group who had undergone neoadjuvant treatment in comparison to the laparoscopic although the possibility that the level of surgical precision achieved by the robot could have been a contributable factor was also considered (68).

Operative Outcomes

Endpoints: *conversions, complications including anastomotic leak rates, blood loss, operative time and hospital stay.*

Open conversions were undertaken in 2.4% (n=7) of robotic cases. These were due to obesity (n=5) and adhesions with progressive tumour growth (n=2). Two further cases required conversion to the conventional laparoscopic technique as a result of the tumour being higher in the rectum than the preoperative workup had suggested, which would have created the need to reposition the robot a second time to complete the TME as the group were using a 3 arm DaVinci™ model (Patrìti *et al*). The conversion rate was demonstrated to be significantly less than the laparoscopic approach in two comparative series (Baik *et al*, Patrìti *et al*; Level 4) (64, 68). Overall mortality was 0.3% (n=1); a result of overwhelming pulmonary sepsis, and a morbidity of 26% (n=108), although some patients experienced more than one complication which was not quantified. Complications in three series were further subdivided into minor and major complications according to the Clavien grading system. The proportion of complications which were defined as “potentially life threatening or involving a significant change in the course of treatment”; Clavien III or IV, was 8.8% (n=12) (64, 70, 81). The most common complications included; a prolonged postoperative ileus 4% (n=17), excessive bleeding as a result of the operation or requiring blood transfusion postoperatively 3.6% (n=15) and wound infection 2.2% (n=9). No significant differences were described between the robotic and the laparoscopic groups.

Table 2.6: Highlights the heterogeneity in the operations, equipment and technique used to perform the Robotic assisted Laparoscopic TME and the respective operative times. (need to check through references)

Name	Study Design	Number of Cases	Type of Operation	Number of Robotic arms	Left Colon and Splenic Flexure Mobilisation	Vessel Ligation	Anastomosis Intra/Extra	Stapled/Hand Sutured	Total Operation Time
Giulianotti et al (75)	CS	8	AR 6, AP 2	3	Rob	-	-	Stapled	AR 270 AP 180
D'Annibale et al (80)	CS	22	R -, L -, AR 10, AP 1	3	Rob	Lap	-	No data	240 §
Braumann et al (76)	CS	2	AR	3	Rob	Lap	Intra	Stapled	Patient 1: 180 (con. to open) Patient 2: 300
Pigazzi et al * (77)	CP	6	AR	3	Lap	Lap	Extra	Stapled	264
Hellan et al * (70)	CS	39	AR 33, AP 6	4	Lap	Lap	Intra	Stapled	285, (TME - 60)
Baik et al ** (63)	RC	18	AR	3/4 ¥	Lap	Lap	Extra	Stapled	204
Spinoglio et al (78)	CP	44	R 18, L 10, T 2, AR 19 AP 7	3	Rob	-	Extra	No data	384
Luca et al (79)	CS	55	L 27, AR 21, AP 7	4	Rob	-	Intra	-	290
Choi G-S et al *** (81)	CS	13	AR 13	4	For LAR - Lap For AR - Rob	LAR - Lap AR - Lap	-	Stapled	261
Baik et al ** (64)	CP	56	AR 56	4	Lap	Lap	Intra	Stapled/ hand sewn	178
Patriti et al (68)	CP	29	AR 24, AP 5	3	Lap	Lap	Extra	Stapled	AR 202, AP 213
Choi D et al ^{v*} (71)	CS	50 ^{v*}	AR 50	4	Rob	Lap	Intra	Stapled	305
Park et al *** (67)	CP	41	AR 41	4	Lap	Lap	Intra	Stapled	232
Baek et al * (65)	CP	41	AR 35, AP 6	4	Lap	-	Intra	-	296
Baek et al *	CS	64	AR 52, AP 12	4	Lap	Lap	-	Stapled/ hand sewn	270
Pigazzi et al * (π) (77)	CS	143	AR 112, AP 31	4	Lap	Lap	Intra	Stapled	297
Bianchi et al (69)	CP	25	AR 18, AP 7	4	20% Lap 80% Rob	Lap	Intra	Stapled	240
Patel et al (72)	CS	5	AP 5	4	Rob	Lap	Intra	NA	204
Koh et al (73)	CS	19	AR 18, AP 1	4	Rob	Lap	NA	Stapled	316
Prasad et al ****	CS	3	AR 3	4	Lap	Lap	Intra	Stapled	340
Zimmern et al ****	CS	58	AR 47, AP 11	4	Lap	Lap	Intra	Stapled/ hand sewn	AR 352, AP 309
deSouza et al **** (74)	CS	44	AR 36, AP 8	4	Lap + Hand assist	Lap	Intra	Stapled/ hand sewn	347. (TME 93)
Kwak et al ^{v*} (66)	CP	59 ^{v*}	AR 59	4	Rob	Lap	Intra	Stapled	270

* - The asterisk next to each published series denotes that the institution from which the data was collected is the same (number of asterisks denotes the institution). Conclusions drawn from examining the method and time course over which patients were recruited in each institution and for each data set suggests that the patients presented have been represented in different ways multiple times. As such only the larger series from the institution, unless otherwise stated in the methods, has been included in this review.

Case numbers highlighted in **bold** denotes cases which have been included for volume analysis of Robotic TME. Data unhighlighted has been represented elsewhere in another series or comparative study.

^{v*} - The institution recorded by ^{v*} may have included some of the same patients for both their represented studies but the second report was a case matched selection of 59 cases from a larger pool of 117 collected over 2 years rather than the first 50 cases presented in in the original case series which was collected over the first year of these 2 years. As such both the case numbers have been included as part of the volume analysis.

¥ - The 3 Arm DaVinci was employed for first 3 robotic cases after which the 4 arm was used.

§ D'Annibale includes benign and malignant disease. Although data included 11 TME cases, separation of the data of the malignant cases from the benign as well as between the colectomy and TME confounds any specific TME related outcome data including the operative time.

▣ - Multicentre trial involving patients from Luca et al, Patrìtti et al and Pigazzi et al. Likely that data has already been presented for each institution previously as time course for patient collection corresponds.

AR – Anterior Resection LAR – Low anterior resection, AP – Abdomino-Peroneal resection, Lap – laparoscopic, Rob – Robotic assisted, TME – Total Mesorectal Excision, CS – Case Series, CP – Case comparison, RC – Randomised Control trial, Intra - intracorporeal, Extra – extracorporeal, hand sewn for low rectal anastomosis from perineal end, - – Not specified, NA – Not Applicable.

Table 2.7: Isolated cases of Robotic Assisted Laparoscopic Total Mesorectal Excision; the operative, oncological and functional outcomes.

	Guilianotti et al (75)	Braumann et al (76)	Hellan et al (70)	Baik et al * (63)	Choi GS et al ** (81)	Baik et al * (64)	Park et al ** (67)	Patriti et al (68)	Choi D et al *** (71)	Baek et al (65)	Bianchi et al (69)	Patel et al (72)	Koh et al *** (73)	deSouza et al (74)	Kwak et al *** (66)
Level of clinical evidence	5	5	4	2b	4	4	4	4	4	4	4	5	4	4	4
Number of cases (n)	8	2	39	18	13	56	41	29	50	41	25	5	19	44	59
Gender	-	2 F	18 F 21 M	4 F 14 M	7 F 6 M	19 F 37 M	17 F 24 M	F 18 M 11	F 18 M 32	F 16 M 25	F 7 M 18	F 2 M 3	F 8 M 13	F 16 M 28	F 20 M 39
Age	-	75 + 82	58	53	54	60	61	68	59	64	69	58	61	63	60
Operation	AR 6 AP 2	AR 2	AR 33 AP 6	AR 18	AR 13	AR 56	AR 41	AR 24 AP 5	AR 48 AP 2	AR 35 AP 6	AR 18 AP 7	AP 5	AR 18 AP 1	AR 36 AP 8	AR 59
AJCC TNM Stage	-	II 1 IV 1	0 8 I 13 II 4 III 13 IV 1	I 5 II 4 III 9	I 4 II 2 III 7	I 22 II 16 III 18	I 13 II 14 III 14	I 11 II 9 III 7 IV 2	I 10 II 19 III 19 IV 2	0 7 I 12 II 4 III 15 IV 3	I 14 II 4 III 7	Salvage Anal Cancer	0 2 I 3 II 6 III 5 IV 3	0 4 I 14 II 15 III 8 IV 3	0 3 I 16 II 23 III 13 IV 4
Distance from the anal verge (cm)	-	20 + 10	>11cm - 2 7-11cm - 16 <7cm - 21	11	- □	10	4 – 8cm 27 <4cm 14	6	7	>11cm - 5 7-11cm - 21 <7cm - 15	-	Anal canal	-	>11cm - 5 7-11cm - 18 <7cm - 21	8
Chemoradiotherapy Adj/NAd (%)	-	-	Adj 84.6	-	-	NAd 8.9	NAd 34	NAd 24 Adj 31	NAd -	NAd 80.5	NAd 52	NAd 100	NAd 9.5	NAd 31 Adj 1°	NAd 8
Operative Outcomes															
Number of Conversions	0	1	1	0	0	0	0	2 (lap) 0 (open)	0	3	0	0	-	2	0
Complications	0	0	Bleeding Wound inf 2 Urinary dis Ileus 5 Others 2	Bleeding Back pain 2 Scrotal swelling	Bleeding □□	Bleeding Ileus Back Pain 2 Scrotal swelling	Ileus Abscess 2 Blood tnsf 2 Atelectasis2 DVT	Wound inf. Bleed. Ileus Urinary retention Eneritis	Anast Bleed. Abdo bleed. Ileus. Stomal obstruct	Ileus 3 Abscess 2 Fistula	Wound Inf Stomal obst	Perineal Seroma	Intraop: Bleeding 2 Dehiscence of stapled stump	Colovaginal fistula Pneumonia 2 C. diffi 3 Periph neuropathy 2	Wound Inf Ileus 5 Anast bleed 4 Resp. Compl
			Total Major Comp 13%(5)	Total major comp 11%(1)	Total major comp 15.4%(2)	Total major Comp 5.4% (3)	Clav III-IV 9.8% (4) Total 29.3% (12)						Postop: Ileus 2 Neuropraxia 2 Gastroparesis	CVA ileus 2 Wound inf 4 Upper limb DVT 2	
Reoperation	-	-	4	-	1(2)	-	-	-	0	-	1	-	-	2	0 0
Blood loss	-	120 + 250	200 \$	180 ¥	-	288 ¥	-	137	-	200	-	150	-	150	-
Hospital Stay	-	16 + 20	4	7	7	5.7	9.9	11.9	9.2	6.5	6.5	5.4	6.4	5	55 -

Anastomotic leak n(%)	1 (12.5%)	0	4 (12.1%)	0	1 (7.7%)	1 (1.8%)	4 (9.7%)	2(8.3%)	4(8.3%)	3 (8.6%)	1(5.5%)	-	0	2 (5.6%)	8 (14%)
30 day Mortality	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0

Oncological Outcomes

Lymph nodes	-	14	13	18	25	18	17	10	21	13	18	7	18	14	20
Distal resection margin	-	-	2.65 R1 0	4 R1 1	4.7 R1 1	4 R1 4	2.1 R1 -	2.1 R1 -	1.9 R 1 -	3.6 R1 0	2 R1 -	-	3.7 R1 1	R1 1	2.2 R1 -
Positive circ. resection margin	-	-	R1 0	-	R1 0	R1 4	R1 2	R1 0	R1 1	R1 1	R1 0	R1 1	R1 1	R1 0	R1 1
Follow up (months)	-	6	13	-	-	14.3	-	29.2	-	-	10	6	-	-	17
Local Recurrence	-	0	0	-	-	0 €	0	0	-	-	0	1	-	-	1

Functional Outcomes

Urinary Incontinence	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Faecal incontinence	-	-	-	-	-	-	-	2 (6.8%)	-	-	-	-	-	-	-
Sexual potency	-	-	-	-	-	-	-	1 (5.5%) <i>α</i>	-	-	-	-	-	-	-
Unpredicted Stoma	-	-	33	-	-	-	0	1	16	33	-	-	-	36 ff	25

* - The asterisk next to each published series denotes the institution from which the data was collected is the same (number of asterisks denotes the institution).

Zimmern and D'Annibale are not included due to the difficulty in differentiating the outcomes of the robotic assisted TME cases from the other benign and malignant colorectal procedures undertaken within the series. Additionally the inclusion dates in the Zimmern series overlap with those included in the deSouza series; collected from the same institute.

§ - 6000ml blood loss from perineal dissection of an APR not robotic involvement.

¥ - Taking 1g/dl Hb loss as 360mls whole blood.

□ - 2 patients underwent Anterior Resection and 11 a low Anterior Resection,

□□ - Haemorrhage from Inferior mesenteric staple line requiring re-operation at 4h post op laparoscopically and in the same patient an anastomotic leak at day 3 which required reoperation managed transanally.

€ - Systemic recurrence in 2 patients – recurrence free survival of 8 and 12 months – both patients Stage III disease, though no local recurrence.

α – measured as erectile dysfunction.

∞ 1 patient received adjuvant radiotherapy but whether or not this was the only one was not confirmed.

ff - unclear as whether this includes the 8 permanent stomas formed as a result of the AP resections as 2 of the defunctioning ileostomies were formed to manage a postoperative complication.

Anastomotic leaks occurred in a total of 8% (n=31 of 381) of AR operations and nine reoperations were carried out in 8 patients, all of them in relation to the management of these leaks. 52% (n=144) of the robotic assisted anterior resections had an ileostomy sited of which 4 were for the management of a postoperative complication with the remainder undertaken electively at the time of surgery to defunction the bowel (68, 70, 74). This is in contrast to only 32% (n=45) for the comparable laparoscopic anterior resections performed (*Table 2.8*). No series included the reoperation and complications associated with stoma reversal as part of the overall outcomes from either the robotic or laparoscopic operations.

Protracted anaesthetic times have been described (*Table 2.7 and 2.8*) with the longest procedure time being 8 hours and 7 minutes (79).

Although this is likely to represent a pure robotic procedure with a 3 arm robot, general operative times for the 4 arm DaVinci™ employed for the TME alone ranged from 2hrs to hours 29 minute to 5 hours 15 minutes (63), more in line with the laparoscopic approach which incidentally was demonstrated to have a significantly shorter operative time over the robotic (level 4) (67). However, the latest series from South Korea which involved a complete robotic procedure claimed an operative time of 270 minutes. From all the pure robotic TME cases performed the mean time taken was 290 minutes with the hybrid approach taking 272 minutes.

Short term outcomes including blood loss appear equivocal to the laparoscopic TME. A statistically significant reduction in hospital stay of two days was demonstrated (Baik *et al*; level 2b) when the robot-assisted technique was employed over conventional laparoscopy (63). This finding was further highlighted by the same institute at their follow up comparative trial (Baik *et al*; Level 4) though all subsequent trials failed to confirm this finding (*Table 2.8*).

Functional outcomes

Endpoints: *Sexual dysfunction, urinary and faecal continence in both sexes.*

Only one series evaluated the functional outcomes. These outcomes were evaluated from interview only without the use of validated scoring tools. 11 patients had pre-existing erectile

dysfunction prior to the surgery and were excluded from the assessment. New onset erectile dysfunction was noted in only 1 patient from the remaining 18 patients in the robotic group (5.5%). From the same series 6.9% of patients experienced faecal incontinence post robotic TME but the evaluation and grade of incontinence is not described. In addition, 24% of the cases received neoadjuvant chemoradiotherapy and 31% adjuvant chemotherapy or chemoradiotherapy 1 month after surgery, which through the effects of radiation related nerve injury could have contributed to any functional difference highlighted between the groups (56).

Table 2.8. Comparison trials undertaken to compare Operative, Oncological and Functional outcomes between Robotic assisted laparoscopic Total Mesorectal Excision and the Conventional Laparoscopic technique.

	Baik ⁽⁶³⁾		Baik ⁽⁶⁴⁾		Park ⁽⁶⁷⁾		Patriiti ⁽⁶⁸⁾		Baek ⁽⁶⁵⁾		Bianchi ⁽⁶⁹⁾		Kwak ⁽⁶⁶⁾	
Level of Clinical Evidence	2b		4		4		4		4		4		4	
	Robotic	Laparoscopic	Robotic	Laparoscopic	Robotic	Laparoscopic	Robotic	Laparoscopic	Robotic	Laparoscopic	Robotic	Laparoscopic	Robotic	Laparoscopic
Cases (n)	18	18	56	57	41	82	29	37	41	41	25	25	59	59
Gender	F 4 M 14	F 4 M 14	F 19 M 37	F 23 M 34	F 17 M 24	F 33 M 49	F 18 M 11	F 25 M 12	F 16 M 25	F 16 M 25	F 7 M 18	F 8 M 17	F 20 M 39	F 17 M 42
Age	53	60	60	63	61	63	68	69	64	64	69	62	60	59
AJCC TNM Stage	I 5 II 4 III 9	I 5 II 4 III 9	I 22 II 16 III 18	I 14 II 19 III 24	I 13 II 14 III 14	I 21 II 37 III 24	I 11 II 9 III 7 IV 2	I 17 II 8 III 10 IV 2	12 I II 4 III 15 IV 3	0 3 I 15 II 3 III 19 IV 1	I 14 II 4 III 7	I 14 II 7 III 4	0 3 I 16 II 23 III 13 IV 4	0 3 I 16 II 23 III 12 IV 5
Operation	AR 18	AR 18	AR 56	AR 57	AR 41	AR 81, AP 1	AR 24, AP 5	AR 34, AP 3	AR 35, AP 6	AR 35, AP 6	AR 18, AP 7	AR 19, AP 6	AR 59	AR 58 AP 1
Mean distances from the anal verge (cm)	11.3	11.0	9.6	9.5	5.7	5.9	5.9	11 ♦	-	-	-	-	8	8
Chemoradiotherapy n (%)	-	-	NAd 5 (9%)	NAd 7 (12%)	NAd 14 (34%)	NAd - 17 (21%)	NAd 7 (24%) Adj 9 (31%)	NAd 2 ♦	NAd 33 (81%)	NAd – 18 ♦	NAd – 13(52%)	NAd – 10 (40%)	NAd 8	NAd 5
Operative Outcomes														
Operative time (mins)	217	204	190	191	232	169 ♦	202	208	296	315	240	237	270	228 ♦

Morbidity %	22.2	5.5	10.7 (major 5.4 ◆)	19.3 (major 19.3)	29.3 (Major 9.8)	23.2 (Major 7.3)	30.6	18.9	22	27	16	24	32	27
Anastomotic leak n(%)	0	0	1 (1.8%)	4 (7%)	4 (9.7%)	6 (7.3%)	2(8.3%)	1 (2.7%)	3 (8.6%)	1(2.9%)	1(4%)	2(8%)	8 (14%)	6 (10%)
Open Conversions	0	2	0 ◆	6 §	0	0	2 (lap) ◆ 0 (open)	7	3	9	0	1	0	2
Mean Hospital Stay	6.9 ◆	8.7	5.7 ◆	7.6	9.9	9.4	11.9	9.6	6.5	6.6	6.5	6	-	-

Oncological Outcomes

Lymph nodes	18	22	17.5	17	17	14	10	11	13	16	18	17	20	21
Distal resection margin	10.9 R0 17 R1 1	10.3 R0 13 R1 3	4 R1 4 ◆	3.6 R1 14	2.1	2.3	2.1	4.5	3.6 R1 - 0	3.8 R1 - 0	2 R -	2 R -	2.2 R -	2.0 R -
Positive circ. resection margin	-	-	R1 4	R1 5	R1 2	R1 3	R1 0	R1 0	R1 1	R1 2	R1 0	R1 1	R1 1	R1 0
Follow up (months)	-	-	14	14	-	-	29	19	-	-	10	10	17	13
Local Recurrence	-	-	0 €	0 €	0	-	0	3	-	-	0	0	1	1

Functional Outcomes

Urinary Incontinence	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Faecal incontinence	-	-	-	-	-	-	2 (6.9%)	1 (2.7%)	-	-	-	-	-	-
Sexual potency	-	-	-	-	-	-	1 (5.5%) α α	3 (16.6%) α α	-	-	-	-	-	-
Unpredicted Stoma	-	-	-	-	0	0	1 ¥¥	0	33 *	14 ◆	10 *	5	25	26

◆ Denotes statistical significance.

§ 6 open conversions were undertaken in the laparoscopic arm; 4 due to a severely narrow pelvis for rectal dissection, one for pelvic wall bleeding and one for a rectal perforation. □ - Intraoperative transfusion in the Robotic TME group 1 (2.4%), and 1 (1.2%) in the laparoscopic TME group. ¥ - Calculated from the drop in Haemoglobin – taken as 360mls per 1g/dl. ¥¥ - Diverting loop-ileostomy for management of anastomotic fistula. *- Stomas relating to a defunctioning loop ileostomy as a means of distal anastomotic protection. € - Although no local recurrence was detected, 2 patients in each group had systemic recurrence. All had TNM Stage III disease with disease free survival of 8 to 13 months.

α - Impairment of sexual function was defined as the impossibility of achieving an erection or ejaculation after surgery and recorded by interview. Patients with pre-existing sexual dysfunction were excluded.

2.6.4. Discussion

Robotic surgery is designed to promote precision, through both enhanced imaging and the clear ergonomic advantages for instrument control and surgical comfort. There can be no debate as to the superior mechanised advantages that the robot brings to any operation over the conventional but the challenge for a platform which seems at first glance ideally suited to cancer resection, the evidence within this field still lacks strength and resilience, including for the more widely promoted RALP. With the predominance of data generated from Level 4 or Level 5 studies, the reliance upon a high volume of cases to support the evidence over well substantiated and peer reviewed randomised control trials or meta-analysis remains compounded by the difficulties in persuading patients to accept the conventional approach as part of a trial when the alternative offered is robotic technology. The challenge experienced by Baik's group (63, 64) when attempting to extend the pilot randomised control trial is testament to this problem. It will be interesting to see whether similar problems have been encountered in other ongoing randomised control trials (RCT) exploring the robotic approach, such as the Lopera trial (London, UK); a multicentre RCT comparing laparoscopic, open and robotic assisted prostatectomy which is due to complete later this year.

Six comparative studies were in total presented in this review, some offering better matched case-controls than others but all used retrospectively matched controls (Level 4) irrespective of whether the controls were prospectively collected. Nevertheless, when the cumulative outcomes of the robotic assisted TME are compared against the respective cumulative laparoscopic outcomes, the most evident finding was the marked reduction in the conversion rate and to a lesser degree hospital stay (Baik *et al*) (Table 2.8). However, these outcomes were confounded not only by the lack of a single agreed coherent robotic assisted TME technique, the heterogeneity of which precluded statistical analysis, but also the discrepancy of the position of each of the surgeons on the learning curves for both the techniques. In consideration, it is likely that each of the surgeons involved were likely to be less advanced along the learning curve of the robotic technique than the laparoscopic. If this is the case, then the differences highlighted between the techniques, particularly the reduced conversion rate seen for the robotic approach, may be even more significant than at first glance.

The potential of a shortened learning curve for the robotic-assisted laparoscopic TME can only be inferred as learning curve analysis is complex and with no data presented, falls outside the remit of this review. However, learning curve analysis has been explored from data surrounding the RALP. Early evidence within the field described that an open surgeon competent in the procedure would be able to undertake a sound robotic assisted surgical procedure after just 15 cases (82) enabling previously surgeons unskilled in laparoscopy to provide their patients with the benefits of the minimally invasive surgical approach with minimal training. This paper however, focused on the technical requirements and not the complex oncological and operative nuances essential to be measured if a true learning curve is to be defined. Carlsson *et al*, presented more extensive work on learning curve analysis for the RALP concluding that outcomes continue to improve after 250 cases (83) which is more aligned to the gold standard open procedure. If this shortened learning curve for the RALP could be mirrored for the RTME, as may be suggested by the reduced conversion rate highlighted in this review, then the increased morbidity and risk of oncological compromise which undoubtedly occurs during any learning curve for trainee colorectal surgeons could be minimised with direct patient benefit.

The two most common arguments against the introduction of the robot into clinical practice are the operative length and overwhelming cost burden. Operative length has always been described as one of the main drawbacks to the robotic procedure. Only one series demonstrated a significant increase in the length of the robotic procedure over the laparoscopic (Level 4) but this was not drawn out across all the studies. The hybrid approach does reduce the operative time through minimising the repositioning of the robot cart during the operation and by its very nature makes the procedure more attractive to laparoscopic surgeons wishing to introduce the robot slowly into their surgical practice. However, the introduction of the 4 arm model has moved to promote the totally robotic approach. It is unlikely that the operative time for a totally robotic TME with the 4 arm DaVinci™ will ever match that for the hybrid approach although it is likely to narrow the gap. Surgeons who undertake the hybrid procedure tend to be proficient in the laparoscopic technique before including the robot into their practice and as such are unlikely to improve further upon this portion of the operation. It will ultimately be through the incorporation of dedicated and trained robotic theatre teams who through the improvement on the robot setup and instrument docking times, will demonstrate the greatest impact on reducing the operative time (84) (85). It is likely that this will impact more significantly on the totally robotic procedure where

more instrument changes will need to be undertaken than for the hybrid technique. Despite this, it is difficult to confer any significant advantage to the use of the robot for the complete procedure over the hybrid from this review since the main impact to the minimally invasive technique by the robot appears to be when it is used for the TME. Further trials will no doubt expose any advantage should there be any but with the benefits of an acceptable operative time coupled with the advantages of precise, oncologically safe robotic pelvic dissection with functional pelvic nerve preservation, is there a need to complicate the procedure further by incorporating a complete robotic bowel mobilisation to the procedure? Arguably this may become more justifiable in time as trainee robotic surgeons become less experienced with the laparoscopic approach transferring their skills to the robot or open surgeons wish to transfer their skills to improve patient outcomes.

Cost is a significant limiting factor for the uptake of DaVinci™. At approximately £1.5 million circa to purchase, together with annual service costs and the average cost of each individual instruments being £2000 for up to 10 uses, the financial burden can be excessive in the absence of scales of economy. However, costs have to be balanced against the effectiveness and benefits gained from using the device for each procedure and although not covered in this review, with increasing dissemination of the robot for the RALP, the cost burden on the hospitals could be significantly reduced with the introduction of further focused clinical applications to which benefits are demonstrated and quantifiable. Baek *et al* reviewed the comparative hospitalization costs between the robotic and laparoscopic TME and found that the average hospitalization cost for each was similar with no significant difference demonstrated (£52,000 compared to £40,000 respectively (1 USD = 0.622044 GBP))(65). However, the methods of how these figures were obtained were not included in the report and individual hospital costs will vary.

Surgical robotics is a young field. After only a decade since inception, the DaVinci™ robot has made such a significant impact on surgical oncology globally. Size and cost of the device have hampered clinical uptake but the escalating demand for the RALP has promoted wide dissemination and with it the encouragement to seek new applications for the device. Although the DaVinci™ is currently synonymous with surgical robotics, it will be the advances in the software; optics, haptics and image registration over and above the system itself, which will ultimately enable the outcomes from surgical oncological management to continue to advance beyond simply the skin incision.

2.6.5. Conclusion

Feasibility of the DaVinci™ robotic assisted total mesorectal excision is demonstrated, with comparable oncologically outcomes presented for rectal cancer excision. One randomised control trial was undertaken to compare the robotic with the conventional laparoscopic surgical approach to the total mesorectal excision though its focus on the short term outcomes limited its use within the review. Only one trial compared functional outcomes which presented no quality of life survival data to support the hypothesis that the DaVinci™ could improve functional outcomes significantly.

Although more controlled trials are required to fully elicit the potential advantages of the technique over the conventional, clear evidence has arisen from the review that the use of the DaVinci™ for TME has a significant impact on the conversion rate to open when compared to the laparoscopic. Further trials are needed to critically appraise this finding more fully and better define what impact robotic assisted Total Mesorectal Excision will have on short and long term quality of life survival as a result.

To critically appraise the DaVinci™ surgical system is controversial given the huge significance of obtaining FDA approval, enabling the enhanced computer aided platform to take its place in the operating theatre. However, there are some significant elements to the current design and thereby robotic-assisted laparoscopy in general, aside from the high cost and marked size of the machine, that suggest over engineering. The requirement for the RTME, the RALP and the Robotic-assisted oesophagectomy is focused on only a small element of the procedure where the operation benefits from the high degree of precision and dexterity that is afforded by the DaVinci™ system. In the case of the RALP, it is the challenge of re-affirming continuity between the bladder and the urethra that laparoscopy is unable to undertake with ease. The side benefits of the nerve preservation in RALP, as is the case in the hypogastric nerve plexus preservation in the RTME, as explored above and the Robotic assisted oesophagectomy, is poorly demonstrated at best. However, greater precision from the robot should attain more effective dissection and thereby better functional outcomes. These attributes may well be demonstrated in future trials but currently are not, remaining for the time being an unsubstantiated marketing avenue for the company.

As a result, the sizeable DaVinci™ which requires its own dedicated operating theatre as a result of both its size and pre-operative requirements coupled with the high costs unsubstantiates the need for perhaps what may only be at best 30 minutes of a complete procedure. Indeed many robotic surgeons, as is evident from the review only use the robot for the part of the procedure which may gain the patient most benefit; in the case above the TME. Surely, the future of surgical robotics requires an on demand system, one which can integrate into conventional laparoscopic practice without the excessive impact in terms of size or attributed cost.

2.7. A Consideration of Robotic Assisted Flexible Access Surgery

The lack of strict clinical evidence to support the use of the DaVinci™ robot in clinical practice has exposed itself to significant criticism. The cost of the device and its overall size has inflamed many surgical departments who feel unable to compete within the growing global healthcare market unless wielding a DaVinci™ robot as part of their armamentarium. The platform is strongly marketed with its well known adjuncts including tremor negation, stereo vision, x10 power magnification, enhanced operative surgeon comfort and greater surgical precision through the use of the patented endowrist™. However, given the lack of clinical evidence to support any significant patient or economic benefit for its use over conventional laparoscopy, are these features relevant or simply examples of well marketed over-engineering? The question as to whether such a costly and considerably domineering surgical platform is welcome within the operating theatre needs to be addressed more pragmatically? If the current evidence is to be considered then no hospital would ever install the system however, healthcare, like many other services today is driven by market trends and monopolized industry and less, as it seems, by true clinical benefit (86). With that in mind, it is here to stay now entwined within the fabric of Surgical Urology. It must always be remembered however, that despite its grandiosity it was the first robot to achieve Food and Drug Administration approval and as a result provides the benchmark potentially smoothing the approval for the introduction of future robotic surgical designs.

Despite the negativity, the term robotic surgery remains synonymous with the DaVinci™ robot and its benefits, if any still under evaluation but one clear advantage to using the DaVinci™ system over the conventional laparoscopic approach may be in the ease with

which the procedure can be learnt and the procedure undertaken, with the potential reduction in learning curve morbidity that can inevitably occur (82). The ergonomic enhancements associated with the daVinci™ best define perhaps the singular true benefit behind its introduction particularly when compared to the laparoscopic technique. This capability is derived from the computer aided interface which is the true revolution behind the success of daVinci™ and for robotic-assisted surgery in general, the ability to integrate software and imaging adjuncts to enhance instrumental control for enhanced precision.

This benefit, empowered by the software augmentation could be extended to incorporate and potentially overcome some of the ergonomic challenges facing flexible access surgery. With the benefits, real or inferred, and the potential future demand for flexible access surgery, this thesis explores whether a Flexible Access Surgical Robot could be developed to overcome some of the challenges faced by conventional flexible endoscopic surgery.

Natural Orifice Transluminal Endoscopic surgery (NOTES) is challenging to undertake. In its current form, it lacks the ease and precision to ensure safety, fuelling dissension and division across the surgical community regarding its introduction (87). However, evidence from multiple clinical user groups as to the benefits of the approach is generating support and as a result a wider global interest (88, 89). Nevertheless, significant disadvantages of NOTES remain, not necessarily about its basic principle, but its current practice particularly surrounding the safe, secure access and closure of the transluminal incision with the consequential risk of associated contamination (89). Optimistically, it is likely that these challenges will be overcome given the level of investment afforded to address the problems. However, equally challenging are the technical issues facing the approach; specifically the ergonomic consideration of the flexible endoscope control, which if not overcome could potentially jeopardise the future of the whole flexible access approach including NOTES (90).

The current flexible endoscope, of which its unique flexibility defines flexible endoscopic surgery, was designed for intraluminal exploration where its flexibility is perfectly suited. However, for use in the spacious intraperitoneal or indeed intrathoracic cavities, a different design is required; one which incorporates a greater degree of control in terms of repeatability, precision and stability. Although multiple procedures using the endoscope have now been described and most are performed by expert endoscopists, surgeons with less

endoscopic experience are unlikely to be able to use such a challenging instrument to perform a clinical procedure, particularly if the technique is not well supported in the literature and when they are familiar with the less demanding laparoscopic alternative.

Laparoscopic surgery, although undeniably far more beneficial in terms of operative outcomes for the patients over the gold standard open approach, also created significant challenges for the surgeons in terms of instrument ergonomics. This results in a lengthy proficiency curve evident by the some of the more complex operations taking many years to come to safe, consistent and widespread clinical application (91). The introduction of robotic-assisted laparoscopic surgery was conceptually a revolution within surgery. Although economically controversial, for the first time it enabled surgeons trained in the open technique to adopt the laparoscopic procedure after a significantly shortened learning curve (82). Despite having limited routine clinical uptake within the wider surgical community, the introduction of such platforms enhanced surgical performance through overcoming many of the ergonomic challenges faced by traditional laparoscopic surgery including a lack of depth perception, inverted movement of the hand to instrument control and the amplified surgical tremor through the long instruments. Negating these challenges significantly reduced the learning curve for a minimally invasive technique with some surgeons claiming operative proficiency for specific procedures after only a small number of cases (82).

It is reasonable to consider, therefore, that the solution to overcoming the ergonomic challenges in flexible surgery also lies within the field of robotics and the benefits imparted by the computer aided platform. Thus far, a number of groups internationally have already explored the potential of this clinical-technical collaboration with multiple designs already in the development phase from roving platforms (92) and magnetically coupled miniature instrument platforms (93) to flexible endoscopic platforms (94). However, before the design of any robot can be undertaken, those areas which expose flexible access surgery as conceptually a unique opportunity for the surgical community to explore, as well as those challenges which may go so far as to hinder its clinical integration, need to be better defined.

Chapter 3

Flexible Endoscopic Navigation

Hypothesis: The challenge of accurately navigating a flexible endoscope within a spatial environment requires significant endoscopic experience.

3.1. Introduction

As techniques such as endoscopic submucosal resection (95) and transluminal surgery (96, 97) gain increasing interest the potential of the endoscope as an operative, rather than an investigative instrument, is fast becoming realised. As surgery strives to develop ever less invasive procedures (98), it is the flexible endoscope which is rapidly becoming central to what is set to be the next advancement in minimally invasive surgery. Ironically, however, it is currently the endoscope itself which most significantly limits this advance (99). Due to the lack of endoscope control, navigation within the peritoneum becomes a far greater task than within the bowel lumen. The lack of luminal constraints, which maintains direction of the endoscope's path, within the bowel are absent within the extraluminal environment. It is this element of navigational control which requires the most significant skill of any endoscopist and where the training in transluminal endoscopy may require an even greater focus of attention than for endoluminal procedures.

Flexible endoscopic navigation whether endoluminal or transluminal is derived from two distinct movements: torque control of the endoscope and the utilisation of the control wheels to alter the angle of the endoscope's distal tip. During endoluminal navigation, tip angulation is essential to maintain directional control of the endoscope with the angle of the tip used to deflect the endoscope off the bowel wall and onto the desired path. During a transluminal procedure the use of this technique provides a less consistent alteration of direction as the spatial environment limits the potential for consistent path modification, with any deflection achieved through the endoscope being forced onto obstructing internal organs or structures. The directional change is therefore predominantly random and could potentially even be

considered unsafe in unskilled hands, enhancing the possibility of inflicting iatrogenic injury to internal organs. It would therefore be reasonable to assume that, for endoscope control within this environment, more emphasis should be placed on the torque control to provide direction changes than perhaps the use of the control wheels which may be more essential for maintaining spatial and visual orientation. If this is the case, then mapping these elements of endoscopic control during a transluminal navigational task could provide a useful indication as to the skill level of each clinician and their appropriateness to undertake such a procedure.

Current evaluation of endoscopic skill is derived predominantly from purely quantitative metrics; the total number of intraluminal endoscopic procedures performed or in the case of colonoscopy; caecal intubation rates. Quality evaluations, however, have proven more challenging to introduce. Rating scores such as the Global Assessment of Gastrointestinal Endoscopy score (GAGES) have recently been validated but are specific for either Upper Gastrointestinal Endoscopy (GAGES-UE) or Colonoscopy (GAGES-C) (100) and as such have not been extrapolated for extraluminal procedures. With simulated training aids already under development for NOTES (101) the need to define a suitable assessment method to quantitatively assess and discriminate movements according to the experience of the operator could be critical not only for determination of user skill, but in the detection of potentially unsafe manoeuvres.

The purpose of this article is to explore the potential of mapping the endoscopist's movements through the use of video motion tracking and to define a novel approach to determining the quality of endoscopic torque control more reliably within an extraluminal environment and potentially expose a method of quantitatively assessing endoscopic skill in the future. It will also enable an estimation of the level of endoscopic skill required to be met to safely perform a transluminal or flexible access surgical procedure using the flexible endoscope.

It is hypothesised that the optical signature of movements as detected would enable the differentiation of the operator skill level and as a result the challenges which are faced with navigating the flexible endoscope within the extraluminal environment. For this feasibility study we rely on optical motion tracking. However, the need to develop a simulated flexible access platform within which to examine these traits is primary. The NOTES approach provides the most extreme example of flexible access surgery as a result of its transluminal

access which reduces the ability to use the external port either to provide stability for navigation or aid in an additional two degrees of motion, found when the port is used as a fulcrum. As such the NOTES approach was the focus for the design of a novel simulator within which to explore spatial flexible endoscopic navigation in greater detail.

3.2. The Natural Orifice Simulated Surgical Environment; Design, Construction and Validation.

The exploration of the ergonomics of the NOTES approach is considerably limited at the current time due the lack of clinical experience that many, if not the majority of, clinicians have of the technique. In the UK the practice of NOTES on human patients has been deemed unsafe and the recommendation is that it remains, for the current time in the research arena. In the United States a more moderated view has been taken in that the procedure can be performed by specific specialists on postmenopausal women via the transvaginal route only, although those restrictions are becoming more relaxed. Nevertheless, given the lack of clinical expertise and exposure, particularly in the United Kingdom, the need for a more robust model on which to trial the technique is essential. The current model in use globally for NOTES research is the porcine model. In the UK, strict guidelines are in place through the Animals for Scientific Procedures Act (1986) to ensure that the proposed use of animals in research is fully justified. It is therefore, essential to ensure that the right focus is given to the research particularly when using animal models and that an alternative trial method could not have been used equally or as effectively to elicit the same objectives before endorsing their use. In essence, if the use of animals cannot be replaced, then it comes down to refinement of the research plan and reduction of the number needed to produce the result. In terms of exploring the ergonomics the need for *in-vivo* models is essential but in terms of the number of animals required to realistically explore the ergonomics of the NOTES technique it could not be justifiable. Simulator models may offer an alternative.

Simulators are being increasingly used in surgical practice as alternatives to initial training on patients (102). With many laparoscopic and endoscopic simulators entering the market, it seems that a NOTES simulator for the purpose of training is a logical extension. The durability of a simulator for training may be difficult to justify in these early stages of NOTES development, however, simple models tend to make the most durable aids both for

research and teaching long term as is evident from the box trainer model for surgical laparoscopic training which remains widely in use. The construction of a Natural orifice simulated surgical environment was proposed to trial the navigation phase of the technique using conventional flexible endoscopes.

3.2.1. Design and Construction of the Simulator Model.

In an attempt to highlight and explore NOTES, and in particular the ergonomic challenges which represent a great proportion of the limiting factors for this approach, the need to design a phantom environment that can be utilised repeatedly to collect data in a standardised environment, be representative of the technique and therefore translatable to the animal model, is essential. The key elements include a spatial environment within which to navigate the endoscope, obstructions upon which the endoscope will deflect during movement, a transluminal access point separate from the external environment by a luminal enclosure and independent internal motion to reflect natural physiological movement.

In this study, the simulator was constructed from an adapted laparoscopic training box with dimensions of 40cm by 40cm by 15cm (Pharmobotics Ltd, Winchester, UK). Any rigid box providing similar dimensions could be used. A hole was drilled in the bottom plate of the box to act as the access point and the simulated rectum (*Figure 3.1*).

Luminal organs including rectum, stomach, small bowel, and transverse colon were made from moulding liquid latex (Magnacraft, Midhurst, UK) and rolled to form a flexible tube. These were filled with polystyrene beads to introduce surface texture. Solid organs, including a liver and ascending and descending colon, were made from expandable foam filler (Evostik™) moulded and shaped. Once dried, these were covered with silicone to smooth and then layered with liquid latex. The spatial cavity of the box was filled with these model organs in a representative anatomical fashion. All the model organs were fixed to individual cut Plastiglass™ sheets which in turn were laid within the box. Each panel was secured to a non slip mat which lined the inside of the box completely. The panels were secured using Velcro™.

The small bowel model was fixed at the point representative of the Caecum (part of the ascending colon) and also at the pylorus of the stomach. A length of 40cm of small bowel

was coiled within the centre of the box but could freely move within the cavity if abutted by the endoscope or instruments. In a similar way, the transverse colon was also attached at either end, to points representative of the splenic and hepatic flexures. This imparted some freedom of movement to this section of the model bowel.

Despite their approximation to the true anatomy, these models can be visually recognisable as representations of their related organs. All the materials used in this simulator can be purchased from a standard textiles and hardware store. The whole internal environment of the phantom was painted to reflect the internal peritoneal environment using acrylic mixed with the liquid latex before moulding (*Figure 3.1(a-c)*).

One of the significant differences of the NOTES technique over laparoscopic surgery is the loss of the fulcrum aspect of the instrument at the port site. This is essential to replicate when designing any simulator for NOTES. For the purposes of this simulator, a model rectum was created. Accessed through an entry made in the bottom panel of the box, the model rectum is convoluted and curves to the bottom right corner of the box to represent the true anatomy. A pre-made full thickness slit in the wall of the model at 5-6cm from the external opening allows the endoscope to pass relatively freely into the transluminal spatial environment (*Figure 3.2*).

In addition to the latex and foam structures, the simulator also includes a moveable diaphragm, the motion of which is achieved through the inflation of two anaesthetic balloons. This can be performed either manually using an external anaesthetic balloon or automatically via a low pressure mechanical ventilator. The balloons are placed within the top section of the box and are connected using a “Y” connector to a ventilation tube, subsequently externalised via a hole in the top panel of the box.

Although the box is currently adapted for a transrectal NOTES approach, it can be adjusted for access via the transgastric route. By removing the anaesthetic balloons, an adapted plastic tube can be passed down from the top of the box to below the model diaphragm. The lower end of the tube allows for the attachment of either the latex stomach as described above or a washed true *ex-vivo* stomach. The challenges of the NOTES technique can then be explored and recreated using both access routes.

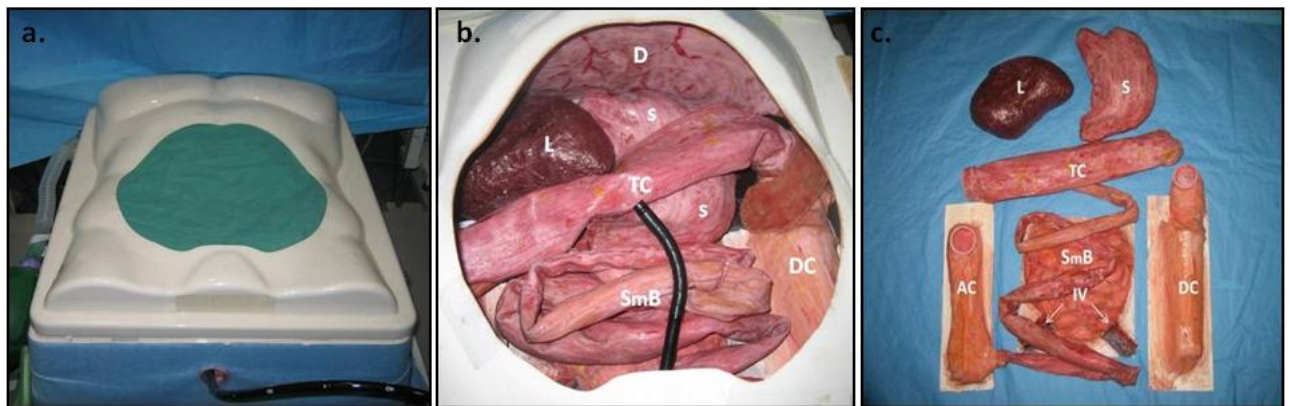


Figure 3.1; Images of the box trainer converted to a NOTES simulator (a, b) and the latex structures created for the internal contents (c). (L - Liver, AC - Ascending Colon, TC - Transverse Colon, DC - Descending Colon, S - Stomach, SmB - Small Bowel, D - Diaphragm)



Figure 3.2; Image of subject performing tests on the simulator (a); Image of the intraluminal portion of the simulator before the transluminal portion (access arrowed) (b) and Image of the internal environment of the simulator showing the endoscope accessing the internal cavity from the endoluminal section (arrowed) (c). (R - Rectum, SmB - Small Bowel, TC - Transverse Colon).

3.2.2. Validation of the Simulator Model

3.2.2.1. Method

The proposed task to be performed within the simulator was a NOTES navigation task. A flexible 10.3mm single-channelled, investigative colonoscope (KarlStorz, Tuttlingen, Germany) was used for the duration of the investigation. With the lack of NOTES experts it was felt that given that the basic concept of the task was to navigate within a simulated peritoneal environment, experts were invited from the fields of both laparoscopic surgery and gastroenterology endoscopy, to trial the simulator. All experts were familiar with the endoscope, although the gastroenterologists were quantifiably more experienced. Laparoscopic surgeons were more experienced in working within the peritoneal environment and perhaps more experienced with the anatomical cues.

10 experts, 5 from each field, were invited to undertake three tasks within the simulator. The first task involved the navigation of the endoscope between two relatively close proximity targets which were set within the simulated peritoneal cavity. The task was to touch the targets intermittently as many times as possible within a 20 second period. This was repeated five times and the number of hits was recorded and reviewed on video replay by three independent reviewers as to whether the targets were hit each time.

The second task was to navigate sequentially around a course of 10 targets set within the simulator. The targets were placed at points within the simulator which could represent specific points which may need to be visited in the peritoneal cavity under the circumstances of a real case; in this case a transrectal NOTES cholecystectomy. The first target was placed within the simulated rectum before the subject could access the simulated peritoneal cavity. The task was timed and the number of targets hit, gauged by a set screen size criteria for the target marked out clearly on the side of the visual display monitor. The task was repeated four times.

All novices were introduced to the endoscope through an introductory video which provided insight into how the endoscope was controlled. The video lasted five minutes during which time the novices had an endoscope to familiarise themselves with. The video also provided a

video playback of the course and a description of what was considered a met target. This was based upon the size of the target seen on the screen which could be compared to markers on the surrounds of the viewing monitors. This size was equivalent to 2cm in real terms of the tip of the endoscope to the target and would be considered to have been met should the target be brought into range of these markers. Each subject was shown a schematic map of the course which could not be reviewed once the trial was undertaken, however, should the subject during the task be lost then position of the next target could be given by means of where it is in relation to the box environment. Any assistance would have to be requested by the subject who was not penalised in any way for doing so.

Each subject was allowed a single trial run of the task, for up to a maximum of 5 minutes before the experiment would then commence. During the trial run the schematic map could be viewed. The experimental trials would then run back to back.

After the procedure the experts were asked to complete a questionnaire. This included 11 questions related to the design and realism of the simulator, the contents and the effectiveness of the task. A linkert scale was used to record the scores from each of the questions on a basis of 0 - 10.

3.2.2.2. Results

Questionnaires

2 experts did not complete the questionnaires in full. One damaged the simulator during the trial and as such the trial had to be abandoned, the simulator was subsequently repaired. Of the remaining 8 experts the questionnaires were completed in full (*Table 3.1*)

Table 3.1. Results from the post-procedural questionnaire.

	Scores from each Subject										
Subject Number	1	2	3	4	5	6	7	8	Mean	SD	Median
Simulator											
Realism of the simulator	8	4.2	7.6	5	6.9	8.8	5	5	6.31	1.72	5.95
Realism of the environment	7	4.2	6.1	3	7.1	8.4	5	5	5.73	1.76	5.55
Represent NOTES approach	8	5	6	5	7.4	8.2	5	5	6.2	1.44	5.5
Realism of movement of the endoscope	10	9.1	7.5	3	9.4	9.4	6	5	7.43	2.53	8.3
Realism of reaction of obstructions to movement	8	2.3	4.5	5	5.7	9.3	5	6.5	5.79	2.16	5.35
Task											
Navigating between targets	7	8.1	7.7	5	9	9.1	5	7	7.24	1.59	7.35
Appropriateness of target positioning	8	7.4	10	10	8.6	9.1	6	8	8.39	1.35	8.3
navigating between two points	7	1.9	7.5	6	5.2	9.3	7	7.5	6.43	2.18	7
Overall											
Do you think simulator meets goals set for the task	10	7	8	5	8.2	9	5	6.5	7.34	1.83	7.5
Does the simulator challenge the subject enough	10	6.9	9.7	8	8.8	9	5	5.8	7.9	1.72	8.4

Task performances

9 Novices, and 10 endoscopic and laparoscopic experts both with variable endoscopic experience ranging from 50 endoscopies to 20000, successfully completed the tasks. The number of targets successfully met and performance times where appropriate, were recorded. In the case of the course navigation task, a performance rating score was allocated to each subject based on the mean number of targets met over the three trials and the mean time in which the trial was achieved. The score was determined by assigning a representative score for the performance based on their position in relation to the other subjects. The fastest time was allocated a score of 10 and the slowest, 1. The remaining subjects were scored accordingly. This was repeated for the targets met variable. With both the speed and number of targets met being assumed to be equally weighted in terms of how an effective performance should be determined, an overall score was obtained by calculating the mean of these two outcomes.

Statistical Analysis

Statistical analysis was performed on the data. The data was subjected to non-parametric statistical analysis, on account of the lack of normal distribution amongst the data, including the Mann-Whitney and the Kruksal-Wallis test where appropriate. A significant difference has been taken as a p-value of <0.05 .

Two target navigation task

The results demonstrated that this task when performed on the simulator can differentiate between the novice and expert endoscopist ($p=0.001$). The task was however, not able to distinguish between the gastroenterologist or the surgeon nor differentiate based on the level of endoscopy experience over the basic understanding of endoscopy (*Table 3.2*).

There was a significant improvement in performance by means of the numbers of targets hit from the first trial to the last ($p=0.04$). This seemed to be demonstrated most significantly amongst the novices (between trial 1 to 3 ($p=0.047$) and between trial 5 and 1 ($p=<0.01$)) with no significant difference in the number of targets hit during trial 1 and trial 5 being demonstrated (*Figure 3.3*).

Table 3.2. Results from the two point navigation task. (GastroE - Gastroenterologist)

Subject Number	Designation	Endoscopy Experience (N ^o of endoscopy)	Numbers of targets hit on each trial of 20 seconds (median values)					Overall (median)
			First trial	Second trial	Third trial	Fourth trial	Fifth trial	
1	Novice	0	2	4	3	3	3	3
2	Novice	0	2	3	1	3	3	3
3	Novice	0	0	2	8	5	5	5
4	Novice	0	0	1	2	2	4	2
5	Novice	0	2	3	3	3	2	3
6	Novice	0	0	2	0	0	1	0
7	Novice	0	0	1	1	0	1	1
8	Novice	0	3	4	4	4	3	4
9	Novice	0	1	1	3	4	5	3
10	Novice	0	4	3	7	7	6	6
11	Novice	0	2	3	3	3	3	3
12	Novice	0	2	3	5	4	6	4
13	Novice	0	1	1	3	3	2	2
14	Novice	0	0	1	1	1	1	1
15	Novice	0	3	4	4	3	3	3
16	Novice	0	1	0	1	0	0	0
17	Novice	0	0	2	1	2	5	2
19	Novice	0	2	2	0	3	3	2
18	Surgeon	500	7	14	14	13	17	14
20	GastroE	200	5	10	10	11	10	10
21	GastroE	6000	5	5	8	9	12	8
22	GastroE	2800	15	17	18	16	18	17
23	Surgeon	500	3	3	4	6	6	4
24	GastroE	20000	9	12	13	12	14	12
25	GastroE	50	6	10	6	4	7	6
26	Surgeon	50	18	17	18	21	18	18
27	Surgeon	350	18	20	22	23	24	22
28	Surgeon	500	16	19	20	20	20	20
29	GastroE	1280	22	22	26	26	30	26

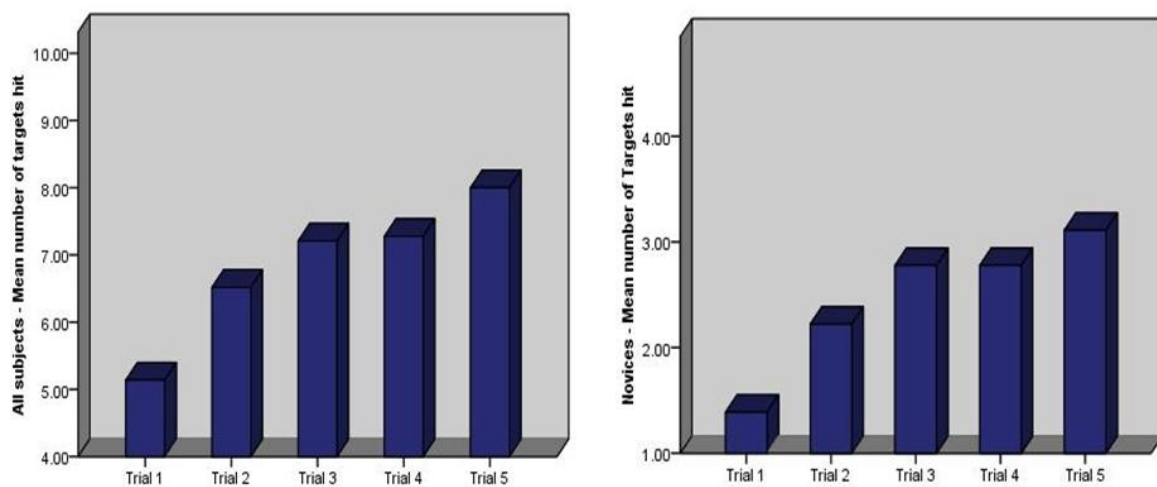


Figure 3.3; Performance improves significantly for all subjects over the 5 trials (left graph) with novices demonstrating the most significant improvement.

Course navigation task

Performance outcome variables including time (seconds), targets met (median), together with the performance rating score demonstrated a significant difference ($p=0.041$, $p=0.006$, $p=0.011$ respectively) between the novice endoscopist (no clinical experience) and the clinicians (*Figure 3.4*).

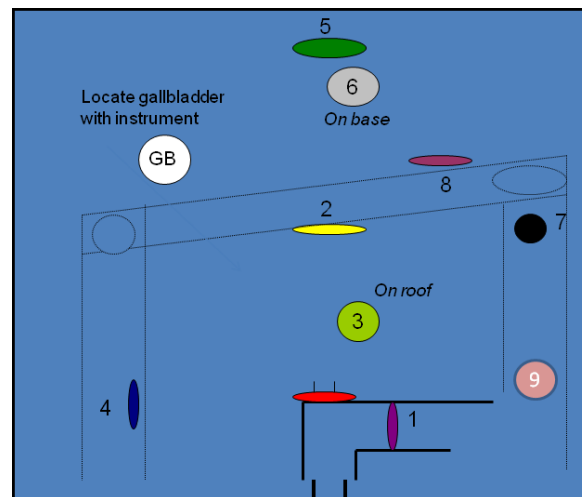


Figure 3.4; Schematic representation of the internal box environment presented to the subjects prior to their trial.

The dashed lines indicate outlines of the colon with the targets numbered sequentially.

The bold lines indicate the outline of the rectum whilst the arrows indicate the optimum paths for navigation of the endoscope between targets.

No significant differences were noted between the gastroenterologists and the surgeons based on the performance outcomes. Both independently demonstrated a significantly better performance over the novices as would be expected.

When the endoscopic experience was separated into three groups based on the quantitative level of experience; novice - nil to minimal, intermediate - 50 to 499, and expert - >500 (*Table 3.3*), the improvement in the performance score is incremental as would be expected in these three groups but although significance is demonstrated between the expert and intermediate group ($p=0.05$) and the expert and novice group ($p<0.01$), no significant difference is demonstrated between the intermediate and novice group (*Figures 3.5 and 3.6*).

No significant improvement in performance could be demonstrated over the four trials for any of the subjects, novice or expert. Trends were suggestive of improvements with some positive increase in the performance score but no significance could be confirmed.

Table 3.3. Performance outcomes from the multi-target navigation task undertaken in the simulated environment.

Subject	Designation	Endoscopy experience § (cases)	Performance time (seconds)	Targets met (median) (n)	Score Time (s)	Score Targets (n)	Performance Score ¥
1	Novice	0	197.10	8	7.48	7.3	7.39
2	Novice	0	340.46	4	4.18	3.25	3.715
3	Novice	0	294.81	6	5.23	5.5	5.365
4	Novice	0	340.93	6	4.17	5.05	4.61
5	Novice	0	327.00	7	4.49	5.05	4.77
6	Novice	0	478.76	3	1	1	1
7	Novice	0	243.80	6	6.41	5.5	5.955
8	Novice	0	270.63	4	5.79	2.35	4.07
9	Novice	0	450.42	2	2.35	1	1.675
10	GastroE	50	351.85	3	3.92	2.35	3.135
11	Surgeon	50	204.33	9	7.31	8.65	7.98
12	GastroE	200	353.04	6	4.11	5.05	4.58
13	Surgeon	350	309.43	7	4.9	5.95	5.425
14	Surgeon	500	106.56	9	9.56	9.1	9.33
15	Surgeon	500	133.43	9	9.05	8.65	8.85
16	Surgeon	500	99.46	9	9.73	9.1	9.415
17	GastroE	2800	87.58	10	10	10	10
18	GastroE	6000	205.98	9	7.28	9.1	8.19
19	GastroE	20000	101.61	8	9.68	8.2	8.94

(§ - Estimated values - results taken from pre-procedural questionnaire) (¥ - Score calculated by taking the mean of the scores assigned for the time taken and targets met) Abbreviations; GastroE - Gastroenterologist

One of the criticisms of the simulator has been the challenge of the operator to move between target one and two. This section of the trial involves passing the endoscope through the latex simulated bowel wall, which has been felt by some experts to be more of a challenge than if performed in the *in-vivo* setting. To explore the potential of this and its effect on performance, the times for the trials and number of targets hit was adjusted as if the trial began from target 2 i.e. once the endoscope had entered the simulated abdominal cavity. Despite the adjustments no improvement in performance for novices, experts or both, either in terms of raw times, raw targets hit or the adjusted performance rating score was described. This included the final trial with and without the extra camera assistance.

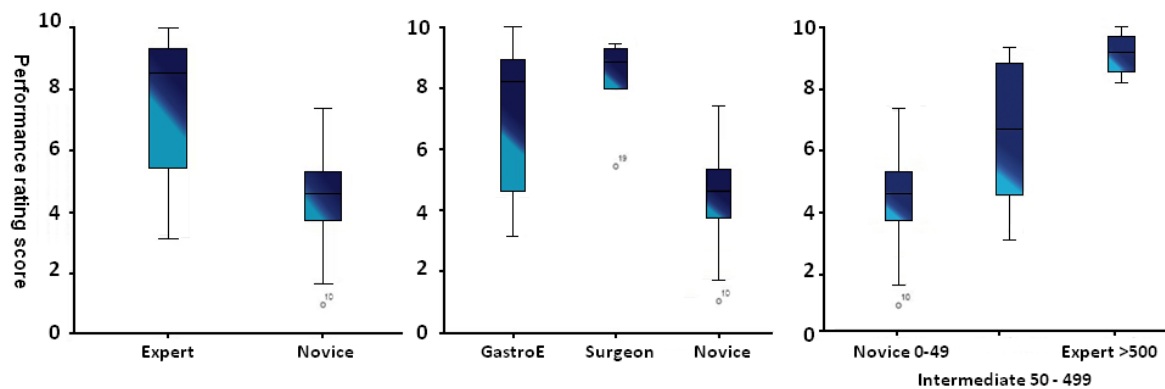


Figure 3.5; a series of box-plot and tail graphs; illustrating differentiation in performance between novice and expert endoscopists.

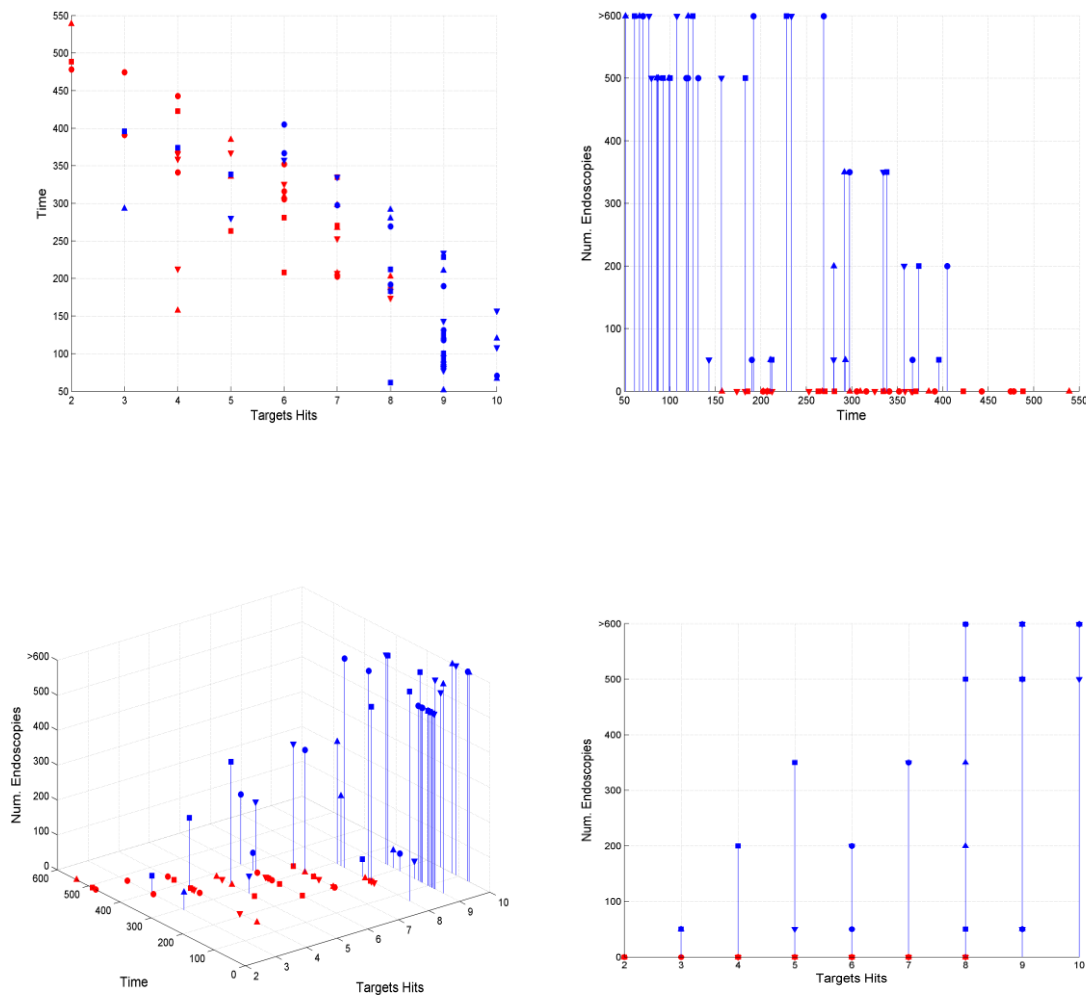


Figure 3.6; Endoscopic experience affects performance in terms of number of targets hit and the time taken to complete the task. (Experts are highlighted in blue and novices in red, the shapes represent the different trials).

NOTES simulators will, in current times, always be challenging to validate. The number of NOTES clinicians available to test and validate any potential simulator is significantly low. Once these numbers are divided according to experience levels, in terms of the number of NOTES procedures performed, the number of experts, intermediate and novice NOTES clinicians required to validate would be too low to gain any significant values.

Considering that one of the major challenges in NOTES is navigating a flexible endoscope in a spatial environment as opposed to one which is constrained by the bowel walls, both gastroenterologist endoscopists and surgeons were invited to trial the simulator under the circumstances. The overall impression of the simulator was that it potentially could be used for the purpose it was intended with facial and content validation results suggesting over 55% of experts felt it had the appearance of a NOTES environment and challenged the user in a way they would predict NOTES would in a true environment.

The tasks undertaken were felt to be suitably appropriate to investigate the trials of navigating a flexible endoscope in a spatial environment with the two point task and the navigation task achieving approval from over 75% of the experts.

The tasks were both successful in differentiating between novices and experts, with some evidence of differentiation between endoscopic skill levels particularly on the two point task. Although, this cannot be accepted as facial, content or construct validity in terms of validating the model as a NOTES simulator given none of the invited experts have had any prior experience in NOTES; simulated, animal or human, the only outcome that can be drawn from these results is that the simulated environment presented as a simulator in which to trial flexible endoscopic navigation within a spatial environment. To this end it may be considered as having construct validity in terms of differentiating the novice and the expert endoscopist when these particular tasks are undertaken in this environment.

3.3. Time and Motion Analysis during Simulated NOTES Navigation; is it all in the Wrist?

It is becoming widely acknowledged that NOTES, as a surgical approach, requires a significant degree of experience with the investigative endoscope, hence the interest by

gastroenterology endoscopists as well as surgeons, with what is in essence a surgical procedure. Although, the debate as to whether gastroenterologists or surgeons are the most appropriate to undertake intracavity flexible endoscopic procedures is out of the remit of this study as the true reflection of the argument involves an exploration of multiple task skills not simply endoscopic experience. In terms of the stages of a NOTES approach (not necessarily involving a transluminal breach of the bowel wall); navigation to the target, operating using endoscopic instruments, tissue manipulation and triangulation, it is this initial phase of navigating the endoscope to the target which will be so markedly influenced by the experience of the endoscopist and as such the most essential from the point of patient safety to be the most proficient.

Using motion tracking techniques, the manipulation of the endoscope by experts and novices is explored during a navigation task to determine potential differences in the effort required to perform the task, explore patterns of movement between the two groups which may influence future investigation either in terms of learning and training of future NOTES clinicians or be used potentially for ergonomic input into future endoscope design.

3.3.1. Method

3.3.1.1. Setup - Motion capture device

In terms of holding and manipulating an endoscope two styles exist. For the majority, the endoscope controls are held in the left hand whilst the right controls the insertion of the device together with the torque required for rotational movement about the axis of the instrument, the drive hand. These are performed simultaneously and the hands tend not to leave either position for the duration unless a procedure is to be undertaken. In this case instruments are required to be passed down the biopsy channels of the endoscope however, for the purpose of navigation both hands predominantly stay in these described positions for the duration.

A video motion capture system; Optotrak Certus™ (Northern Digital Inc, ON, Canada), was used to capture the motion of experts and novice endoscopists controlling the endoscope whilst performing a navigation task within the simulated model. The motion capture system records the position of strobe markers in 3 dimensional space and in real time. It maintains an

accuracy of 0.15mm^{-1} of these position markers within this environment. Markers have to be in direct view of the video capture system. Once out of view the position of the strobe markers are not able to be accurately defined.

3.3.1.2. Rigid bodies and their positioning

Rigid bodies, braces in which to hold the strobe markers in position, were designed in-house specifically to be attached to the subject's right side (for right handed clinicians) (*Figure 3.7*); wrist, proximal radius, proximal humerus and temporal region of the head for this initial pilot series of experiments, in addition to a separate custom made rigid body for the endoscopes control handle held in the other hand. The rigid bodies each have four markers embedded into them to ensure that if one marker was out of sight then three others remained; enough to determine positional and rotation coordinates in free-space.

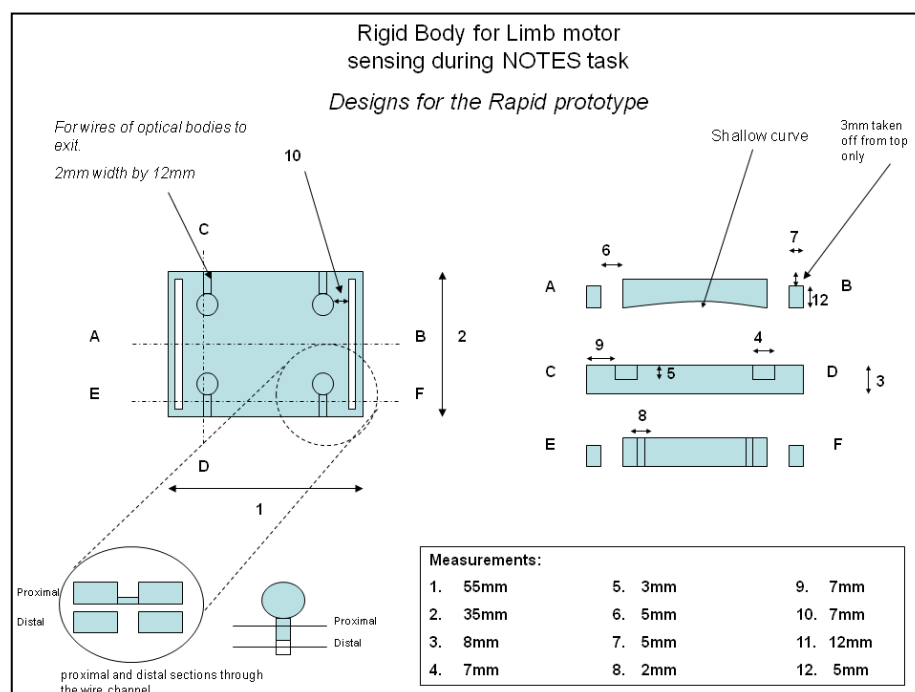


Figure 3.7; Design schematic of the rigid bodies required to mount the optical tracking markers

For the purposes of these trials the rigid bodies for each of the measured elements were custom made in-house. Rigid bodies were placed on the subjects drive hand side, usually the right, positioned on the wrist overlying the radioulnar joint, on the supinator muscle when the forearm is in supination and on the deltoid muscle, overlying the humeral head when the arm

is in the resting anatomical position. The final rigid body was customized to fit the endoscope control head without interfering with the operator or the control wheels. Optimum positioning was checked prior to each subject performing the task ensuring that each rigid body would be visible through the full potential range of motions expected to be performed by the subject during the task (*Figure 3.8*).

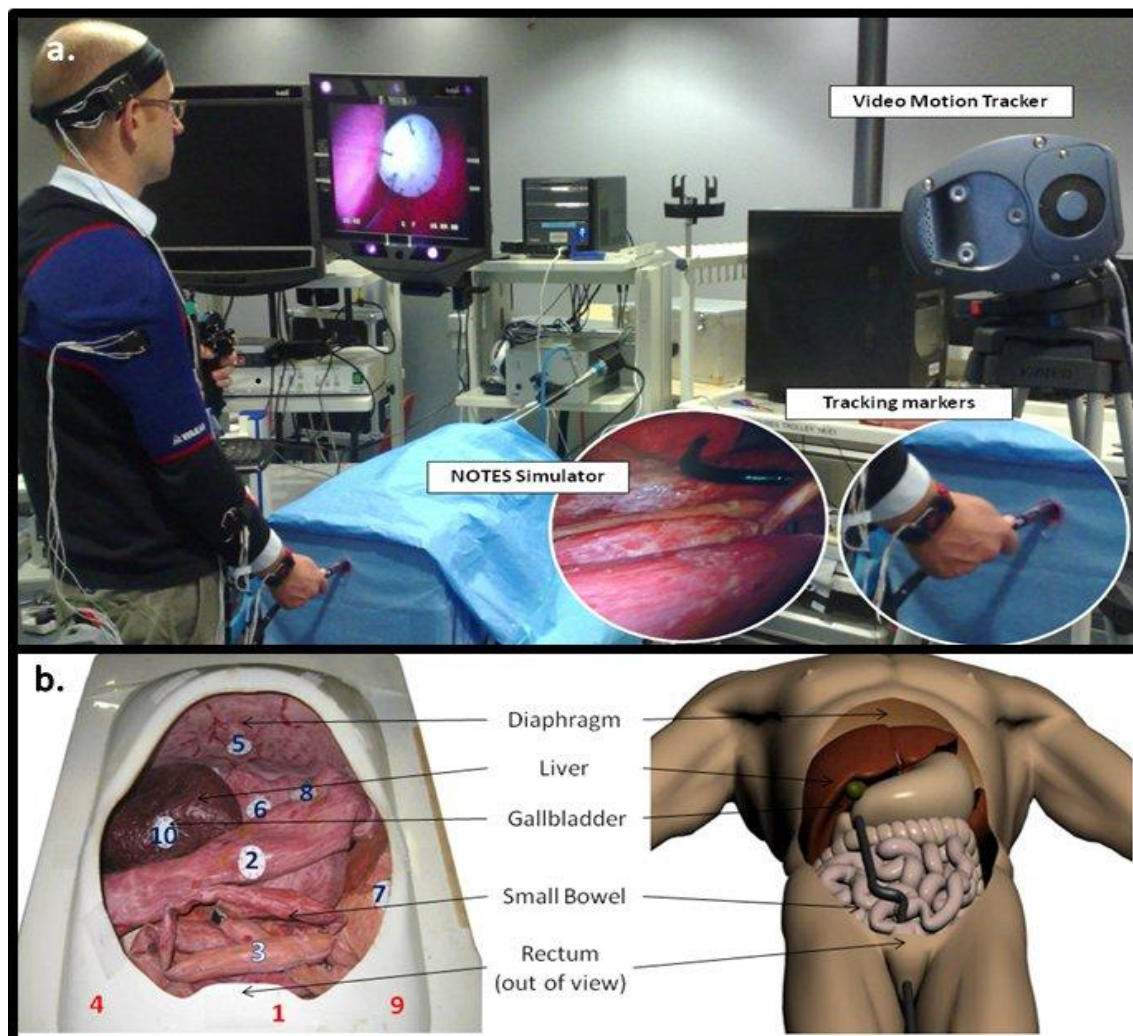
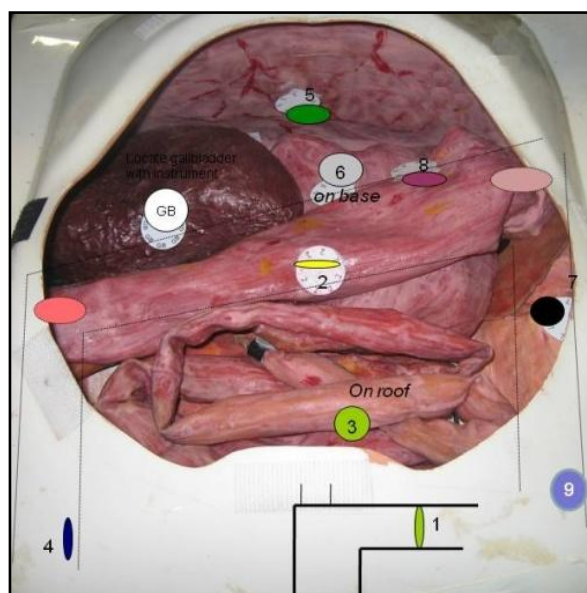


Figure 3.8; Illustration of the setup of the experiment with the insets highlighting the internal view of the simulator during the task and the tracking markers on the wrist set within a rigid body (a), with an image of the course of targets within the simulator with their relation within the simulator to the actual anatomy (b).

3.3.1.3. Navigation Task

The task was performed within a Natural Orifice Surgical simulator (6) as defined above. Subjects were required to navigate a flexible 10.6mm, single-channelled, investigative colonoscope (KarlStorz; Tuttlingen, Germany) through the same series of numerically

labelled targets within the simulator. The targets were to be reached sequentially with the first target situated in the simulated rectum as the endolumenal portion of the task, and the second and remaining targets requiring a transition of the endoscope through the wall of the rectum into the spatial environment of the simulated abdomen (*Figure 3.9*). The targets were placed within the simulator to be representative of points within an abdominal cavity that the operator may explore if the task were a true NOTES approach to an assisted cholecystectomy undertaken within the *in-vivo* setting. This task within the simulator has been validated to differentiate between novice and expert endoscopists.



Possible movements required for each target destination

1. Forward and either Right wheel or (Alt. right rotation and down wheel).
2. Straight push with up wheel.
3. Up wheel and backward motion.
4. Left rotation and backward motion.
5. Reorientate (right rotation) and forward push with up wheel.
6. Down wheel.
7. Right full rotation and backward motion.
8. Reorientate to 5 then Full Right wheel.
9. Backward motion and right rotation.
10. (GB) Reorientate (left rotation) and forward with over compensated left rotation.

Figure 3.9; A schematic of task overlaid onto the simulator with the targets in place. The sequence of motions of the endoscope required to meet the targets is described alongside.

Subjects received a standardised introductory video tutorial on endoscope control and a 3 minutes run through of the task for tool familiarization. The target was considered to have been met when the visual display of the target had reached 50% of the screen size confirmed by predetermined markers placed around the periphery of the monitor. This accounted for a distance of approximately 2 - 3 cm from the tip of the endoscope to the target; a distance felt to be sufficient enough to enable

The task took the same format as described in the previous chapter with 10 targets. The targets were to be reached sequentially with the first target situated in the simulated rectum as the endolumenal portion of the simulation and the second and remaining requiring a transition through the wall of the rectum into the spatial environment of the simulated abdomen.

The positions of the targets with respect to their sequential partner were also considered. The sequence of simplistic movements of the endoscope required to reach the next target was defined. However, the position of target 8 was set to disorientate rather than to express a specific movement. (*Figure 3.9*)

Each subject was recorded using video motion tracking as described. Their trials were subsequently replayed and their movements subjected to manual segregation. A graphical user interface designed using Matlab™ software (version 7.6.0324 R2008 Mathworks) enabled playback of the trials for scrutiny, separation and recording of each of the movements (*Figure 3.10*).

19 subjects underwent a navigation task in the Natural Orifice Simulated surgical Environment. Their motion was tracked throughout each trial. Motion tracking from one trial was scrutinised for each of the eight subjects; 4 expert endoscopists and 4 novices. The trials chosen were the third attempt at the task so each subject was aware of the course.

The total displacement of each of the rigid bodies; i.e. the distance that the calculated centroid of the rigid body had moved at each recorded time stamp (frequency 30Hz), was undertaken to explore the areas of the body most interesting in terms of instrument control (*Table 3.4*). In all subjects the predominant displacement was recorded from the endoscope and wrist rigid body (*Figure 3.11*). This does concur with what would be expected in terms of current instrument control; the wrist producing rear drive and torque and the instrument hand the wheels that apply pitch and yaw to the instrument tip. However, the rigid body on the instrument head is not measuring the movement of the wheels but purely the subject's movement of the instrument irrelevant of whether the control wheels are being used so how useful a measure this is will need to be determined.

1. →

2. →

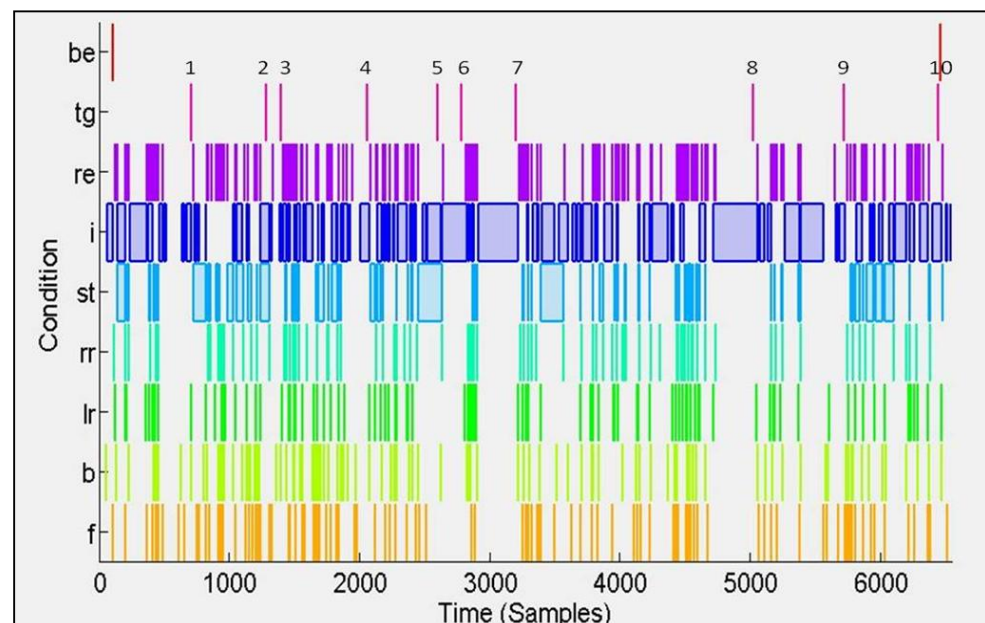
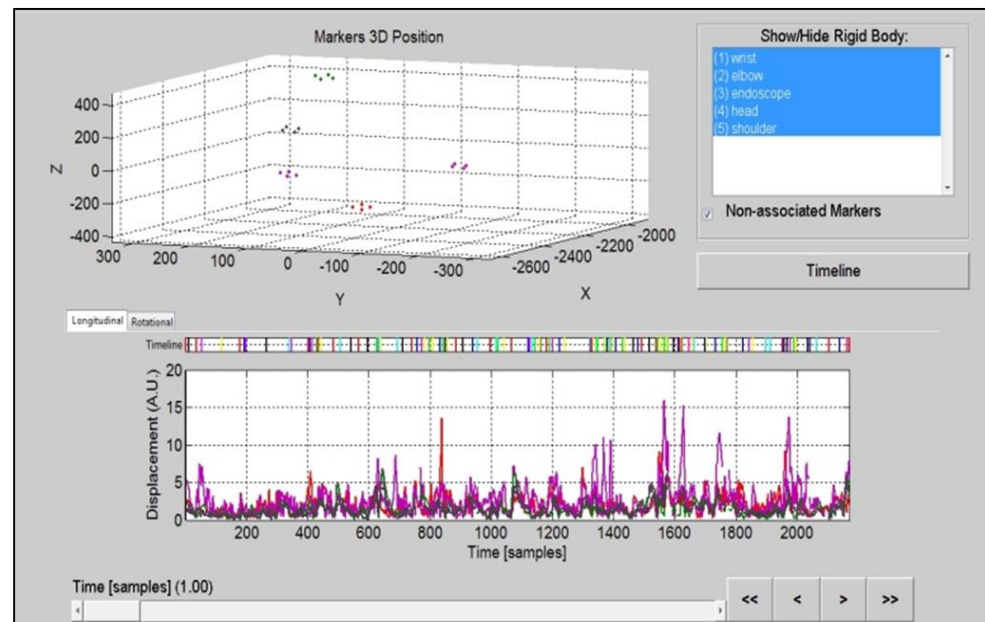


Figure 3.10; The graphical user interface (top) designed in Matlab™ (Mathworks Software Inc R2008) with the strobe markers 3D position (1) is visible with the function of playback. The extent of displacement of the markers can also be seen displayed graphically (2). The manually determined timeline of the events that occurred through monitoring the wrist during the whole task is recorded (bottom) with the target (tg) labelled sequentially.

(be – beginning and end time points, tg – targets met/passed, re – rotation ends, i – indifferent (marker static), rr – right rotation, lr – left rotation, b – back, f – forward.)

3.3.2. Results

The rigid bodies placed on the head and shoulder, reflect total body movements, in particular the shoulder whose predominant movement reflects movement of the upper body. The extent of displacement demonstrated at the wrist appears to be the most important in terms of determining instrument control for NOTES navigation however all of the experts demonstrate higher movements at the upper body, reflected by the higher displacement recorded at the shoulder rigid body particularly when time is taken into consideration. This may suggest that although wrist manipulation is an important aspect of instrument control, upper body flexibility rather than rigidity is of benefit. Further evaluation to confirm this is required.

3.3.2.1. Time and motion analysis

In terms of exploring potential patterns or strategies of movement which most appropriately reflect the control of the instrument, the wrist was chosen for examination. The movements relating to the wrist were segregated into a forward, backward or no motion in addition to a rotation; right or left (*Figure 3.10*). A positional magnetic tracking marker was also attached to the endoscope to determine when the wrist was in or had passed through the neutral position. Segregated movements were time stamped at the beginning of the event and the end.

Table 3.4; The total displacement of all the rigid bodies for all subjects (shaded) and the time taken for each to complete the trial. (AU - Arbitrary units).

Subject Experts		1		2		3		4	
Rigid Body		Time (AU)	Displacement (AU)	Time (AU)	Displacement (AU)	Time (AU)	Displacement (AU)	Time (AU)	Displacement (AU)
Wrist	2027	5413.914	6344	13969.49	3648	9489.907	1758	4526.498	
Elbow	2027	4405.887	6344	10649.67	3648	7946.803	1758	3685.12	
Endoscope	2027	6617.952	6344	20387.08	3648	10208.93	1758	5584.639	
Head	2027	4362.915	6344	9750.094	3648	7213.92	1758	3695.316	
Shoulder	2027	3622.046	6344	6961.906	3648	5510.304	1758	3062.436	
Total		2027	24422.71	6344	61718.24	3648	40369.86	1758	20554.01
Shoulder to wrist ratio (%)			66.90		49.84		58.06		67.66

Subject Novices		5		6		7		8	
Rigid Body		Time (AU)	Displacement (AU)	Time (AU)	Displacement (AU)	Time (AU)	Displacement (AU)	Time (AU)	Displacement (AU)
Wrist	8124	8591.13	5586	6851.229	9250	9009.408	6297	6481.502	
Elbow	8124	6667.042	5586	5458.248	9250	7323.04	6297	5271.471	
Endoscope	8124	9141.125	5586	11117.26	9250	16743.43	6297	9163.394	
Head	8124	4241.215	5586	5353.343	9250	7858.985	6297	5351.191	
Shoulder	8124	3884.897	5586	3924.835	9250	4564.228	6297	3642.626	
Total		8124	32525.41	5586	32704.91	9250	45499.09	6297	29910.18
Shoulder to wrist ratio (%)			45.22		57.29		50.66		56.2

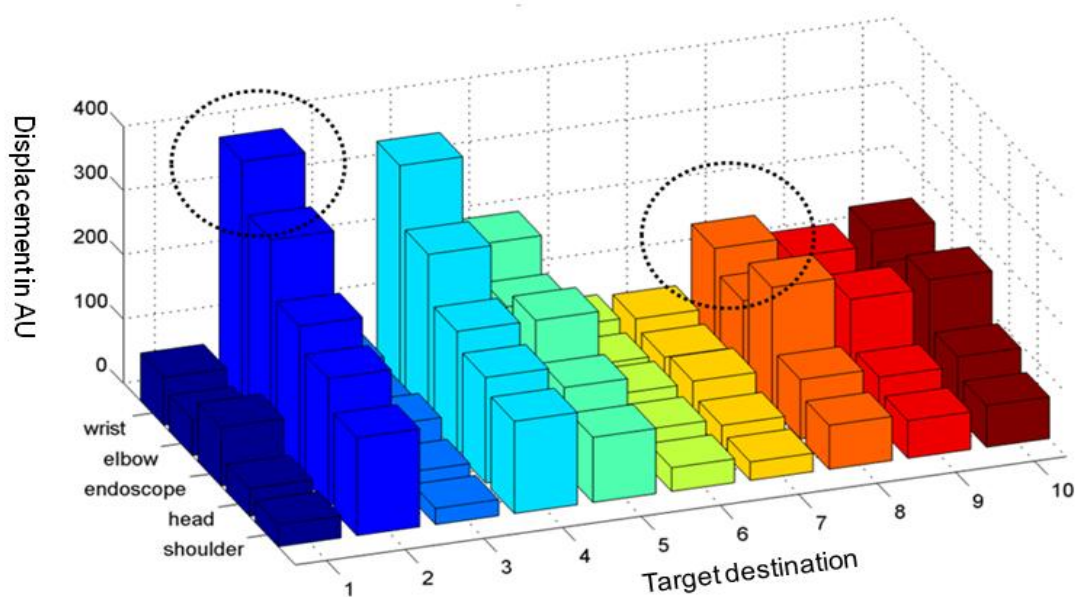


Figure 3.11; Average displacement of each of the rigid bodies during the set navigational task. Dashed circles highlight the displacement of the rigid body on the wrist.

Duration was included for the times when the wrist was in the neutral position or when it demonstrated no forward or backward motion. The complete time stamped events recorded from eight of the subjects can be visualised in *Figure 3.12*.

The number of events was totalled for each subject across each of the 10 target destinations. Significant correlation was evident between the number of events and time (($p < 0.01$) Pearsons correlation) with the trend demonstrating that the longer the time taken to perform the task the more events performed. This would not be wholly unexpected, given that more movements take longer to perform but it does indicate a lack of ineffective movements, as a faster series of multiple movements may achieve the target in a shorter time if those movements were more effective. It is evident from above that some of the number of movements undertaken by the experts (subjects 1-4) had been the same as those in the novices for example subject 3 destination target 5 took 27 moves to complete the task in a time period of 335 AU (equivalent of approximately 11 seconds) whilst subject 6 during the same task took 25 moves but completed it in a slower period (figures highlighted in red (*Table 3.5*)).

Experts

Novices

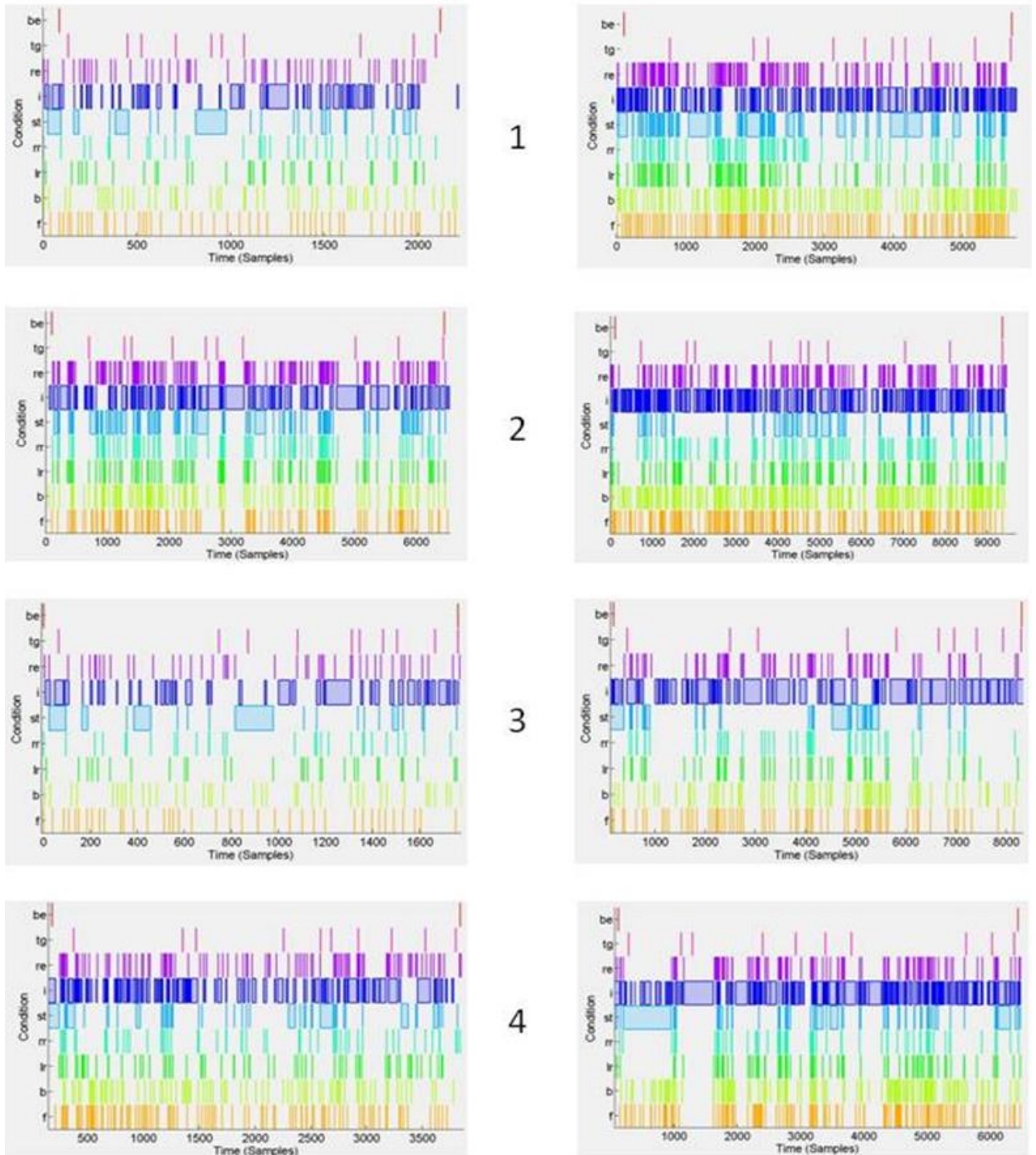


Figure 3.12; Representative events occurring at the wrist during the whole navigational task for each of the subjects; 4 novices and 4 experts.

Table 3.5; Time and motion analysis. The number of movements required to complete the navigation task and the associated time.

Expert Endoscopists								
Subject	1		2		3		4	
Target	Events (n)	Time (AU)	Events (n)	Time (AU)	Events (n)	Time (AU)	Events (n)	Time (AU)
1	4	46	32	597	17	191	6	64
2	27	315	52	577	105	977	53	680
3	5	76	5	113	7	117	8	122
4	16	183	58	663	51	784	10	210
5	12	189	34	533	27	335	19	230
6	4	55	2	191	7	94	6	33
7	6	118	20	410	24	240	14	101
8	54	621	112	1820	25	299	5	59
9	19	283	27	696	19	303	13	160
10	9	116	47	723	17	271	7	98
Total	156	2002	389	6323	299	3611	141	1757

Novices								
Subject	5		6		7		8	
	Events (n)	Time (AU)	Events (n)	Time (AU)	Events (n)	Time (AU)	Events (n)	Time (AU)
1	37	273	75	657	21	623	8	157
2	27	2053	107	1208	83	1102	46	834
3	53	549	27	206	6	191	2	173
4	39	1792	59	943	96	1802	69	1108
5	23	968	25	457	55	713	48	524
6	9	838	23	396	13	184	32	467
7	6	307	4	183	18	474	19	415
8	13	456	16	366	102	1840	140	1802
9	4	519	43	642	70	1076	13	409
10	1	360	61	514	77	1245	17	353
Total	212	8115	440	5572	541	9250	394	6242

This ineffective movement that may be demonstrated by novices can be confirmed by relating it to the overall performance. A positive correlation suggesting that an increased number of movements during the task relates to a poorer performer is demonstrated, although it is not significant ($p=0.063$).

Although, there is a difference between the numbers of wrist movements performed by the novice compared to the expert in terms of completing the task, this difference using the Mann-Whitney U test was not shown to be significant ($p=0.083$) although with more samples this may demonstrate this better. However, the question may not be related directly to the number of motions but the number of effective motions.

3.3.3. Extrapolating Patterns of Wrist Motion

The method of quantifying the number of events which occurred during the task is a relatively straight forward way of determining the effectiveness of instrument manipulation for the task of navigation over a particular target point. However, it is confounded by the speed and duration of the movement over which the event occurred. A single event may be a slow but steady manoeuvre which reaches the target although in a slower time than the two events which were of a shorter duration but reached the target faster. Which is the most effective is difficult to establish on event counting alone. An alternative may be pattern recognition. A method of determining what defines an effective manoeuvre may be visualised through patterns of movement behaviour.

As is evident in the pictorial format of the event marking for the wrist in *Figure 3.12* above, it is evident that the images created by the movement over the task for the experts appear lighter than the novices on the right. This evidently related to the density of the number of events that occurred during each task performance for these subjects. Whether this was as a result of the length of time undertaken to perform the task or fewer motions was explored further. The initial aim of this was to extrapolate these events into a series of patterns which could then be better scrutinised for any differences.

Using the custom developed Matlab™ based software tool which recorded of each separate movements as they occurred during the task, a timeline for each subject was created from the wrist enabling the recording of each of the four separate basic movement gestures; forward, backward, left and right rotation, as they had occurred with respect to each of the successive targets. From these segmented timelines, movement initiation was isolated and coded into a binary texture; movement (white) or no movement (black) (*Figure 3.13*).

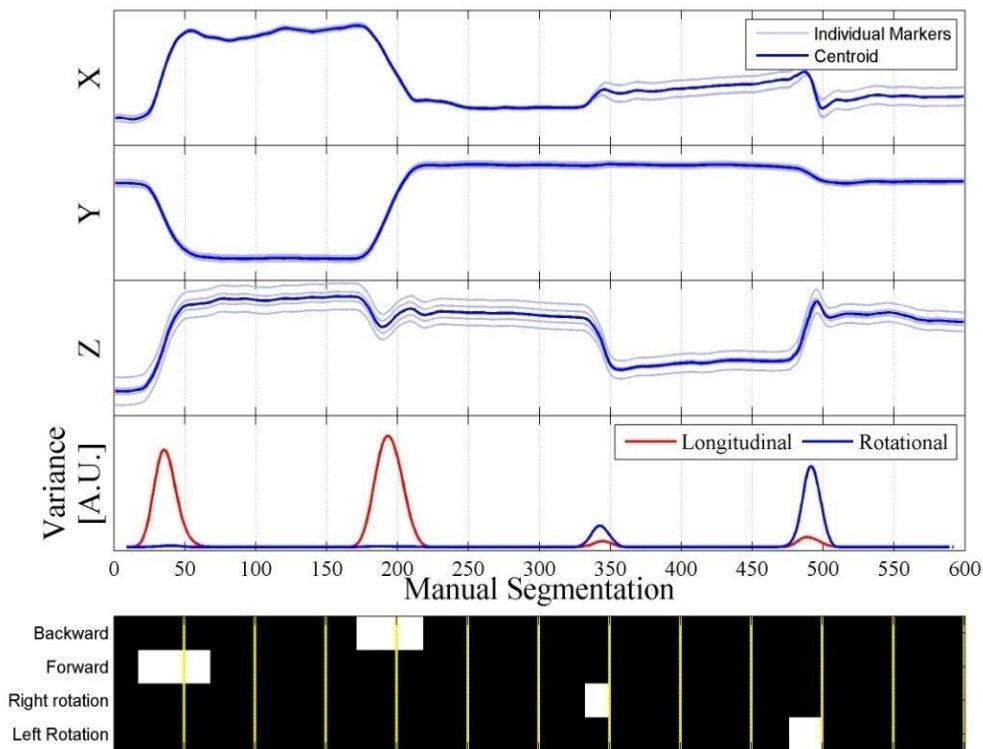


Figure 3.13; A series of the four gestures recorded from the wrist as recorded in terms of the displacement of the markers over time and the binary representation of each of these gestures as they occurred.

In the initial circumstance, the duration of each event was calculated and recorded for each subject and each target. This was represented in binary form with all movements depicted in white with no movement in black. The position marker representing the neutral position of the wrist during rotation was also recorded in white although strictly speaking does not represent a movement event.

Patterns which may indicate effective navigation or indeed difficulties with target navigation were explored. Three patterns were evident from this which required further examination (Figure 3.14). These patterns were felt could be representative of different levels of how the subject coped with the task. The first; a distinct and deliberate movement, the second; a chequer board appearance of repeated opposite movements indicating that some problem in achieving the task exists but the movements can still be considered definite and deliberate, and the third; an accentuated version of this with an almost slatted appearance reflecting rapid repetitive movements which could be considered as potentially irrational movements. In this latter case the movements are sharp and erratic often with repetitive rotations of the wrist across the neutral plane which may suggest the subject is disorientated or being challenged by

the simulator as the movements are not precise or deliberate and could even be considered unsafe.

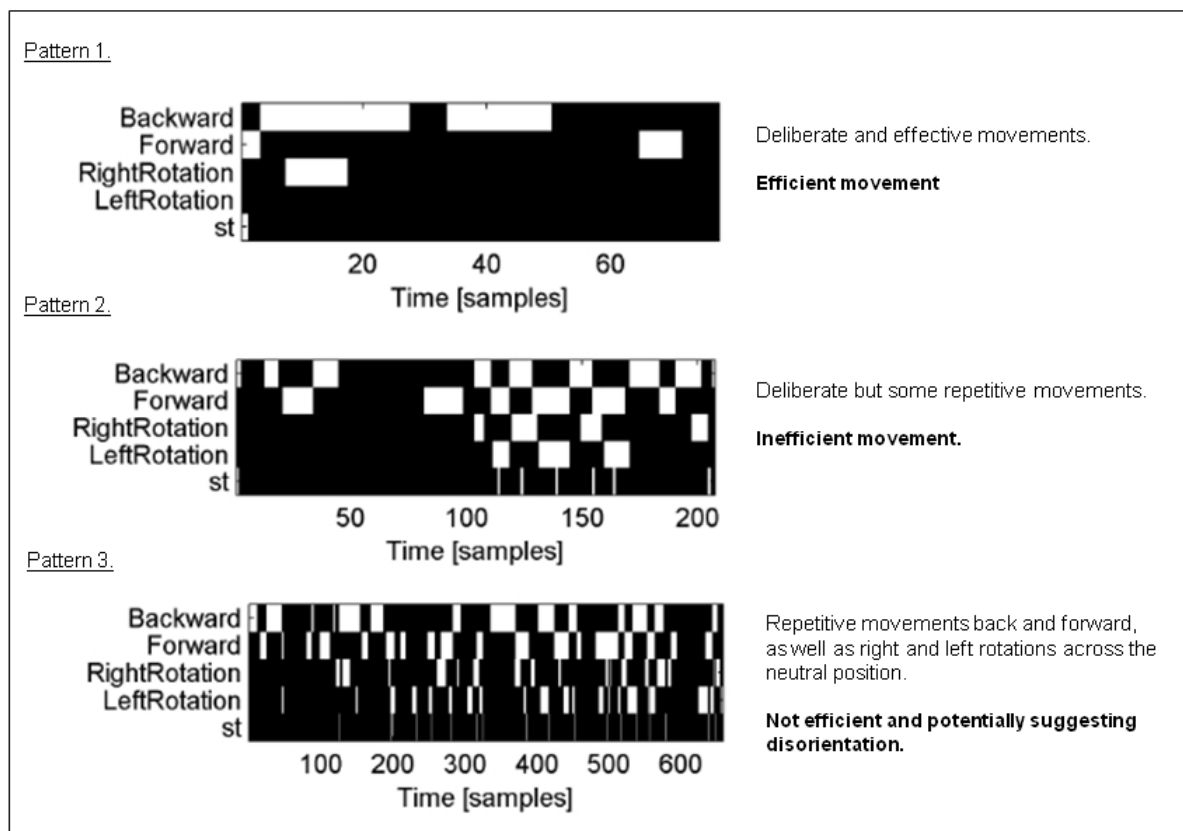


Figure 3.14; Binary patterns derived from the manually recorded events from the wrist. Each motion is recorded in white and a static period in black. The relevant movement is recorded alongside its label. (st – straight – this is an event which determines whether the endoscope is orientated)

Similar patterns can be seen during other target navigation sequences. When using these patterns the examination of a known simple navigation task (target destination 6) and challenging one (target destination 8) are compared the patterns are evidently more visible (Figure 3.15 and 3.16 respectively). It is evident that in subjects 2, 7 and 8, the target 8 was not in the end successfully reached.

It may be considered that Patterns 2 and 3 are indeed the same in terms of movement behaviour but due to the time distortion through the image scaling different patterns are recognised. To some extent this may be true, but the repetitive forward - back or right rotation - left rotation across the neutral point is indicative of disorientation. Perhaps it may be assumed to be in an attempt to find a recognised cue which those showing pattern 2 signs were able to find and those demonstrating pattern 3 not necessarily.

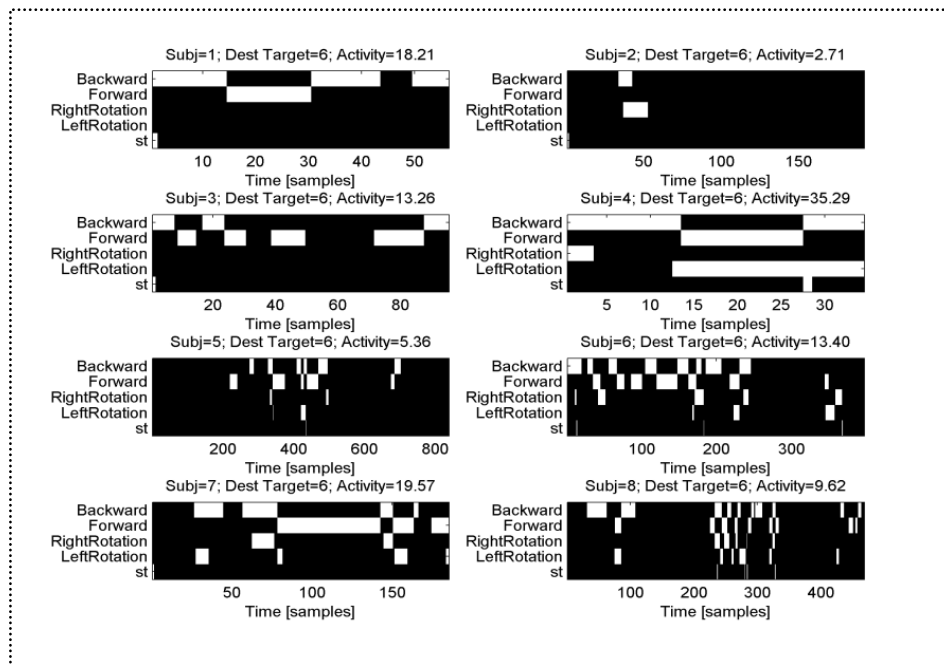


Figure 3.15; Navigation to Target 6 - a relatively simple maneuver - predominant patterns 1 and 2 some element of pattern 3 recognized in Subject 8.

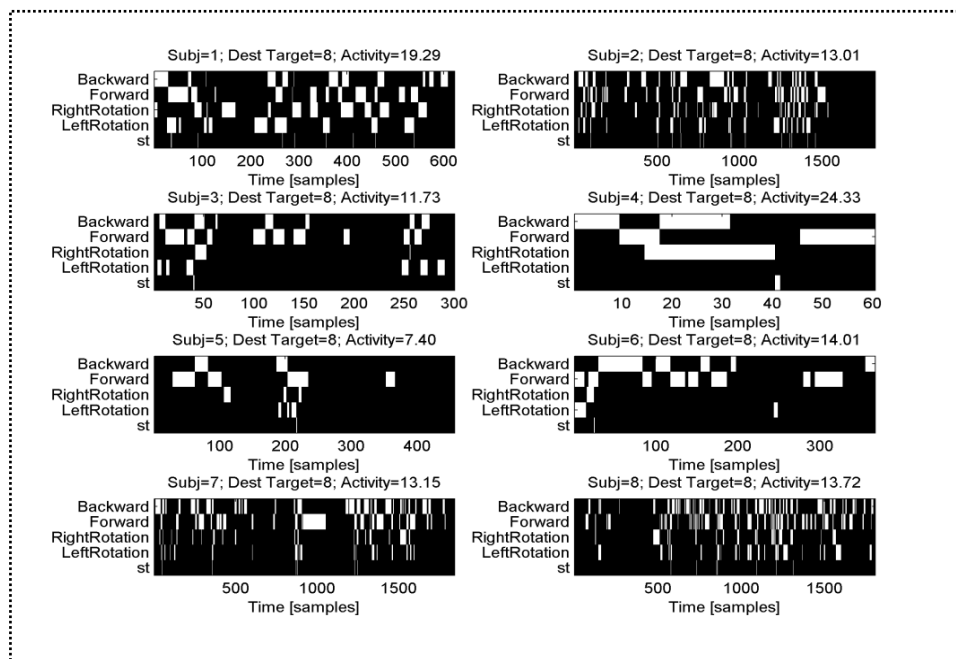


Figure 3.16; Destination Target 8; a more challenging maneuver - predominantly patterns 2 and 3.

However, there are times when pattern 3 can be recognised in the middle of what may be considered a pattern 2 sequence - subject 8 destination target 6 above (highlighted). In this case there may have been a brief period of disorientation during which this behaviour was performed before reorientation occurred and the target successfully met. Whether the patterns

are significant in terms of recognising inefficiencies in movements, further investigation and indeed validation needs to be performed. Further studies need to focus not only on validating these patterns as suggested but taking the issue of the time scaling into consideration and ensuring that the patterns seen are not just an effect of this.

3.3.4. Validation of the Defined Patterns as an Assessment of the Level of Endoscopic Experience Required to Navigate within a Spatial Environment.

The aim was to explore the patterns recognised in the preliminary work to determine whether a quantitative skill assessment tool could be derived which could also be used to estimate the level of the skill required to perform flexible endoscopic navigation within the spatial environment.

The task and setup was as has been previously described. Each subject was required to meet each individual target sequentially (*Figure 3.17*). A target was considered missed if either the subject passed on the attempt or a period of sixty seconds from the previous target had elapsed, at which time the subject was asked to move on. The number of targets met and time taken to complete the task were also measured.

3.3.4.1. Data processing

The data was processed as described above. The binary timelines were subsequently fragmented into 10 smaller frames as determined by the time when each target was either met or passed. Each separate frame was then scaled to a common size using nearest neighbour interpolation, a rescaling technique which maintains the relationship of the movements within the time frame irrespective of the time taken to reach each target by each subject while still yielding a binary output. With each subject, a total of 10 binary coded motion pattern sequences were made available for review and assessment.

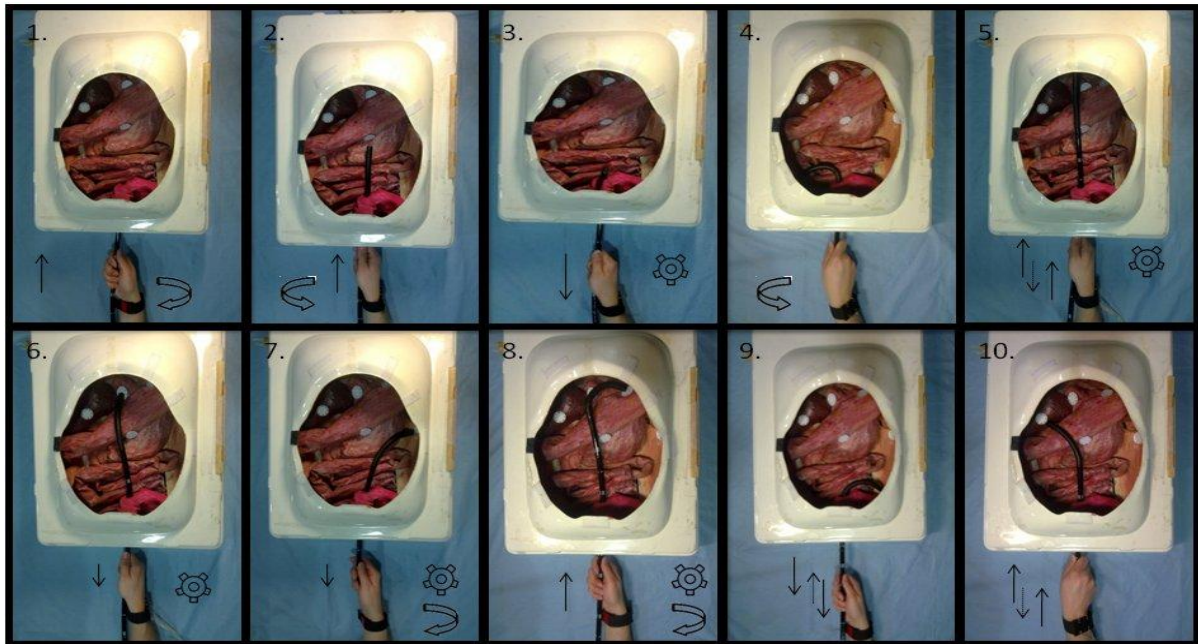


Figure 3.17; The target course presented in terms of the movements at the wrist required to reach each of the targets. The movements presented are not the sole method of endoscope navigation through the task but offers an optimum comparison.

Key:

Small image of a control wheel - Indicates control wheel adjustment required.

Circumferential arrow next to the endoscope - Indicates a rotation of wrist.

Solid arrows indicate linear directional movement with dashed arrows indicating movement at the wrist but with no contact of the endoscope.

The rectum and position of the first endoluminal target is indicated by the solid black arrow.

The frames from the task were isolated and subsequently presented to three blinded independent assessors (A, B and C) who were asked to score each one according to three subsequently defined patterns. Each assessor was given an example of each of the patterns for guidance (*Figure 3.18*). The assessors were clinicians each with *in-vivo* porcine NOTES experience. The time axes from all the binary frames were hidden before being randomly shuffled and presented to the assessors. Scores for each subject were then summated across the 10 target course and displayed alongside endoscopic experience (*Figure 3.19*).

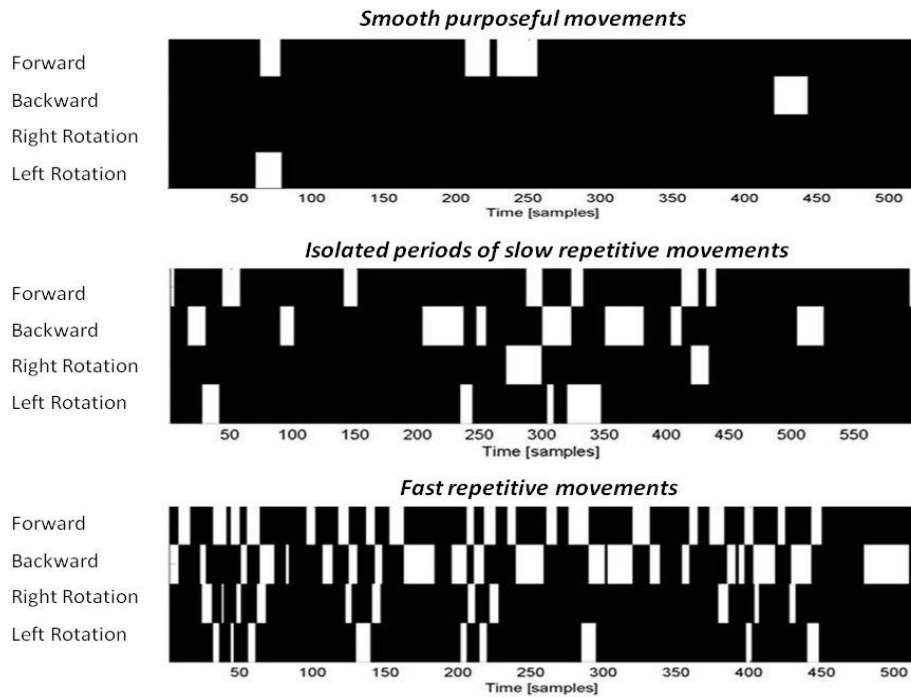


Figure 3.18; A further example of each of the three recognised binary patterns which represent the smoothness of endoscope control during endoscope navigation. Note the differences are independent of time.

3.3.4.2. Statistical analysis

The scores for each behavioural frame were collated for each subject and a total score assigned. An inter-rater reliability analysis using the kappa statistic was performed to determine consistency among the raters and Cronbach's alpha used to assess the internal consistency between all the outcome scores. These techniques determine the strength of this method as a viable assessment system.

When comparing measured outcomes between the subjects, the data, being non-parametric, was analysed using the Mann-Whitney-U test where significance was considered as $p < 0.001$. Spearman's rank was used to determine the correlation between the assessment scores and endoscopic experience as a method of validating the patterns as a potential assessment tool.

3.3.4.2. Assessment Results

14 subjects, which included the data recorded from the initial 8 preliminary subjects, navigated the endoscope across 10 targets which including 8 clinicians with variable

experience in endoscopy, of which 5 were gastroenterologists and 3 surgeons with endoscopic experience ranging from a total of 10 to 20,000 as well as 6 subjects with no endoscopic experience. As a result 140 binary coded frames delineating each subject's pattern of wrist motion from one target to the next was presented for evaluation.

When the task binary codes were visually inspected, a clear differentiation in the pattern of movement was apparent across all subjects and for each target. Movements which were smooth and purposeful were evident particularly when navigation was relatively simple independent of time. Conversely, instances in which the subject appeared lost or challenged yielded sequences of multiple repetitive movements which could be interpreted as random, unpredictable or even potentially unsafe if translated into the clinical environment. In view of these evident patterns, a score of 1 to 3 was assigned to each pattern with 3 representing the more purposeful manoeuvre pattern (*Figure 3.19*).

Scores were compared between each of the manual assessors using inter-rater reliability with the kappa statistic function. The reliability value in scoring between assessors A and B was 0.751 $p < 0.001$ 95% (0.659 - 0.843), between A and C; 0.722 $p < 0.001$ 95% (0.626 - 0.818) and between B and C; 0.637 $p < 0.001$ 95% (0.529 - 0.745). The internal consistency between all variables using Chronbach's alpha function was 0.948 ($p < 0.001$) (*Figure 3.20*).

The scores were then adjusted to take into account of any targets that were missed. The assigned scores for those targets missed were subtracted from the total score for that subject such that a score of 0 was assigned to any frame that resulted in a missed target. This generated an overall performance score. A significant correlation of this score with endoscopic experience was found 0.874 ($p < 0.001$), although interpretation should account for the heterogeneity of experience amongst the endoscopists and the small study size. The overall scores for each subject together with the other measured outcome variables; time and endoscopic experience and their effect on the overall rank order of the subjects in terms of a performance metric was evaluated (*Tables 3.6 and 3.7*).

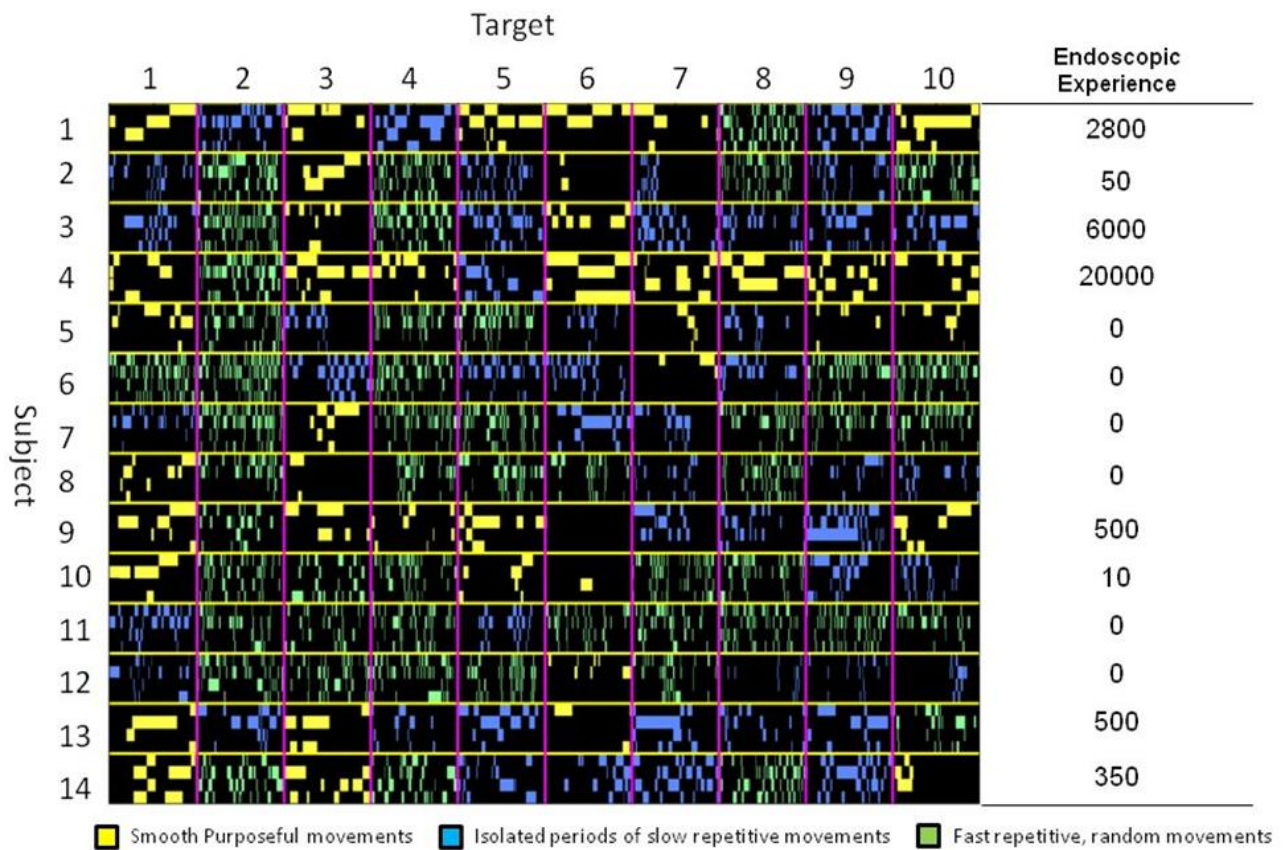


Figure 3.19; The binary frames for each of the 14 subjects across all the targets. The individual frames have been colour coded determined by the median score assigned by the assessors. The relevant endoscopic experience of each of the subjects is included for comparison.

Time to complete the navigation task ranged from 61.5 to 422.6 seconds with the mean for the clinicians being 128.7s (± 76.9) and novices 286.6s (± 86.6) ($p=0.014$), whilst comparing the total adjusted score for each subject, mean for novices 16 (± 3) and clinicians 22 (± 7), a significant difference between the groups was evident ($p=0.006$).

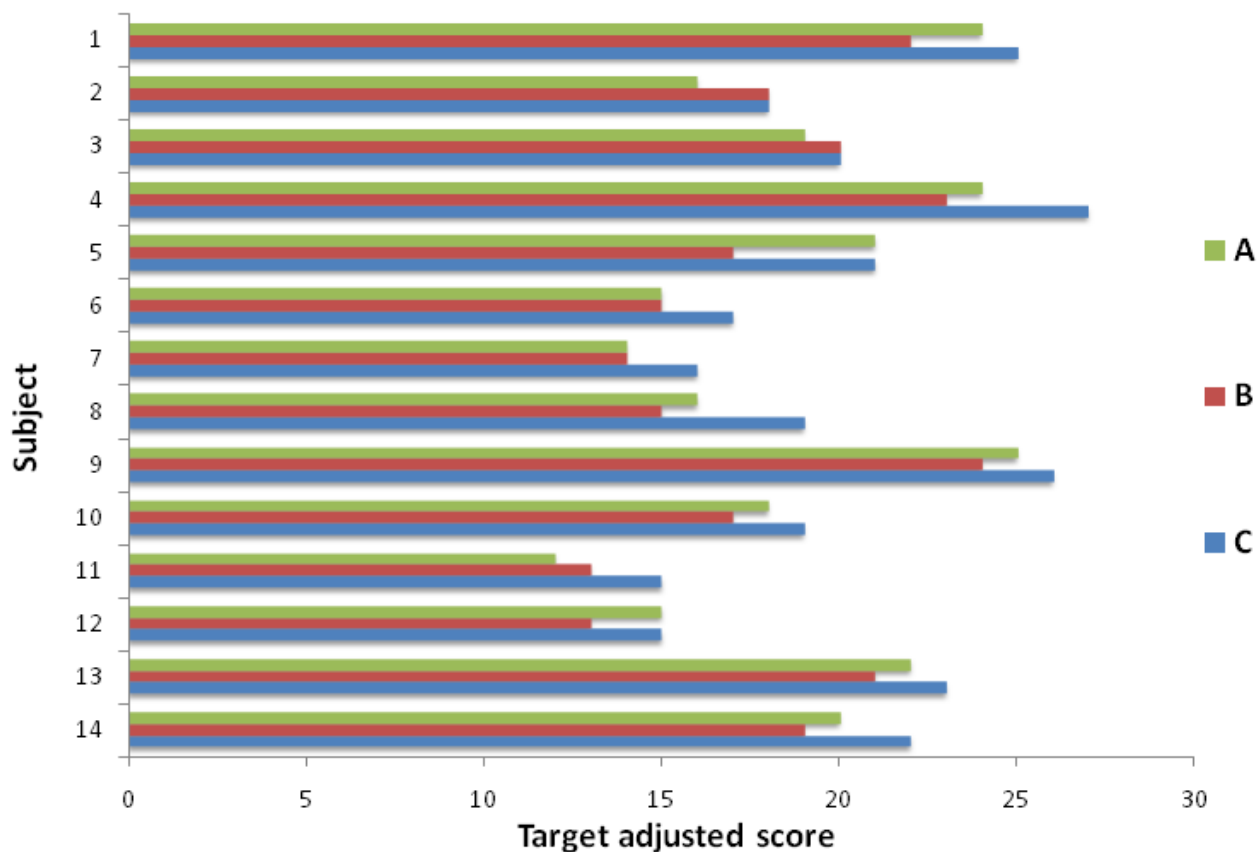


Figure 3.20; A comparison of the adjusted scores as assigned by each of the assessors (A, B and C) for each subject.

Table 3.6. Summary of outcomes from each of the subjects.

Subject	Endoscopy experience (number of endoscopies performed)	Time to complete task (seconds)	Score adjusted for missed targets
1	2800	66.75	24
2	50	210.77	17
3	6000	120.36	20
4	20000	61.45	24
5	0	185.73	17
6	0	208.08	13
7	0	270.5	11
8	0	298.02	13
9	500	100.3	23
10	10	280.35	11
11	0	334.86	9
12	0	422.64	8
13	500	85.9	19
14	350	103.9	19

Table 3.7; The ranking as determined by the various measurable outcomes; time, raw score and target adjusted score compared to the numbers of endoscopies (Endoscopy) each subject has previously performed.

Ranking	Time	Endoscopy	Score	Endoscopy	Adjusted Score	Endoscopy
1	61.45	20000	25	500	24	2800
2	66.75	2800	24	2800	24	20000
3	85.9	500	24	20000	23	500
4	100.3	500	23	500	20	6000
5	103.9	350	21	0	19	500
6	120.36	6000	20	6000	19	350
7	185.73	0	20	350	17	0
8	208.08	0	19	10	17	50
9	210.77	50	18	50	13	0
10	270.5	0	17	0	13	0
11	280.35	10	16	0	11	10
12	298.02	0	16	0	11	0
13	334.86	0	15	0	9	0
14	422.64	0	12	0	8	0

3.3.5. Automating the Analysis Process

To enable the quantitative analysis to be both viable and usable within the clinical setting, the requirement for human involvement needs to be removed in an attempt to reduce both the time to perform the analysis and any potential bias. Existing machine learning techniques and pattern recognition software have been successfully integrated to develop a unique fully automated system to evaluate quality of endoscopic torque control based on the demonstrated results.

Automation of the assessment system is achieved in two stages. First, a template matching algorithm temporally segments the optical stream and derives a binary texture, similar to the ones evaluated by the scorers. Then a neural network based classifier assesses the manoeuvre skills. A sliding window is shifted along the optical tracking multidimensional signal. The windowed sequence is compared against predefined sequence templates recognising each of the *mean* wrist *gestures* using a multidimensional constrained Dynamic Time Warping (MD-cDTW) metric. Given two time series S_1 and S_2 the recursive expression of the DTW distance is given by Equation 1.

Equation 1;

$$\begin{aligned}
DTW(F, F) &= 0; \\
DTW(S_1, F) &= DTW(F, S_2) = \infty; \\
DTW(S_1, S_2) &= d_{base}(head(S_1), head(S_2)) \\
&\quad + \begin{cases} DTW(S_1, tail(S_2)) \\ DTW(tail(S_1), S_2) \\ DTW(tail(S_1), tail(S_2)) \end{cases}
\end{aligned}$$

Where F represents the empty sequence, $head(\cdot)$ and $tail(\cdot)$ indicate the first and all but the first samples of the sequence respectively and d_{base} is an underlying base distance, which in this case was the cosine correlation distance. Pre-defined wrist gestures templates were obtained by averaging manually segmented gestures sequences stretched to a median length in samples. The labelled time series is represented as a binary texture and five run-length features extracted. The feature vector is input to a neural network classifier trained with mode scores from experts. The first stage yielded segmentation accuracy of 81.66% for longitudinal and 90.28% for rotational gestures. Manoeuvre recognition reached 93.6% success rate after ruling out over fitting.

3.4. Conclusion

The results suggest that the pattern of movements extrapolated from the wrist could potentially be used as a method of assessing endoscope torque control during a transluminal navigation task. More subjects are required to fully ascertain the strength of this as an assessment tool. However, the reliability scores suggest that the method has substantial internal consistency, demonstrating that a clear visually discernible pattern of behaviour can be differentiated between skilled and unskilled endoscopists such that the assessors were able to successfully and reliably differentiate. The individual scores and their correlation with endoscopic experience suggest that the use of this tool as a quantitative measure of endoscopic navigation skill within this environment is feasible. Wider applications in terms of endoscopic NOTES training, future NOTES endoscopic instrument evaluation and the potential for determining unsafe manoeuvres needs to be evaluated further with a broader and more substantial endoscopic skill range to fully elicit the benefits of the method as an effective quantitative assessment tool for endoscopic control.

The outcomes demonstrate that to navigate the flexible endoscope within a spatial environment effectively, requires a significant level of flexible endoscopic experience. At least 500 previous clinical investigative experiences with the flexible endoscope within the endoluminal setting appears to be suggestive from this study, although only a limited graduation of endoscopic experience was evaluated. This is a very limiting factor to the whole flexible access approach. This level of experience is only found in only a small proportion of surgeons; a level of experience few surgeons may meet which may not be enough to bring the technique to the forefront. This study highlights the very clear need for a more controllable device, one that is flexible yet stable and one which has a shorter learning curve.

However, in the short term the technique defined here could be used for performance evaluation. One of the most significant challenges currently facing the wider adoption of Flexible Access Surgery is the mastering of the endoscope within the transluminal environment. As noted, this can be achieved through re-designing elements of the endoscope and its controls but in the short term the primary aim should be on developing a suitable training program with particular emphasis on endoscope control. Training aids and assessment methods are currently only in developmental stages but it will be through these research streams that the continual expansion of the technique will be assured (101).

The introduction of a simplified method of assessing endoscopic skill as part of the training program will be essential however qualitative assessment methods for endoscopy are limited even within the endoluminal specialty. Methods have previously been explored in an attempt to quantitatively measure endoscopic skill. One such approach used feature tracking of images taken from the endoscope's camera during an endoluminal procedure (103). This enabled endoscope movements during the task to be tracked and extrapolated to determining the quality of endoscope control from the recorded footage

The scoring of the direct interaction of the endoscopist with the instrument exposes a novel approach for quantitatively evaluating endoscopic control during a transluminal procedure. However, the approach could also be used to quantify the ergonomics of the instrument in terms of controllability and usability. With novel surgical endoscopes entering the market place it is essential that a method of quantitatively evaluating their usability is available. This

method offers an objective non-biased evaluation of any novel endoscope designed for extraluminal navigation and enables a direct comparison to be made to the current form.

The time taken to complete the task evidently affected the witnessed patterns of movement and therefore the assigned score. Of course, it is clear that over a longer time frame the number of wrist movements will always be greater than over a shorter time frame and this has been a problem for all manner of research themes exploring time and motion analysis in the past (104). However, a measure of the quality of a procedure should include not only the time taken to complete the task but also the efficiency. A slow procedure, demonstrating a smooth and purposeful behaviour to reach the target must be considered more skilful than the same task being completed within the same time frame but performed with movements that occur faster, which are repetitive in nature and appear more random or unpredictable. The temporal normalization of the binary frames is an attempt to compensate for this.

One limitation to the current method is the lack of deriving the extent of movement of the control wheels during the navigational task. Large periods of time reflecting no movement at the wrist were noted in a number of the patterns. These periods may in proportion indicate periods when the subject was holding the endoscope still and manipulating the control wheels alone to visualise the target. Exploring the radial displacement of each of the control wheels through the use of attached optical tracking markers may offer an insight into whether this is the case and how important these manipulations are in the transluminal navigation over the endoluminal.

This study was conducted within a validated box simulator. The small study size, particularly the number of endoscopists involved in addition to the small number of assessors limits the conclusions that can be drawn from such a study in terms of its suitability as a measure of endoscope skill. However, it highlights a quantitative approach to endoscope control, currently lacking in endoscopy. This method has been demonstrated to be feasible within this setting and encourages a larger more robust evaluation.

Chapter 4

Clinical evaluation of Flexible Access Surgery

Hypothesis: Navigation and Instrumentation are progressive limitations of the technique.

4.1. Introduction

Flexible access surgery using the flexible endoscope aims to expose and push the envelope for new advances in surgical application and surgical technology. The ability to undertake any surgical procedure from any incision site may be considered farcical or ill minded given the current trend in surgical thinking, particularly when considering such bizarre techniques as the flexible access cholecystectomy via the axilla; as had been indicated by the questionnaire from the general public presented in the previous chapter. However, the acceptance of such an approach may be more patient driven than we anticipate particularly in the current body conscious times we live in. This drive will ultimately force the development and design of innovative technology that will enable this technique to become a part of clinical practice or at least enable more techniques along similar lines to develop as a result. Instruments, capable of being driven beneath the skin to the appropriate operative site, drop into the desired cavity space and perform the necessary surgical procedure may seem far-fetched but it is not such a great leap from where we are in current times. We don't need to look too far to see this potential technology fast developing and indeed evolving in fields such as interventional radiology and interventional endoscopy. Although with the current innovations within these fields, the potential of what can be therapeutically achieved is relatively simple, however if a surgical tool was placed at the end of either, that potential would exponentially increase and expose a whole new area of surgical research. Perhaps such procedures as the endovascular mitral valve repair from a radial artery puncture or the full thickness resection of T1 and T2 colonic tumours endoscopically with an exploration through the defect to examine the sentinel mesenteric lymph nodes before closure of the transluminal defect could be considered. This later technique has already been explored in the animal model with some success (105). What challenges are required to be overcome to enable these techniques, perhaps leaving the endovascular consideration aside, to expose them for the real potential they hold?

4.2. Defining the Challenges through Pre-clinical and Clinical trials

This study aimed to objectively define the most significant challenges associated with the use of the endoscope for flexible access surgery and determine the most important areas for further analysis. The study also aimed to explore some potential applications for the use of the flexible endoscope under the bracket of flexible access surgery.

Live porcine, human cadaveric as well as human clinical trials were undertaken to explore the potential applications and through them, the potential challenges affecting flexible access surgery.

4.2.1. *In-vivo* Porcine Trials; The Transrectal Retroperitoneoscopy and Para-aortic Lymph Node Biopsy.

The ability to access the retroperitoneum without the transabdominal approach particularly for potential surgical targets as localised kidney biopsy under vision, total or partial nephrectomy, adrenalectomy or para-aortic lymph node sampling for gynaecological or germ cell tumours, is achievable. Indeed the transvaginal route for retroperitoneal access has already been successfully described for a total nephrectomy in a clinical setting using rigid instruments. The approach in this case was simply transferring the single port concept to the vagina and performing a SILS nephrectomy, with all the ergonomic challenges. In this setting the approach to the retroperitoneum was via a peritoneal route (106). However, an alternative route which has been described in the pig model is the transanal route.

This approach was replicated within our study to explore the potential of the transanal mesorectal approach to the retroperitoneal space and the potential clinical applications which it may offer. Under ethical and approved home office license, a transanal flexible access approach to the retroperitoneum was undertaken through the wall of the rectum and into the mesorectal plane in a live porcine model.

A posterior lateral incision was made under direct vision in the rectum just above the border of the anal canal – human equivalent to the dentate line. Access was obtained using a custom made trocar with a length of 40cm attached to a 15mm bariatric trocar which was inserted

under vision through the mesorectum to the retroperitoneal space. Insufflation through the endoscope enabled the avascular tissue within the retroperitoneal space to separate. The kidney, renal hilar including the vascular structures, were clearly visualised (*Figure 4.1*)

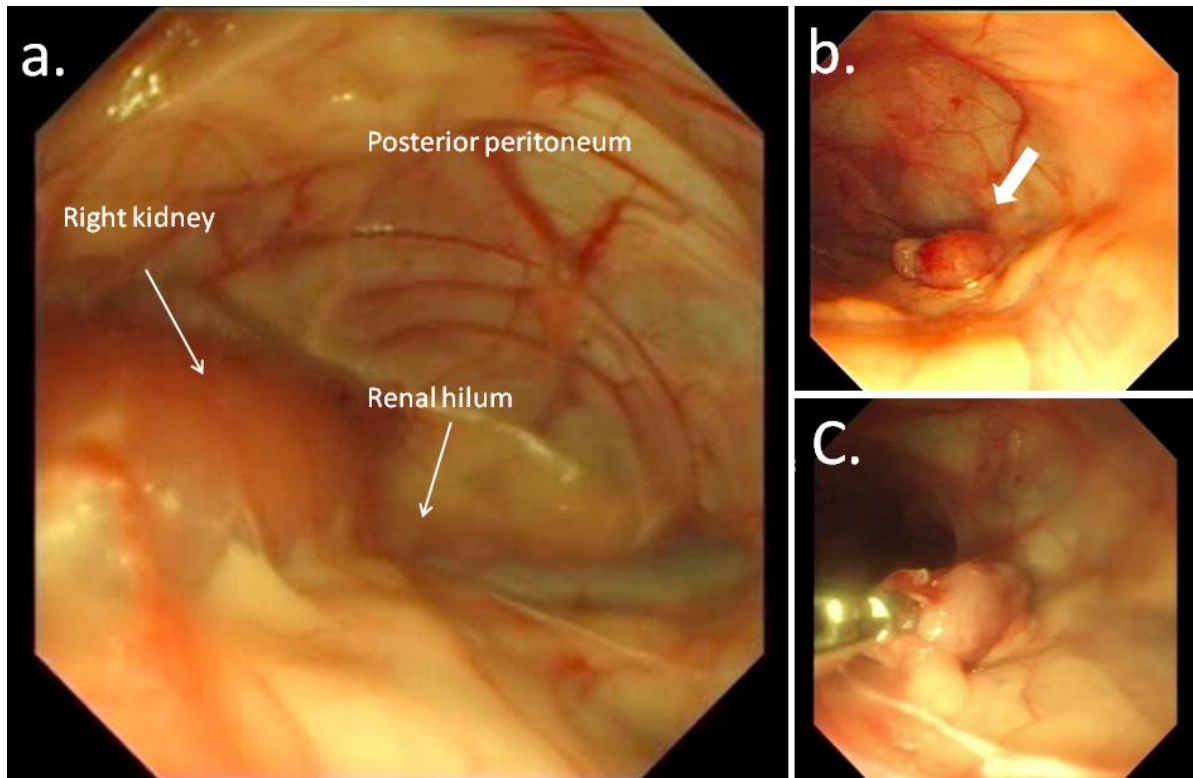


Figure 4.1; Flexible endoscopic image of the right retroperitoneal space (a) with the right kidney and hilum visible. A para-aortic lymph node noted (b) (white arrow) sampled using endoscopic biopsy graspers (c).

4.2.1.1. An objective determination of the challenges faced:

1. Flexible endoscopic navigation within a cavity space; difficulty in navigating to target site.
2. Parallel instrument presentation prevents any dissection from being undertaken. Simple biopsy grasping or tissue ablation possible but not controlled.
3. Unable to maintain a stable platform from which to base any intervention; even simple diagnostic intervention as endoscope would retract as graspers were presented to the tissue bed.
4. The range of instruments available for use with the flexible endoscope for dissection and safe clipping and ligation of structures.

5. Inability to provide enough force by the instruments for effective tissue dissection.

4.2.2. Exploring the Sub-Dermal Tissue Planes for Distant Flexible Access; a Pre-Clinical Human Cadaveric Trial.

Subcutaneous tunnelling is a technique which has been used extensively for many years within surgery and across a number of different specialties including vascular surgery for the placement of prosthetic grafts in patients with peripheral vascular disease and in cardiac surgery for minimally invasive long saphenous vein harvesting (107). More recently breast surgeons have begun to successfully harness these subcutaneous avascular planes to undertake breast augmentation via the umbilicus (108). The technique within this section explores the use of the flexible endoscope as a surgical platform, introduced into the body distant from the target organ and approached using the subcutaneous planes.

For all the cases described within this section the procedure followed the same steps. A supraumbilical incision was made with dissection continued to the pre-fascial plane. A long tapered introducer and hollow over-tube (*custom made in-house; Figure 4.2*) was introduced through this incision. The internal diameter of the tube is 13.5mm with an external diameter of 15mm. A 15mm bariatric trocar (Applied Medical, United States) was attached to the end of the tube and air sealed.

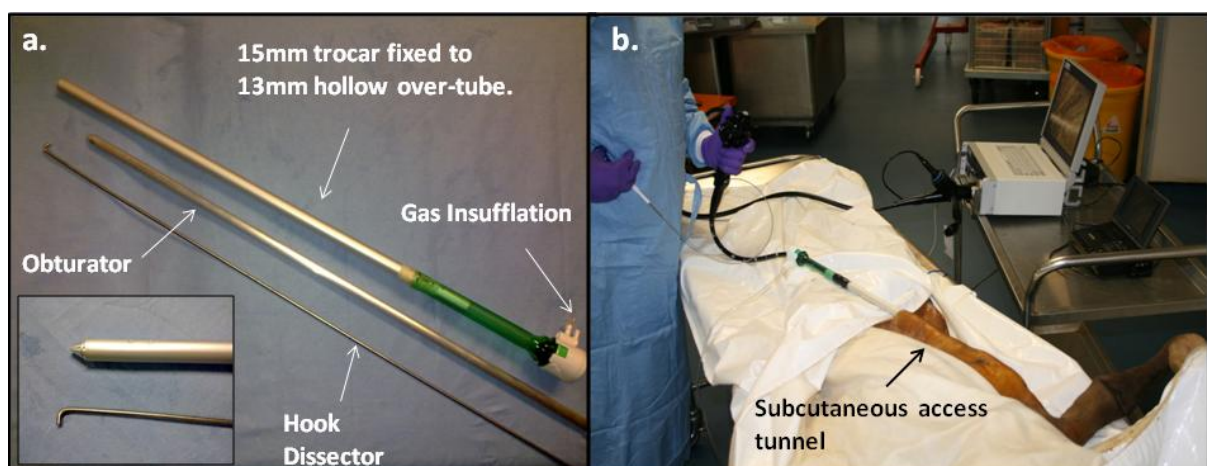


Figure 4.2; Images of the custom made tools used for the trials which included an introducer with 14mm diameter over-tube. A 15mm by 150mm trocar secured to the over-tube and a hockey-stick blunt dissector (a) and the external setup (b) . Note the Right arm of the cadaver is flexed and abducted at the shoulder during the initial trial for better access to the axilla (b).

Once in place, the flexible endoscope was introduced through the delivery tube to the region requiring dissection. For the series of trials described this included the submammary plane, which was subsequently opened using instruments passed through the biopsy channels of the flexible endoscope.

4.2.2.1. Transumbilical Level 1 -2 Axillary Lymph Node Dissection for Breast Cancer Treatment.

Method

Four axillary lymph node dissections were attempted in three soft preserve human female cadavers. Alcohol, phenol, glycerine soft preservation allows for greater tissue manipulation than formalin fixation though some colour differentiation of the tissues does tend to be lost and pliability is less compared to living tissue. One of the cadaver models had a breast cancer lesion for which she had undergone palliative treatment with no breast excision. However, unilateral axillary lymph node dissection had been performed. Within this trial setting bilateral axillary dissection was performed on this cadaver using the transumbilical approach both to explore the feasibility of the technique on the contralateral side and to explore whether the same technique could be used to approach an axilla when the associated breast has advanced cancer. In light of the previous axillary dissection on this axilla a complete level 1 and 2 axillary lymph node dissection was only performed on the remaining three axillae. Access followed that described for the Transumbilical Breast Augmentation (TUBA) technique (108) (*Figures 4.2*).

The introducer and overtube were used to create a subcutaneous tunnel to the sub-mammary space aiming for the lateral edge of the inferior mammary fold. Once at the fold, the introducer was removed and the trocar valve replaced. Controlled air insufflation through the tube exposed the sub-mammary space, aided initially by a long blunt dissector instrument (custom made *in-house*) which enabled a 12mm dual channel flexible endoscope (Karl Storz, Tuttlingen; *Germany*), to be inserted through the overtube and further dissect the space to expose the axillary borders.

Dissection with controlled air insufflation enhanced this avascular space which enabled further blunt dissection of the areolar tissue to be performed using the endoscope tip under vision. With the relative redundancy of the Pectoralis Major muscles and a more lateral angulation of the overtube, the inter-pectoral space can be found with relative ease. The primary anatomical landmark for the axilla with this approach was the lateral border of the Pectoralis Minor muscle (*Figure 4.3*).

With the arm abducted, dissection of the axilla was undertaken using existing flexible endoscopic instruments which included endoscopic graspers (Olympus Keymed, United Kingdom (UK)), electrocautery Insulated-Tip knife (Olympus Keymed, UK) and endoscopic diathermy scissors (LSVP medical supplies, United States (US)).

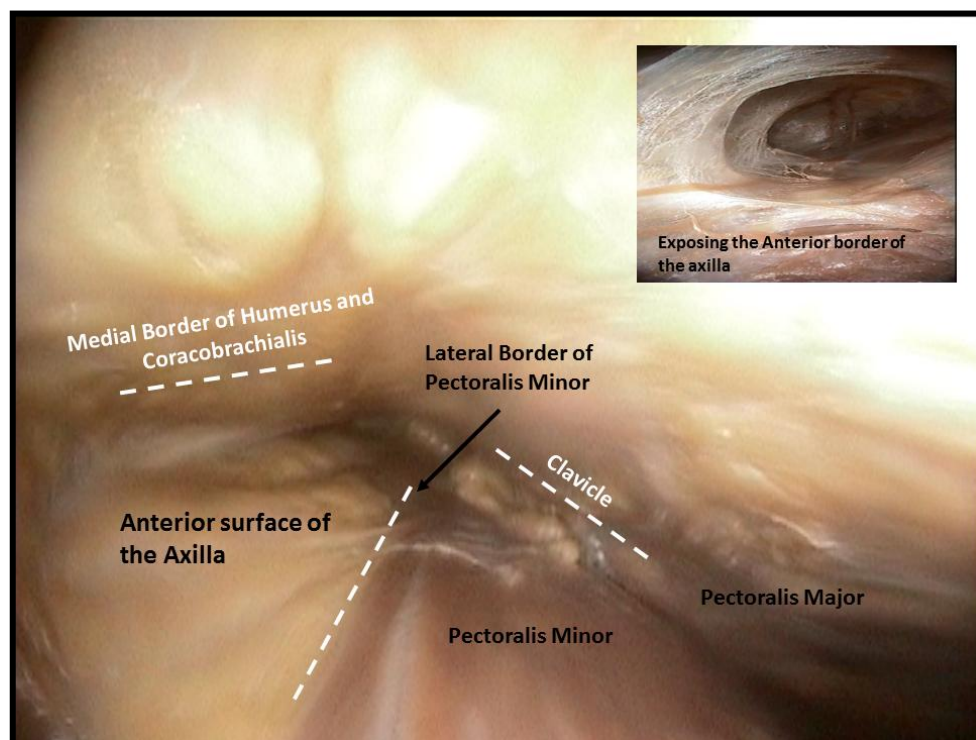


Figure 4.3: Images of the anterior border of the axilla as it appears once exposed by the endoscope. Inset; shows the images of the submammary space when initially viewed by the endoscope. Note the loose avascular tissue.

Using electrocautery, an incision was made down the lateral border of the Pectoralis Minor muscle keeping close to the muscle itself dividing a thin fascial layer overlying the anterior aspect of the axilla and attaching to the Pectoralis Minor muscle. Once divided the axillary fat is freed but remains attached to the chest wall and the focus can be turned to exposing the

axillary vein using cephalad directed dissection. Dissection was continued using a combination of blunt and sharp dissection. In all cases an anterior cephalic vein was noted before the axillary vessels became visible. These were followed medially under Pectoralis (Figure 4.4). Controlled air insufflation and blunt dissection exposed the sub-pectoral space enabling a Level 2 dissection to be completed using endoscopic graspers coupled with air insufflation and blunt dissection.

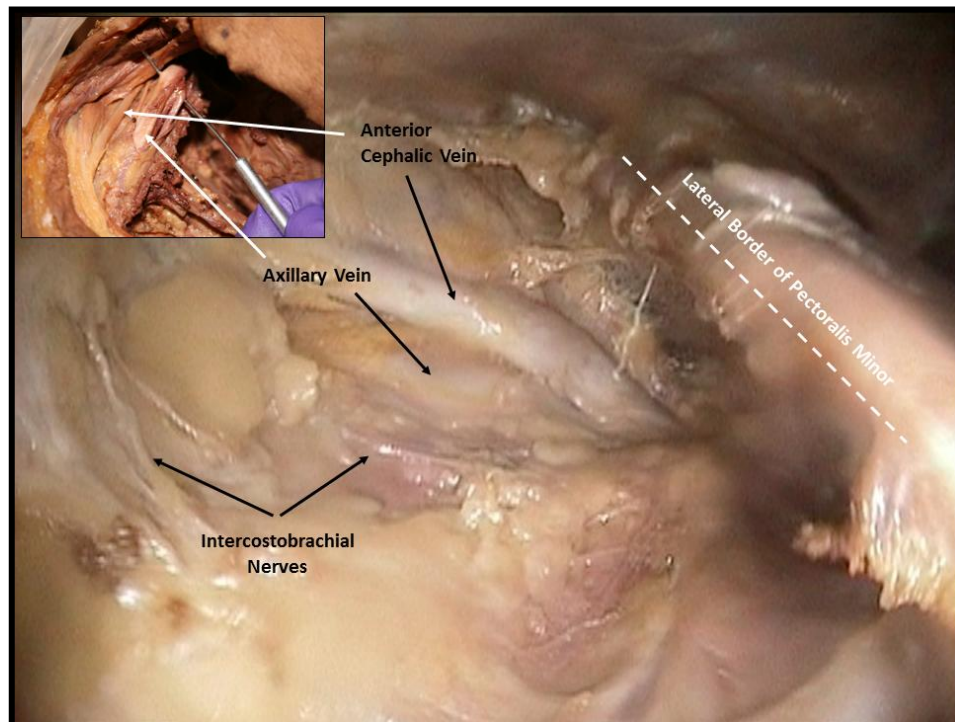


Figure 4.4: The internal anatomy of the axilla as viewed from the endoscope with the sub-pectoral space visible on the right. Inset shows the corresponding anatomy after completion of the surgery.

The posterior border of the fat was approached from the inferior angle of the axilla. Caudal extension of the incision along the lateral border of the Pectoralis Minor was required. Blunt dissection enabled this inferior aspect of the axilla to be teased away from the Latissimus Dorsi muscle at the posterior border. Electrocautery was not used until the Thoracodorsal pedicle could be positively identified. Once defined the lateral border and the attachment to the underlying subcutaneous fat of the skin was divided using diathermy scissors as far cranially as the axillary vein. The Intercostobrachial nerve, which crosses within the axillary fat was identified but in all cases was not spared. Division of the fat from the inferior border of the axillary vessels marked the completion of the excision. On the last two cases, a 2.3mm

mini-laparoscopic instrument (Stryker, USA) was inserted into the axilla via a needle incision on the upper lateral border of the Pectoralis Major muscle. The axillary fat was grasped and placed under tension to enable the final portion of the dissection to be completed more efficiently.

The specimen was removed en-bloc through the subcutaneous tunnel and exteriorised at the umbilical incision (*Figure 4.5*). Current endoscopic tissue retrieval techniques were trialled including a Dorma basket (Olympus Keymed, UK) but the size of the specimen far exceeded current basket sizes. The tunnel and axilla were re-examined for any remaining tissue before the overtube was removed and the wound closed. All specimens were sent for histopathological analysis to assess lymph node yield. In each case the axilla was opened and examined for neurovascular injury. Any injury or residual tissue left within the axilla was verified by a second examiner.

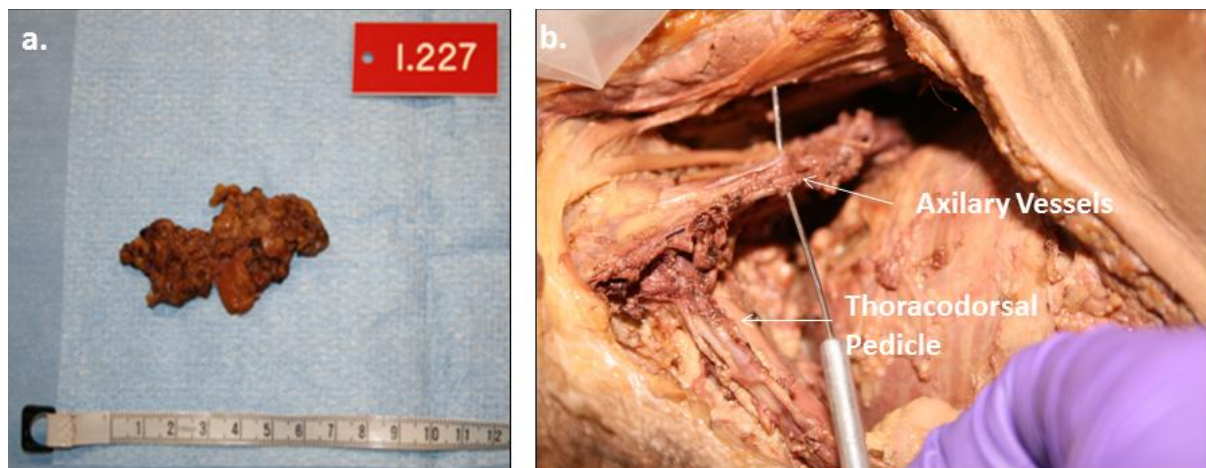


Figure 4.5: The axillary specimen excised from the cadaver (a) and the image of the axilla opened to expose the neurovascular bundles intact.

Patient motivation and acceptance

A questionnaire was created to assess whether such an approach would be acceptable within the general population when presented against the current conventional open and peri-areolar laparoscopic techniques. The level of complication risk that patients were willing to accept should they choose the transumbilical technique was also assessed through a series of questions which targeted their operative preference when presented with various statements of increasing risk severity for the techniques both in isolation and all together. Questions

included risks of infection from the bellybutton to the armpit, a risk of shoulder stiffness and sensory discomfort at or around the armpit as well as a hypothetical risk of cancer recurrence compared to other approaches. Since the complications of the technique can only be assumed, incremental risk stratification was adopted in the questionnaire to assess at which point a given population would be willing to accept the technique and at what point observers would revert to an alternative hypothetically safer technique. By this method the answers given would provide a level at which the technique has to reliably perform before it could be accepted by the general public.

The questionnaire was validated using three independent general and breast surgeons whose comments were incorporated into the questionnaire before further review and re-evaluation. The questionnaire was also trialled on 10 members of the general public, whose comments and suggestions were incorporated to ensure the language used was not technical and the instructions clear enough for the questions to be completed without assistance. The focus population for the questionnaire was women, although not exclusively, and from the age of 18 and upward. The general population was targeted with questionnaires left within the jury suite of a Crown Court as well as hairdressers and schools with verbal permission granted at all sites for the questionnaires to be left. Members of the public could pick up the questionnaire on their own volition. The questionnaire was anonymous but a request was made to initial and date the front page to confirm that the individual agreed to be involved in the survey. Internal validation of the questionnaire was undertaken with the addition of a duplex question presented in a different format to the original.

Questionnaires were excluded when either the subject had not initialled the agreement to participate on the front page or when answers to the internal validation question did not agree. The questionnaire presents the general public with three techniques to approach the axilla for axillary dissection. This was shown in the form of images of the scars which would be associated with the transumbilical, open and peri-areolar laparoscopic techniques.

Results

Questionnaire outcomes

127 questionnaires were returned, 32 were excluded, 8 of which were as a result of disagreement with the answers to the validation questions. 95 questionnaires were therefore

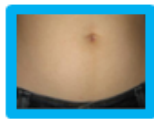
accepted for analysis which included 87 women and 8 men with a combined mean age of 41.6 (+/-12.3) years. Of the population surveyed, 3 women had previously been treated for breast cancer, 1 had required axillary surgery. 7 women had experienced some form of breast surgery for benign disease. Full demographics of the surveyed population are shown in *Table 4.1*. The survey was part of the same survey presented in chapter 2; hence the same population demographics.

When given no information regarding risk or complications relating to the three scar site options, 73% of the population group questioned would prefer the transumbilical approach over the transaxillary or peri-areolar techniques. When presented with a potential complication of a “treatable infection under the skin from the bellybutton to the armpit” for the transumbilical approach without any complications disclosed from the other techniques, 19% changed to prefer the transaxillary approach though 54% still maintained their preference for the transumbilical technique. Once again when this was presented in conjunction with complications associated with the other approaches; shoulder stiffness and wound discomfort, the preference for the technique increased to 82%. However, when the TU approach was presented with a potential risk of cancer recurrence, preference fell to 15% although when quantified as a risk of 1 in 500 for cancer recurrence and presented with a reduction in the risk of shoulder stiffness and wound discomfort, 20% preferred the transumbilical approach suggesting the improvement in shoulder stiffness and wound discomfort may influence their decision. When further quantified with an even higher cancer recurrence risk of 1%; 11% of the public still preferred the technique over the alternative open axillary approach which was presented with a theoretical no risk of cancer recurrence (Summarised in *Figure 4.6*). This suggests that cosmesis plays an extremely important role in any operative decision made for the subgroup evaluated in this survey.

Table 4.1: Demographics of the population who met the inclusion criteria for the questionnaire.

<i>Sex</i>		<i>Marital Status</i>	
Female	87	Married	52
Male	8	Single	32
		Divorced	4
		Widowed	1
		Not answered	6
<i>Age</i>		<i>Ethnicity</i>	
18-30	20	Caucasian	70
31-40	30	African	10
41-50	20	Asian	5
51-60	17	Oriental	3
61-80+	8	Middle Eastern	2
Mean Age	41.6	South American	1
		Not answered	4
<i>Surgical History</i>		<i>Religion</i>	
Previous Surgery	61	Christian	62
Previous Laparoscopy	17	No religion	24
Previous Endoscopy	20	Muslim	2
Previous Cancer	3	Budist	2
Previous Breast Cancer	3	Other	2
Previous Breast Benign	7	Sikh	1
Previous Axillary Surgery	1	Not Answered	2
<i>Education</i>			
Secondary School	11		
Sixth form college	12		
Undergraduate	28		
Postgraduate	42		
Not answered	2		

Techniques



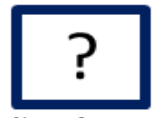
Bellybutton



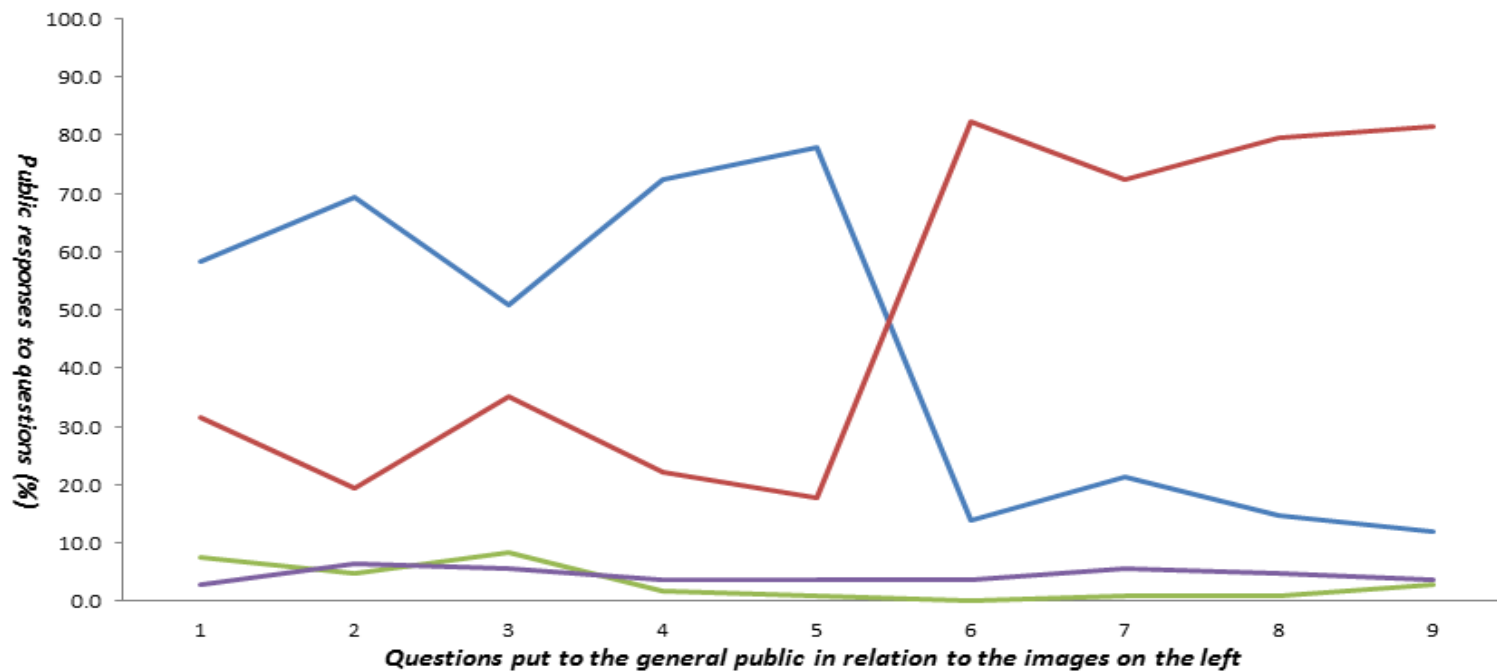
Armpit



Nipple



No preference



Prefix to questions... ➡

...Questions. ➡

The three techniques are equally safe and have a similar risk of cancer recurrence but...

If the three techniques are all equally safe but....

No information on techniques other than the images presented on the left.

The Armpit technique may cause shoulder stiffness and sensory discomfort at the wound site.

The Bellybutton technique may cause a treatable infection under the skin from the bellybutton to the armpit.

The Bellybutton technique may cause a treatable infection as in (3). The Armpit technique may cause shoulder stiffness and sensory discomfort at the wound site and a treatable infection in and around the wound. The Nipple technique may cause a treatable infection under the skin of the breast and shoulder stiffness and sensory discomfort.

The Bellybutton technique which may cause a treatable infection under the skin, reduces the risk of shoulder stiffness and sensory discomfort at the wound site; associated with both the Armpit and Nipple techniques.

The Bellybutton, Armpit and Nipple all may cause long term shoulder stiffness and sensory loss at the armpit. BUT in addition there is an increased risk of cancer recurrence with the Bellybutton and Nipple techniques.

The Bellybutton and Nipple techniques reduce the risk of shoulder stiffness and sensory discomfort (associated with the Armpit technique) with no risk of infection. BUT both have an increased risk (1 in 500 patients) of cancer recurrence.

Same question as (7) BUT both have an increased risk (1 in 300 patients) of cancer recurrence.

Same question as (7) BUT both have an increased risk (1 in 100 patients) of cancer recurrence.

Figure 4.6: Graphical representation of the outcomes from the questionnaire. The questions which were presented to the general public in the questionnaire are summarised below each of the respective responses.

Operative outcomes

Transumbilical levels 1 and 2 axillary dissection was successfully undertaken in three soft preserve human female cadavers. The transumbilical axillary approach conducted on the cadaver with a fixed breast lesion was successfully performed. The submammary space was opened using pulsed air insufflation and blunt dissection. The presence of the advanced breast lesion did not restrict access to the axilla, confirmed with the anatomical demonstration of the pectoralis minor muscle. However, scar tissue and distortion of the axillary anatomy restricted further endoscopic dissection and would suggest that the technique would not be suitable for recurrent axillary disease.

The contralateral axillary Level 1 and 2 dissection in the same cadaver and the other 2 cases was successfully performed. In the second cadaver, electrocautery was only intermittent felt to be due to the age and therefore decomposition of the cadaveric specimen which in turn reduced the electrical conductivity of the tissue. As such sharp dissection was used considerably lengthening the operative time for this procedure on this cadaver.

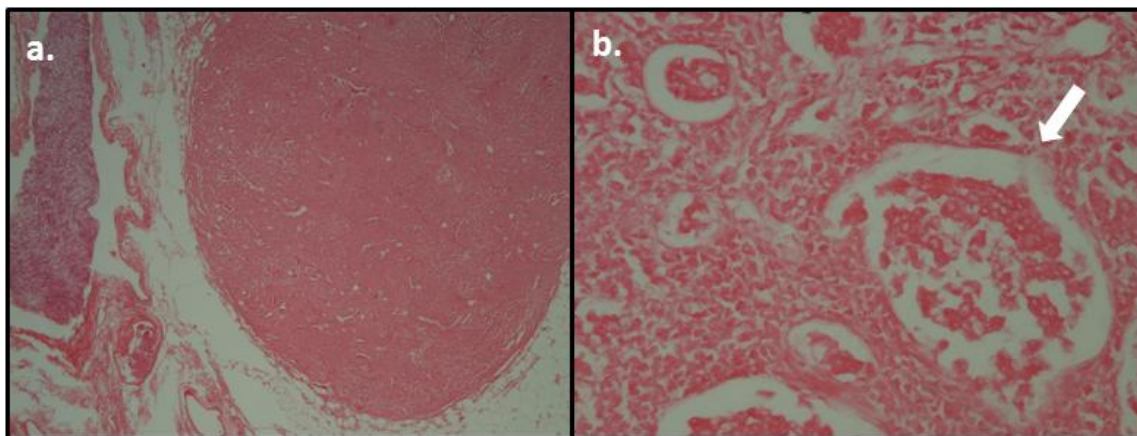


Figure 4.7: Low power histology of one of the excised lymph nodes (a). High power magnification demonstrates evidence of tumour deposits; the largest is arrowed (b).

Operative times for the endoscopic level 1 and 2 axillary dissection in each of the cadavers was 1080, 840 and 390 minutes (in sequential order) with a clear improvement in the times noted from the first to the last attempt. In each case, the whole of the specimen was put through for histological examination by a senior pathologist. Although, as expected, the

lymph nodes were autolytic they were clearly identifiable. Lymph node harvests were 12, 11 and 14 respectively. In the case where the specimen was extracted from the cadaver with a contralateral breast lesion, 4 lymph nodes were identified as being positive for cancer (Figures 4.7).

Open examination of the axillae revealed that in all three cases the intercostobrachial nerve was sacrificed, however, the axillary vessels, thoracodorsal pedicle and long thoracic nerves were all identified in each case as being undamaged.

4.2.2.2. Transumbilical Approach to the Thyroid in a Human Cadaveric Model; a Feasibility Study.

Flexible access surgery is not so much new by design but perhaps a new bracket to encompass an array of different approaches to the same surgical problem. When considering a gland like the thyroid for example numerous approaches to it have already been explored. These include not only the conventional open approach through a mini-neckline incision but also the transaxillary approach; currently favoured by robotic-assisted surgeons, the transoral approach through the floor of the mouth and the peri-areolar approach with the camera inserted through a peri-areolar incision. Already, the extent of approaches to the thyroid gland is high with the versatility perhaps only limited by the requirement of a straight shot from the incision to the gland.

In this human cadaveric trial the transumbilical subcutaneous approach to the thyroid gland was explored in a similar way to the axillary dissection above. The method and approach was similar other than one at the sub-mammary fold the flexible endoscope was inserted into the centre of the sub-mammary space and cranially toward the left clavicle.

Minimal electrocautery was required to reach the clavicle due to the avascular planes that were visible through the use of intermittent pulsed insufflations and the blunt dissection using the endoscope tip. Once the clavicle was reached the requirements for instrumentation became essential. The elevation of the subcutaneous tissue off the clavicle required a combination of intermittent electrocautery and blunt dissection. Once overcome, access to the anterior triangle of the neck was achieved. The access to the neck in this way had enabled the endoscope to approach the thyroid from below the sternothyroid and sternohyoid muscles.

The trachea was initially noted and the thyroid gland encompassing. The nerves were delineated and confirmatory biopsies were taken of the thyroid gland (*Figure 4.8*).

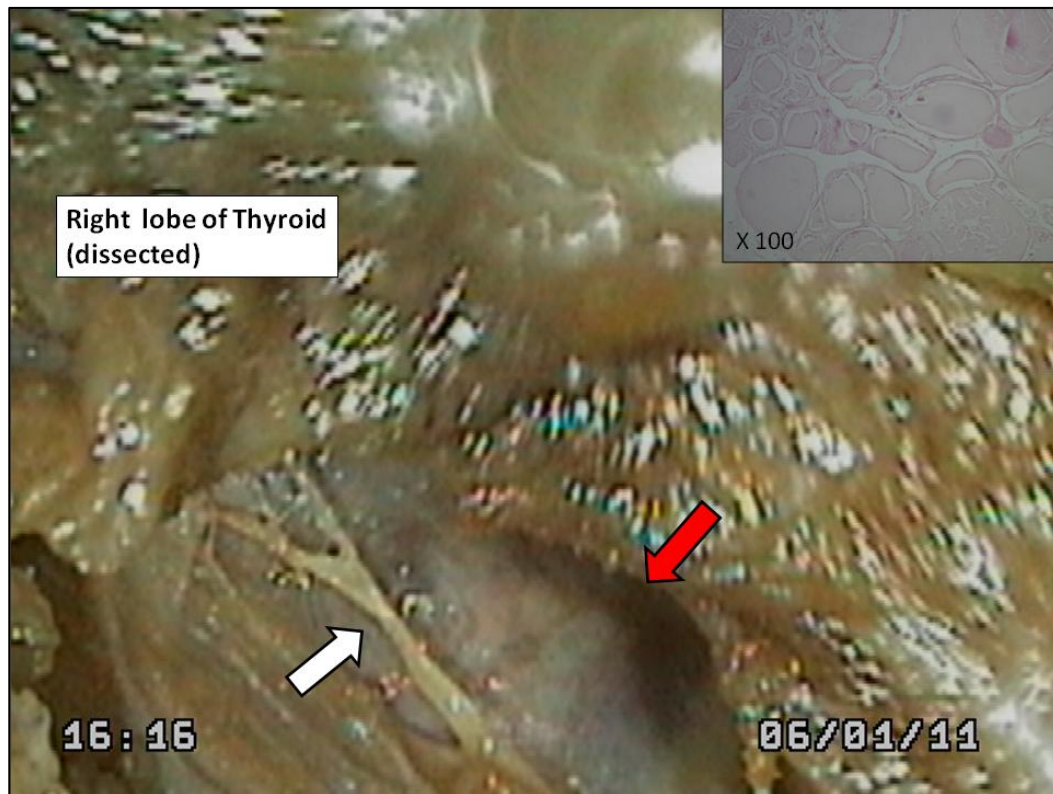


Figure 4.8; View from the flexible endoscope during the transumbilical approach to the thyroid demonstrating the trachea with its cartilaginous rings (red arrow) and the recurrent laryngeal nerve (white arrow) closely approximated. Histology X100 inset showing thyroid colloid cells.

4.2.2.3. Transumbilical Transthoracic Exploration in a Human Cadaveric Model.

This approach is perhaps an extreme example of the potential of the flexible access approach idea. This trial explored the potential of the flexible endoscope to access a body cavity from a distant site. In this case the right thoracic cavity was explored.

On this occasion the same approach was used as for the two previous applications. The flexible endoscope was directed subcutaneously to the fifth intercostal space on the anterior axillary line. At this point the ribs are slightly angulated inferiorly with the intercostal space presenting in-line with the endoscope. Access was made using an Insulated-Tip Endoscopic Knife to the intercostals muscles whilst within the subcutaneous plane. The access was created and the endoscope directed into the right thoracic cavity. Visual confirmation was

made of the visceral and parietal pleura (*Figure 4.9*) with identification of the pulmonary hilar. Pleural biopsies were taken for histopathological confirmation.

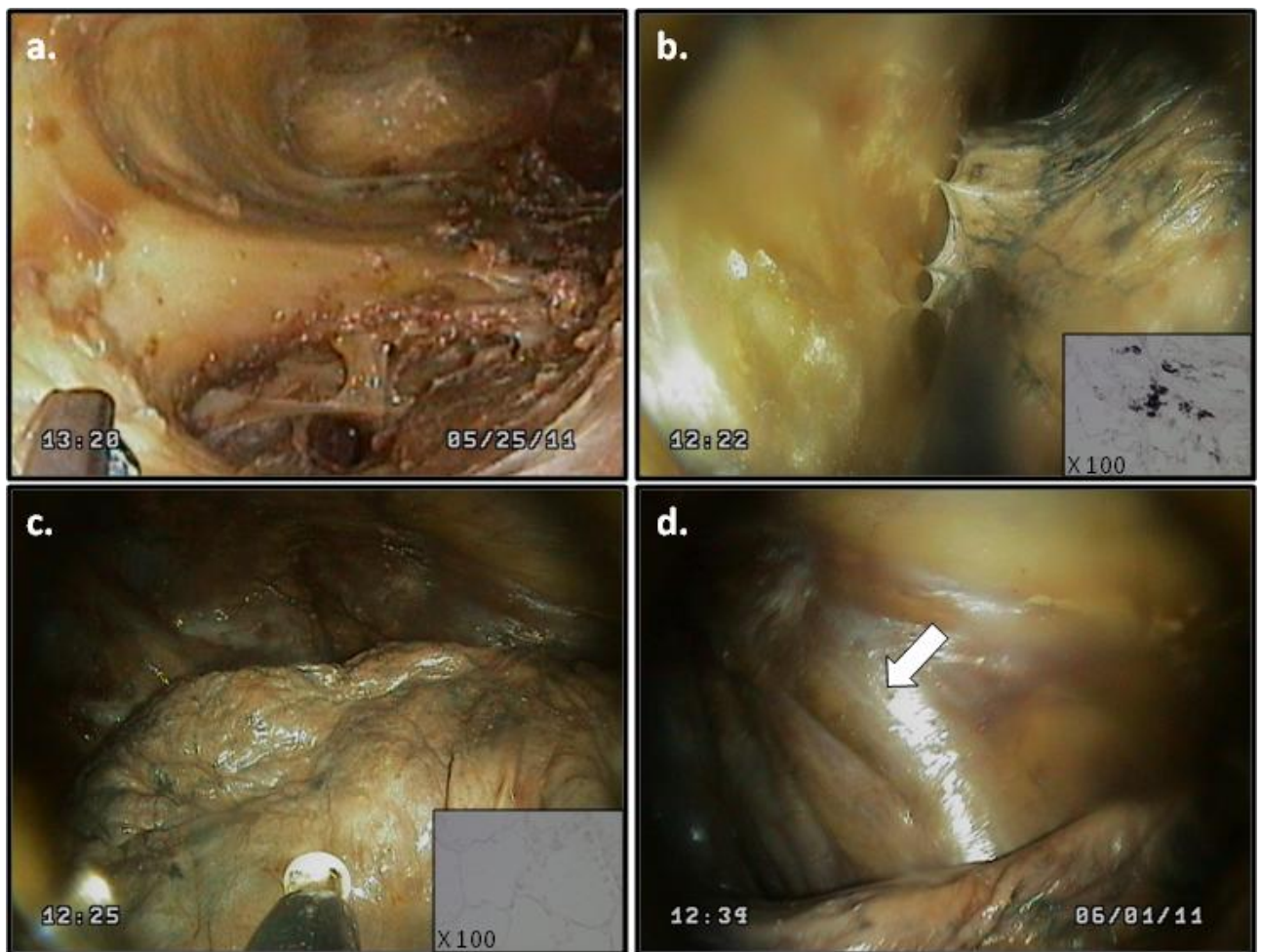


Figure 4.9; Intrathoracic images from the flexible endoscope during the transumbilical flexible access approach to the right thoracic cavity. a) shows the intrathoracic access route, b) the visceral pleura adhered to the thoracic wall, (Inset histology of pleura magnification x100) c) the lung looking caudally (inset histology of lung magnification x100), d) the pulmonary hilar vessels can be seen in the mediastinum (white arrow).

4.2.2.4. An objective determination of the challenges faced in the human cadaveric model:

1. Instrumental triangulation of the instruments and endoscopic tip stability during intervention.
2. Force transmission of the instruments on the tissue bed.
3. Better control of the instruments for dissecting purposes is required. The instruments and in-particular the diathermy enabling devices (needle knife, IT-knife, diathermy scissors) were more precisely controlled when exteriorised only by a short length (maximum 2cm) enabling control of their position on the tissue to be almost entirely

managed by the endoscope control wheels. If exteriorised further they had limited control leading to imprecision but at the closer length collateral heat damage to the endoscope itself was noted.

4. Within the chest cavity, orientation of the endoscope became a sufficient challenge and although the horizon and knowledge of the anatomy aided to some extent, a precise location or orientation was not always possible.
5. Endoscope ergonomics; the control wheels, instrument changes coupled with diathermy pedal, wash and suction creates a complex number of elements requiring control.

As demonstrated by the reduction in time to complete the procedure over the course of the three successful trials the final trial showed a sufficient reduction which was beyond the effect of the learning curve entirely. This last trial employed the use of an adjunctive mini-laparoscopic instrument, inserted into the axilla percutaneously, to enable additional tension to be placed on the tissue to enable final dissection, highlighting the clear need for effective tissue triangulation in flexible access surgery.

In the cadaveric model although more relevant to the human in terms of anatomy, the challenges are of course far less evident than within a live model. In this setting there is no blood loss to occlude the vision and additionally the lung does not need to be deflated to achieve the thoracoscopy. However, the idea is a conceptual one, determining the potential of what could be achieved and not per-se the actual procedure.

The transumbilical approach to the axilla was not discredited by the general population surveyed even when potential complications were presented and even the potential risk of cancer recurrence did not deter a small proportion of the sample. This being said, under no circumstances would such an approach be considered if there was even the slightest risk above any of the others that it could result in cancer recurrence though it does move to support the approach and the desire of a proportion of the general population to want a better cosmetic outcome to their surgery.

4.2.3. Clinical trial; part of the NOTESuk trial.

4.2.3.1. Natural Orifice Cholecystectomy in a Human Being; feasibility and accessibility!

In the past, the desire to reduce the impact of surgery on the patient led to the minimally invasive surgical revolution and the consequential, almost overnight success of laparoscopic surgery. The momentum of such revolutionary concepts has been maintained with new emerging techniques such as single incision surgery, single incision natural orifice surgery and natural orifice transluminal endoscopic surgery (NOTES), each in their own way portrayed as the next generation of surgical intervention.

Ever since the first human Natural Orifice Transluminal Endoscopic operation was undertaken three years ago (98), the drive to develop a repeatable and safe NOTES technique has become an ongoing research commitment. Whilst the lack of specifically designed endoscopes (99), effective endoscopic instrumentation (109) and safe repeatable closure methods (110) still limit the technique as originally described (17), the exploration of a more hybrid approach; particularly with the advent of long articulating semi-rigid instruments (111), acts as an interim measure to ensure surgical outcomes and patient safety can be maintained during any transition from the transabdominal to the natural orifice. However, even with such a mediating step available, much of the technique is yet to be fully defined. Aspects such as the primary incision, endoscope stability, maintenance of pneumoperitoneum (110), access methods and instrument selection are all essential to refine to ensure that the most effective, technically proficient surgical procedure can be carried out repeatedly with the highest quality results.

As a result of its extensive use within gynaecology and the well documented security of wound closure, the natural orifice transvaginal approach has been the most widely used access route undertaken in NOTES to date. Although a safe technique to gain closed access to the peritoneum through the posterior fornix has been established using hydroperitoneum, the choice of access port to enable stable instrumentation in addition to maintaining a secure pneumoperitoneum throughout the procedure has been less considered. The majority of natural orifice transvaginal trials described in the literature have utilised the conventional

bariatric 12mm by 150mm port for access (112), with a further 5mm 150mm port placed laterally, for the use of any additional articulating instruments. However, the vaginal vault varies considerably in anatomical dimensions between women. This creates the problem that any single port may not be suited for all women, with port instability, inadvertent removal from the culpotomy and subsequent re-insertions more likely to occur throughout the procedure.

Alternative single port devices have been trialled as a means to overcome this problem including the “Tri port” (Advanced Surgical Concepts) (96), a single access port originally designed for the transabdominal approach. However, its suitability for the vaginal incision beyond a single documented case has not been explored. One port which, however, which was designed specifically for the transvaginal approach and trialled extensively within gynaecology but as of yet not within the setting of NOTES, is the McCartney tube (Gate Healthcare Pty Ltd, Victoria, Australia) (113, 114).

This manuscript describes the technique we employed to complete a transvaginal hybrid NOTES cholecystectomy in an adult female patient and our experience in using the McCartney tube as the transvaginal access port. The potential that this port offers towards the expansion of the NOTES technique is discussed.

Materials and Methods

Full ethical approval was obtained for undertaking the procedure within a clinical trial setting (09/H0716/72). The patient was a 21 year old woman who presented with symptomatic cholelithiasis; confirmed on abdominal ultrasound. Magnetic resonance cholangiopancreatography revealed an uncomplicated biliary anatomy apart from a low insertion of the cystic duct on the common bile duct, with no intra-ductal stones.

The patient is a mother of a 2 year old daughter, and has no previous medical history including any pelvic or abdominal surgery. Consent to enter the trial was obtained by the senior investigator as per protocol. The procedure was undertaken within a multidisciplinary team setting which included senior gynaecologists, endoscopist and general surgeons.

Operating room setup

In total seven clinicians, including the anaesthetist, three abdominal surgeons, two gynaecologists and an endoscopist, as well as two nurses were involved in the initial trial. However, only a maximum of five were required at the operating room table at any one time. The patient was placed on the operating room table in the lithotomy position. Two surgeons were on either side of the patient at the abdomen and two between the legs, initially the gynaecologists to obtain access and later the second assistant for gallbladder retraction and the endoscopist. Once the operation was completed these clinicians would step out for the gynaecologists to return and close the colpotomy (*Figure 4.10*).

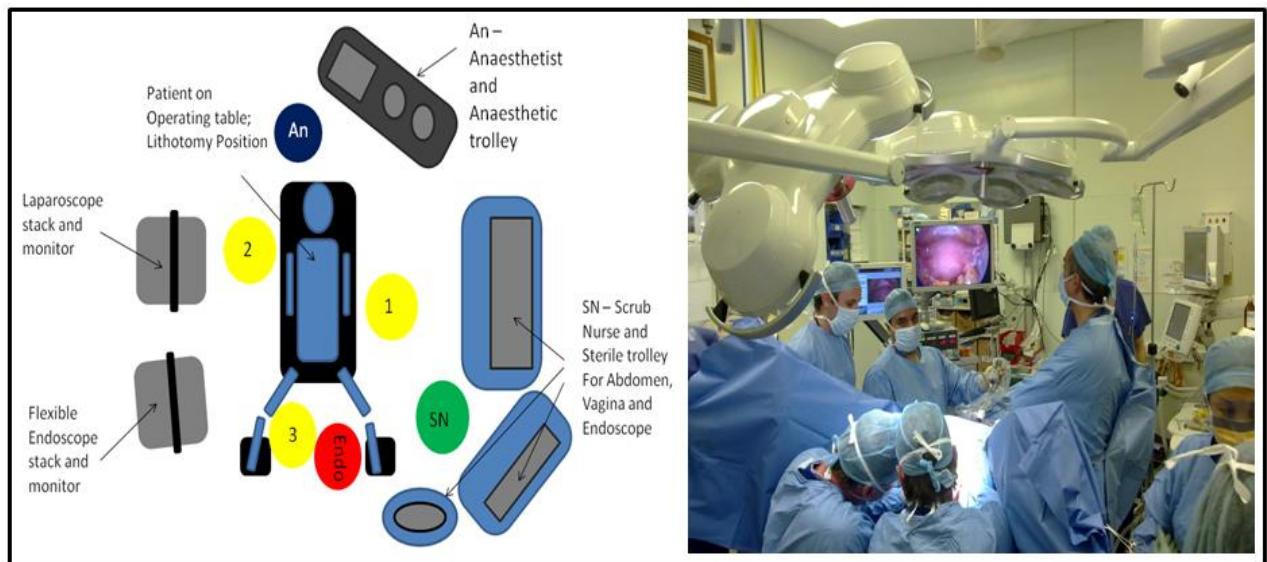


Figure 4.10; The operating room setup for the undertaking of the transvaginal hybrid Cholecystectomy with the primary surgeon (S1) and two assistants (S2, S3 - Yellow) as well as the endoscopist (Endo - red), Scrub nurse (SN1 - green) and Anaesthetist (An - blue). (Gy - Gynaecologist)

Equipment for access; The McCartney tube

The McCartney tube, is a soft silicone access tube purposely designed for transvaginal surgery. It is a 200mm length tube with an outer diameter of 35mm but can be found in a larger 45mm size for postpartum women or those with a larger vaginal vault. The external handle enables both placement and correct orientation of the tube to ensure the upwardly angled bevelled internal end is correctly sited within the pelvis.

The tube has a sealed interchangeable cap at the rear with two valves capable of accepting an instrument up to 12mm in size and one 5mm instrument. Pneumoperitoneum can be maintained successfully through the port with a nozzle incorporated to enable tube attachment for gas insufflation (*Figure 4.11*). Further caps are now available with two 5mm and a 13mm valves to enable multiple instrumentation and the larger dual channel operative endoscopes to be passed.

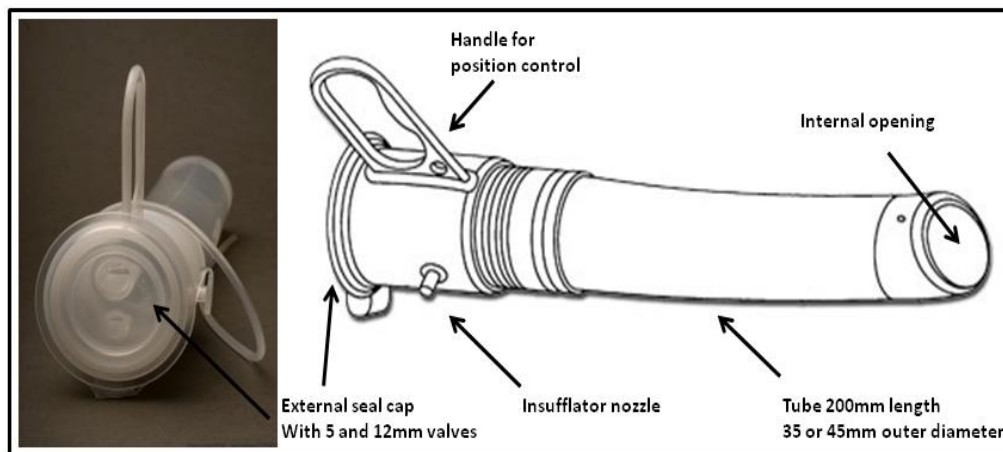


Figure 4.11; The McCartney transvaginal access tube.

Laparoscopic assisted NOTES; the technique used.

The patient was given a full general anaesthetic as for a conventional laparoscopic cholecystectomy, placed on the operating table in the lithotomy position and prepared and draped in the standard fashion for a joint pelvic and abdominal procedure. A 5mm trocar was inserted transumbilically using the open technique and pneumoperitoneum was established. A 5mm rigid laparoscope was inserted through the transumbilical port and a visual inspection of the peritoneal cavity and the pelvis performed to explore for any congenital adhesions or previously undefined anatomical variants. The patient was subsequently placed in the head down position enabling a full visual inspection of the pelvic adnexa to be undertaken prior to transvaginal access being performed.

Transvaginal access was performed through a one inch incision in the posterior fornix made under direct vision using a Sims speculum for cervical exposure. A 35mm diameter soft silicone port (McCartney Tube; Gatemedical Healthcare, Aus) was inserted into the incision enabling transluminal peritoneal access to be obtained. The internal position of the access

port was confirmed using the 5mm laparoscope and enabled anatomical structures including the ureters and iliac vessels to be visualised to ensure no pressure was being exerted upon them prior before continuing with the operation (Figure 4.12).

The operating table was flattened and a dual channel, 11.8mm gastroscope (Olympus Medical, UK) was inserted into the peritoneal cavity transvaginally. The 5mm laparoscope was removed and visualisation from this point was obtained only through the gastroscope camera. A 65cm semi-rigid articulating (Novare, Cupertino, US) ratchet toothed grasper was inserted through the transvaginal port which enabled retraction of the gallbladder and liver cephalically to expose Calot's triangle.

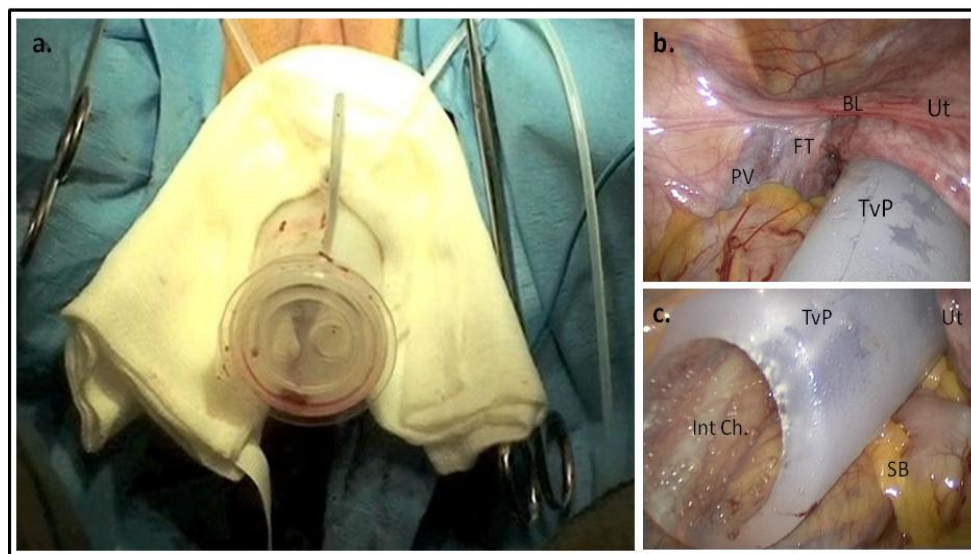


Figure 4.12; The McCartney Transvaginal Access Tube in-situ (a) with the position within the pelvis confirmed by the 5mm laparoscopic (b and c).

(Ut - Body of Uterus, TvP - Transvaginal access port, Int Ch. - Internal Channel of access port, BL - Broad Ligament, FT - Left Fallopian tube, PV - Pelvic vasculature, SB - Small bowel.)

The operating table was placed in the head up position. A mini-lap (2.7mm) grasper (Stryker, UK) was inserted into the upper right quadrant of the abdomen to aid in the retraction. For safety, the dissection of Calot's triangle was performed using single incision laparoscopic curved grasper via the transumbilical port (Roticulator; Covidien, US). A 5mm dissector exposed the cystic duct and artery with Calot's lymph node clearly visualised as the landmark. The cystic duct and artery were isolated and clipped using a 5mm clip applicator with two clips placed proximally and one distally for each. Once ligated the clips were checked to ensure secure placement before the remaining tissue of calot's triangle was divided using endoscopic instruments. Tension was placed on the gallbladder using the mini-

lap retractor to aid in the dissection. The Insulating Tip (IT-) knife (Olympus Medical, UK) was used to dissect the gallbladder from the liver bed (*Figure 4.13*).

The long semi-rigid retracting grasper maintained a hold on the gallbladder throughout the procedure and for extraction, enabled the gallbladder to be removed via the wide vaginal access port without the need for a bag. The gallbladder bed and para-hepatic spaces were inspected and toileted with normal saline before closure. Endoscopic visual confirmation of clip position on the cystic duct and artery was obtained before the operation was considered complete (*Figure 4.14*).

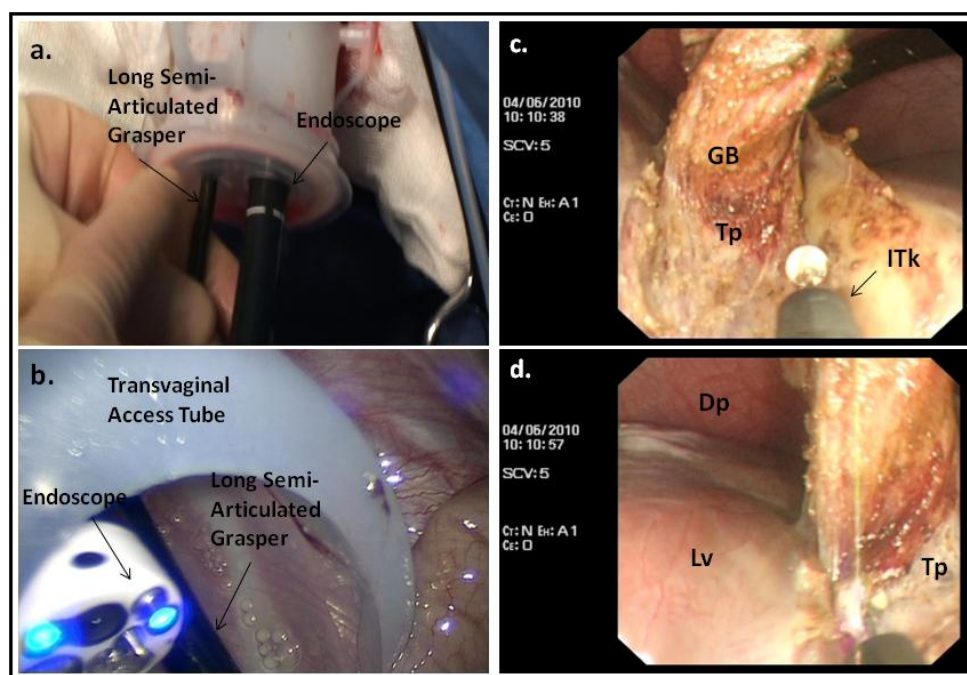


Figure 4.13; The endoscope and long semi-articulating grasper within the access port (a - external and b - intraperitoneal views) with the use of the Insulating Tip Knife (ITk) dividing the gallbladder (GB) from the Liver (Lv) (c and d). (Tp - Tissue plane, Dp - Diaphragm)

Follow up

Telephone consultation was undertaken daily for 1 week as a means of highlighting any early postoperative complications followed by outpatient consultation at 6 weeks with both gynaecologists and surgeons in attendance.

Operative outcomes

Operation time 127 minutes, despite an early postoperative temperature spike to 38°C which settled within 12 hours without intervention. No complications were evident and the patient was discharged home within 24 hours with the advice to refrain from sexual intercourse for 2 weeks. Routine telephone consultation was undertaken as part of the trial protocol daily for 1 week after the operation during which time no complications were highlighted.

Formal outpatient follow up was undertaken at 6 weeks with both the Gynaecologist and the General Surgeon.

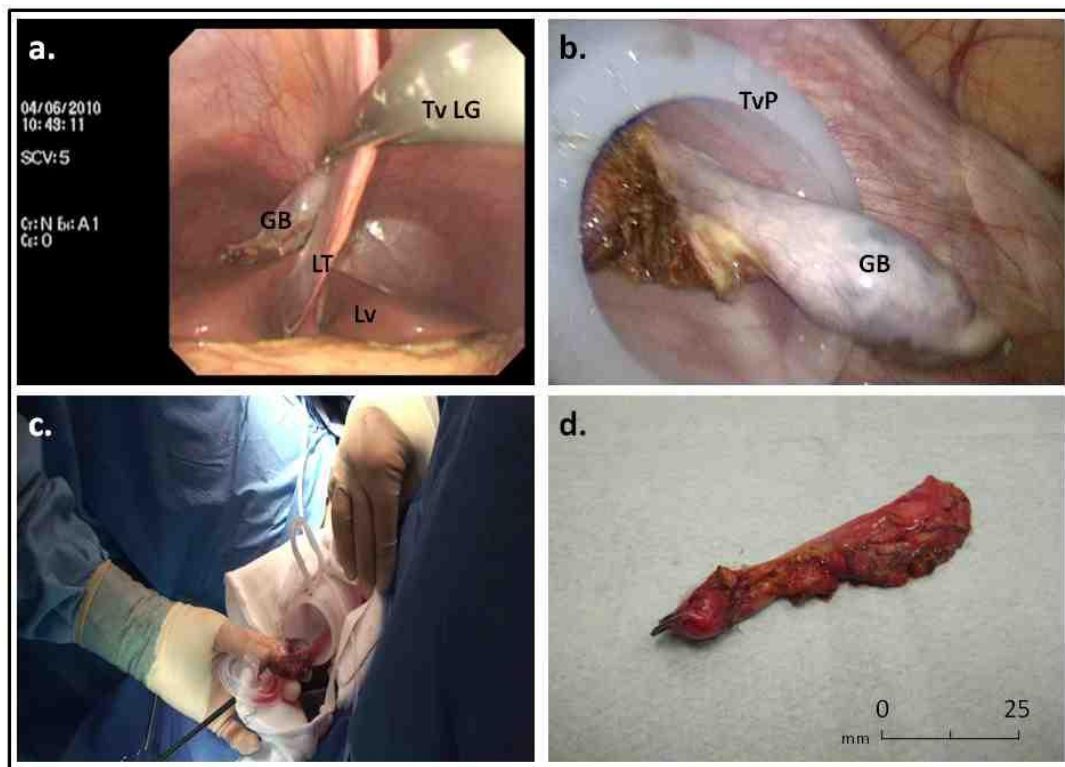


Figure 4.14; Removal of the gallbladder (GB) from the abdomen using the long transvaginal semi-articulated graspers (TvLG) (a). The GB can be removed without the need for a bag due to the wide internal bore of the tube (b and c). (TvP - Transvaginal Port, Lv - Liver, LT - Ligamentum Teres)

The patient had remained well with no evidence of complications either gynaecological or abdominally. The abdominal 5mm incision had healed well with no sign of the mini-lap insertion point (*Figure 4.15*). No symptoms relating to the transvaginal incision were

described. She was discharged but will remain on the trial with open follow up for a further 2 months to document any unforeseen long term complications.

4.2.3.2. *An objective determination of the challenges faced during the human clinical trials:*

1. Navigation of the endoscope within a spatial environment; the abdominal cavity.
2. The number of clinicians involved in a single cholecystectomy operation.
3. Access challenges; as this is only suitable for half the general population.
4. Aspects centred surrounding the sterility of the endoscope.
5. Instrument triangulation as indicated by the need for the additional surgeon to maintain tension on the gallbladder.
6. The lack of flexible endoscopic end-effectors capable of safely securing a blood vessel or in this case the cystic duct.
7. Force transmission of the instruments on the tissue bed.



Figure 4.15; 6 weeks post hybrid natural orifice transluminal endoscopic cholecystectomy. No visible scarring from either the transumbilical 5mm port or the minilap 2.9mm insertion site is noted.

4.3. An Overview of the Challenges which are currently facing the Flexible Access Surgical Technique.

The technique is without contestation in its infancy, with many hurdles yet to be overcome before widespread clinical acceptance is assured (28). From the trials, the challenges to be overcome are predominantly centred on two distinct yet intimately linked areas; patient safety and clinical usability or technical ergonomics. Both have to be addressed before Flexible Access Surgery can be addressed in the mainstream.

To ensure that both of these requirements are met, the predominant focus of research can further be divided into:

1. Improving the equipment; endoscopes, instruments and closure devices.
2. Defining and overcoming the technical challenges; Navigation, orientation and spatial awareness.
3. Basic sciences; physiological effects, psychological effects and peritoneal contamination.

All of these hurdles are closely linked however uniquely individual and must be approached as such (*Figure 4.16*). For example no matter how the endoscopes are improved to make them more ergonomic and responsive to the user, the concept of the technique still requires the navigation of a flexible instrument through a spatial environment and as such the challenges of disorientation and spatial awareness are still disabling factors.

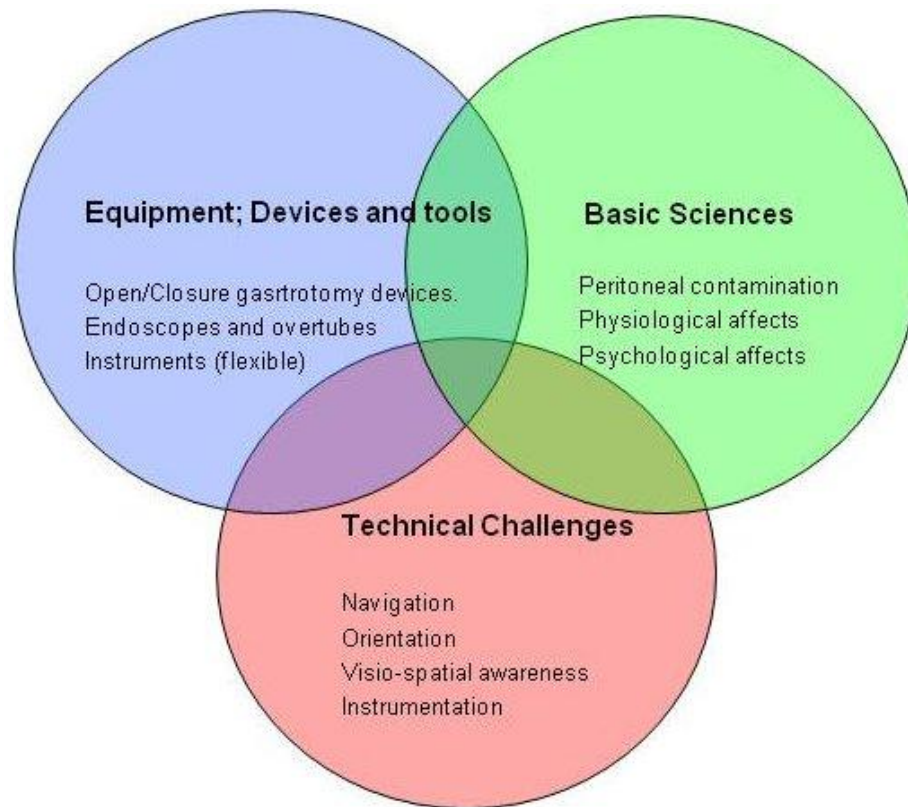


Figure 4.16; Defining the challenges hindering the acceptance of Flexible Access Surgery into clinical practice and their intimate relationship to one another.

The Technical Challenges

One of the significant hurdles in developing a wider acceptance for NOTES is to improve the design application to equate it to a more user friendly technique taking into consideration mental workload, decision-making, skilled performance, human-computer interaction, human reliability, work stress and training. In view of this the main challenges to overcome and the main focus of current and future research should be on:

1. Improving Navigation with advanced flexible endoscopes;

Current endoscopes in use for NOTES are based on the design of the investigative endoluminal endoscope. Their design was for use within a luminal environment; constrained by the bowel walls. Rear drive from the operator moves the instrument through the bowel using the walls for directional guidance. The tip is controlled from the control wheels which allows for finer camera manoeuvrability to investigate pathology. Within the spatial

environment of NOTES these constraints do not exist and manipulation of the endoscope for navigation is reliant upon the operator manipulating the endoscope externally with the drive hand and the control wheels. The lack of constraints challenges navigation. Directional changes can only occur within this environment through the deflection of the instrument off anatomical structures, which will receive a sustained force from the operator as the instrument is advanced. Many of the structures within this environment will not have the capacity to absorb this force and may damage potentially with morbid consequences.

2. Overcoming disorientation;

The fixed nature of the camera at the tip of the endoscope means that the navigation of the endoscope and the visual display from the camera are tied. Certain manoeuvres of the endoscope will therefore render an inverted or misaligned image of the environment or target (Figure 4.17).

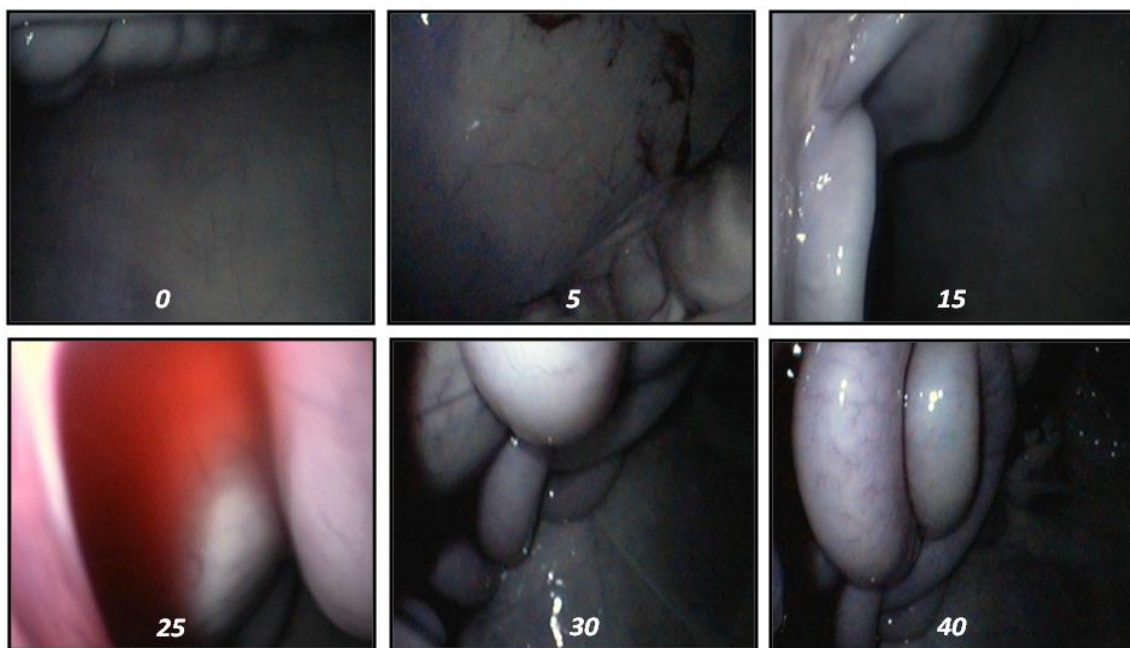


Figure 4.17. Sequential time images taken from footage during a NOTES procedure performed on a porcine model. It illustrates the disorientation that can occur during exploration of the peritoneal cavity using a flexible endoscope. (Numbers indicate the time sequence in seconds).

Disorientation in such an environment can lead to irrational and unsafe manoeuvres being undertaken in order to re-orientate. The camera only gives a forward view of the environment with the lagging tail of the instrument remaining out of vision. For this reason an irrational re-orientation maneuver under these circumstances could be unsafe particularly if the trailing endoscope is abutting delicate structures such as the spleen.

3. Improving awareness of the position of the endoscope within the environment (Visio-spatial awareness);

The fixed forward facing camera is unable to visualise the trailing section of the endoscope. The knowledge of the position of surgical instruments with conventional minimally invasive surgery has not been a significant problem due to the rigid nature of the instruments. In this case, using triangulation techniques from the tool tip, the path of the instruments can be extrapolated back. Furthermore, with conventional rigid endoscopy, the camera is off-axis, separate from the instruments and as such unlike in NOTES, visualisation of the tool path can be performed. The instrument flexibility and this fixed forward facing camera combine to prevent the user knowing precisely their position within a spatial environment a safety issue if the trailing section is abutting delicate structures.

4. Instrumentation and force requirements

One of the most significant challenges associated with the flexible access technique and the use of the flexible endoscope as a surgical platform is the instrumentation. There are three very clear distinctive elements which contribute to this problem:

1. The stability of the flexible endoscope during intervention.
2. The triangulation of the instruments at the end effectors.
3. The stiffness of the instruments themselves; determined by the force requirements of the instruments to manipulate tissue effectively to enable precise dissection.

As has been experienced with the recent introduction of single port surgery, standard instruments inserted from a single point in the abdomen, like the umbilicus, have lacked the ability to triangulate at the tissue bed requiring a total redesign of the instruments to accommodate. The challenges for Flexible Access Surgery in this setting are effectively the same. A single point of delivery of the instruments close to the tissue bed will be challenged to achieve a wide angle for retraction and tissue dissection.

4.4. Conclusion

The introduction of the flexible endoscope into surgical practice exposes a huge potential for a range of novel surgical approaches to be developed. The unique flexibility of the platform

coupled with the delivery of interventional tools to the tip (e.g. scissors, graspers and dissectors) enables the position of the incision to be distant from the target organ; an advantage which may provide significant benefits in terms of reducing scarring in and around the operative area positively impacting on the associated co-morbidities. The advantage of being able to make the incision distant from the target organ has been exploited by the NOTES community for the cosmetic benefits it provides (98). However, the major obstacle to NOTES deployment is the closure of the unavoidable transluminal breach, where leakage and contamination could prove disastrous; hence the limited indications for NOTES thus far. Nevertheless, this challenge should not result in the flexible endoscope for surgical applications being abolished.

The potential opportunity raised through NOTES, re-iterated by the questionnaire described, points to the value that the population places in the cosmetic outcomes from surgery. Furthermore, the importance placed by each individual and even the differences of opinions as to what may be considered cosmetically appropriate is also evident; potentially relating to their own individual preferences of their body (Chapter 2). It is about time the question as to whether surgery should be targeted more to the individual rather than a generic approach is considered. The possibilities of personalised surgery have the potential to be realised with flexible operative platforms such as the endoscope being introduced more widely into operating theatres. Scars could be placed at any location on the body and targets approached using the subcutaneous techniques described. Operative choice is already presented in other operative scenarios such as the thyroidectomy, which has been successfully undertaken both through the transaxillary or the peroral approach (115) (116).

As an endoluminal investigative tool the flexible endoscope is well suited, however as a therapeutic surgical platform, the broad design presents numerous imperfections. Designed for navigating within the confines of the bowel lumen, the uncontrollable flexibility essential within this environment, confounds not only accurate and effective target navigation but also its stability whilst flexed, a requirement essential for precise instrumentation when the platform is taken into the spatial environment of the peritoneal or axillary space. Within the setting of the TU axillary approach, the rigid overtube and subcutaneous tunnel provides some of the support required for navigation and, to some extent, the stability during intervention but not enough for an effective and reliable procedure to be completed within an acceptable time frame.

The ergonomics are further impeded by no instrument triangulation at the endoscope tip. The lack of both interventional control and triangulation were most evident when the operative times for the transumbilical axillary dissection in the human cadaver were considered, particularly in the last of the three trials when the deployment of an additional instrument was required to complete the task. This trial demonstrated a markedly shorter operative time than the initial two, demonstrating its significance as a problem which needs to be addressed before translatable flexible access surgical applications are ever realistically achievable.

The introduction of more specifically designed instrumentation for the flexible approach will also aid in reducing operative time. The need for flexibility as well as stability are now well regarded but the need to interchange instruments needs to be considered as well as broadening the range of flexible instrumentation available. This includes energy delivery devices as well as secure and effective methods of not only enabling safe and secure vascular control but also duct ligation; fallopian tube or cystic duct.

The final hurdle to overcome is the challenge of endoscope ergonomics. The learning curve associated with intraluminal endoscopy is significant and to obtain proficiency requires significant experience. With the challenges of navigating the endoscope within a spatial environment such as the abdominal or thoracic cavity, it is likely that this will be even more significant and will as a result impact directly on the translation of the technique clinically. A more challenging technique to learn is unlikely to translate to the routine clinical setting.

It will only be through innovation that these challenges will be overcome. Novel platform designs have already been developed to explore these problems but many have been based on the flexible endoscope with devices which either deal with the uncontrollable flexibility (eg Shapellok, USGI Medical) or the triangulation (eg Anubis; Karl Storz) but not both. It is likely that the answer may eventually lie within the field of robotics. Articulating robots which provide stability as well as the control with interventional capabilities are under development (117) but the additional requirement to overcome the triangulation still remains a significant research and engineering challenge (Chapter 2).

Chapter 5

Evaluation of the Instrumental Force Requirements

Hypothesis: The forces required to manipulate tissue for clinical application are measurable and the level can be optimised through appropriate tool-tissue placement.

5.1. Introduction

The previous chapter of flexible access *in-vivo* trials has highlighted a number of significant problems aside from the navigational challenges associated with the uncontrollable flexibility of the endoscope, which need to be addressed. One particular area which is overwhelmingly evident is surrounding the delivery and effectiveness of instrumentation through the flexible endoscopic platform. As can be seen from the devices currently under development within the commercial market for flexible surgery (Chapter 2), the most significant design iteration is in the overcoming of the parallel delivery of flexible instruments to the tissue bed towards a greater element of instrumental triangulation so by enabling one instrument to place the tissue under tension providing a more ergonomic alignment for the second to dissect or undertake intervention. However, this is only one element to the problem. Evident from a number of platform designs which have already been developed with adequate triangulation of the instruments yet remain unable to undertake a full surgical procedure even without significant tissue pathology, likely to challenge the instruments even further. The problem is multifactorial (118) and relates not only to instrument triangulation but also to overall platform stability, a flexible platform that provides on-demand stability during intervention as well as instrumental force integration, all of which are essential and inter-related.

The challenge of instrumental force integration is significant. This relates to the need for the instruments to remain flexible to negotiate the flexibility of the platform but also be rigid enough in their own right to deliver enough force to the tissue bed for surgical application. To better design and integrate such instruments for flexible access surgery, it is essential to first map the force requirements that may be encountered during any given intervention.

A number of groups have explored the force requirements within the *in-vivo* setting. Varying sensing methods have been adapted to explore these force requirements during certain procedures and for variable tasks. Tissue cutting forces for example have been trialled on various *ex-vivo* tissue samples and were found to be in the order of 13 – 35N (119). Sensed laparoscopic instruments have been developed to explore forces within minimally invasive surgery (120) predominantly within the *ex-vivo* setting for training and assessment purposes (121, 122) with little formal assessment of the *in-vivo* force requirements ascertained. One Canadian group however did place force sensors on flexible endoscopic instruments and trialled them *in-vivo* to determine the level of force imparted during a trans-gastric and trans-peroneal NOTES appendicectomy. The outcomes from this study suggested that the maximum force requirements for tissue manipulation in this setting were in the order of 8 to 16N (123) concluding that instruments designed for flexible access surgery should be able to meet these force requirements.

It is reasonable to assume that the forces imparted within the body are related to fixed and measurable factors. These include the weight of the organ in question, the degree to which it is tethered to its anatomical attachments and the elasticity of both the tissues in question and their attachments all coupled with the speed at which the force is imparted or in the case of these trials, measured (Young's tensile modulus). These forces would therefore be the similar whether measured using a force sensed flexible instrument or a rigid one.

This chapter describes the design of a laparoscopic instrument capable of measuring force at its instrument tip as a means of defining the force requirements for surgical application. A quantitative systematic definition of the forces required to manipulate a range of tissues within the abdominal cavity of a pig model is described as well as those that required during a focused clinical procedure; the laparoscopic cholecystectomy.

Force minimisation is also explored through investigating the effects of tissue force requirements through optimising instrumental triangulation as well as exploring the effects of surgical experience on force and its relationship if any to the level of tool-tissue interaction that occurs during any minimally invasive procedure.

5.2. Materials and Methods

5.2.1. Constructing a Laparoscopic Force Sensing Instrument.

The objective was to adapt a laparoscopic tool which can be used through a standard laparoscopic port to measure the forces that are imparted on the instrument during laparoscopic tissue manipulation. As a result the force requirements can be better defined. It was also essential that the adapted tool was capable of being passed through a conventional laparoscopic port for easy access to the appropriate cavity and be able to grip and hold the tissue effectively as for normal surgical application. A conventional 5mm laparoscopic grasper (Ethicon, Cincinnati, Ohio, US) was used and integrated with force sensors.

5.2.1.1. Laparoscopic Instrument structure

The laparoscopic instrument consists of two shafts: inner-shaft, and outer-shaft. The inner-shaft, a solid shaft made of steel, is used to actuate the surgical tool (e.g., the gripper). The outer-shaft, which is made of Aluminum, is used for changing the roll orientation of the tool. A CAD drawing of the instrument shaft with the surgical tool is shown in *Figure*.

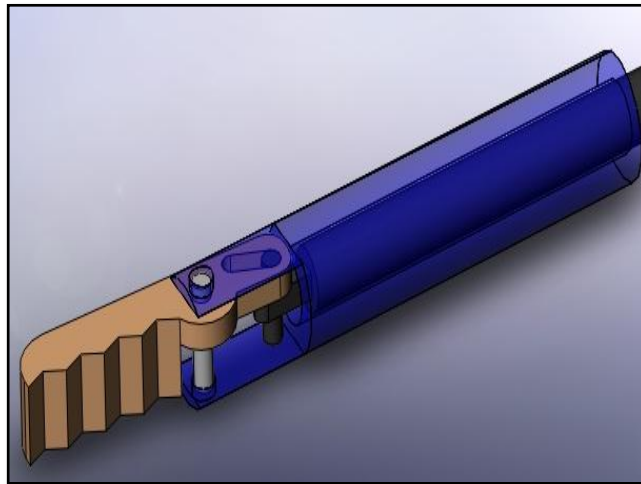


Figure 5.1; A CAD drawing of the instrument showing the inner-shaft, the outer-shaft, and the surgical tool (cut).

5.2.1.2. Integrating Force Sensors

Strain-gauge sensors were employed for the detection of radial forces. The strain-gauge sensors

used in this case were Aluminum foil strain gauges having the size of 5 mm x 1.8 mm, and gauge resistance and gauge factor of 120 Ω , and 2.1 respectively.

To provide a proper mounting for the strain-gauge sensors to the outer-shaft, the shaft is shaved with a milling machine until only a fine slice of the aluminum of the outer-shaft remains (*Figure 5.2*). There are two pairs of strain-gauge sensors, with a pair sensing force at the instrument tip in vertical direction (+Y, -Y) while the other pair in horizontal direction (+X, -X). The strain-gauge sensors in each pair are mounted opposite sides of the shaft. Arrangement of a pair of strain-gauge sensors, and associated resistors in a Wheatstone bridge circuit is shown in *Figure* .

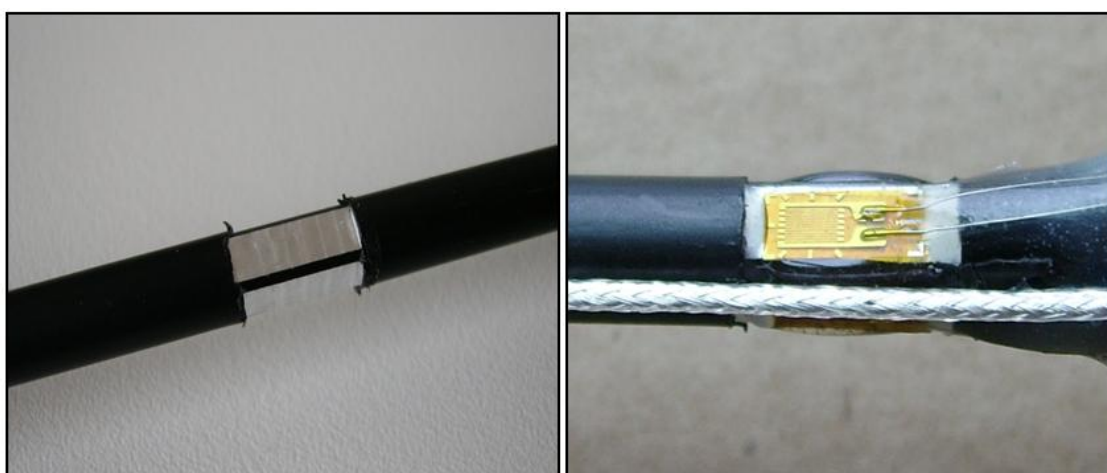


Figure 5.2; Modification made to the instrument outer-shaft for strain-gauge attachment and the strain-gauge sensors attached to it he instrument outer-shaft.

The Wheatstone bridge configuration integrated is the half-bridge configuration, employed to compensate for the effect of temperature changes on the strain gauges which in essence, provides a more accurate force reading. Since the output of the bridge is in the range of only a few millivolts, the output was amplified using an instrumentation amplifier (*Figure*) to improve Signal-to-Noise Ratio (SNR). The amplified output is acquired by a conventional personal computer via a data acquisition device NI USB-6009 [14 bit, 48k Samples/sec] (National Instruments, USA). A block diagram of the force sensing system is shown in *Figure* .

The software required to acquire the force data is written in LabView (National Instruments, USA). The force data was acquired and displayed at 40 Hz. Calibration of the force sensing was performed by placing known weights at the tip of the instrument while clamping the instrument at the handle

using a vice. Just before each trial, the force values were all zeroed. The drift in force measurement due to temperature change during each trial is negligible since the trial period was not especially protracted.

Since force has both magnitude and direction, it is essential during formal *in-vivo* trials where the laparoscopic instrument is continually being rotated along its shaft that the position of the X and Y strain gauges relative to their original position and therefore it's calibration, is still determined so that the forces and their direction can be accurately and appropriately measured.

As a result the laparoscopic force sensing instrument developed for these trials was coupled to a 6 degree of freedom (DoF) magnetic motion tracking marker (Aurora; Northern Digital Incorporated, Ontario, Canada). This marker enabled the rotational element of the instrument to be accounted and as such the orientation of the X and Y strain gauges essentially mapped at all times to ensure that the direction of the force, as well as the magnitude could be predicted (*Figure 5.6*).

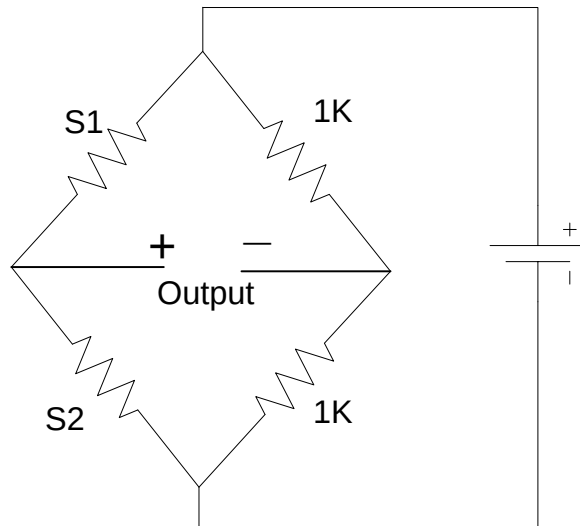


Figure 5.3; A Wheatstone bridge circuit with a pair of strain-gauge sensors and associated resistors. S1 and S2 represent strain-gauge sensors.

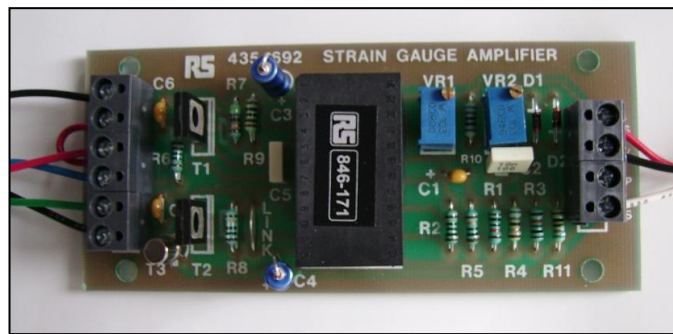


Figure 5.4; An instrumentation amplifier used to amplify an output signal from Wheatstone bridge output.

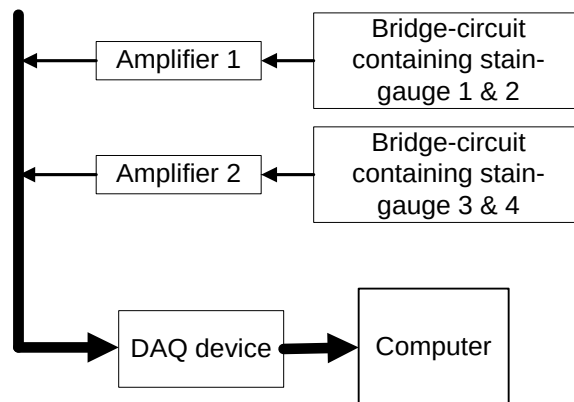


Figure 5.5; Overall block diagram of the force sensing system.

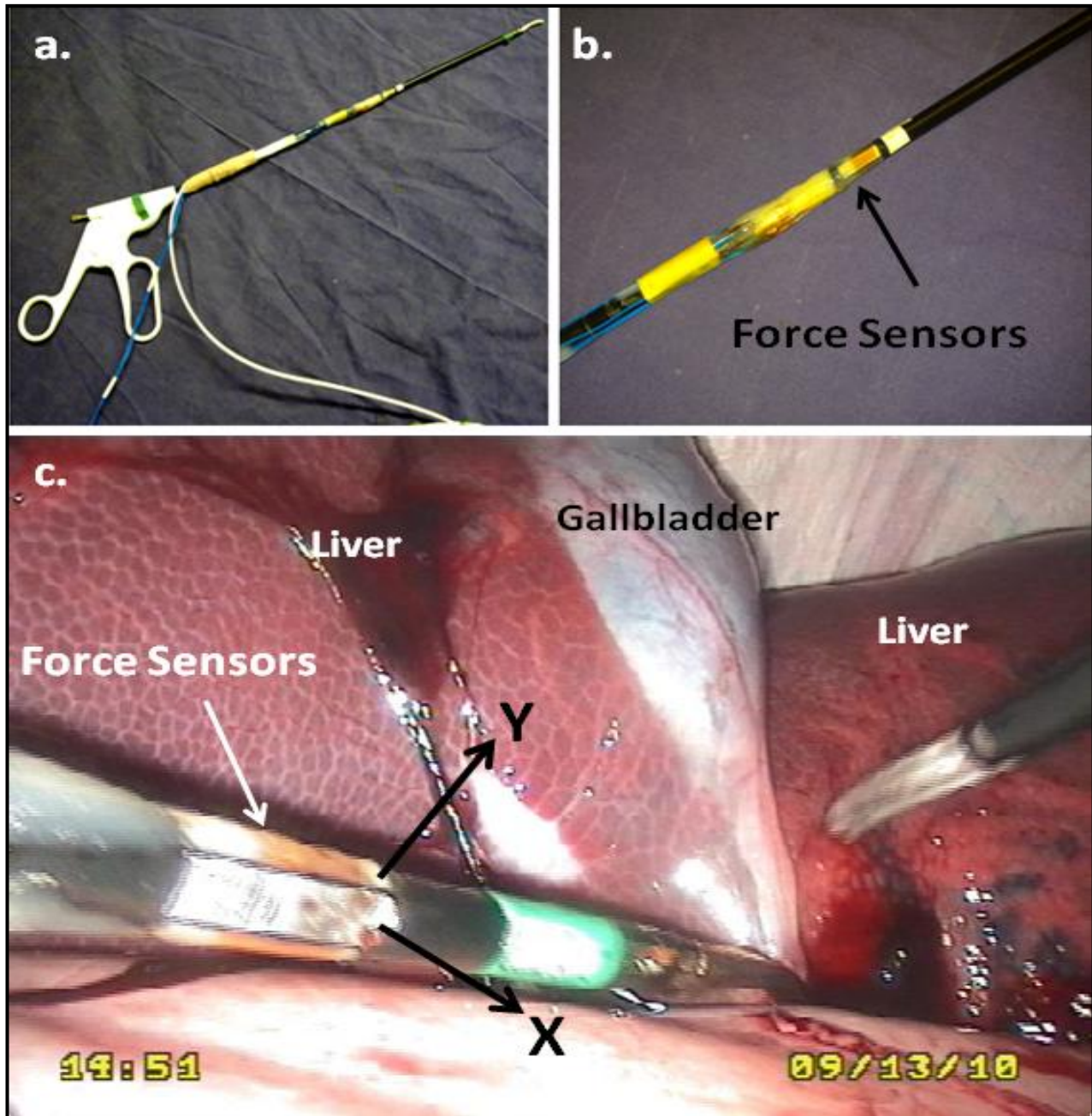


Figure 5.6; The laparoscopic force instrument with aurora magnetic tracking marker attached (white cable) (a) with the force sensing instrument and force sensors clearly visible (b and c). The force readings in the X and Y plane are demonstrated in the *in-vivo* image (c).

5.3. Tissue Force Mapping.

With the increasing requirements to design instruments, which will in essence pass through a flexible port; i.e. the flexible endoscope in this case, the need to understand the forces required to manipulate tissue within the body is essential. It would be reasonable assume that, given their flexibility, these instruments will be affected more by the tissue resisting forces than the conventional rigid alternatives. Using the laparoscopic force instrument described above, the tissue forces required to manipulate tissue within the abdominal cavity of a pig was recorded and defined as a reflection of the potential force requirements for future instrumental designs.

5.3.1. Method

The laparoscopic force instrument performed a number of manipulation tasks within the abdominal cavity of a live porcine model under ethical approval (80/2297). A 75kg modified Large Gloucester White pig was used in the trial. Tissues included in the study were small bowel, large bowel, uterine horn, bladder, stomach, liver and gallbladder. Tasks varied according to the tissue under investigation and the relevance to the clinical application which may involve the tissue type but in general the tasks consisted of elevation, placing the tissue under tension with another instrument and elevation with dissection using a separate instrument.

Tasks were performed multiple times and over three separate trial periods. The trial period was recorded using a standard 10mm 0 degree laparoscope and the video sequence analysed post-trial. A pre-defined instrument strike against the liver bed (see sequence in *Figure 5.7*) or anterior abdominal wall was undertaken once recording of the forces had commenced. This enabled, during post processing to accurately enable synchronisation of the force data stream with each video frame (*Figure 5.8*). For this to be enabled it was essential that both the video frame rate and force data stream were running at the same frequency of 40hz. Once achieved and with the synchronisation confirmed, the video could then be analysed to define the start and end points of the performed tasks during the trial using frame numbers as these reference points. A open source software program; Virtual Dub (www.virtualdub.org), was used to run the video files during analysis as accurate frame numbers for the desired tasks could be read. With the frame numbers realised for each particular task undertaken, the aligned forces from the X and Y strain gauges which were gathered during that time could be accurately determined.

The force vector could be determined from both strain gauge readings using the standard formula ($\sqrt{F_x^2 + F_y^2}$). Where F_x is the square of the force readings from the x strain gauge. The mean force requirement to perform the task was then determined from the multiple readings ascertained and the values recorded.

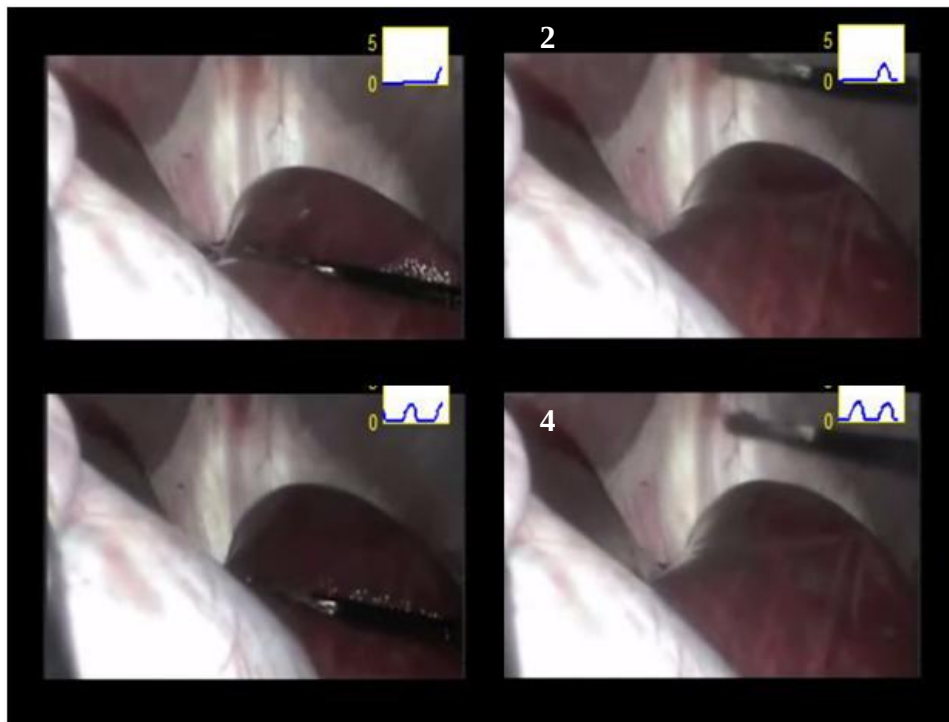


Figure 5.7; Images depicting the synchronisation between the instrument on the tissue and the force recording inset graph. The images are screen shots from a video sequence which combined the force data and video frames in post production (numbered sequence in frame order).

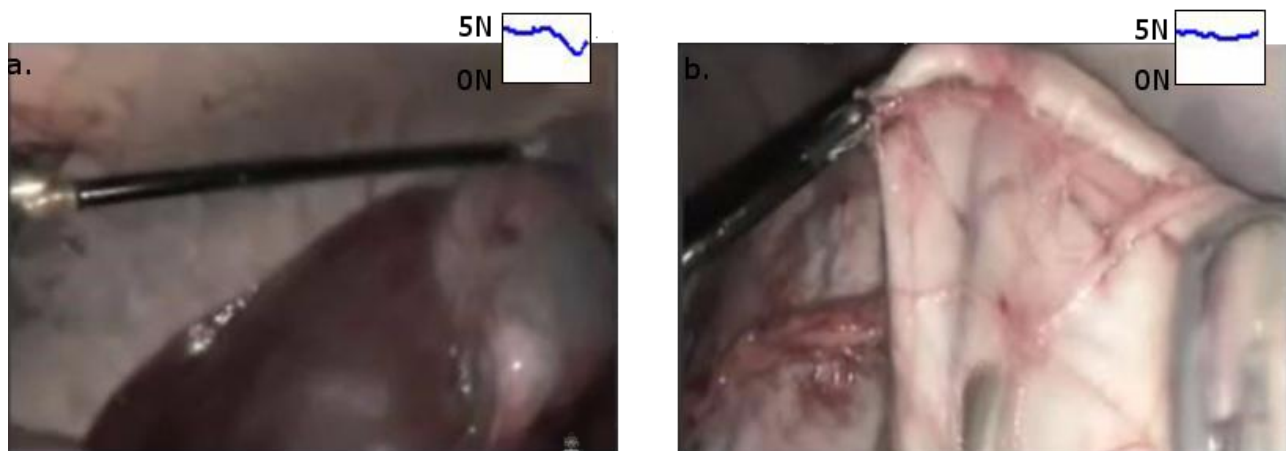


Figure 5.8; Images of the use of the laparoscopic force sensing instrument during *in-vivo* trials. a) elevating the Gallbladder over the liver and b) elevating the stomach to tension.

5.3.2. Results

Eighteen separate tasks were performed during the trials with a focus on six main anatomical areas; the small bowel, large bowel, stomach, hepatobiliary, uterine horn and bladder. Each task was repeated median 4.1 (range 1 – 9) times with those sustained forces measured during a lengthy time frame; as is the case for some of the dissection or manipulation tasks.

The mean, minimum and maximum forces isolated for each of these tasks was determined and are expressed in (*Table 5.1*), *Figure 5.9* demonstrates these results in an anatomically representative format.

The force requirements necessary to manipulate tissue was analysed and the variation between different tissues recorded as well as the overall force requirements instruments are required to meet to enable effective dissection within the porcine model.

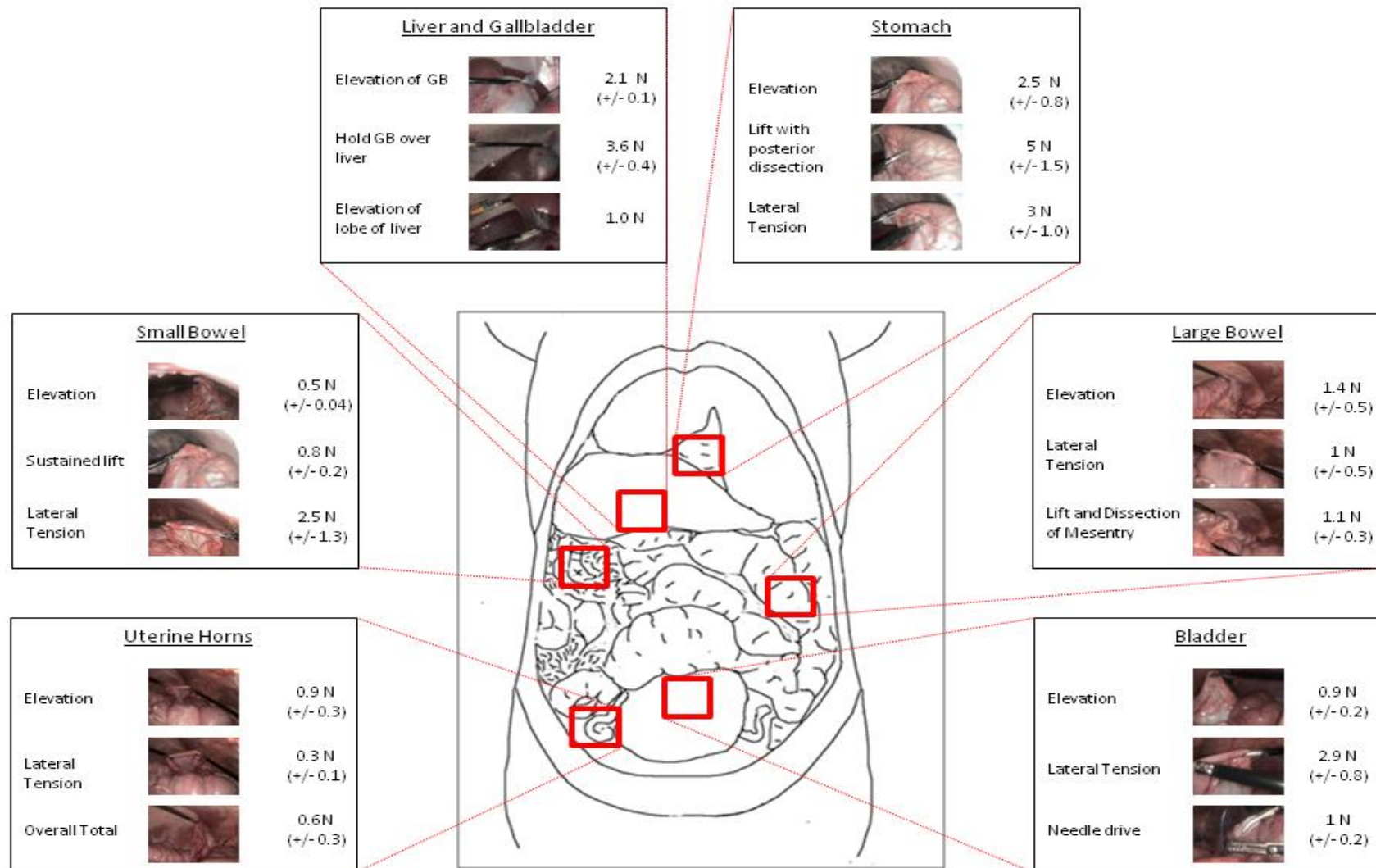
Evidently the relationship between the pig tissue and human tissue bed will vary and the values registered within this trial cannot be considered to be the same as those required for human tissue manipulation however objectively it was apparent that the with the variation in the anatomy of the pig from the human particularly when considering the abdomen it is likely these values are higher than in the human. The pig has a spiral colon strongly adhered to the posterior wall and to each length of approximating bowel Furthermore the pig has a significantly larger liver often being overlaid by a very large spleen. Both these organs also overlay the stomach restricting its visibility during laparoscopic manipulation even with liver retraction. All these features expose the instrument to objectively higher forces but this will only be confirmed with clinical *in-vivo* trials.

Nevertheless, it is likely that any novel flexible access devices with instrumentation will require trialling within the pig model before moving into the human and with that the essential knowledge of what forces these instruments will meet within the pre-clinical trial setting is defined here.

Table 5.1; The force measurements determined during each of the manipulation task

	Force Magnitude (Newtons)				
	Number of task repetitions	Mean	Min	Max	SD +/-
Small Bowel					
Lift	6	0.51	0.16	0.97	0.18
Lift under tension	4	0.58	0.26	1.42	0.35
Lateral tension	8	2.53	1.89	3.26	1.31
Lift and draw across field	2	0.37	0.01	1.32	0.58
Large Bowel					
Lift (spiral colon)	7	1.36	0.44	2.00	0.51
Lateral tension (non-spiral colon)	5	0.95	0.48	1.66	0.51
Elevation and dissection of mesentry (spiral colon)	2	1.12	0.12	2.54	0.33
Stomach					
Lift	4	2.48	0.76	3.87	0.80
Elevation and Dissection	3	4.92	4.09	5.88	1.55
Lateral tension	4	3.03	1.99	3.78	1.03
Hepatopancreatico - Biliary					
Liver lift (rt lobe)	1	1.05	0.60	1.47	
Gallbladder Lift	3	2.11	0.22	4.45	0.11
Sustained lift over liver	3	3.65	1.54	5.08	0.35
Uterine Horn					
Lift (proximal, mid and distal)	3	0.86	0.28	1.23	0.29
Lateral tension	3	0.30	0.03	0.80	0.07
Bladder					
Lift	6	0.88	0.10	1.97	0.21
Lateral tension	8	2.93	0.07	4.90	0.82
Needle drive	2	1.00	0.07	2.49	0.23

Figure 5.9; Image defining the forces required to manipulate various tissue within the porcine abdomen.



5.4. Optimise Instrument Triangulation, Minimise the Force.

It has long been appreciated that performance with regards to a surgical task is enhanced with more pronounced instrument triangulation. This has, in the past only been assessed using predominantly task performance metrics such as time and pre-trial defined task end points with the optimum angle considered to be around 60 degrees (118).

It could be hypothesised that the force imparted on the instrument, and therefore in reflection upon the tissue, during dissection would reduce the closer to the optimum triangulation. An *ex-vivo* study was designed to test this hypothesis using the in-house designed force instrument.

5.4.1. Method

The task involved the dissection of skin from a chicken breast within a laparoscopic box trainer. A pre-defined circle with standardised diameter of 5cm was inked onto the skin of the chicken breast for the subjects to dissect around. The instruments used were only the laparoscopic force sensing grasper and endoshears (no force sensing). Each subject would perform the task through a series of four different instrument triangulating angles; 10 degrees, 40 degrees, 90 degrees and 140 degrees (*Figure 5.10*). These angles were chosen to cover the range of potential instrument triangulations seen during clinical practice from single incision surgery to wider angles seen during laparoscopic abdominal surgery. Each subject was randomly assigned to which angle they would start and follow on with, so as to minimise any effect of learning.

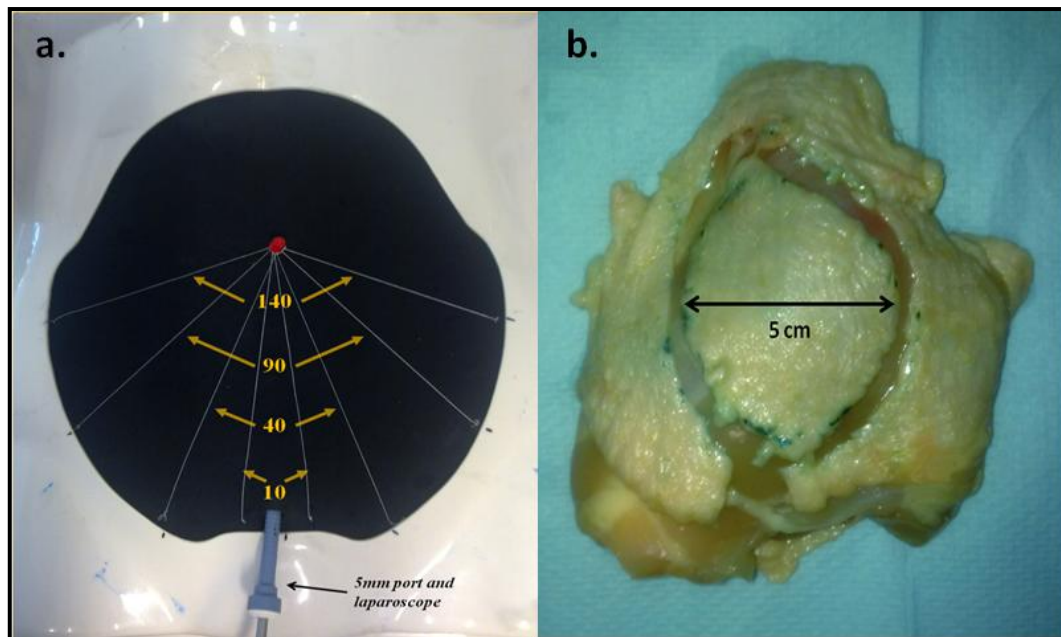


Figure 5.10; (a) Laparoscopic box trainer with the angles through which the task was performed highlighted and (b) the disc of chicken skin required to be dissected as the task.

For each of the tasks the ports were placed in the peripheries, adjacent to the marks on the box trainer. These correspond to the appropriate angles and was standardised for each subject.

The measurements from the X and Y strain gauges were recorded and the vector magnitude of the force calculated. Statistical analysis was performed using non-parametric tests – Wilcoxon Rank (SPSS software) with significance taken as $p < 0.05$.

5.4.2. Results

11 surgical trainees; 3 females and 8 males, undertook the dissection task at each of the four pre-defined angles. Each subject was experienced with conventional laparoscopic surgery with a variable range of experience levels and each subject performed the dissection with close adherence to the outlined marked disc. The force measurements for each of the subjects are shown in *Table 5.2*.

Subject	Degree of triangulation			
	10	40	90	140
1	0.94	0.78	0.58	0.52
2	1.03	0.59	0.61	0.65
3	1.00	0.88	0.27	1.14
4	0.71	0.526	0.39	1.17
5	0.77	0.76	0.83	0.66
6	0.45	0.39	0.34	0.40
7	0.79	1.30	0.55	0.86
8	1.05	0.60	0.68	1.29
9	0.78	0.59	0.42	0.82
10	1.62	1.08	1.32	1.53
11	0.78	0.23	0.40	0.46
Mean	0.90	0.70	0.58	0.86
SD +/-	0.29	0.30	0.29	0.37

Table 5.2; Table of the vector force magnitude for each subject and for each of the triangulating angles.

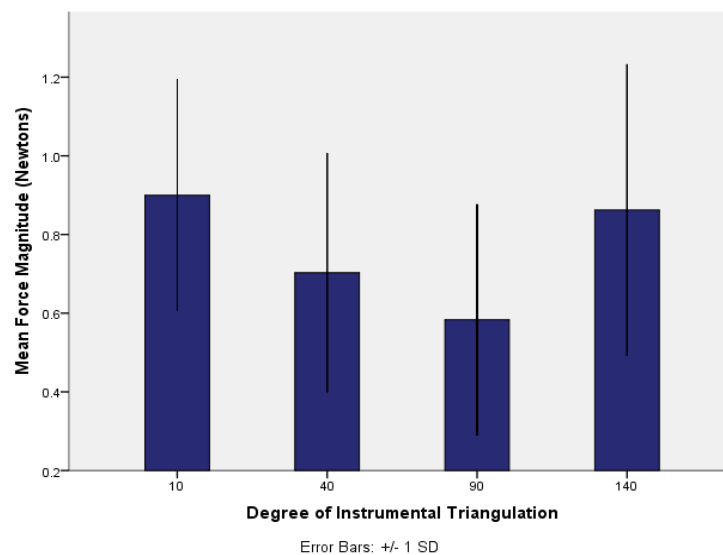


Figure 5.11; Graphical representation of the mean vector force magnitude from all eleven subjects.

The outcomes highlighted a reduction in the amount of force required to undertake the dissection as the triangulation of the instruments increased towards 90 degrees with a

significant reduction ($p=0.042$) when 10 degrees was compared to the 90 degree triangulation. Further triangulation beyond this level further raised the force requirements though in this trial this was not significant.

This short trial demonstrated that the level of force required to perform a laparoscopic task can be reduced by optimising the angle of instrument triangulation. Although only four angles were examined during this trial it highlights not only the importance of instrument triangulation during surgery, whether during laparoscopy or when considering instruments designed with flexible access surgery in mind.

One argument as to the results of the findings may include the lack of measuring the force derived through the Z-axis of the instrument which is with this instrument unable to be measured. With increased triangulation the use of the instrument to place the tissue under tension through the Z-axis would increase up to 180 degrees in relation to the tissue. However, if the result of the finding was related to this deficiency then it is likely that the findings of the forces at the 140 degree level of triangulation would be lower than that found at 90 degrees which doesn't appear to be the case. However, more detailed analysis with instruments capable of measuring the force through the Z-axis as well as the X and Y-axis would more precisely define optimisation. Further investigation into the declination of the instruments in relation to the tissue bed may also demonstrate an optimal angle in terms of force reduction. One other aspect which may confound these results is that at the narrow 10 degree angle the level of instrument interaction and clashes is larger which could have an influence on the high level of force seen at this triangulation. Nevertheless, once again if this were a significant factor then the level of force at 140 degrees would also not be high. However, this aspect cannot be completely ruled out from this trial.

5.5. The Forces Required for a Focused Clinical Application.

It is essential when considering instrument design for tools aimed at the abdominal flexible access market to have a basic understanding of the forces required to perform simple tasks. However, this will only provide information on a solitary force. To design an instrument that is clinically relevant will require a more in-depth assessment of the forces that are involved when performing of a full clinical procedure.

When examining the forces undertaken during such a complex task multiple confounding influences could potentially cause inaccuracies in the data. Of note is the instrument interaction, such as the clashes noted in the previous trial. These can produce high spikes in the force readings with variable effects on the data leading to inaccuracies. In addition, many surgical procedures rely on a variety of instruments which are altered and changed during the procedure. This also challenges the results often creating readings of forces from the instruments being applied to external elements such as the anterior wall or the port. In order to gain a greater degree of accuracy relating to these force requirements, it is essential that these are considered and overcome.

5.5.1. Mapping the Instrumental Forces for the Laparoscopic Cholecystectomy.

This trial aims to explore the instrumental force requirements during a laparoscopic cholecystectomy. It aims to better quantify the force magnitude and most common directions of force applied during each step of this procedure.

5.5.1.1. Materials and Methods.

Experimental setup and task

An *ex-vivo* porcine laparoscopic cholecystectomy was undertaken in a standard laparoscopic box trainer (Pharmobotics Ltd, Winchester, UK). The liver was fixed to a cork board using pins placed at standardised position around the mesenteric attachments of the organ to secure it in place; anatomical variations aside. The cork board was secured within the laparoscopic box trainer in a set position. In order to reduce the need for instrument changes particularly at the point of clipping the cystic duct, two clips were placed on the duct before the task was started. The gallbladder was elevated with a secure laparoscopic grasper to the fundus to place it under stretch as it would be in the real environment, and held by an assistant throughout with direction as to when to release undertaken by the subject.

Subjects of varying skill levels in laparoscopy and laparoscopic cholecystectomy; defined by a short questionnaire relating to each subjects case experience in terms of both experience in laparoscopic cholecystectomy as well as laparoscopy over the past five years, were asked to perform the task in the normal fashion. The questionnaire included three questions which enquired over each subjects laparoscopic experience base through a two five points scales relating to case numbers of laparoscopic cholecystectomies and general laparoscopic surgery. Seniority as a baseline of experience was used to differentiate for rank order those subjects who had the same score when both 5 point scales were calculated.

The task was to undertake a full laparoscopic cholecystectomy using the force sensor and a pair of endoshears without diathermy (*Figure 5.12*). The lack of diathermy was essential as the high current used in electrocautery, even if the instruments were not touching, distorts the force sensor readings.

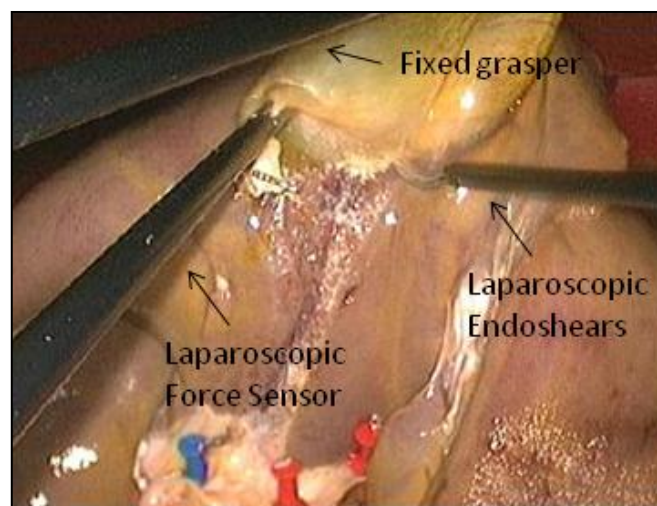


Figure 5.12; Ex-vivo porcine laparoscopic cholecystectomy trial using the laparoscopic force sensor and conventional laparoscopic endoshears for dissection.

The positions and orientations of the laparoscopic tools were tracked using an NDI Aurora electromagnetic tracking system (Northern Digital, Inc, Waterloo, ON, Canada). The endoscopic video was captured using a PC video capture card connected to the S-video output feed of the endoscope control unit. Synchronisation of the tracking and video was performed using in-house software. This enabled not only both the direction of the force sensor readings and the force magnitude to be determined but also to define the particular video frame that this force and direction was relevant to. Once the video feed and force sensing laparoscopic tool was synchronised; using a simple visually recognizable sequence of

tapping of the force sensing instrument and correlation to the X and Y strain gauge responses in post processing, then all forces defined during analysis could be attributed directly to the appropriate frame of the subject's task.

5.5.1.2. Data Analysis

A custom engineered Matlab™ software graphical user interface was created to enable visualisation of the force data collected throughout each subject's task, which was coupled with the aurora magnetic positional tracking data to enable force direction to be ascertained (See *Figure 5.13*). Forces which appeared to be erroneously elevated could be highlighted and the appropriate video frames, synchronised to the data set, analysed to confirm the reasons.



Figure 5.13; Raw data from the X and Y strain gauges for the entire length of the procedure is seen on the left. Force is highlighted in Newtons with the time in unit samples. On the right the display highlights the direction of the force for a particular time point indicated by the arrow and the magnitude by its length.

Forces attributable to causes other than those related to tissue dissection and gallbladder retraction could then be cut and removed from the data set so as not to affect the overall force readings. This included instrument strikes against each other and the neo-abdominal wall, as well as on occasions when the instrument needed to be removed from the operating area as a result of the need to re-apply a clip to the gallbladder to prevent bile leak complicating the dissection. This in effect enabled the data collected from the tasks to be cleaned in post

processing to isolate only those forces directly attributable to the procedure before formal analysis of the data was undertaken.

Although, major events could be visualised using this technique, smaller instrument strikes, which often give high spiked force readings and can skew the results were difficult to see even when close scrutiny of the relevant video frames was undertaken. As such these were not removed but the whole data sequence was subjected to a low pass moving average filter which was able to smooth the high spikes of the data without removing them entirely enabling these high spikes not to significantly interfere or skew the overall analysis of the data.

The user interface also enabled the time course events to be marked out during the task and time frames and the force data relating to these events analysed in separation. Videos of the laparoscopic cholecystectomy from each of the subjects were reviewed and the time points relating to the precise period when the cystic duct was ligated; the initial part of the operation, was recorded. This time point was marked on the user interface for each of the subjects together with the precise start i.e. when the initial contact was made with the force sensed instrument onto the tissue bed, and the end point i.e. when the last cut was made to remove the gallbladder from the liver, as determined from the videos. With these points set, the data could be processed to include these events independently or the procedure as a whole.

Evaluation of both the force and the direction of the forces across the whole task were performed with the minimum, maximum and average force determined. With the time points for the reference events defined, the force data could also be analysed for ligation of the cystic duct (time point “*start of dissection*” to “*ligation of Cystic duct*”) and removal of the gallbladder from the liver bed in isolation (time point “*ligation of Cystic duct*” to “*gallbladder removed*”). Non-parametric statistical analysis was used to analyse some of the comparative data with significance taken at $p < 0.05$.

5.5.1.3. Results

11 subjects with experiences ranging from <50 to >500 laparoscopic cholecystectomy and general laparoscopic cases as the primary surgeon, were recruited from within the Imperial

College Healthcare NHS trust, Department of Surgery. 3 experts, 5 intermediates and 3 junior trainees took part in the trial. The minimum, maximum and mean forces together with the standard deviations were recorded and are highlighted in *Table 5.3*.

From all the subjects the minimum force required to undertake the whole procedure was 2.4N (Newton) with an overall mean force requirement from all 11 subjects being 1.4N (+/- 0.6) with the mean maximum force occurring during the task being 4.4N (+/-1.7). Although differentiation between the instrument-tissue force between junior trainees and experts could be visualised, these differences were only weakly significant with experts imparting a mean force for the procedure of 0.94N and the junior trainees 1.56N ($p=0.050$). This difference was noted when each section of the operation was separately reviewed with similar levels of significance. No difference could be determined between the intermediate level trainees when compared to the junior trainees or experts across the whole task or when separated.

In addition to the magnitude of the force, the direction of the applied force was also evaluated. This was determined both through the use of a radial 2 dimensional heat map which highlighted not only the raw directions of imparted force with their corresponding magnitude during each part of the procedure but also the direction of the most prominent force direction. The most prominent direction was determined using principle component analysis (PCA). This could be overlaid onto the radial map and a visual comparison can be made with the raw directions.

Table 5.3; The minimum, maximum and mean values of the force magnitude measured by each of the subjects for the complete *ex-vivo* porcine laparoscopic cholecystectomy.
(The subject requiring the least force to complete the procedure is highlighted in bold red)

Laparoscopic Cholecystectomy										
Subject		Whole procedure			Division of Cystic Duct			Dissection of gallbladder from liver bed		
	Experience score	Min	Max	Mean	Min	Max	Mean	Min	Max	Mean
1	3	0	4.08	1.62	0	4.08	1.64	0.01	3.71	1.59
2	7	0	5.94	2.15	0.05	4.75	2.1	0	5.94	2.17
3	13	0	2.98	0.93	0.01	1.96	0.85	0	2.98	0.95
4	9	0	5.67	1.83	0	5.67	2.14	0	2.59	1.2
5	3	0	4.46	1.47	0	3.84	1.13	0	4.46	1.54
6	9	0	4.25	1.32	0	3.19	0.9	0	4.25	1.42
7	5	0	3.7	0.76	0	3.11	0.81	0	3.69	0.74
8	13	0	3.52	1.25	0	2.79	1.01	0	3.52	1.39
9	7	0	2.43	0.64	0.01	1.59	0.26	0	2.43	0.67
10	13	0	3.12	0.64	0.01	2.50	0.53	0	3.12	0.68
11	3	0	8.53	2.37	0	5.03	2.35	0.03	8.53	2.38
Mean			4.43	1.36		3.50	1.25		4.11	1.34
StDev (+/-)			1.73	0.59		1.30	0.70		1.76	0.57

It would be anticipated that the in cases where there is low variance in the direction of the forces, the most prominent direction of force would point in the same general direction as the raw presentation, as indicated on the radial heat map, however this does not always appear to be the case. This can be explained by examining the underlying distribution. There may be cases for instance when there is a multimodal distribution and the most prominent direction points to none of the modes; in these cases the direction may point to the darker areas of the disc (*Figure 5.14*) as the most prominent direction represents the direction which explains more data variability, i.e. higher variance which is necessarily computed over the number of samples pointing to a particular direction.

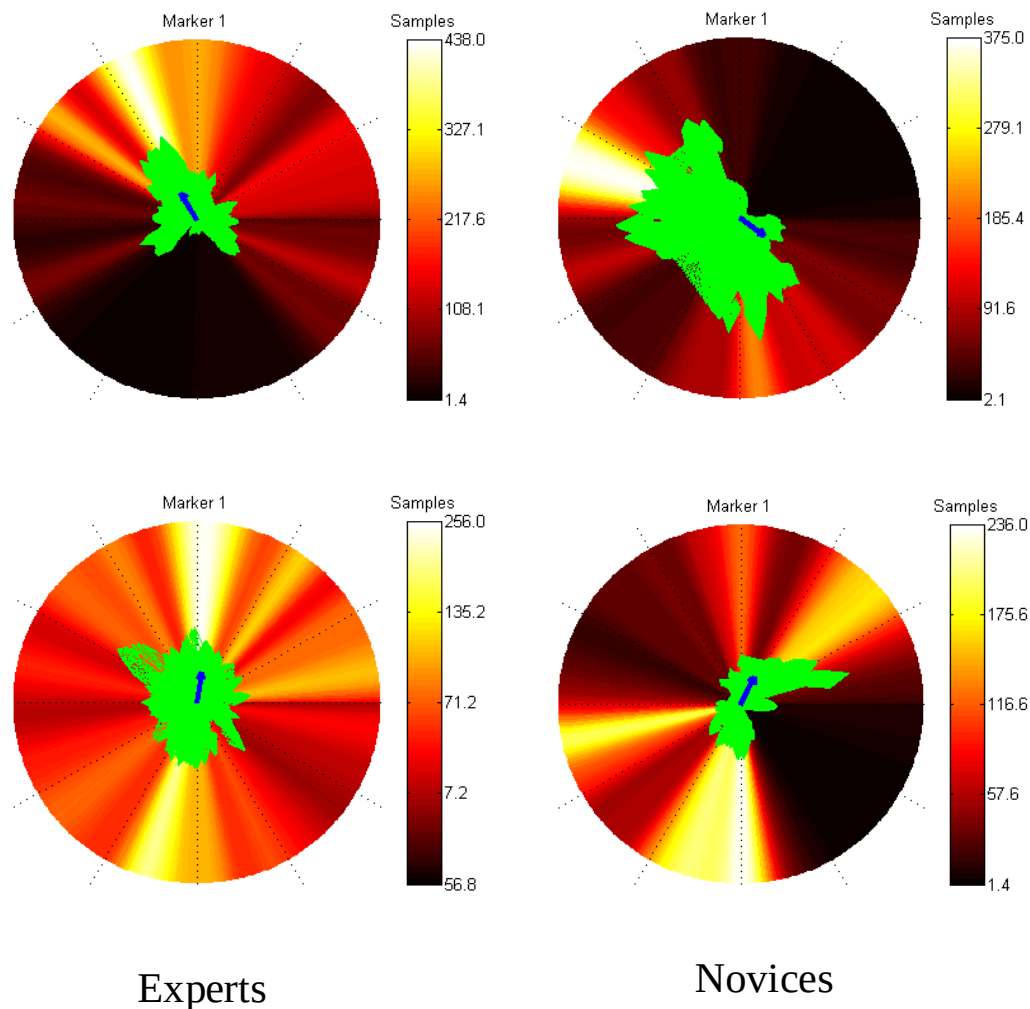


Figure 5.14; Four *radial force maps* extracted from four subjects; two experts (left images) and two novices (right images) and represent all the elements of the forces that occurred during the complete *ex-vivo* laparoscopic cholecystectomy.

The maps highlight the magnitude of the force (green) with the scale of the circle set so the radius is equivalent to a force of 6N. The intensity of the direction of the forces is demonstrated through the use of the radial heat maps with the white highlighting the direction of highest sample intensity and the most prominent direction of force (direction of the blue arrow) calculated using PCA.

It may therefore, be reasonable to consider that expert laparoscopic surgeons undertaking the cholecystectomy are more precise in where the force is placed on the gallbladder to create the instrument triangulation more efficiently than the novices, and as such, it would be expected that the most prominent force direction would align with the sample intensity more frequently in these cases. For the junior laparoscopists, who perhaps are less adept with the operation, the forces that can be applied without tissue damage and the best placement of the instrument to enable continuous traction for tissue plane demonstration requires more experience. A continual replacement of the instrument in an attempt to realign the retracting instrument, or in this case the force sensing instrument, to maintain the most appropriate level of traction force could be one explanation. Furthermore, it is felt in clinical practice that trainees often forget the use of the retracting instrument with the concentration firmly placed on the dissecting instrument. Without constant tension on the tissue the dissecting tissue plane is lost and the trainee tends to reposition the instrument more frequently whilst the expert continually adjusts to maintain tension without the need for replacing the tool at regular intervals.

Although this is demonstrated to some extent when the radial force maps for all the subjects ranked in order of experience are compared (*Figure 5.15*), it is difficult to quantitatively assess, and given the lack of the third dimensional element to the force sensor readings, may only at best infer this difference rather than confirm a definitive causal relationship. However, the concept of this lack of precision of placement of the force could be demonstrated through exploring the impact in the sustained length of time a given force is placed on the tissue. Through approaching the problem from this angle it may offer an alternative method of demonstrating this lack of precision for force placement which is suggested by the data as associated with the trainee surgeon. This will be explored later in this chapter.

The mean direction from all the most prominent directions of force each segment of the procedure and from all subjects was estimated. The X and Y vectors, determined from the PCA evaluation from each subject was converted into radians ($=\text{atan2}(x,y)$) and further converted to degrees ($=\text{Rad} \times (180/\pi)$) where 0 degrees lies along the horizontal positive X-axis with increasing degrees moving anti-clockwise. The mean direction was calculated from these values and plotted. It is evident that the predominance of force applied to the tissue bed

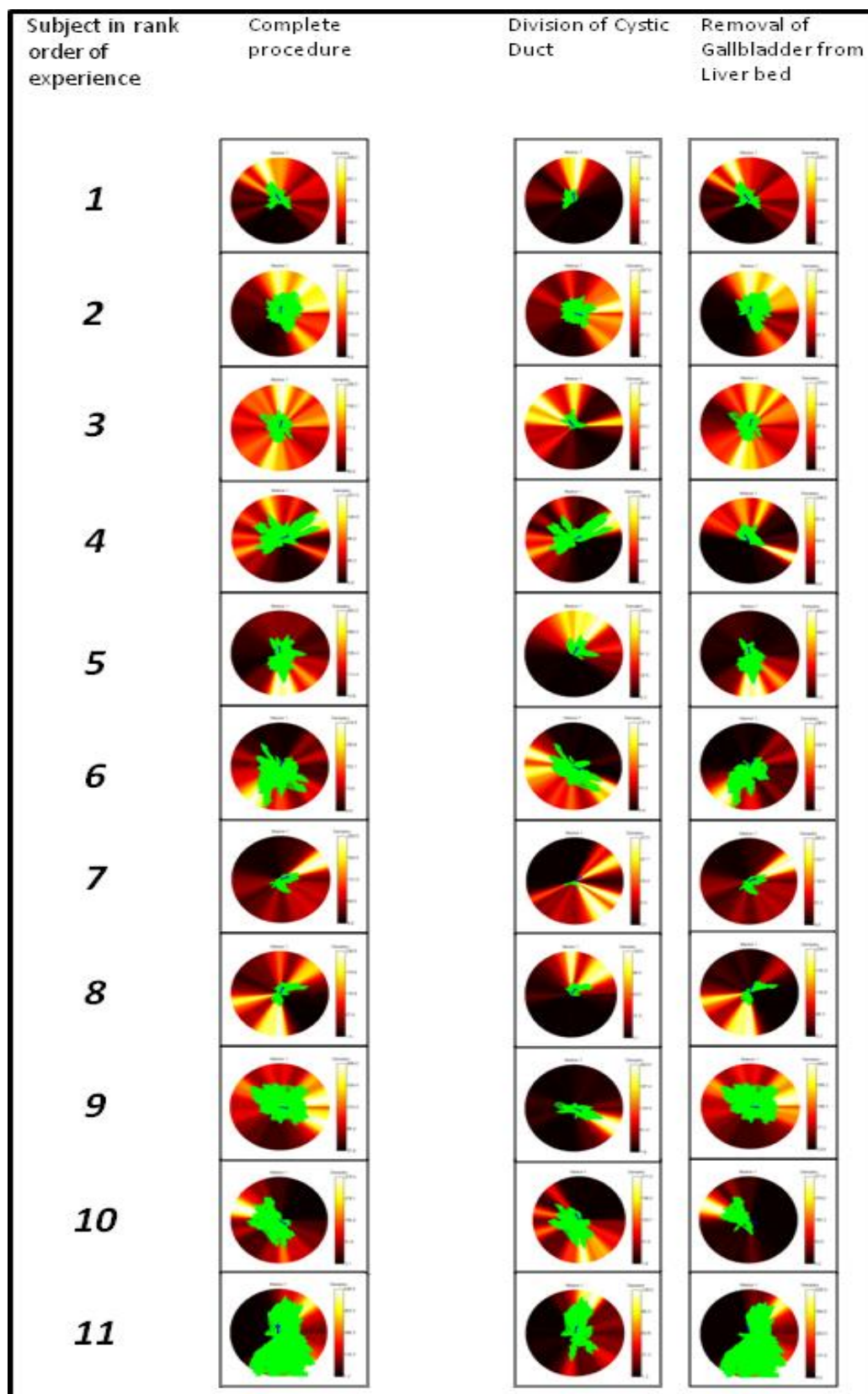


Figure 5.15; Radial force maps for all subjects placed in rank order of laparoscopic experience. The magnitude of the forces (green) and the alignment of the most prominent direction with the sample intensity cannot be used as independent markers of laparoscopic skill. (scales of the maps are as described above.

was in a direction which ranged from 51 degrees to 215 degrees. The overall mean prominent direction of force for performing the whole laparoscopic cholecystectomy was 120 degrees from the horizontal with 146 degrees for the dissection and ligation of the cystic duct and 131 degrees for the gallbladder removal. This implies that the most prominent force applied was towards the upper left of the tissue bed when considered in a 2 dimensional plane which would be anticipated given the taught approach to the laparoscopic cholecystectomy in terms of dissecting Callots triangle and then elevating the gallbladder to show the tissue plane between the liver and the gallbladder when dissecting the gallbladder off the liver bed. Independently it appears that experts operate with more tension placed in the upper half of this plane with the juniors trainees more prominent towards the left and lower left quadrant, which may indicate that with experience of the procedure and adaptation of the retracting instrument to best suite dissection, the force imparted tends to be moved more towards the anterior abdominal wall (*Figure 5.16*)

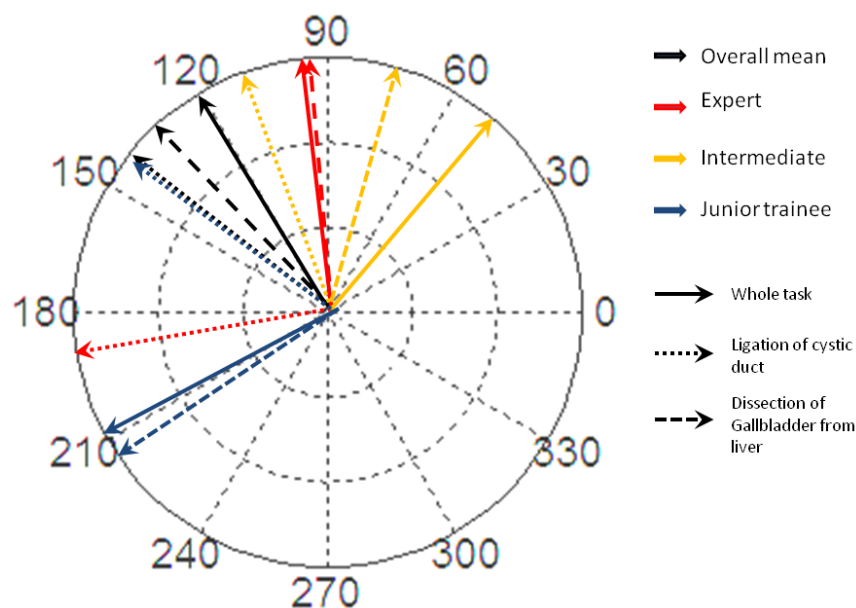


Figure 5.16; Image representing the mean of the most prominent directions of force extrapolated from all the subjects and calculated for junior trainees, intermediate trainees and experts as well as for each part of the procedure.

In all the level of force required to manipulate tissue is at a maximum of 6 Newton within the porcine model at an optimum force triangulation of between 60 and 90 degrees.

Without the retraction force for the gallbladder over the liver bed, the force requirements to undertake a laparoscopic cholecystectomy were reviewed across each section of the operation with a mean of 1.34 N and a maximum of 4.11 N required for the removal of the gallbladder from the liver bed; the highest level of force required for the procedure (*Figure 5.17*).

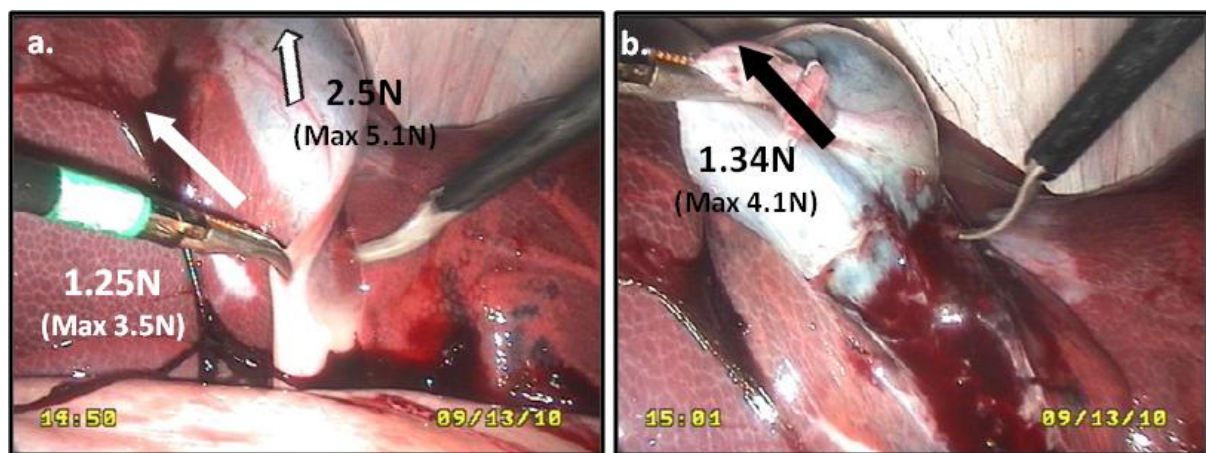


Figure 5.17; Summary of the force requirements to undertake a laparoscopic cholecystectomy. Images from *in-vivo* trials using the force sensing instrument; left image shows dissection of Calots triangle and right the removal of the gallbladder from the liver bed. Arrow with black border in left image represents force required to lift gallbladder to demonstrate Calots triangle.

5.5.2. Can the Forces on the Tissue Bed be reduced through more Precise Instrument Placement?

It has always been considered that the junior surgical trainee interacts with the tissue more frequently than the expert surgeons and that the undertaking of the surgical procedure could be performed with less frequent changes of the tool position on the tissue bed. However, the evidence is anecdotal at best with only subjective evaluation undertaken; more often at the operating table during a training case.

The radial force maps, reviewed above, when considered in combination with the prominent force direction (blue arrow on the radial force maps), inferred that there may be some element of disorder associated with the distribution of the forces through the instrument relating to the junior trainees. The experts on the same maps tended to demonstrate a more ordered delivery of the forces, with the prominent direction visibly mapped to the most common force direction when overlaid. It is unlikely that this disco-ordination seen amongst the novices

relates to anything other than chance, nevertheless the discrepancy was further evaluated to ascertain whether the variation of the tool tip position upon the tissue bed could be relevant to these findings. It may be considered that with a significantly lower overall force provision as demonstrated from the experts could it be that this lower force is as a result of more optimal placement of the instruments on the tissue bed during dissection.

To evaluate this further, the signal variation recorded by the force instruments created during the cholecystectomy task for each of the subjects, was analysed. To determine the frequency variation associated with each of the force data sets, a Fourier Transform was applied. This enabled the visualisation of the frequency variation (Hz) that occurred during each of the samples to be evaluated between subjects (*Figure 5.18*). The extent that a specific frequency of force variation (X-axis) is determined within the dataset is summated as power (ms^2) for that frequency (Y axis).

For the purposes of primary data analysis using the Fourier Transform, the section of the operation relating to the *removal of the gallbladder* was assessed in isolation. This consideration was predominantly due to the pig's anatomy of the Calot's triangle, which although similar to the human, the operative similarities do not compare to the true complexities of that section of the operation within the clinical setting. The removal of the gallbladder from the liver bed, however, offers a greater sample range to analyse and clinically resembles more closely that section of the laparoscopic cholecystectomy within the human being.

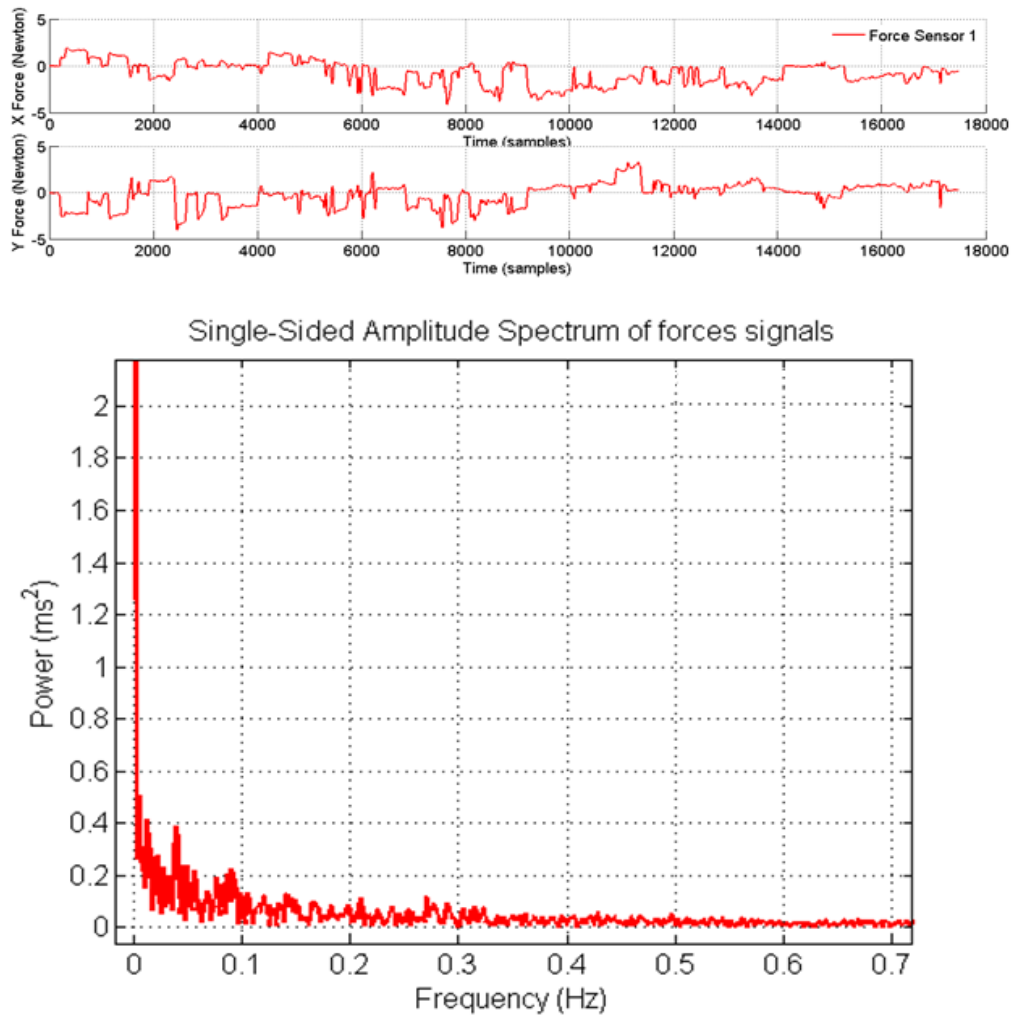


Figure 5.18; The Fouriers Transform (bottom) of the combined force dataset from both the X and Y strain gauges, shown separately above.

5.5.2.1. Method.

Fourier Transform of the force sensed data associated with removing the gallbladder from the liver bed was undertaken for all subjects and analysed to explore whether any differences between the subjects in relation to the levels of force variation could be identified. It is hypothesised that junior trainees re-position the retracting instrument excessively during the task.

The Fourier Transform analysis technique was used due to its ability to quantify the magnitude of the frequency ranges that exist within a given time domain relating to the tool tissue interaction as expressed from the readings from the force sensors on the instrument.

The magnitude of various frequency variations can be defined by recording the area under the curve in the frequency domain between a given frequency range.

Furthermore, the frequency at which the power (amplitude of the frequency) dropped below a predetermined threshold provided some evidence as to the range of frequencies of tissue-instrument interaction which that subject had undertaken during the task; the higher the frequency range that occurred during the task the greater the amplitude recorded for that frequency. As a result this aimed to provide some insight into whether the instrument was being frequently altered in terms of its position on the gallbladder during the task. In all cases these values were compared against the laparoscopic experience level as determined from the initial questionnaire. It is hypothesised that the level of variation, and therefore the level of tool-tissue interaction across the subjects would be lower in the expert group when compared to the junior trainees.

Data analysis

The Fourier Transform (FT) was graphically presented in a similar manner for all subjects with the predominance of power, demonstrated across all subjects to be broadly within the lower frequency range; 0 to 0.5Hz with fluctuations extending into very high ranges thereafter at lower power which could be considered as noise. An arbitrary power level of 0.1ms^2 was chosen after visually evaluating the graphs, as the level which could be considered as being of significant power to suggest instrument-tissue interaction and not simply noise.

Each of the subjects FT was reviewed and a common frequency range of 0 to 0.5Hz evaluated. This was considered to be a reasonable range as there was a visual drop in power across most subjects after 0.5Hz. This range was further subdivided into frequency ranges which corresponded to *Low Frequency (LF)* 0 – 0.1Hz, *Medium Frequency (MF)* 0.1 – 0.2Hz, *High Frequency (HF)* 0.3 – 0.4Hz and *Very High Frequency (VHF)* 0.4 – 0.5Hz. The area under the curve (Hz/ms^2) for each of these ranges was calculated to explore the extent of the variation that occurred in the force readings across the particular range during the sampled event and compared across the groups. In addition the area under the curve (AUC) for the range 0 – 0.5Hz as a total was also calculated, together with the ratio of the lower and higher frequencies with this value calculated as a percentage of the total AUC.

Statistical analysis of the data was undertaken using the Kruskal-Wallis and further the Mann-Whitney U test for independent non-parametric data with the level of significance set at $p=0.05$. Correlation between specified data where appropriate was assessed using the Spearman's rank co-efficient with significance of any correlation again set at $r=0.05$.

5.5.2.2. Results

The time taken to complete the task across all the subjects ranged from 79 seconds (s) to 975s, mean 479s (± 272). No significant difference was determined between junior trainees, senior trainees and experts ($p=0.827$). When a threshold power level of 0.1ms^2 was considered, the last frequency that dropped below this power varied between subjects and ranged from frequencies of 0.0223Hz to 0.271Hz with a significant difference noted when these levels were compared between the experienced surgeons (mean 0.078 ± 0.105) and junior trainees (mean 0.181 ± 0.096) ($p=0.05$) with, in addition, a significant difference noted between the intermediate trainees when compared with the experts ($p=0.025$).

The overall AUC for the frequency ranges of 0 to 0.5Hz also varied between subjects with the mean values for the junior trainees, intermediates and experts being 0.014 (± 0.002), 0.030 (± 0.016), and 0.033 (± 0.013)Hz/ ms^2 respectively which was found to be significant $p=0.034$. This difference was found to be the case across all the frequency ranges defined as may be expected with the significance across the groups using the independent test for non-parametric data being $p=0.049$ with the significance being seen between the experts and intermediates ($p=0.025$) perhaps more strongly than between the experts and juniors ($p=0.05$) with no difference noted between the juniors and intermediates. A similar significant difference was noted when each of the frequency ranges were taken in isolation and compared. When the ratio of the lower frequency ranges, 0 to 0.2Hz was taken as a percentage of the overall AUC for 0 – 0.5Hz no significant difference was found between the groups ($p=0.886$) (Table 5.4).

These results move to suggest that there is a greater degree of tool-tissue interaction amongst junior trainees which clearly differentiates this subgroup and intermediates from the expert laparoscopic surgeon. Although it may have been considered that the expert would impart predominantly a lower frequency; i.e a more sustained force application onto the tissue bed

rather than varied intermittent tissue manipulations, it seems that this is not the case and that all frequencies of instrument interactions are reduced to a similar extent. It therefore suggests that it is likely that the expert as expected undertakes the task in general more efficiently with less tissue interaction than the junior trainee.

Table 5.4; Table showing the results of the areas under the curve (Hz/ms²) for the pre-defined frequency ranges and the frequency drop (Hz) below 0.1ms² for each subject.

Subject	Experience Score	AUC (LF) 0 – 0.1 Hz/ms ² x10 ³	AUC (MF) 0.1 – 0.2 Hz/ms ² x10 ³	AUC (HF) 0.3 – 0.4 Hz/ms ² x10 ³	AUC (VHF) 0.4 – 0.5 Hz/ms ² x10 ³	Ratio of LF to HF	Ratio of MF to HF	Frequency (Hz) drop below 0.1ms ²
1	3	24.8	6.4	3.4	2.5	1.209	0.311	0.2712
2	7	23.9	6.8	2.6	2.1	6.755	1.916	0.1688
3	13	9.0	2.0	1.3	1.0	7.001	1.588	0.0650
4	9	25.0	8.2	5.9	3.9	2.816	0.929	0.2732
5	3	10.0	3.1	1.4	1.2	4.824	1.485	0.0870
6	9	10.6	3.1	1.7	1.3	5.836	1.670	0.1092
7	5	12.2	4.2	2.0	1.6	4.082	1.393	0.1102
8	13	8.6	2.7	1.3	0.8	5.099	1.616	0.0645
9	7	8.6	3.0	1.6	1.1	4.13	1.463	0.0759
10	13	5.8	2.3	1.2	1.0	3.891	1.576	0.0624
11	3	16.9	7.5	4.0	2.5	4.284	1.491	0.2580
Mean		14	4.5	2.4	1.7			

On considering the mean and maximum force magnitudes, which also demonstrate significance between the junior trainees and the experts (Chapter 5.5.1), the force variation determined here does not correlate with the mean force magnitude $r=0.083$ or the maximum $r=0.326$. Given that the length of the operative task also demonstrates no significant difference between the groups it would appear that the force variation, thereby the degree of tool tissue interaction and the magnitude are separate factors in determining operative skill for this procedure.

Furthermore, the difference noted in the variation of force and therefore tool tissue interaction between the novices and experts could be as a result of either the experts better placing their instrument on the tissue bed to apply the force required to undertake the dissection, or the novice surgeons are indecisive about their instrument placement and have a tendency to change the position of their tool more frequently. This may move towards the possibility that better or more optimal tool placement on the tissue bed, as seen by the experts, could enable the procedure to be performed with less force imparted.

5.6. Conclusion

This chapter defines the level of forces required to manipulate tissue within a clinical *in-vivo* setting. The design and utilisation of a laparoscopic tool which had been adapted to measure forces during surgery was described within the *ex-vivo* and *in-vivo* setting to explore the levels of force that are required to not only lift and manipulate tissue but also perform a particular procedure; the laparoscopic cholecystectomy. Furthermore, the degree of instrument triangulation was also evaluated to explore the optimum degree of tool tissue triangulation through defining the level of force imparted on the tissue bed during a laparoscopic task.

However, there was evidentially a variation in this force across the subjects, with junior trainees demonstrating a higher mean force and indeed maximum force when compared to the expert surgeons. This was only weakly evident and further analysis revealed that the variation in the instrument – tissue interaction was significantly less with the experts over the novice and intermediate trainees suggesting the possibility that experts placed their instruments more precisely on the tissue bed as a means to demonstrate the appropriate dissection planes. It also suggested that experts, once the instrument is placed, tended to leave the retracting force imparting in the same direction rather than intermittently changing it; as reflected by the force variation analysis.

This work should enable engineers developing novel instrumentation for flexible access surgery to have a more precise gauge of the force requirements imparted during surgery and also the potential ways of being able to minimise this force through optimal tool triangulations as well as more precise placement of the instruments onto the tissue bed before embarking on dissection.

Chapter 6

A Robotic-assisted Flexible Access Platform

Hypothesis:

A clinically relevant hyper-redundant robotic endoscope can be engineered to reliably and repeatedly be used to access a target within the in-vivo environment from two separate single incision sites one of which includes using a natural orifice.

6.1. Introduction

The previous chapters have highlighted and explored a number of factors which are essential for flexible access surgery to be realistically achievable and clinically translatable. This includes the provision of a flexible surgical platform capable of navigating from a single access point to a distant target site which may be out of direct line of sight from insertion. Once at the target it is essential that the platform offers on-demand stability from which instruments can be delivered and interact with the tissue bed without recoil. For more complex surgery, clinically relevant triangulating instrumentation capable of providing enough force to manipulate and dissect tissues with greater reliability and precision would be required.

Uncontrollably flexible platforms like the investigative dual channel colonoscope are unable to provide the repeatability and safety essential for navigation within the *in-vivo* clinical environment, or the stability required when preparing to undertake any form of procedure. Aside from these and as has been shown in Chapter 3, the experience required to be proficient and thereby safe at undertaking the flexible access technique using such a device is far too long for it to be considered viable by the general surgical community. The result of which would be a disregard of the technique before it had even been formally trialled.

The problems surrounding flexible access surgery are well described across the NOTES community (109) and as such novel designs have already been explored and circulated in an attempt to meet them, as was described in Chapter 2. However, evidently they fail to meet the full combination of essential elements required for the technique within a single platform. As

a result smart devices; enhanced mechatronic and robotic, have been explored as potential natural orifice platforms within the research setting which could be adapted for the flexible access technique. The benefits of introducing smart platforms into this surgical field enables the promotion of not only greater opportunity towards overcoming the main highlighted challenges; safe access, target acquisition and navigation, but also the ergonomic challenges of manually manipulating a flexible device within the body cavities as was seen the introduction of the previous generation of minimally invasive surgical operating systems; the DaVinci™ (Intuitive Surgical, California, US). Overcoming the ergonomics and shortening the proficiency curve will ultimately promote greater opportunity for the technique to be accepted into clinical practice. With all factors taken into consideration it seems that the only practical way flexible access surgery will enter the clinical field is within the realm of robotic-assistance.

Furthermore with enhanced mechatronics and autonomous sensing, the true advantage to this adjunct will be through the introduction of the computer aided platform into flexible access surgery. As a result this will not only open up the potential of overcoming the basic elements hindering the technique as described but also enhance it further through promoting even greater reliability, precision and most importantly safety over and above any manual or direct drive design.

It may be argued that under some circumstances the simplest answers to the most challenging questions are often the most effective. With NOTES currently being performed only by experienced endoscopists, perhaps the answer to simplifying the technique is to robotically actuate the controls of the standard endoscope and mimic the expert's manipulations with automation. Of course this would only work if the whole endoscope could be controlled in a consistent manner for a given procedure (1). The dynamic flexibility and therefore the lack of predictable navigation of the endoscope within the anatomical compartment, limits its capability for full automation. Similarly, the Direct Drive Endoscopic System (Boston Scientific, MA, USA), a device which boasts tendon driven instrument triangulation and end effector manipulation for endoluminal surgery with the capability of instrumental interchange. Although, this platform is manually controlled over mechatronic or robotic, it effectively provides all the requirements for end organ instrumental manipulation required. However, the device once again relies upon manual manipulation to navigate the instruments to the target organ. Mechanising and therefore robotically actuating such a device would be

feasible in relation to the instrumental controls however the instigation of a shaft lock device would be required to enable the curved path to be rigidly maintained throughout its length during use of the end-effectors. The shaft lock would need to be released before further positioning of the instruments is obtained and then re-locked before use, a system which is not smooth or entirely ergonomic. The consideration to robotically actuate the controls of a standard endoscope, control the flexibility of the shaft during navigation or decouple the instruments to individual arm controls, overcomes only a selection of the numerous challenges for flexible access surgery to be truly successful. As a result, this approach limits the true potential that a dedicated flexible robotic design meeting many or all of the limitations could provide.

Software developments capable of being incorporated into surgical robots have continued to be engineered over the last decade as a means of exposing the true significance of the era of robotic assisted surgery and how it can impact on surgical safety through ever less invasive techniques. One particular area targeted for the robotic-assisted laparoscopic field is in image overlay or Augmented Reality. Major blood vessels and vital structures can be highlighted during surgery in real time onto the view screen of the surgeon as a means of both reducing the risk of inadvertent injury or in the case of structures such as tumours, defining their borders deep within paranchymal tissue. This enables the potential resection margins to be clearer and more precisely dissected during excision (125). When considering the future of robotic assisted flexible devices, the ability to highlight vital structures will enable these platforms to autonomously determine the safe zones within which to navigate and personalise it for each individual patient (126). The potential of which could be autonomous navigation from the incision point to the target zone without human interference and based on patient specific imaging, once at the target the surgical hand can intervene. Of course this is all conjecture and perhaps even bordering on fantasy however the most effective platform for flexible access will undoubtedly be smart.

The DaVinci™ robot, as an enhanced laparoscopic tool, developed in parallel to the introduction of the laparoscopic surgical era with the overall aim to present a surgical platform which could mimic the technique with the long term aim of overcoming the difficulties the technique presented ergonomically. With flexible access surgery, there is no true conventional instrument upon which to compare. Although the investigative flexible endoscope would be considered as the instrument for flexible access surgery the challenges

both ergonomic as well as significant integral design issues related to controlled navigation, stable platform and instrumental-tissue interaction are too significant to enable it to ever be an effective tool. Re-engineering with pure clinical focus in mind, is the only way flexible access surgery will become a true clinical reality and as such it is important to goal direct the design of such a device to reflect both its clinical relevance as well as taking into consideration its integration into the operating theatre so that all of the benefits of the computer aided platform can be presented through the single incision of the flexible access technique.

One example of a robotically designed flexible access system already trialled is the Neoguide™ robotic endoscope. A highly effective flexible platform designed initially as an endoluminal device although it was evidently capable of transluminal and intracavity navigation. Its ability to maintain its shape in whatever form along its entire length promoted itself as a strong potential platform for the technique. However, despite the hype, instrument triangulation was not in place with the system prior to its take-over. It may be that the difficulty of integrating tendon controlled end effectors into the tendon driven flexible shaft was too challenging.

There was minimal public exposure related to the platform or any related *in-vivo* trials before it was acquired by another major market competitor and suppressed. Therefore, outside of this company and the former Neoguide Systems Inc, only speculation can be made as to the clinical relevance of the platform. It is believed that the design was based on extended lengths of tendons, which passed through the centre of the device and attached to each jointed segment independently. The computational requirements for the kinematic modelling enabled each joint position to be recognized by its preceding and proceeding joint. There is no doubt that this was or is a strong competitor for robotic flexible access surgical platform and with the tendon drive offered not only superior control, an aspect not often assigned to the tendon drive systems but also strength in terms of robustness. The alternative design is the micro-motor system. Independent jointed segments within which the drive motors are embedded making up the articulating section of the device.

The benefits of using a micro-motor design is in the potential ability to overcome both the challenges of navigational flexibility and potentially more realistically integration of instrumental end-effector manipulation. With independent segments, the potential advantage

is in its ability to form long chains to a desired length without the need for any required diameter increase to the shaft in order to accommodate the increasing lengths; a problem often seen with tendon driven designs. Furthermore, there is also some evidence to support the benefit in terms of maintenance as only the faulty joint need be replaced rather than the whole device, a problem associated with all tendon driven designs.

It is considered that using an articulated hyper-redundant snake robot platform using the micromotor concept, a flexible access platform could be developed that can reliably and repeatedly be trialled within an *in-vivo* setting.

6.2. Materials and Method

A series of pre-clinical termination porcine trials were conducted to explore this hypothesis using a prototype device designed with clinical guidance based on a broad clinical gap analysis of the underlying requirements. In all cases a female “Large White” pig of approximately 70 – 80kg weight was used for each of the trials. These were conducted under full ethical approval according to the animal for scientific procedures act (1986); license number (80/2297) (Appendix 1 – UK Home Office Approval).

Each trial was conducted to explore and define the challenges associated with the clinical introduction of a prototype articulating device into the clinical environment and explore the design iterations that would enable reliable and repeatable access to be performed. The problems and challenges that presented themselves are described and the methods used to overcome them documented.

6.2.1. Clinical Considerations for the Design of a Prototype Flexible Platform

For an effective clinically relevant and potentially translatable flexible access platform, the features essential for its successful introduction into clinical practice need to be established at the initial design phase both through clinical gap analysis as well as through formal *in-vivo* feasibility and usability trials to determine the most important design elements and requirements.

The aspects already discussed in previous chapters allude to the requirements essential to the basic design of a flexible access robotic platform; the flexibility to access appropriate target organs from distant sites through a single incision and once at the target enable a form of surgical intervention to be undertaken with the benefits of a stable platform. The conceptual design of the individually controlled multi-segmented snake like design, as described above, focuses upon these essential features as prime. One of the most significant of all features of any new robot aimed at clinical translation is the overall size of the system both external to the patient and internal. The encroachment of a large device within the operating theatre, given the space constraints already restricted with anaesthesia, may not be as tolerated with newer devices as it is with the current clinical robot; an aspect that is essential to be taken into consideration at the earliest design phase.

The dimensions of the robot need to be of suitable size and strength to safely access the *in-vivo* environment yet capable of, if possible, utilising conventional laparoscopic ports. This would not only promote a robot which could be used as an on-demand device; inserted during any laparoscopic procedure at the times when high precision and image guided surgery is of most benefit and removed when no longer required, a theme of *pro re nata* robotic assisted surgery with appears to be well supported by the literature when robotic assisted surgery is reviewed (3, 127), but also promote an economic benefit for the overall cost of the product if it went to market. From a clinical perspective the small diameter of the articulating shaft will also enable enhanced manoeuvrability once inserted into the *in-vivo* cavity. Aside from the dimensions, clinical guidelines of the additional requirements for a flexible access platform are tabulated below (*Table 6.1*).

Table 6.1: Clinical gap analysis for the ideal flexible access robotic platform.

Articulated Flexible Access Robot	
Robot dimensions	
Length	400 – 1400 mm
Lumen diameter (reduce as current instrument sizes reduce)	12 mm
Max diameter (reduce as current instrument sizes reduce)	16mm (preferential aim 10 – 12mm)
Instrument dimensions	
Number required	2 min, 3 ideal

Interchangeable instruments	
Instrument arm length	60mm
Jointed instrument arm for full range of motion at instrument shoulder and wrist (triangulation)	360°
Force requirements	0 – 5 Newton (minimum range)
Image Requirements	
Cameras	1 minimum, 3 ideal (2 for stereo and 1 for off axis visualization)
Field of view	Wide angle 150cm ² at 15-20cm
Motion stabilization	1 – 2 Hz (Cardiac pulse and physiological respiration)
Physiological tremor negation	2.5 – 13Hz (physiological tremor frequency)
Variable Magnification	X10-15
Theatre requirements	
Setup time	<20 mins
Total operative time	e.g. Cholecystectomy <40mins
User interface	1 person operable
Theatre staff requirements	3 (nurse, anaesthetists, engineer (initially))
Short learning curve	<25 cases

One of the further elements, essential for the successful translation of such a product, will be in the theatre staff requirements to set up and manage the device during the procedure, this will also include the number of assistants required to use the device. Although, overall size will play a significant role in this aspect, the simplicity of the device to setup and control will enhance the promotion of the device. The current robotic systems require a team of dedicated trained staff to drape, set up and perform the procedure so the minimum number of people required will aid in promoting the dissemination of such a tool together with a reduction in the overall cost burden particularly in terms of training. The current time taken to set up the DaVinci™ is 15 – 20 minutes given a dedicated highly trained theatre staff (128). The overall aim for any new device should be at least to match if not better this setup time.

6.2.2. Flexible Prototype Designs and System Configuration

The design of the robotic flexible access platform is based on the snake robot. A multi-jointed robotic design which has been explored for its flexibility in a number of other research and commercially based settings such as within the Nuclear Power station environment to examine for cracked fuel rods (OC Robotics, Bristol, UK). However, the size of many of these designs precludes them from the far smaller surgical environment. They are large with sizeable external hardware. This may simply be because the specifications for the required task did not restrict the engineering. Large motors could be placed externally to the main body of the snake which could provide high torque and therefore high force through tendons to each individual joint. This not only increases the external component of the system but also the complexity of the kinematic modelling required to navigate the system effectively. With each articulation of each joint the tendon path length changes for all the other joints distally. This means that each tendon to each joint distally needs to be adjusted with each motion to maintain the tension. This is a significant engineering challenge. The method derived to overcome this problem within this setting was to place the drive motors closer to each joint and shorten the tendon length so it does not cross any articulating joint during motion other than its own.

6.2.2.1. Engineering articulation

In regards to all the prototype designs discussed within this chapter, each of the articulating modules was designed on the repetition of a housing segment and interposing joint actuated through a coupled micro-motor and tendon drive system (*Figure 6.1*). In reference to the *Figure 6.1a*; for each joint to provide one degree of freedom of motion a micro-motor (1) drives a pinion (2) which is coupled to an external ring gear (3). The rotation of the ring converts the tendon (4) into linear translation which is fixed to the ring gear (5). The tendons translational direction is altered by pulleys (6) which are then translated to termination points (8) on a common member (7). When the gear rotates, one tendon is drawn in and the other pulls out which rotates the common member about the X axis. To provide an additional degree of freedom to the joint a further motor tendon drive system is installed mirroring the first across the common member, the tendons of which terminate on the opposite sides of the common member to where the first terminated, enabling it to rotate about the Y axis.

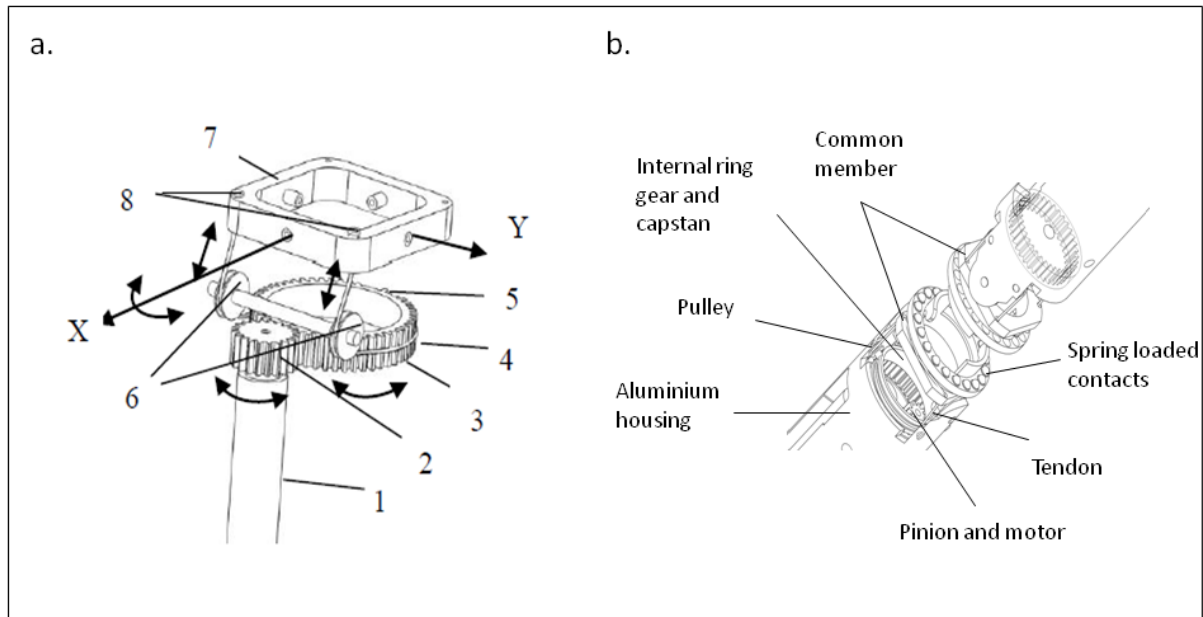


Figure 6.1; A computer aided design sketch of the universal joint which underpins the capability of providing controlled flexibility of the platform. a) a single degree of freedom joint design b) the universal joint with internal ring gear within 12.5mm housing.

The initial design of the joint was 16mm in diameter (*Figure 6.1a*), too large to fit within the conventional laparoscopic ports widely available in the market. As a result the joint was redesigned to a diameter of 12.5mm through internalising the pinion motor and gear so that it drove the ring gear from the inside. The internal ring gear joint (*Figure 6.1b*) enabled the design to be used with a 15mm bariatric trocar.

The motors for the joints were 4mm brushless DC micro-motors which had a 337:1 planetary gear box (Namiki Precision Jewel, Japan). A pinion from the motor pin is fixed to the internal gear which drove the capstan upon which the tendons attached. The capstan was attached to the ring gear which upon rotating drew the tendons, routed over the pulleys, to mobilise the joint. The weight of each module as well as all the frictional elements, were reduced in order to maximise the potential of the capabilities of the motors. The motor size coupled with the fine drive wires used as a result of minimising the whole module size, reduced the capabilities of the motors in terms of their torque. PEEK, a self lubricating material, is used on the common member and the ring gear within the joint to stop them moving axially. Micro balls of 0.5mm diameter are placed between the ring gear and aluminium housing to further reduce the friction.

Each module was made of aluminium casing hollowed out to create four central channels (Figure 6.2). The larger housed the 4mm micro-motors and pinion gear, of which for those associated with universal joints would have two. A 3mm channel contained camera and illumination cables with a further smaller 1.8mm channel directly in the centre for the motor wires. The final channel was 3.5mm and was maintained from the rigid shaft for the passage of flexible endoscopic instruments. It had an internal lining to maintain continuity across each of the joint segments so instruments could smoothly be passed without disruption to the joint mechanism.

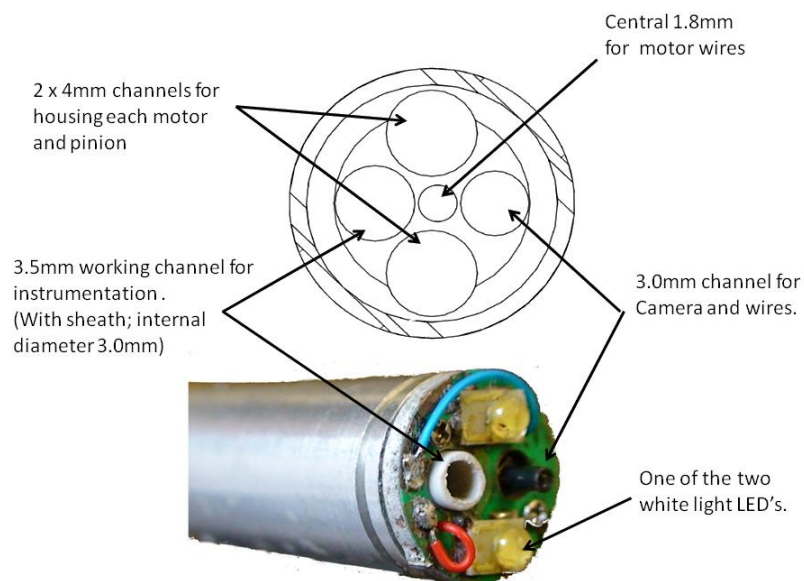


Figure 6.2; A diagram to illustrate the working channels inside each module and a photograph of the distal tip of the final module with the working instrument channel, the camera and illumination highlighted.

The addition of the working instrument channel is core to the flexible platform in essence promoting the device as a flexible access platform over a flexible laparoscope. Its capabilities have both diagnostic as well as a minor therapeutic abilities determined by the devices that are currently on the market for the flexible endoscopes. More advanced instrumentation for the more complex and precision based surgery, is considered at a later stage in the trials with as the device evolves.

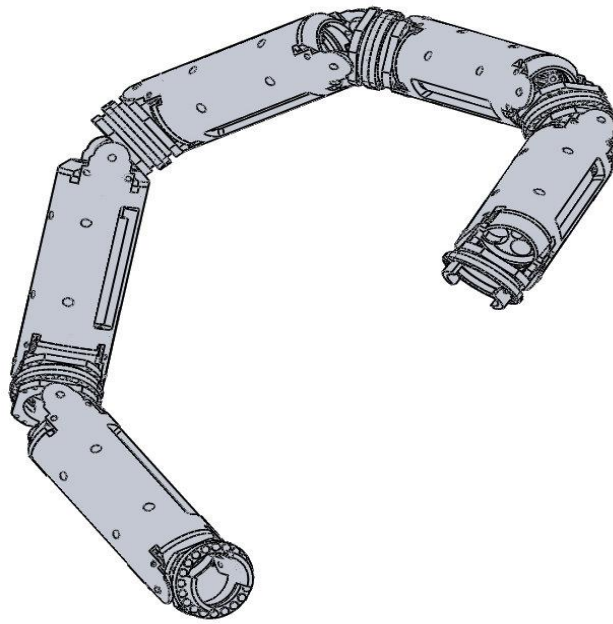


Figure 6.3; A computer aided design model of the potential articulation that is achievable with serial coupling of multiple modules with each joint providing 2 degrees of freedom of motion.

Early laboratory based trials with this joint design demonstrated that the force-torque ratio from the motor to the tendons was insufficient to lift the combined weight of the distal articulating segments without additional tissue elevation requirements which may be required. As the joint design evolved the problem was to some extent overcome through greater optimisation of the tendon routing through the joint with an increase in the gear ratio of the motor to the internal ring. Despite these efforts, the capabilities of articulation were ultimately limited by the force-torque provision of the micro-motors. Engineering constraints meant that early designs could only successfully integrate two universal joints at the distal tip with the remaining joints working only on the horizontal plane providing one degree of freedom. However, even with this setup the distal joints were too weak to provide reliable force and as such required to be turned to 45degrees off the normal axis to compensate. This was noticeable when driving the device but despite the motion being off-axis, the control was still easily manageable a level that was formally tested in user trials, described later. This remained for the duration of the trials described within these chapters.

6.2.2.2. System control

The design for the overall setup was kept to the minimum required. These included the control box; designed and engineered in-house containing the drive electronics, a graphical

user interface which could run on a personal laptop using Labview™ software, the flexible access platform itself and a control handle.

A number of different control handles were trialled. In the initial prototype the control was coupled to the device creating in effect a handheld articulating instrument. Later iterations were decoupled from the device and the prototypes were operated remotely. On all models, each joint could be individually selected by pressing a trigger on the control handle and thereafter the selected joint moved by directional control. Linear translation of the device into the port, where used, could be controlled with a further push button on the controller.

The user interface enabled the user to determine which joint had been selected visible on the screen marked by an illuminating light or box. The direction of the control movement is also visualised as a basic four point compass with illumination of the corresponding point as the direction is activated. Linear translation is also noted to be an on-off symbol when deployed.

The linear translator was developed for the second prototype version. It is in effect a sequence of angled motor driven wheels which grip the outside of the rigid shaft of the robot and when fixed, is capable of driving the whole platform forward. This was only trialled in one sequence of *in-vivo* trials as a proof of concept with manual insertion undertaken during the remaining.

6.3. Live *in-vivo* porcine Trials; Flexible Platform.

6.3.1. Conducted Trials

8 pre-clinical live termination *in-vivo* porcine trials were undertaken to explore whether such a device could be engineered to be reliably and repeatedly used within the clinical setting as a flexible access platform. Trials were conducted with multiple iterations of the prototype device described above, using various access points to approach various parts of the anatomy. Early limitations were noted in using the device within the thoracic cavity due to the variation in the porcine anatomy in terms of size and shape of the thorax when compared to the human. The pigs thorax is triangular in shape and often a large heart which tends to fill the small amount of space available. Access and therefore the trials, was restricted to the abdominal cavity in all of these trials.

6.3.2. Trial outcomes

6.3.2.1. *Prototype Version 1 (V1).*

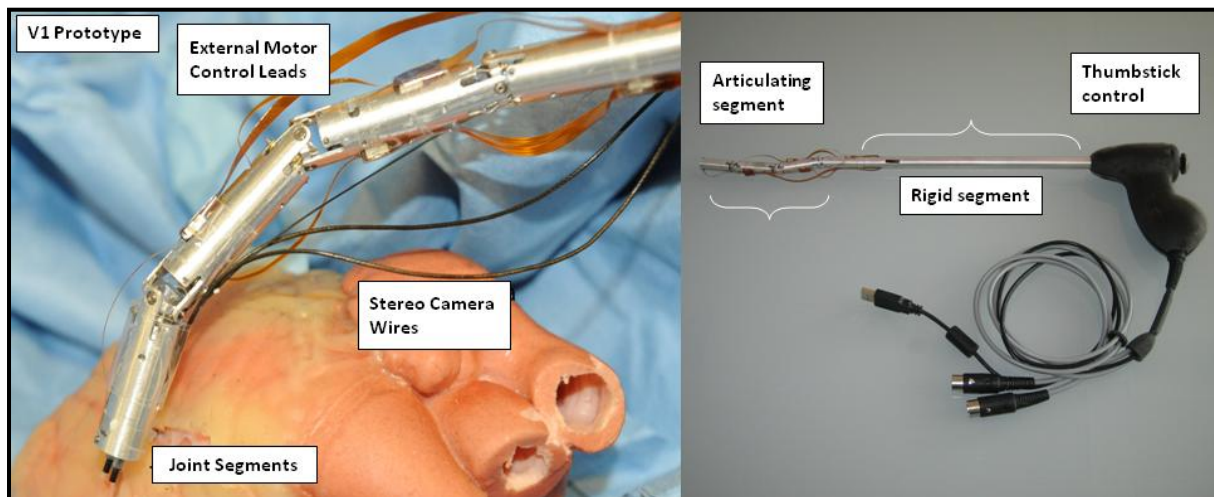


Figure 6.4; The Version 1 prototype showing the articulated sections with the flat external motor cables and stereo camera.

The initial prototype design was a three jointed handheld design with 5 degrees of freedom; two universal joints and a horizontal joint (*Figure 6.4*). The control handle was coupled to the device and held as any other standard laparoscopic instrument. The outer diameter with the drive electronic wires external to the device restricted the use of known conventional laparoscopic ports and a custom made port with no valve was manufactured to enable initial access to be obtained. The articulating segment was covered using a thin, widely sourced, latex sheath to prevent foreign body contamination.

The V1 was inserted into the abdominal cavity through the custom made port until the entire length of the instrument was in situ (*Figure 6.5*), however, by the time this was performed the proximal joint had been broken and the middle joint only working in one plane. This was due to a number of initially highlighted problems including the loss of pneumoperitoneum that occurred as the device was inserted through the port and once inside, the challenge of inserting what was in essence a laparoscope with a weak articulating section which would not sustain any bend forces beyond the motions of the articulating segments, and the inrurnment of the latex sheath into the joints due to the pressure differences between the internal elements of the device (low pressure) and the abdominal cavity (high pressure).

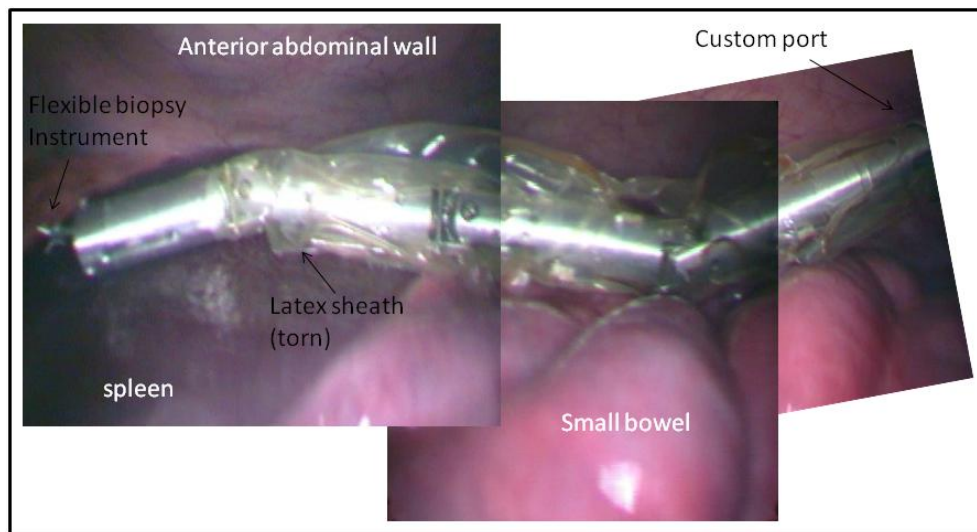


Figure 6.5; Image reconstruction of the V1 prototype fully inserted into the abdominal cavity. The articulating sections of the device can be visualised.

An instrument was inserted through the central channel of the device but no tissue biopsies on this occasion were taken as a result of the difficulties in navigating the space to any significant extent. The ability to pass a flexible instrument through the device was noted to be a problem at this stage. The instrument has to be passed through each of the joints under vision before the whole device is inserted into the model otherwise it would have a tendency of deviating out at one of the joint segments and cause damage to that joint. It was evident that a continuous internal channel that crossed each joint was needed if instrument interchanges were to be undertaken in the future.

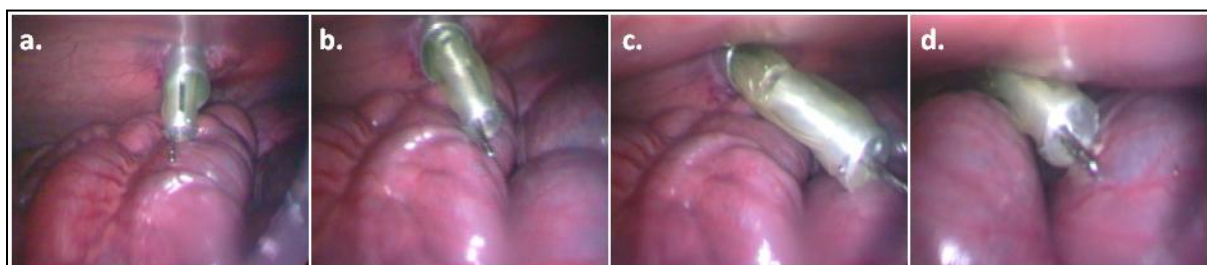


Figure 6.6; Image sequence of the device during initial insertion demonstrating the collapse of the abdominal wall and the loss of pneumoperitoneum.

The loss of pneumoperitoneum was a significant problem for safe insertion. The collapse of the abdominal wall on the device caused irreparable damage to the joints due to the force imparted (Figure 6.6). This was found to include damaged to one of the ring gears and a snapped tendon. On a similar note, the difficulties of inserting the device whilst attempting to

control each individual joint, and perhaps in retrospect was again secondary to the lack of space, was found to be difficult to undertake manually without causing pressure on the articulating section. The device needed to be inserted straight but as it was inserted each segment internally each joint needed to be articulated into the space so it was parallel to the bowel rather than perpendicular. Whilst undertaking this, additional stress was placed on the articulating section by the user as difficulty in judging the joint position internally whilst trying to maintain the remaining as joints straight (*Figure 6.7*). The stress imparted on both the internalised and externalised joints was the cause of significant damage to this prototype.



Figure 6.7; Image of the V1 *in-vivo* trial with the handheld prototype being steadied for insertion. A manual abdominal lift is being used to overcome the problem of sustained pneumoperitoneum.

6.3.2.2. *Prototype Version 2 (V2).*

Similar to the V1 the V2 is a three jointed device providing 5 degrees of freedom with the motor cables external (*Figure 6.8*). However, on this prototype the cables were custom designed and reduced in size but still required to be exteriorised due to the spatial constraints within the device segments. In addition, a pair of cameras was installed at the tip to explore the potential for stereo vision. The sheath remained the same as for the V1; a loose latex cover.

The other element which provided a marked improvement to the outcomes from the V2 trials was the decoupling of the control from the shaft. On this model, control of the device was undertaken using a fixed custom made joystick. The tip was fixed to the table with a clamp

and the ball and socket type joint between the clamped tip and the handle provided the control interface. An activation switch for the linear translation was also built in to this control creating a truly remotely operated device (*Figure 6.9*).



Figure 6.8; The second version prototype (V2) showing the custom made motor cables wrapped externally (inset) and its trials within the *ex-vivo* (bottom right) and *in-vivo* (top right) environments.

One of the most significant hurdles to overcome for the forthcoming trials was the control of the pneumoperitoneum. For the V2 trials and remaining *in-vivo* trials a 15mm diameter x150mm bariatric port (Applied medical, California, US) had been sourced. This proved to be sizeable enough to accommodate the outer diameter of the device with the external cables and maintain pneumoperitoneum throughout insertion of the prototypes. This simple find was one of the most significant in enabling reliable future trials to be conducted.



Figure 6.9; Images of the insertion and re-establishment of pneumoperitoneum with the V2. The conventional 15mm trocar valve can be seen both on the rigid section of the device and on the trocar in-situ. The linear feed mechanism can be seen in both.

The V2 was trialled through both a transabdominal lateral incision as well as a transvaginal posterior fornix incision. For the percutaneous approach, pneumoperitoneum was established through the newly sourced 15mm bariatric trocar placed under vision, as would be considered appropriate within the clinical setting. Pneumoperitoneum was maintained at a pressure of 12mmHg. With this and every subsequent trial, a separate trocar head was placed onto the prototype before insertion of the prototype. This in effect was set to replace the trocar head which is already transabdominal and securing pneumoperitoneum. When this head is removed pneumoperitoneum is lost but the articulating section can be inserted and securely sited within the 150mm chimney of the trocar before the head of the trocar on the prototype is attached to the chimney in-situ and pneumoperitoneum re-established. This technique was employed for every subsequent trial of all later designs without any damage being caused by insertion; confirming reliability of access through this route.

Once inserted through the abdominal wall, the V2 was clamped and stabilised using a clamp over the linear feed mechanism, which as described earlier was use to enable some linear translation of the device into the pig, the first time it was introduced. Access to the upper abdomen was secured and multiple users could trial the device (*Figure 6.10*). *In-vivo* user trials were conducted using the V2 with motion tracking of the control handle. These are discussed in more detail in Chapter 8. However, objectively it was felt that although the control setup was manageable wrist strain was experienced by the users during long repetitive tasks.

The transvaginal route proved to be more challenging with the V2 in part due to the length of the pelvis in the pig model which was greater than 150mm from vaginal vault to peritoneal space. As such the trocar was not long enough to safely secure access for the V2 without damage. Damage was sustained to the V2 during attempted access and although transvaginal access was obtained minimal joint manoeuvrability existed to enable any reasonable trial. However, even if secure access was obtained due to the size of the animal it was not possible to reach the upper abdominal organs from this incision with the prototype as it was designed.

Stereo camera views were taken for explorative purposes. A light pulsed LED source was used for illumination during the task and although the camera could be used the power of the illumination was not sufficient within the abdominal cavity to clearly visualise the structures to the detail required clinically. The light source from the laparoscope was therefore used to test the cameras definition and clinical suitability.

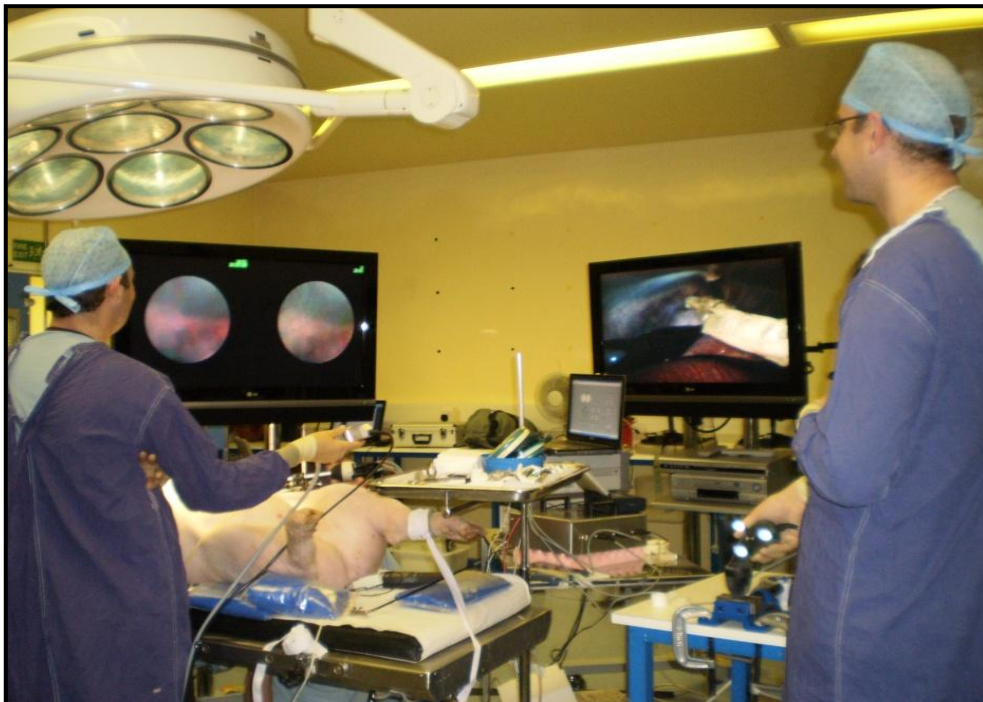


Figure 6.10; The *in-vivo* setup with the V2. The user on the right is controlling the device remotely with the controller. The on-board stereo camera view (left screen) as well as the external laparoscope view (right screen) is seen.

6.3.2.3. *Prototype Version 3 (V3)*

The V3 aimed on overcoming some of the challenges highlighted with the V2 particularly the sheath, the length of the overall device and the internal channel. It remained with three joints

imparting once again 5 degrees of freedom although it was widened to 12.5mm outer diameter to accommodate and incorporate all the wires within the shaft of the device itself. This also enabled an internal instrument channel of 3mm outer diameter; 2.4mm internal with a continuous sheath which ran down through the centre enabling instruments to be passed across the joint without interference. The stereo cameras had been replaced with a single 1.8mm camera at the tip with no light source fitted as it was felt that as an initial design stereo vision was not an essential requirement and that a single 2D camera would suffice particularly in these early design phases where the central space within the device is more important to keep free for the motor wires and the instrument channel (*Figure 6.11*).

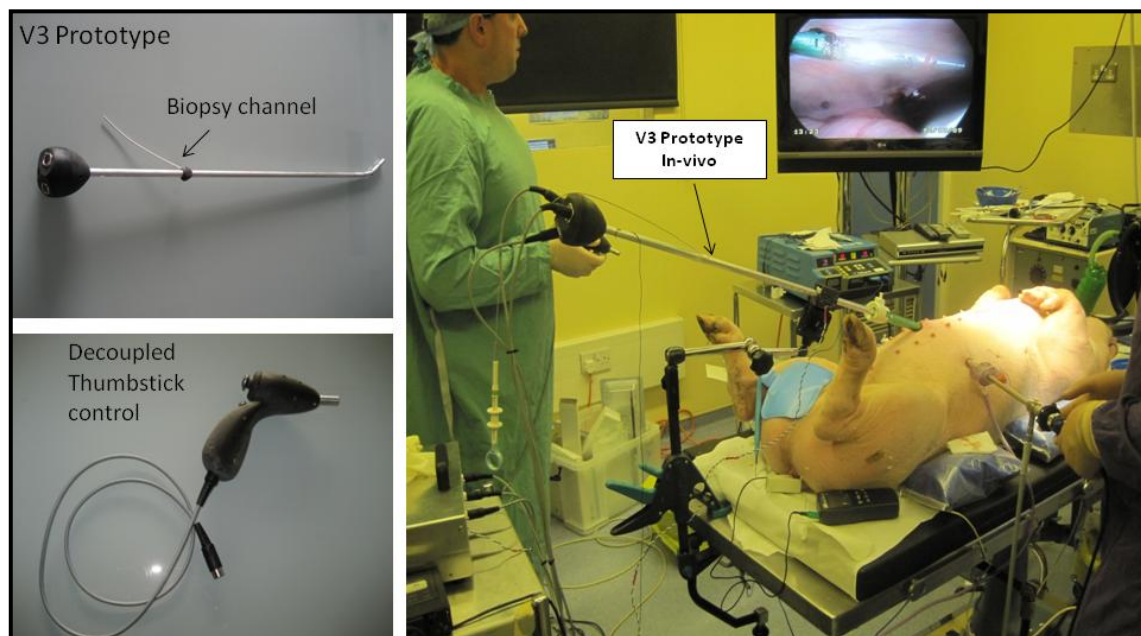


Figure 6.11; The elongated V3 model with decoupled thumbstick control. The user can be seen controlling the device remotely.

The control interface had returned to the concept of a thumbstick but remained decoupled from the device. This provided significant freedom of movement for the user who could now stand and operate the device whilst standing over the pig and at the same time introduce and control the flexible instruments that passed through the central channel.

A strong custom made latex sheath was developed to cover the V3. Although durable, it caused excessive stiffening of the joints reducing articulation. This reduction was also worsened by the presence of flexible instruments through the internal channel. Once inside the peritoneum this, coupled with the sheath, significantly impaired the joint manoeuvrability.

The length of the V3 was markedly increased to cover for the suspected length of the animal and despite the stiffness of joint articulation was successful in obtaining access to the upper organs both through a transabdominal as well as transvaginal incision (*Figure 6.12*).

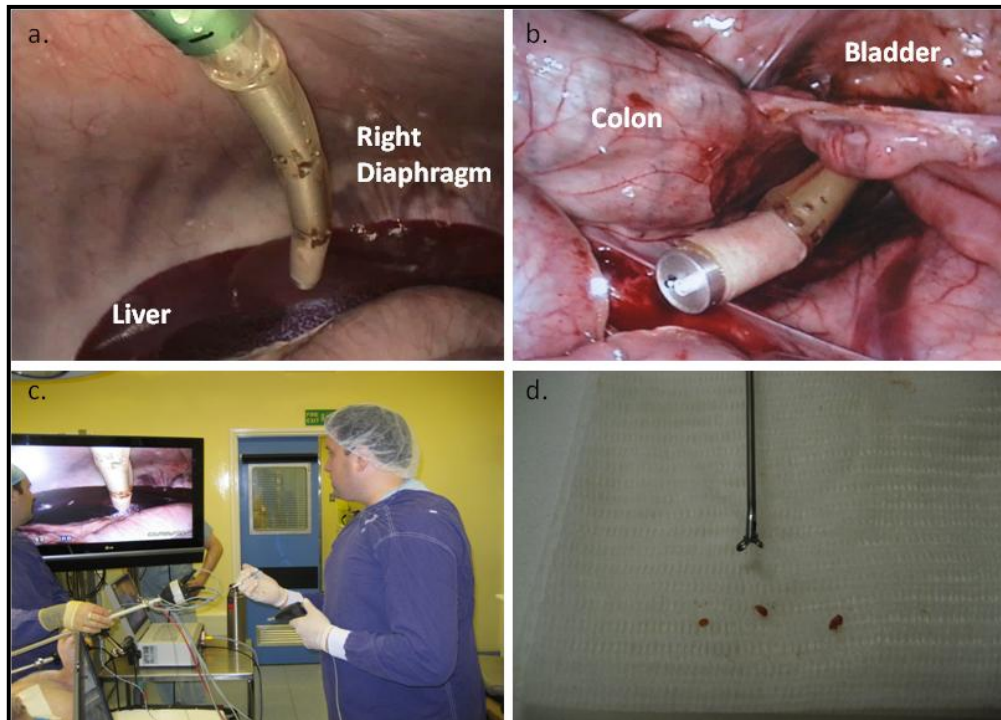


Figure 6.12; Images from the V3 trial demonstrating access to the upper abdomen from the transabdominal approach (a) with pelvic access through the transvaginal approach (b). The independently operated V3 control enabled the same operator to control the flexible instrument (c) to enable minor intervention to be undertaken; liver biopsies shown in (d).

The transabdominal access was successfully undertaken as described previously with the V2 device. The transvaginal approach however, still required significant laparoscopic assistance as a result of difference noted between the human and pig anatomy. As is well understood the human bladder expands within the intra-abdominal wall with no intraperitoneal connection. Within the pig the bladder is entirely intra-abdominal with only a loose connective band which connects it to the anterior abdominal wall. For the purposes of the trial in order to enable secure access through the pigs pelvis the pig was catheterised with an in-out catheter to reduce the bladder filling and an extracorporeal straight needle passed through the skin to hitch the bladder up on to the bladder wall with the knot tied externally. This coupled with some positional alterations to the table opened up the pelvis significantly to enable access to be obtained using the conventional 15mm trocar. Once inserted the V3 could access the upper abdominal organs with ease. Liver biopsies were obtained with instruments passed down

through the central channel and removed with repeatable attempts demonstrating the capability of the device to cater for minor interventional tools up to 2.4mm in diameter.

A number of significant challenges were highlighted at this trial. This included the restriction of movement of the joints with the external latex sheath and the further restrictions associated with the presence of instruments within the external channel. Furthermore, the instruments that could be used were restricted to only those with a diameter of 2.4mm or less. Many of the more advanced instruments including energy delivery devices are 2.8mm and could not be used with this device. Visualization and manoeuvring the device with the use of the on-board camera alone remained an engineering challenge and bespoke custom made designs were being sought from the market place.

6.3.3.4. Prototype Version 4 (V4)

The V4 was a significant upgrade from the previous prototypes and although it had the same outer diameter as the V3 as well as the same central channels, its joints were shortened and the angle of motion about each joint optimised. An additional horizontal joint was added to the articulating section which created a further degree of freedom to the device.

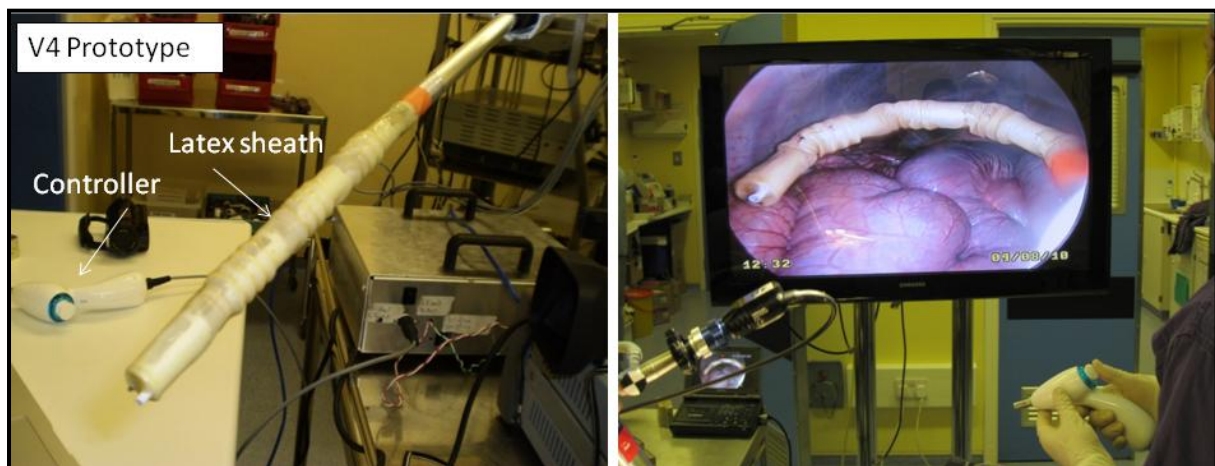


Figure 6.13; The V4 prototype with the latex sheath and remote thumbstick control handle. The V4 can be seen retroflexing on itself in the abdominal cavity.

With 6 degrees of freedom the V4 was more hyper-redundant than any of the previous models and a second custom made durable latex sheath with bellows in the latex designed to be sited at each of the joints, was created to enable this enhanced manoeuvrability to be demonstrated to its maximum potential (*Figure 6.13*). The camera, latex sheath and lack of fixed illumination were the same as for the V3. Trials with the V4 involved the attempt to

access both the upper abdominal organs and the pelvic organs from both the transabdominal as well as the transvaginal approach.

The transabdominal approach followed the same principle as for the previous trials. The transvaginal trials however were modified through the inclusion of a customized alteration to the 15mm x 150mm trocar. Previous trials had highlighted the challenges of access with the trocar and the need to manipulate the bladder on to the anterior abdominal wall with laparoscopic instruments before access could be attained. An extension to the trocar had been developed to overcome the length of the pelvis and also ensure that the articulated section of the V4 could be safely held within the now 300mm chimney whilst pneumoperitoneum was re-established prior to insertion.

Trials were conducted to evaluate the robustness of the device and the potential of what could be done with this more versatile device. For the transabdominal approach an epigastric port was placed for access to the pelvis. A straight approach was simply undertaken and the right uterine horn was targeted. An endoscopic clip (Boston Scientific, US) was passed through the central channel and using the guidance from the V4 the clip was able to be placed on the target.

Transvaginal access was made in the way described previously but on this occasion using the new lengthier trocar. Access was successfully obtained and the V4 inserted into the pelvic cavity. All the upper abdominal organs were successfully reached with an optical biopsy probe; Celvizio pCLE (Mauna Kea Technologies; Paris, France) confirmed the liver, spleen, stomach and anterior abdominal wall could be met from this access point.

Using the transvaginal access retroflexion of the V4 was attempted to explore the limits of the capabilities of the joint articulation and whether what had been achieved with through the transabdominal access with the clipping of the uterine horns could be replicated. Retroflexion was undertaken but was extremely difficult and multiple failed attempts were trialled before a retroflexion was finally achieved with the prototype. However, full retroflexion i.e. the capability of examining the access port, was not achievable. Nevertheless, the left uterine horn was visualised and although instrumentation proved challenging a flexible endoscopic grasper was passed through the internal channel and grasped and elevated the left uterine

horn. An endoscopic clip was attempted to be passed but was unsuccessful due to the size of the instrument and the restriction of the internal channel.

6.3.3.5. Prototype Version 5 (V5)

This prototype was designed to enable full retroflexion and an additional joint was added to the system enabling 7 degrees of freedom of motion about the articulating segment of the device. The additional joint was once again a horizontal joint which meant that the V5 had 2 universal joints and three single joints (*Figure 6.14*).

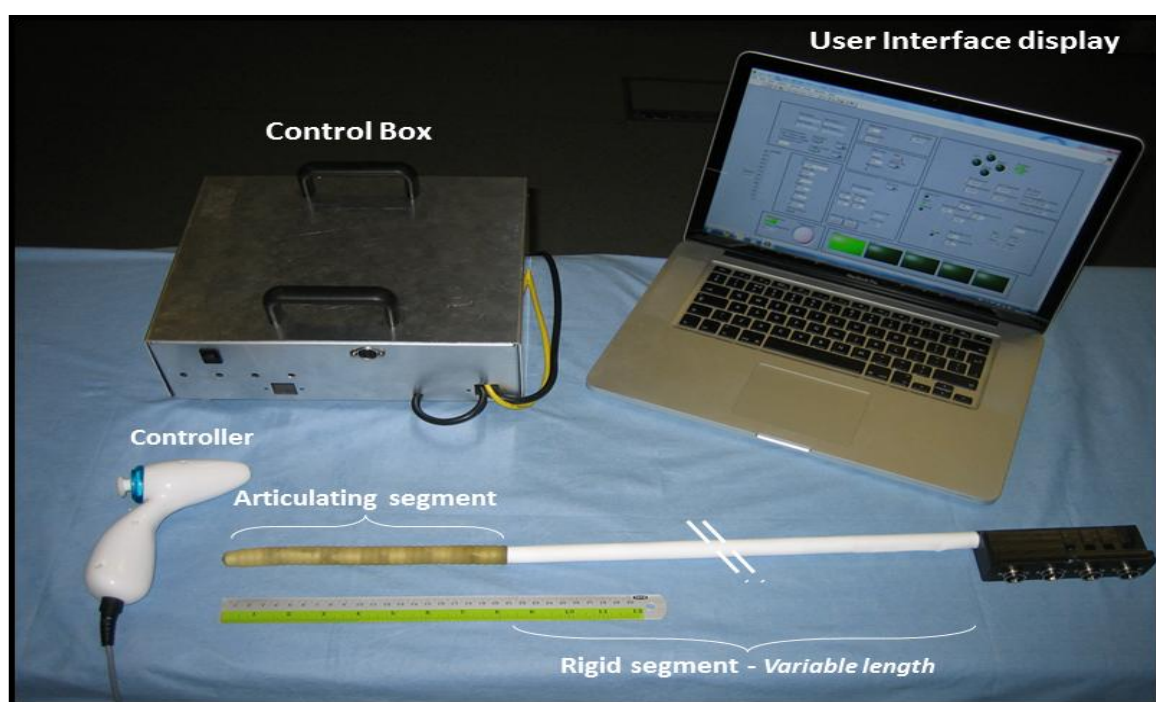


Figure 6.14; The system setup of one of the V5 prototype with the thumbstick control handle, compact control box and the later version of the graphical user interface displayed on the laptop. (Image also shown as part of ICRA 2011 Conference paper J.Shang et al; 2011 (117))

This design also incorporated a wider internal channel so the design now incorporated two internal channels, one 3mm and one as 3.5mm outer diameter. The 3mm channel incorporated the motor and camera wires whilst the larger channel, lined by a copper wire strengthened composite plastic inner sheath; custom designed for the device, enabled the passage of larger flexible instruments currently available in the flexible endoscopic market place, to be passed freely. The camera remained as a single 1.8mm externally sourced camera as for the V3 and V4. Separate trials had explored the potential for suitable illumination

sources over the sequence of *in-vivo* and *ex-vivo* trials once this had been highlighted as a significant issue to overcome. Outcomes from a range of trials suggested that White light LEDs offered the greatest potential for illumination within this environment (129), though these experiments are considered outside the scope of this chapter. The on-board camera with suitable illumination in the format of the heat-sunk white LEDs enable the tubes to be targeted without the support of the external laparoscope (*Figure 6.15*).

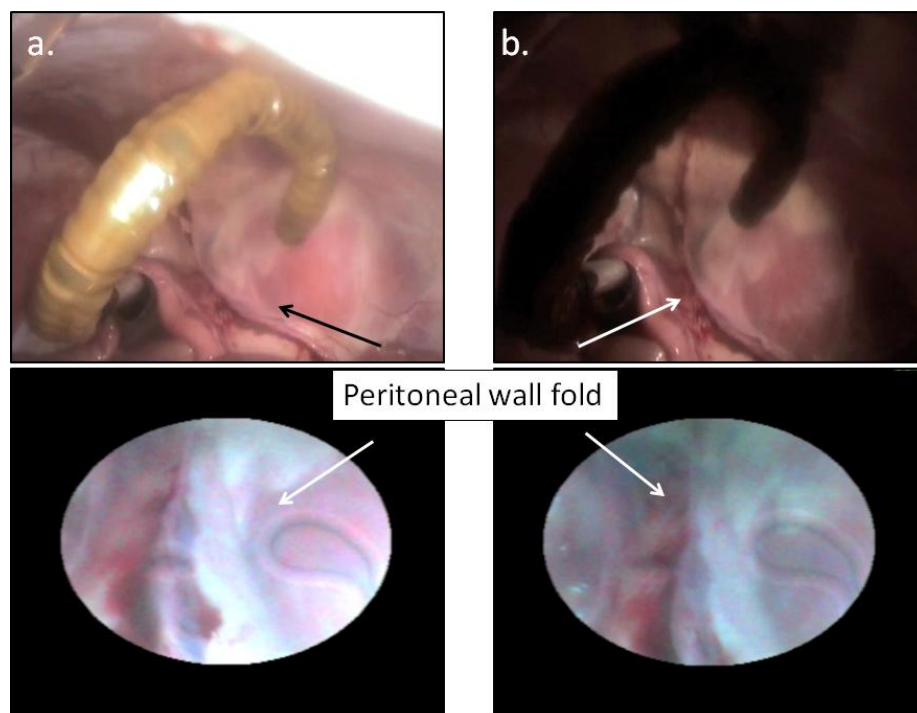


Figure 6.15; Image from external camera taken with the additional support of the external laparoscopic illumination and with the on-board illumination alone, demonstrating objectively the satisfaction of illumination with the white light LEDs.

The main goal for the V5 was to retroflex within the pelvis to access the pelvic structures from a transvaginal incision. *Ex-vivo* trials confirmed the capabilities with the *in-vivo* trials confirming it. The device was inserted transvaginally using the access technique as described above with the extended custom made trocar. No laparoscopic manipulation of the pelvic organs including the bladder was necessary before access was undertaken. The V5 accessed the abdominal cavity and the right uterine horn was targeted. Retroflexion was undertaken with rotation of the device from the horizontal so the distal camera was looking down onto the uterine horn. A 2.8mm flexible grasper (Olympus, Southend, UK) was passed through the internal channel of the V5 and the uterine horn was grasped (*Figure 6.16*).

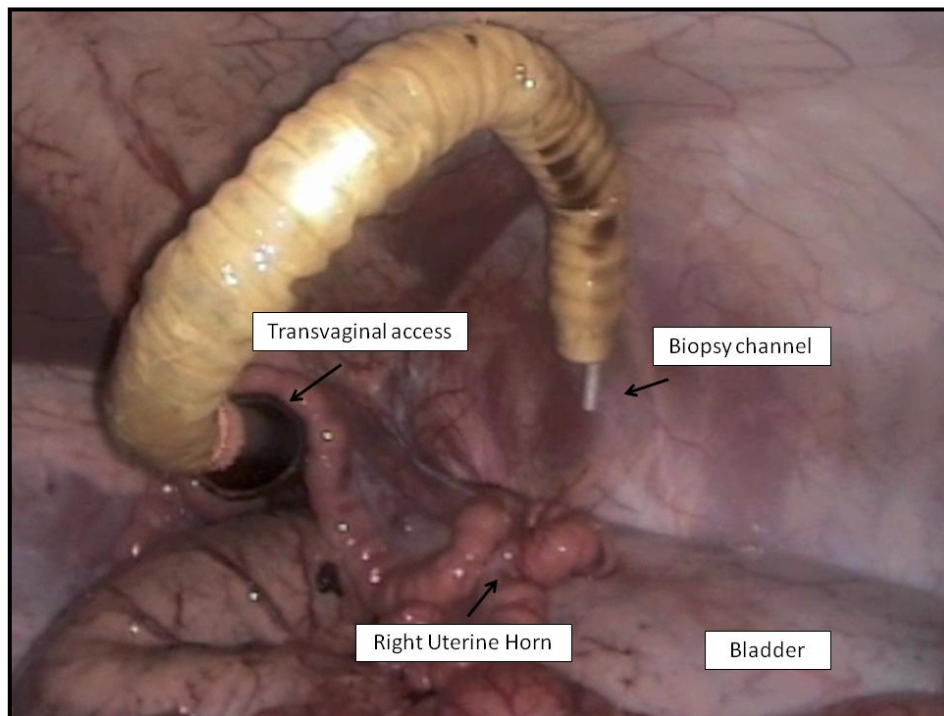


Figure 6.16; The V5 prototype retroflexing in the pelvis to target the right uterine horn.

Multiple further trials were conducted using the version 5 prototype both to re-confirm the ability to retroflex within the pelvis and meet the capabilities demonstrated but also to trial the use of further flexible instrumentation in both the upper abdomen and the pelvis through both access routes as a means of exploring the potential of what can be achieved with a single channel flexible robot.

6.3.4. Summary of the in-vivo results

The outcomes from all these *in-vivo* trials have in effect confirmed the essential principles required for the design of a successful clinically relevant flexible access platform (*Table 6.2*). The strength and robustness needs to be sufficient to cope with the stresses and strains imparted on the device within the *in-vivo* setting; such as the unexpected collapse of the abdomen due to a loss in pneumoperitoneum. However, this in itself acted as a basis for robust testing of the device, each time an unexpected event occurred which either incapacitated the device or rendered it in-operable suitable design consideration could be placed on the area which broke. With each passing trial, the strength and robustness of the

prototypes became more evident with trials of the V5 lasting in essence some six hours longer than the initial V1 prototype. This was in effect overcome through two main design alterations; the shortening of the joint segments, which became possible as a result of sourcing smaller motors, and micro-welding of the joint components rather than using glue.

The sheath not only drew the attention for the need for a lightweight material to prevent abdominal content including blood and tissue from entering the joint mechanisms but also highlighted the long term need for a sterilizable sheath. Several sources were explored as to which would be most appropriate if the device was to go to clinical market; material such as ePTFE (polytetrafluoroethylene) which has the potential to be sterilized using gamma-irradiation and the lightweight requirements essential for the device were considered. This consideration also meant that aspects such as disposability of aspects of the device could be considered instead of sterilization. Modular joints had been developed for the distal tip of the V4 and V5 as a proof of concept that joints could easily be detached and re-attached without the re-wiring requirements making the possibility of disposability of the articulating section a true reality.

Of the problems which have not been met with the V5 prototype it is the instrumentation which is of significant interest. A camera which is of high enough resolution will be outsourced in the long term and can be integrated as has been demonstrated; the problem is one of sourcing not of overall design.

Table 6.2; A table of the challenges highlighted by the *in-vivo* trials (✗) and the prototype whose design iterations enabled them to be overcome (✓).

	V1	V2	V3	V4	V5
					
Robustness	✗	✗	✗	✓	✓
Maintenance of Pneumoperitoneum	✗	✓	✓	✓	✓
Control	✗	✗	✗	✗	✓
Sheath	✗	✗	✓	✓	✓
Biopsy Channels	✗	✗	✗	✓	✓
Illumination	✗	✗	✗	✗	✓
Visualisation	✗	✗	✗	✗	✗
Instrument triangulation	✗	✗	✗	✗	✗

However, the limitations of small flexible instruments which neither have the number nor capability of triangulating expose a significant weakness of the device which will ultimately limit its clinical capability. Currently only those instruments used in flexible endoscopy for diagnostic and minor therapeutic intent can be used with these prototypes, many of which are not suitable for surgical application even with the addition of triangulation.

6.4. Bimanual Instrument Design and System Configuration

6.4.1. Design alterations to flexible platform

It became evident during the trials for the flexible robotic platform that the lack of instrumentation and particularly triangulation was a significant limitation to the capability of such a device if it were to be used for clinical application. However, the flexibility of the

device was proven in multiple trials as being capable of accessing the same targets, upper and lower abdomen and pelvis from two separate incision points including the natural orifice transvaginal route. Nevertheless, for clinical application, instrumentation is limited and focused efforts to explore options were considered. As a result a bimanual instrument based on the outcomes from the *in-vivo* trials, was developed.

The general design of the bimanual prototype differed from the flexible devices with a number of novel design features incorporated, yet with the structural concept of the SSPD joints, as had been refined from the V5 trials, still integral. These included an articulating neck, based on multiple small segments linked together into a spinal formation and manipulated using a tendon drive system, to which distally the articulating joints were fixed (*Figure 6.17*).



Figure 6.17; The bimanual instrumental platform

The centre of the neck was hollow enabling the passage of wires and the internal channel to be maintained. Once the device was inserted swan-neck was capable of being lifted from straight into a swan-neck pose with the articulating segments then elevated above the tissue plane. Between the rigid shaft and the neck a split plug had been incorporated which distracted the instruments as they are passed through the rigid shaft to promote separation at the tissue bed. Tendons attached to the instruments, fixed at various points along its length,

enabled manipulation of the tip of the instruments ultimately enabling them to meet and even cross over when medial translation at the tip was maximised.

The design maintained the flexible articulation but this was reduced to only 3 degrees of freedom of motion with 1 universal distal joint and 1 horizontal both of which were placed distal to the swan-neck. The distal tip, as for the V5 flexible model, maintained a 1.8mm camera, a white light LED and a 3.5mm biopsy channel for flexible instrumentation as before. (Figure 6.18)

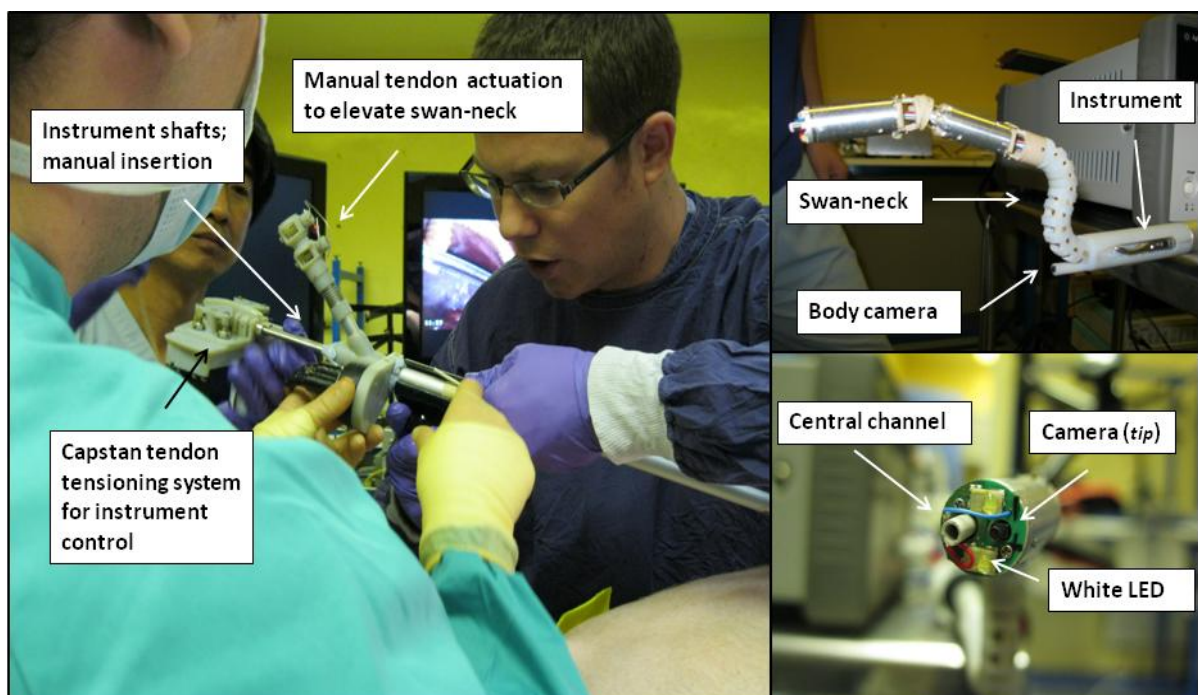


Figure 6.18; The bimanual instrument design demonstrating the rear actuation pack as well as the tip and unique swan-neck elevation design

Instruments were custom made in-house to fit the design of the bimanual prototype. The instruments had been designed using long endoscopic flexible instrument wires coupled with a standard laparoscopic end-effector; a Maryland's dissector or Endoshears, with a laparoscopic pistol grip handle attached proximally for end-effector control. It was essential that the instruments were flexible enough to pass down the long rigid shaft and be separated at the split-plug before exiting the device into the cavity yet provide an element of stiffness and rigidity not only to provide strength and force at the tissue bed but also to enable effective manipulation and triangulation. This semi-flexibility was achieved through the inclusion of a nitinol tube which was placed over the distal 15cm of the instruments. Each

nytinol tube was cut with millimetre horizontal sections at intervals down its length (*Figure 6.19 – right image*). The tendons were attached to the outside of the nytinol tubing with all the elements secured and set within heat-shrunk plastic.

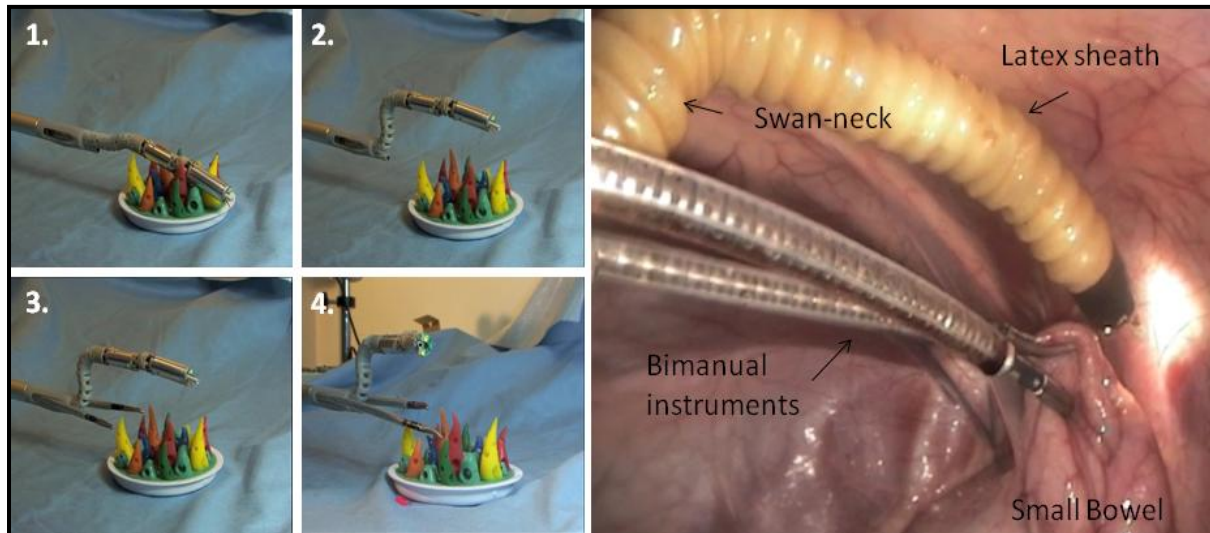


Figure 6.19; Images of the bimanual instrument prototype showing the sequence of change from a 16mm single shaft device (1), to an elevated position with the lift of the neck (2) followed by the instrument insertion through the split plug (3 and 4).

Two cameras were installed for the purpose of enhancing the ergonomics of controlling the device. A camera was embedded, as for the flexible prototype, into the joint segment distal tip. However, with the bimanual design, a further camera was placed at the base of the swan-neck and directed toward the instrument end-effectors enabling an elongated rear view of the instruments as they were manipulated.

6.4.2. System Control

For the purposes of enhanced ergonomics within the operating theatre, the goal for the system control for this platform was to once again enable a single operator to control the instrument arms, the instrument end-effectors and the articulating head altogether. For the purposes of the arm control, two Omnitrak™ control handles were linked to the instrument arms for all trials, these provide a full range of motion within 3D-space. A number of different control systems for the head and end-effectors were explored during each of the trials, with the control of the articulating head being consistently based on the previously demonstrated thumbstick design as defined in the previous *in-vivo* trials for the flexible platform.

Modifications to all elements of the design were trialled with *ex-vivo* and *in-vivo* trials undertaken. In total four *in-vivo* trials together with a sequence of *ex-vivo* trials were conducted to explore clinically the most suitable design iteration for this prototype device.

6.4.3. Live *in-vivo* Porcine Trials; Bimanual Platform.

6.4.3.1. Bimanual instrumental prototype Version 1

Trials were conducted in the same way as for the flexible endoscopic platform. Access was trialled using both the transvaginal and percutaneous methods. This early prototype required a minimum of three users to enable the device to be used (*Figure 6.20*), a fourth was required if an instrument was needed to be passed through the central channel. A coordinated team effort was required for these initial trials.

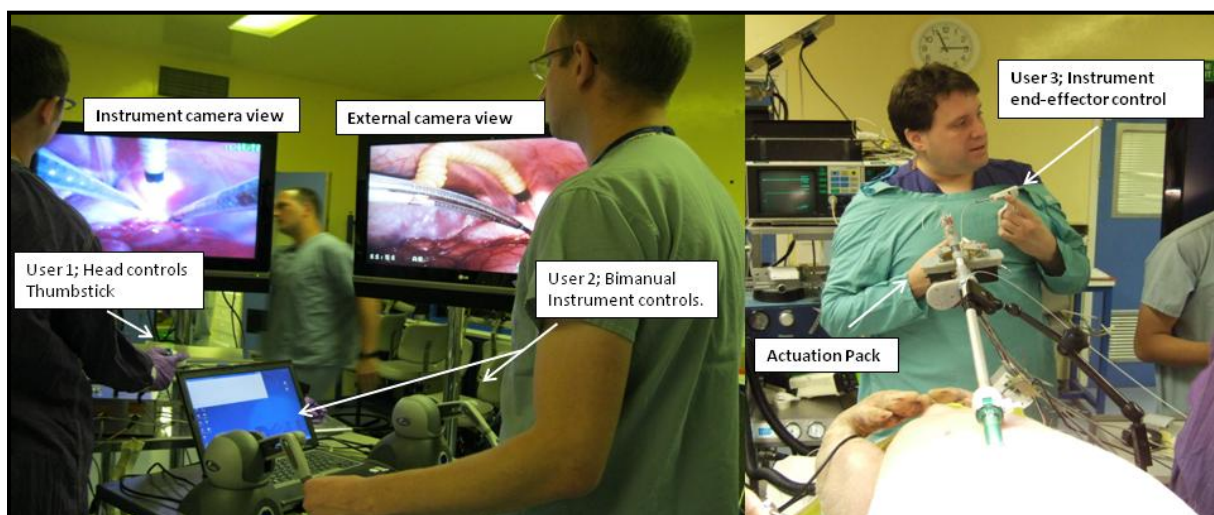


Figure 6.20; System control of the initial bimanual instrument platform demonstrating each of the parts of the device which required independent user-control. In the initial prototype three users were required as labeled in the image.

Early challenges of the trials were centred once again around establishing and maintaining the pneumoperitoneum. The redesign of the prototype to suite more therapeutic surgical intervention created new problems in terms of sealing. The large hollow rigid shaft previously closed off was now exposed to the intraperitoneal cavity through the much larger instrument channels as well as the previously 3mm channel which continues through to the tip of the device. Although the instrument arms, once pushed out from the shaft provided a better seal, a significant problem of air leak was evident. For this initial trial where the

problem was noted, standard lubricant grease was improvised to provide enough seal to enable *in-vivo* tasks to be undertaken.

Once pneumoperitoneum was established and suitably maintained the device was able to undertake a series of coordinated trials. Tissue manipulation within the abdominal cavity was performed using both the transvaginal and the percutaneous access routes (*Figure 6.21*) with the small bowel being targeted due to the ease of access.

Percutaneous Access



Transvaginal Access



Figure 6.21; Percutaneous and transvaginal approaches to the abdomen. The small bowel can be seen passed from one instrument arm to the other and back again in the sequence of images. With the transvaginal sequence (bottom) linear translation of the instrument end effectors is required to reach the tissue.

Further trials focused once again on the pelvis through the percutaneous approach with the dissection of the uterine horns seen with the flexible instrument now replicated. A successful grasp of the uterine horns with both arms enabled tension to be placed on the structure through a lateral draw by the instruments. This placed the tissue perfectly in-line with the articulating head and the central channel. A flexible endoscopic needle knife was passed through the channel enabled a complete ligation of the uterine horn and mesentery to be undertaken (*Figure 6.22*).

Broadly speaking these initial trials were highly successful particularly considering it involved a completely newly designed prototype however upon reflection and aside from the very obvious ergonomic issues of the device in terms of the personnel requirement; a number of significant areas for clinical consideration were raised as a result. The tissue manipulation highlighted an evidential lack of capability in the instrument arms to perform independent

tissue elevation which included even the very light uterine horns. This lack of force was overcome in the trials through an elevation of the whole device using the trocar port as a fulcrum whilst maintaining a strong grasp on the tissues with the instrument end-effectors. This enabled the uterine horns, for this part of the trial, to be placed in the most optimum position to be dissected. Although this is not strictly a problem it does demonstrate the device as less than an automated platform. The trials demonstrating tissue manipulation also demonstrated an overwhelming need for linear translation of the instrument end-effectors in relation to one another. During these trials, due to the lack of fixation of the flexible instruments to the Nitinol tube, the end effectors could be decoupled by external manipulation and pushed forward to provide some linear translation although this was not automated nor controlled to any extent. It was evident that this was an essential element to be incorporated into future designs. In a similar manner the need for the end-effectors to rotate was also evident.

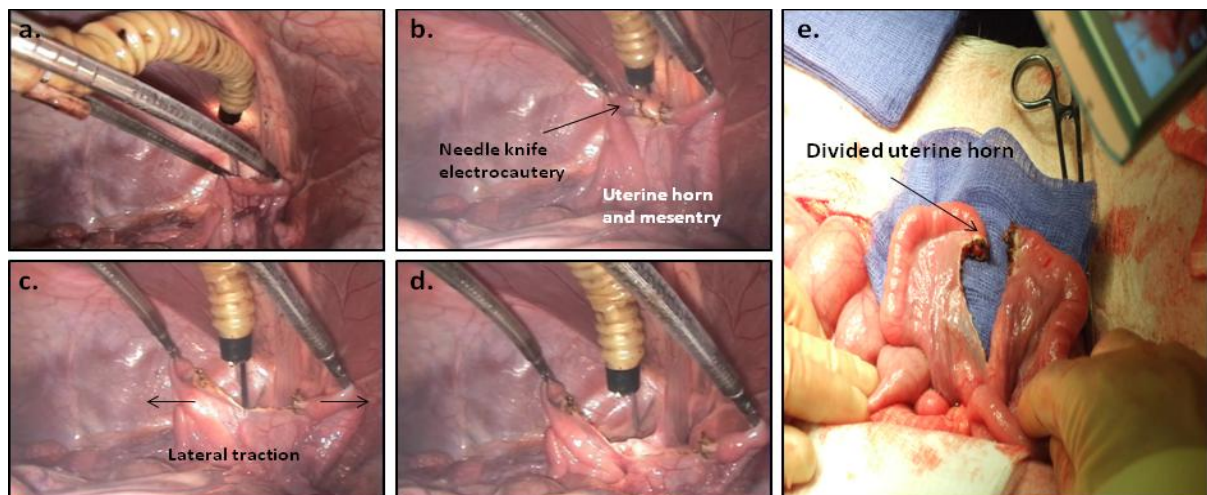


Figure 6.22; Transabdominal division of porcine uterine horn using the first prototype version of the bimanual instrumental platform.

Finally the central channel through the actuator head, once again provided problems with respect to the type of instruments that could be passed. Boston scientific clips, the larger flexible endoscopic tools which are used in clinical practice as well as a pair of flexible endoscissors were not able to be passed. The curve in the channel created by the swan-neck was angled to too greater degree and the internal sheath too weak to direct the instruments around its bends. In due course with repetition the scissors damaged the sheath preventing further use. The passage particularly of flexible endoscissors would have greatly enhanced

the speed of dissection during the ligation of the uterine horn and the lack of universality of the channel is restricting the overall capabilities of the device.

6.4.2.2. Bimanual instrument platform; Version 2

The second prototype aimed to address the majority of these problems with a further redesign of a number of features of the device but particularly in relation to the actuation pack at the rear. The platform was re-designed as a fully automated system once insertion and transformation into the bimanual instrument had occurred internally.

The actuation pack at the rear now contained high powered motors to power not only instrument motion but also the linear translation of the end-effectors which had been automated to approximately 10mm, together with their rotation about 360 degrees. The articulating section of the device remained powered by the micro-motor – tendon system of the joint design with the same number of degrees of freedom as had been trialled previously. The whole rear pack was contained within a sealed unit which was fixed with silicone sealant before use. Pressure testing using a sealed box and air insufflators enabled the platform to be tested for potential air-leak sites within the laboratory setting prior to the trial. Although, some leaks were noted, these were small and would likely be overcome with a slightly higher pneumoperitoneal pressure and gas flow rate during the trial to maintain the pressure.

As part of a move to reduce the sharp angles provided by the swan-neck in response to the challenges noted with the central channel, an alternative design was put in place for this prototype. This was based on a parallelogram. This could be folded straight when inserting the device and opened up into a parallelogram once internalised to lift the articulating segment up. The reduced angles for the central channel internal sheath would in theory enable a wider range of flexible instruments to be used.

In-vivo trial with this device was unfortunately rendered in-effective soon after insertion. Due to an unforeseen event soon after the platform was inserted into the abdomen pneumoperitoneum was lost and the weight of the abdomen on the parallelogram of the neck bent the bars and prevented it from being drawn up to enable actuation of the platform. The event in question was that of the instrument rods. These rods are fixed rigid shafts that run within the main hollow shaft of the platform. At the front end they are fixed to the instruments with the nitinol tubing as before and in the rear the capstan and actuator pack for

each arm. When the device is inserted into the abdomen the shaft and the rods need to be moved at the same time otherwise the rods draw the instruments back into the shaft. This would not be such a significant problem aside from the fact that once they are in the shaft each arm needs to be manipulated back into the relevant side of the split plug situated at the base of the neck. The difficulty was that once this was realised the neck had been forcibly been elevated by the reduced space in the abdominal cavity and the instrument rods could not be re-inserted into their correct split plug side. With this pneumoperitoneum was lost and the parallelogram neck buckled (*Figure 6.23*) putting a halt to any further trials. Labelled as a destructive test for the re-design of the neck, the future iteration and testing of the bimanual instrument re-established the swan-neck concept due to its more robust tendencies over past trials.

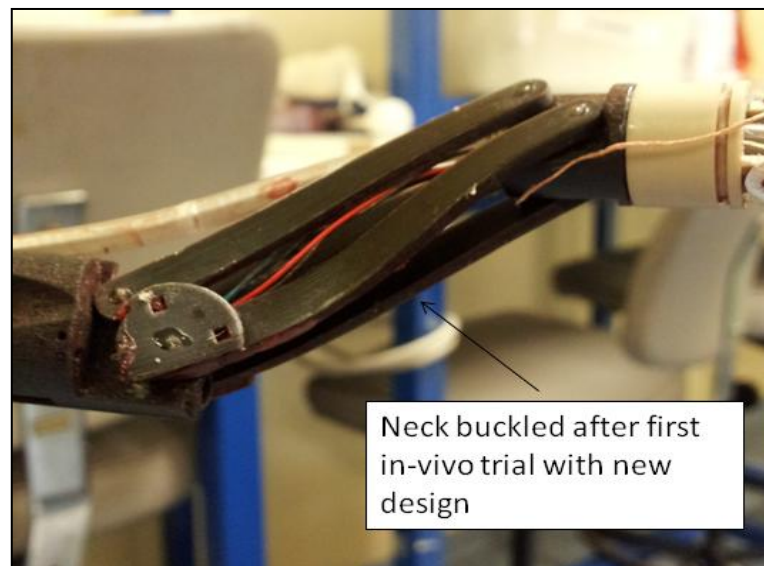


Figure 6.23; the swan neck of the bimanual platform buckled after pneumoperitoneum collapse

6.4.2.3. Bimanual instrument platform; Version 3

This version was a replication of the previous design but as previously documented, re-initiated the segmented swan-neck as the preferred design for the elevated section due to the potentially greater robustness. Although the internal channel may be narrower at points through this neck greater focus has been placed on strengthening the internal sheath through this portion to enable a wider variety of flexible instruments to be utilised through it.

In-vivo trials were conducted using the device with access predominantly undertaken through the transvaginal route. Trials were based upon similar formats with insertion, control of the

prototype and tissue manipulation being the main focus. The transvaginal access was chosen as it enabled insertion of the device along a course which was in effect parallel to the peritoneal contents rather than perpendicular as would be the case with the percutaneous approach. In doing so more space was available for the device to transform from the single incision shaft into the bimanual instrument once pneumoperitoneum was established.

Successful initiation of pneumoperitoneum was established with maintenance confirmed to be at a pressure of 14mmHg. Although the prototype was successful in terms of accessing the abdominal cavity from both routes, any tissue manipulation was found not to be possible. The forces imparted by the instrument arms were still not suitable to comfortably manipulate tissue, an attribute which requires some significant consideration and potential re-engineering within the laboratory setting to overcome.

The control mechanism however could be trialled and this had been significantly integrated to enable a single operating surgeon to undertake the task once the device was inserted and made ready. The use of the Omnitrak™ wands were used as previously for gross control with slight modifications made to each of the control wands to enable an in house custom made pistol grip to be attached, similar to the freehand pistol grip used in previous trials. The right hand grip had been integrated with the same thumbstick design which enabled the articulated joint section to be manipulated in the same format as before but this time it was all attached to the Omnitrak™ wands. With each pistol grip a trigger was installed which when activated enabled the end effectors to open or close. Linear translation of the end-effectors was activated by drawing the grippers in and out referenced by a central point in space. Similarly rotation of the grippers enabled rotation of the end-effectors. (*Figure 6.24*)

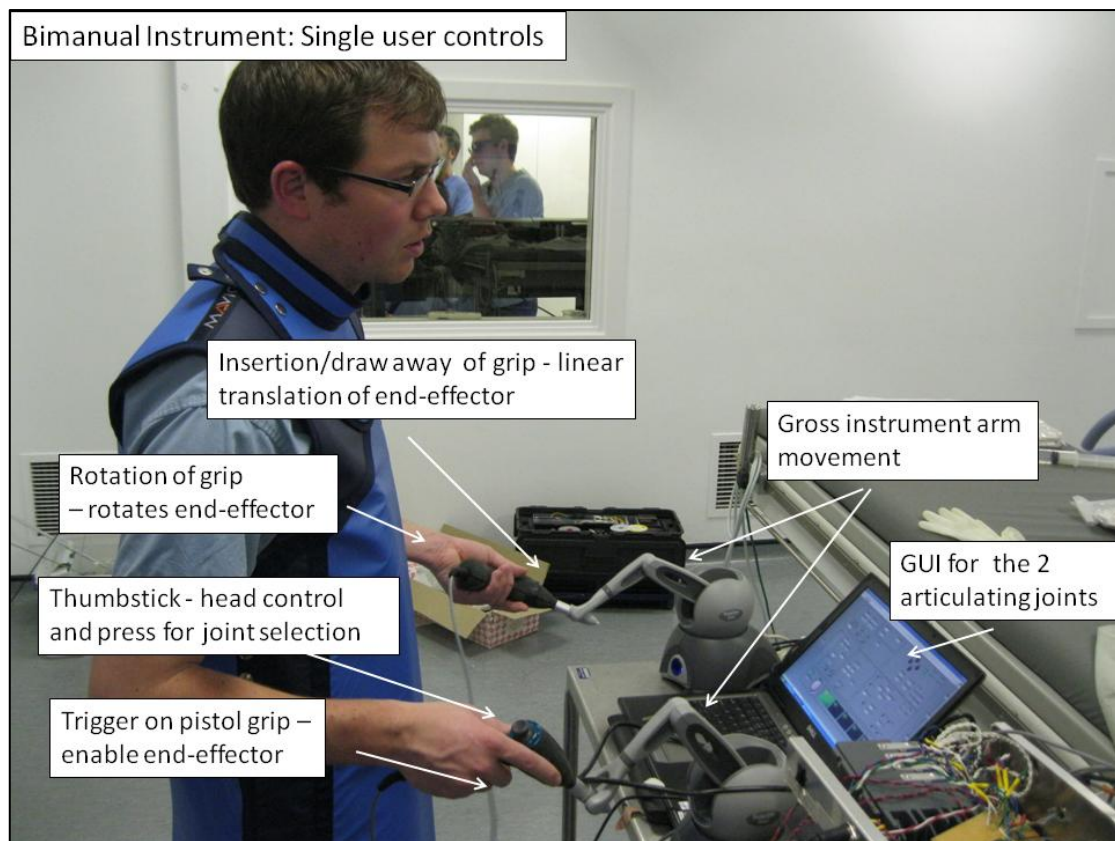


Figure 6.24; Image highlighting the single operator control for the device during the *in-vivo* trials

Although, assistance would be required to insert and actuate the device once internalised, in terms of gross movement the instrument was in essence single operator controlled. Some problems with the controls from a clinical perspective were noted which included the lack of precision and repeatability in terms of the motion of each actuation. The arms would for example move generally in the appropriate direction but the degree would be difficult to control. This was also found to be the case with all the other actuated elements with inaccurate representation of the desired motion.

6.4.2.4. Summary for the *in-vivo* results for the Bimanual Instrument.

Clinically relevant *in-vivo* evaluation of a single incision bimanual instrument for surgical application has been successfully undertaken. Damage to the device during trials has rendered a more robust device capable of coping with the stresses encountered during surgical application. Access through both the percutaneous and natural orifice routes have been trialled with repeatability confirmed with the latest design.

This design is still far from full clinical translation. Some significant engineering challenges still remain unresolved. Of particular note is the weakness of the instrument arms to deliver a force suitable to manipulate tissue successfully. This is perhaps the most crippling element to future trials as no clinical procedure can be trialled until this is overcome. Nevertheless, the device is capable of single operator use with the potential to undertake a minor clinical procedure based on the dexterity and potential of the prototype as examined within the ex-vivo setting; see chapter 8 for formal quantification.

6.5. Conclusion

The inception, design and engineering of an enhanced mechatronic flexible access platform, capable of overcoming many of the challenges facing the FAS technique, has been successfully undertaken. The integration of a micro-motor tendon drive system enables joints with multiple degrees of freedom to be serially arranged and independently controlled to provide the hyper-redundancy which is essential for the flexible access approach and the precision at the tip to enable instrumentation with a stable platform epitomised by the instrumental approach to the pelvis using the transvaginal access route.

The evolution of this platform from an engineering platform has been undertaken through multiple *in-vivo* trials to ensure that the design is not only robust enough to overcome the challenges which are met within the true *in-vivo* environment such as the loss of pneumoperitoneum, are addressed. This secures a design which can be considered as one which is clinically relevant. The design is engineered to be used through conventional sized trocar ports. It can access and maintain the internal environment during *in-vivo* tasks as well as provide instrumentation to the tip of the instrument through an internal channel. Instruments can be viewed using the on-board camera to deliver therapeutic or diagnostic applications with precision to the tissue bed.

The lack of instrumental strength within this design drove the development of a second platform. This design overcame the instrumental problems seen in the first design presenting a device which, although remained true to form with single trocar access, promotes a full surgical operating platform with triangulating instrument arms and the articulating head to

oversee the instrument tips once the whole platform is internalised. In essence this project has led to the development of currently two separate platforms.

In-vivo testing of two flexible access enhanced mechatronic prototype designs was undertaken. Each device was capable of accessing targets both in the upper abdomen transabdominally as well as transvaginally. The hyper-redundant flexible access platform was capable of accessing a broader workspace within the abdominal cavity from a single access point whether this was natural orifice or otherwise with the ability to retroflex upon itself to perform minor therapeutic applications. However, it was limited by the lack of instrumental support which may limit its broad clinical potential. The bimanual instrument design with its instrument triangulation overcomes this problem, within the extent of the engineering capabilities, was limited in terms of its flexibility. This restricted its use only to targets which could be accessed from a straight approach.

The rigidity of the shaft and the current instrument design inhibits the shaft from being as flexible as perhaps would be preferred, limiting its capabilities to reach the pelvic organs from a low natural orifice approach or indeed limits the natural orifices to only the straight access approaches, ruling out the transgastric approach which may conceptually be the most universal natural orifice approach for true Natural Orifice Surgery. However, even the flexible access platform in its current form is not able to undertake this access route, but the limitations of the device do not extend to the fixed rigidity of the shaft as is the case with the bimanual and it is only a small leap to change the flexible access platform to incorporate a more semi-flexible rear shaft to conquer the advanced navigational requirements of the transgastric route.

Chapter 7

Exemplar applications of Robotic-assisted Flexible Access Surgery

Hypothesis:

The flexible access platforms can be validated to confirm translatable clinical applications.

7.1. Introduction

This project has led to the design of a platform which has the potential to meet many of the requirements for flexible access surgery. However, it is very apparent that over the course of the project two clear designs, each with their own unique advantages have evolved. The single hand controlled flexible hyper-redundant endoscopic platform with multiple joints integrated with an internal channel for minor therapeutic intervention and diagnostics, as well as the single-incision bimanual instrument which has the benefit of triangulation.

To design and engineer a mechanised device which can be inserted into a clinical environment could be considered by some as relatively straight forward however, to develop a platform capable of true clinical intervention is the essential next step. The questions that need to be reflected are whether the designs are clinically relevant and project a clinical advantage over the conventional platforms currently available, namely the flexible endoscope as well as the designs currently under development highlighted in Chapter 2. Once assured and subsequently integrated with imaging, sensing and some degree of automaticity, a truly novel robotic assisted flexible access platform can be developed and packaged for the clinical market place.

Up until this point the *in-vivo* trials have predominantly been focused on exploring the requirements in clinical design for a flexible access platform. As a result a number of the applications have only been highlighted as possible given the early prototype designs,

however, now a more structured and fixed design is in place the true capabilities of each platform clinically needs to be addressed. This will include not only the potential advantages for given clinical procedures but also where each design may fall short in terms of clinical relevance. This will enable the engineers to focus on those areas in the design which will need to be refined before complete clinical applications are realised.

With a more relevant design in place, the potential clinical applications that could be approached are explored in this chapter both with and without integration of various instrumental adjuncts, the nature of which are explored for inter-cavity surgical application rather than their widely described endoluminal applications. Validation of the platforms for clinical use is explored in relation to the complexity of procedure that each design could undertake once fully refined.

7.2. Methods

The methodology behind exploring this hypothesis will be in focusing upon the two platforms individually in terms of workspace analysis and where appropriate user trials, with formal analysis of the potential for the device to meet the clinical workspace requirements of a clinical application and what further iterations to the design if any may be required as a result. The potential clinical applications which both devices are felt to be able to meet are explored within the porcine model with assessment of a range of instrumental energy delivery devices which may be effective when used in conjunction with the platforms.

7.2.1. The Multi-articulated platform

The clinical suitability of this design was assessed through examining both the usability of the flexible articulated device and the clinical relevance of the workspace it is able to meet, as defined by the volume of a given region which is accessible by the tip of the device. The usability trials were performed within an ex-vivo simulated model as well as within the *in-vivo* live animal trials.

The clinical relevance of the workspace was examined using a computer generated mathematically accurate, simulated model of the Prototype version 5 platform. This was evaluated not only within the NOSsE phantom (Chapter 3) but also within a computer generated anatomically referenced model, to evaluate whether the design would be able to be articulated and be effective within the constrained anatomical space of a human.

The Prototype version 5 was the design which was evaluated on all occasions within this chapter apart from the *in-vivo* usability trial which used its predecessor; the Prototype version 4. Clinical translatability was further assessed and potential clinical applications discussed.

7.2.2. The Bimanual Instrument platform

The most important aspect of the bimanual instrument design is in the effectiveness of the two instrument arms, which is predominantly force application and dexterity. These were measured independently within the laboratory setting.

The clinical relevance of the dexterity of the instruments was determined through matching the volume capable of being met by the tip of the instrument against the average volume required for a focused clinical procedure, determined through evaluating multiple surgeons undertaking the procedure within the ex-vivo setting.

Clinical translatability was further assessed and potential clinical applications discussed.

7.3. Results; The Multi-articulated Flexible Platform

7.3.1. Usability trials

The aim of these trials was to ascertain the effective controllability of such a hyper-redundant multi-articulated device using the bespoke hand held controllers; thumbstick and joystick. It also explored the usability of the device within the pre-clinical setting. The trials aimed to test both the repeatability and robustness of the design to repeated joint activations.

7.3.1.1. Materials and Methods

Ex-vivo usability trial.

Multiple trials were undertaken both within the ex-vivo as well as *in-vivo* setting. For the ex-vivo trials a simulated model of the pelvis (Limbs and Things Ltd Part 60283, Australia) was used to undertake repeated usability trials of the device providing both a measure of the reliability and robustness of the device as well as the simplicity of novice users to grasp the control interface. Access was created using a posterior rectovaginal incision in the simulated vagina and a 15mm 150mm bariatric trocar was inserted as the introducing port. This would be in-line with the current transvaginal approach to the peritoneum defined in the previous chapter. A surgical clip was applied to each of the simulated fallopian tubes on the simulator which would act as the targets for the users to touch (*Figure 7.1*).

The task consisted of the subject articulating the device into the retroflexed position from its straight position and targeting each surgical clip in turn. The users were only allowed to use the on-board camera to navigate. Targets were considered met when an endoscopic biopsy grasper, passed through the central channel of the device, was able to touch the base of the clip which attached to the fallopian tube. Completion of the task was when the device has been returned to a straight position which was confirmed through visualising a target positioned centrally visible only once the robot was straight. This reflected the need for the user, when in the real anatomical environment, to return the instrument to a straight position so it can be removed efficiently from the abdomen.

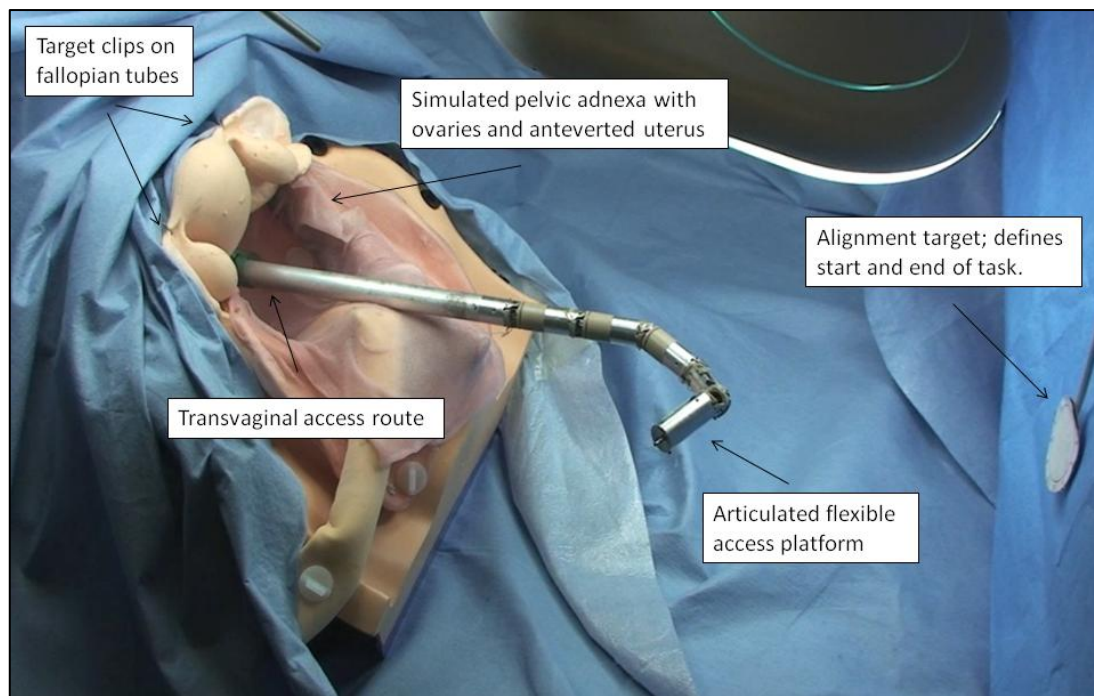


Figure 7.1; User trial task setup using simulated pelvis.

Ten subjects were enrolled onto the trial. Each subject performed three trials each consisting of three runs. Each trial was separated by approximately 3 - 4 days. Each subject was shown a pre-made video of an expert performing the task, with a clear description of the relevant steps required to navigate to the target prior to each trial. This was undertaken in conjunction with a full description of the control interface.

All trials were video recorded. Videos were analysed and the number of motions of the device performed by each user and the completion time was recorded. A single motion was defined as a definitive movement of a joint, rotation of the device or a single linear translation without interruption from another motion. Statistical analysis of the data was undertaken using a Mann-Whitney test for non-parametric data and significance was taken as $p < 0.05$.

In-vivo usability trials

The task required each subject to control the articulated laparoscope using the bespoke joystick design to visualise a set of sequentially numbered targets. Targets were placed in the upper abdomen and the robot clamped externally to ensure that visualisation of the targets was solely achieved through the control of the robot's distal joints using the on-board camera

for guidance. The presence of a rigid laparoscope was used to provide enhanced illumination for the on-board camera during the trial but subjects were not able to visualise images from it.

Outcome metrics

Performance was determined using the number of joystick motions required to complete the task as determined using video motion tracking (Polaris, Northern Digital Incorporated), and the overall time taken. Passive markers were attached to the bespoke controller to whose position in 3D space could be determined. Using a MatlabTM based software program the movements of the active markers on the controller could be isolated and manually segmented. Each definitive movement of the markers represented a movement of the controller and the direction and number of movements were recorded (*Figure 7.2*).

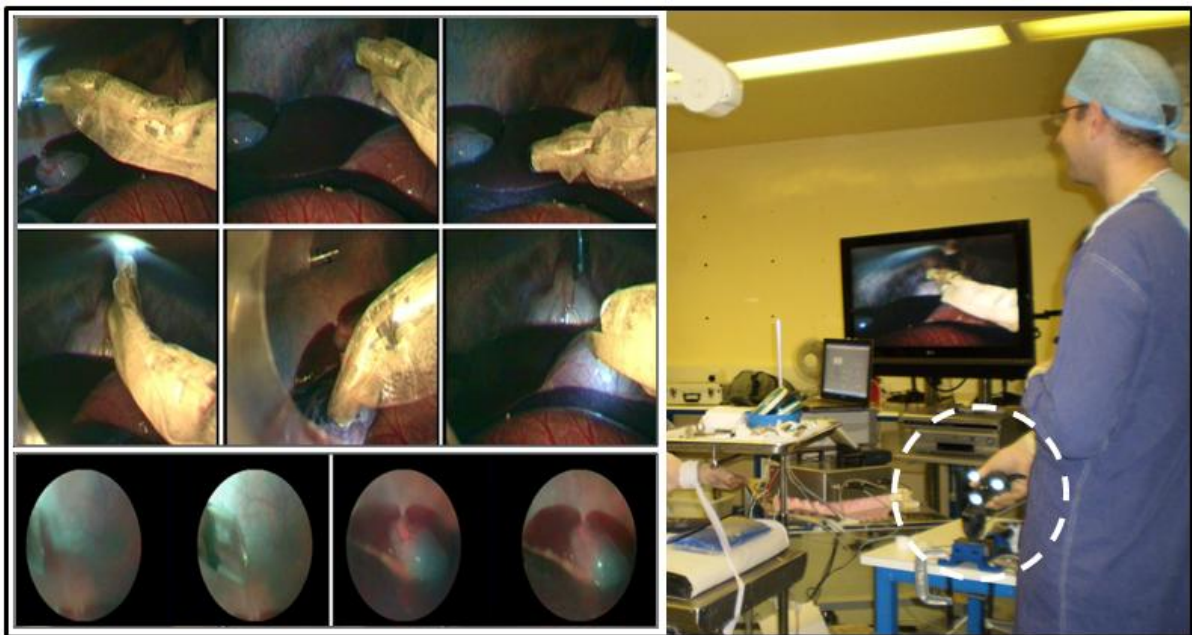


Figure 7.2; Images highlighting the setup for the *in-vivo* animal trial. (Left) *In-vivo* images of the robot performing the target task in sequence with the on-board dual camera visualised by the subject below. (Right) Image of the bespoke control handle for the robot with the optical markers placed onto the side for motion tracking – highlighted within the dashed circle.

7.3.1.2. Results

Ex-vivo trial results

The robot performed all trials successfully without sustaining any fatigue damage. 10 subjects undertook the user trials. In all cases the task was completed in full with a mean

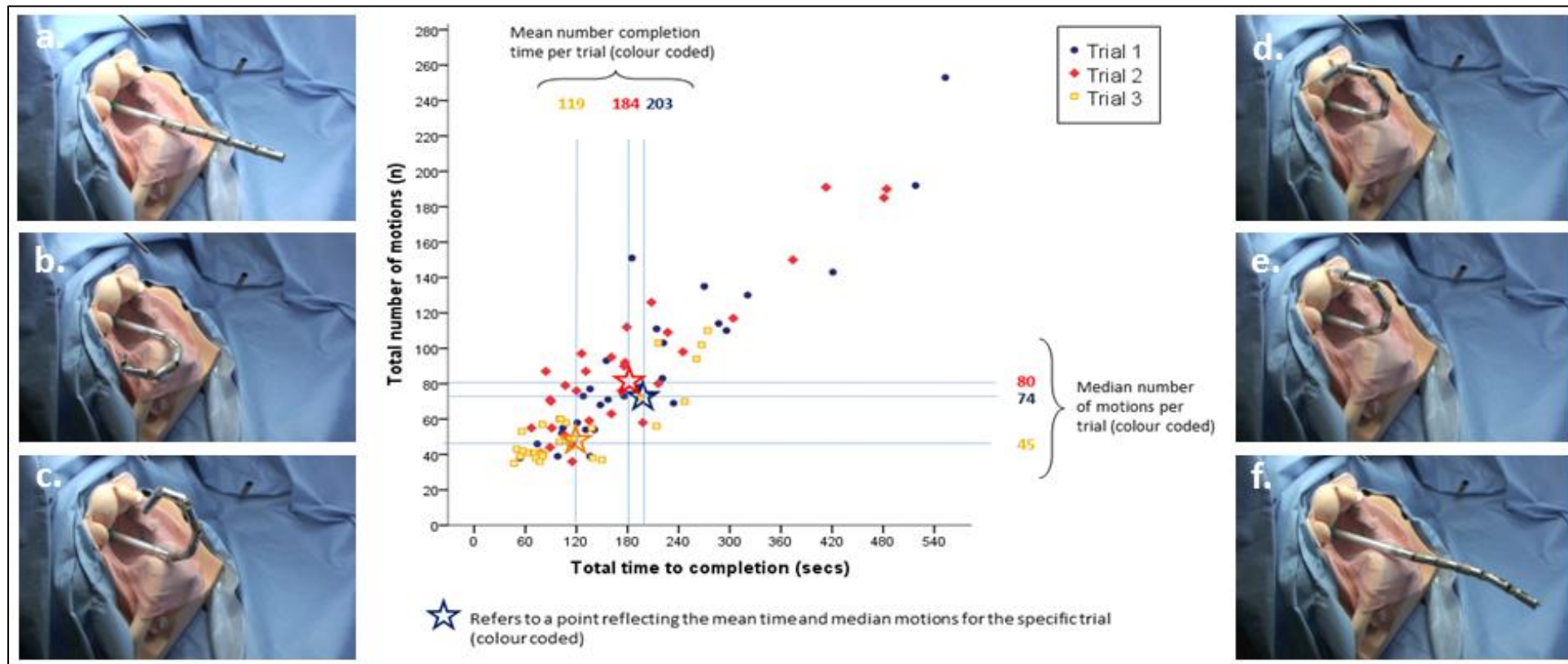


Figure 7.3; Simulated tubal sterilisation in a pelvic model with graphical display of the outcomes as to the learning curve for users of the device. Sequence a) to f) define the ideal position for the robot to undertake the targeted procedure.

completion time of 167.9 (+/-109.4) seconds. This was performed with a median of 68 (35 - 253) controlled robotic movements. The times and motions for trial 1 and 2 were similar with no significant difference highlighted. However, for trial 3 the mean time 119.3 (+/-70.6) and median motion 45 (35 - 110) demonstrated significant improvements $p=0.001$ and $p<0.001$ respectively in comparison to trial 1 with a similar significance when compared with trial 2 (*Figure 7.3*).

Due to the nature of the task, complete retroflexion of the device was required for accurate targeting. It was visually evident from the trial videos that a clear workflow was required to complete the task. This included retroflexion on the horizontal plane, rotation to the vertical and linear retraction to bring the ovary into sight. From this point, focused targeting of the first clip with the distal joint was required. Once met, the instrument is inserted and rotated to the contralateral fallopian tube and the second clip is targeted with some linear retraction of the device performed to approximate the tip to the target. The device is then reinserted and rotated to the horizontal before being straightened (*Figure 7.3*).

In-vivo trial results

Four clinicians licensed to operate on animals, performed a navigational task across a series of five targets positioned within a live 70Kg porcine model. The users visualised each target in sequence successfully without the need to manipulate the device externally and completed the trial within an acceptable time frame. The times to completion ranged from 28.9 –164.6 (mean 57.5 seconds) *in-vivo*. The number of movements of the operating control needed to complete the task ranged from 21 - 96 (median 58) and 14 - 68 (median 41.5) respectively (*Figure 7.4*).

A significant reduction in time taken and the number of motions required to complete the task was demonstrated between the first and last run performed in the simulator ($p=0.026$, $p=0.011$) indicating that each subject was not simply moving the controller faster but controlling the instrument more effectively after only 2 attempts.

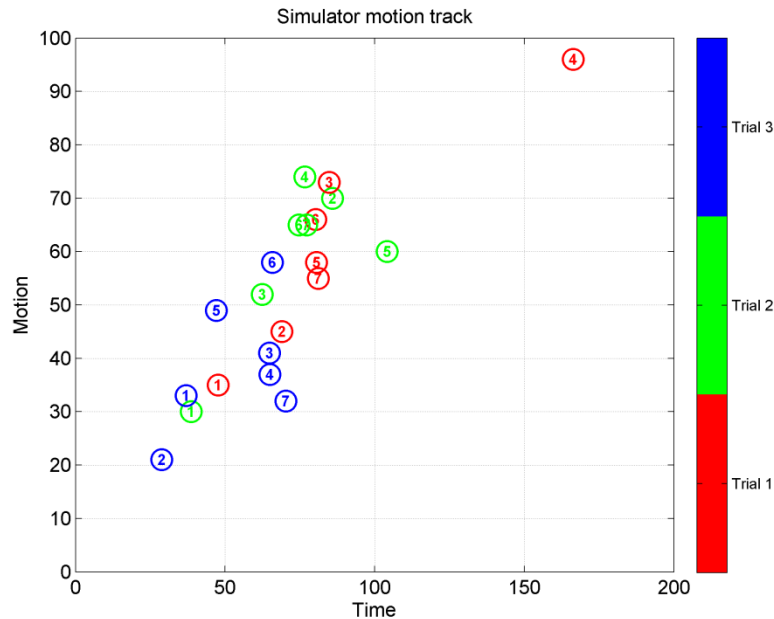


Figure 7.4; Graph highlights the time and motion analysis of the navigational trial within the *in-vivo* model.

(Numbers represent the subject and the colour the trial sequence number – the task was performed with fewer control stick motions and in less time by the third (blue) trial than the first trial (red))

These user trials have demonstrated that the device, in its current configuration, is both controllable in terms of the design and able to be navigated and utilised by novices who are able to grasp the nuances of its control within only a short space of time.

The method of control in this setting was by means of independent joint actuation, a method more in keeping with enhanced mechatronics than robotic control. However, with the planned integration of joint position sensing into future designs, control of the device will be made even more efficient. Motions from the control console, directed by the user according to the alignment with the view from the on-board camera, will then be translated to all the joints which will move as a single entity, with only the most efficient joints activated to complete the navigation required.

These trials have also highlighted the reliability of the device particularly in the ex-vivo pelvic trial where the robot sustained and lasted for what was in effect 90 trials within a week; 3 trials of 3 attempts by 10 people, whilst remaining in an effective usable order. This highlights the security of the design in terms of its strength and resilience to undertake repetitive procedures.

7.3.2. Workspace analysis

The aim of this trial was to explore the potential workspace capabilities of the flexible hyper-redundant platform and to ascertain whether it could effectively articulate within the confines of the human *in-vivo* environment.

7.3.2.1. *Materials and Methods.*

The platform used for this study was the prototype version 5. It is a 12.5mm diameter, multi-articulated enhanced mechatronic endoscope with a hybrid micro-motor/tendon design (117) as described in the previous chapters. The total length of the articulating segment is 185mm. Its joints enable the robot to be controllably flexible throughout this length providing a total of seven degrees of freedom serially arranged into two universal joints with two axes of movement and three single axis joints. Forward drive and rotation provides two additional degrees of freedom.

As described earlier a 3.0mm central channel, transmitted through the entire length of the device and exiting at the tip, provides a route to pass and interchange standard flexible endoscopic instruments and flexible sensing tools to enable the device to provide both diagnostic and minor therapeutic intervention (130)(131). The instrumentation can be passed through the entire device irrespective of the individual joint configurations. The device is capable of controlled retroflexion of the instrument towards a maximum angle of 225° and a minimum inner radius of curvature of 42.5mm.

The robot was trialled both within an ex-vivo NOTES simulator; the NOsSE (Chapter 4), as well as within a computer generated model of an anatomical cavity of a human, defined by true magnetic resonance images of human patients and using a kinematically accurate computer representation of the device.

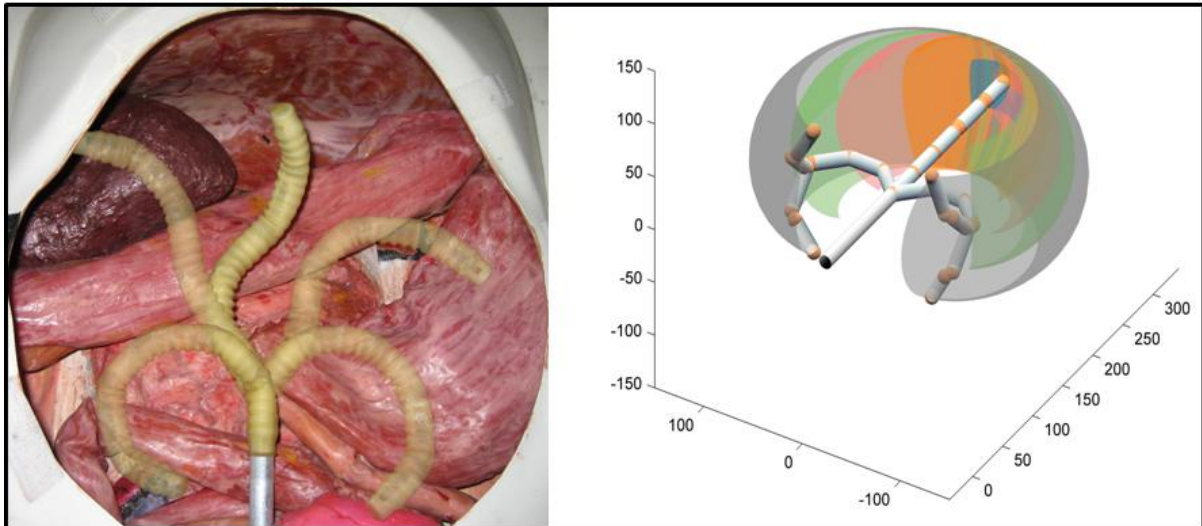


Figure 7.5; (Left) The workspace of the flexible robot visualised using image overlay of the multiple positions that the robot is able to flex into from a static insertion point. **(Right)** A kinematically accurate model of the device visually demonstrates the workspace area reached by the tip of the device with each degree of freedom used from the straight (2 DoF at tip - blue, 4 DoF - orange, 5 DoF - pink, 6 DoF - green, 7 DoF - grey) the articulation of each joint (courtesy of Dr Valentina Vitello PhD).

The capabilities of hyper-redundancy of the robot are evident within the NOsSE simulator with all quadrants of the box trainer capable of being reached by the tip of the robot with minimal linear translation of the shaft of the robot at its insertion point required (*Figure 7.5*)

However, the ability to articulate and in particular retroflex, a unique aspect to this design, within a modified laparoscopic box trainer or within a computer model demonstrates its full capabilities but for clinical relevance the device needs to articulate within the real anatomical environment of a human patient. With the ability of the robot to retroflex exposes significant clinical opportunities within the gynaecological remit to explore through potentially a single incision transvaginal access route. Applications such as endometriosis ablation or tubal sterilisation could be potential clinical targets if the robot can articulate within the conformities of a human female pelvis.

To evaluate the suitability of the design for adhering to the volumetric constraints of the pelvis, a kinematically accurate computer simulated model of the device was created. Pelvic dimensions were estimated from Magnetic Resonance images of the pelvis from eight pre and post-partum (1:1) women. Estimations were based on the mean inter-anterior superior iliac spine distances, the diameter of the sacral promontory and the height of the pelvis from the levator muscles to the midpoint of the inter-ASIS line measured using CRMtools™

(Cardiovascular Imaging Solutions, London, United Kingdom). A mean cone volume ($\frac{1}{3}ht\pi r^2$), representing an estimation of the pelvic shape, was created on the basis of these values. This was estimated by creating a single large inverted cone with the base representing the pelvic outlet. This was undertaken by estimating the diameter of the pelvic outlet and the pelvic inlet. The distance between two points considered as central points to each of these circles was estimated. Lines drawn to connect similar points around the circumference of each circle were joined and extended until they intersected. At that point one large cone was created; pelvic outlet (*base*) to intersected points (*apex*) and a smaller cone; the pelvic inlet (*base*) and the intersected points (*apex*). With the smaller cone subtracted from the larger an estimated volume of the human female pelvis could be determined from measuring the volume of the cone; assuming the pelvis is a pure cone which it is of course not to any precise measure nevertheless, it offers a reasonable guide to the anatomical restrictions (*Table 7.1*).

Table 7.1; Table highlighting the values measured from the MRI of the pre- and post-partum pelvises as an estimate of the anatomical volume of the average female pelvis.

Subject	Diameter (D)		Height (ht)		Length(cm)		Volume (cm ³)		Pelvic workspace
	(cm)		(cm)		$\sqrt{(0.5D)^2 + ht^2}$		$(\pi(0.5D)^2 \times ht) \div 3$		volume (cm ³)
	(do)	(di)	(H)	(h)	(L)	(l)	(LC)	(sc)	(LC – sc)
1	22.9	11.9	15.1	8	19.0	10.0	2073.0	296.6	1776.4
2	22.2	11.6	24.9	13	27.3	14.2	3212.6	457.9	2754.7
3	20.2	9.6	17.1	8.6	19.9	9.8	1826.6	207.5	1619.2
4	22.4	9.7	12.2	6.2	16.6	7.9	1602.6	152.7	1449.8
5	19.6	9.1	12.9	6.5	16.2	7.9	1297.4	140.9	1156.4
6	22.4	8.3	13.4	5	17.5	6.5	1760.2	90.2	1670.0
7	21.7	9.5	13.8	6.3	17.6	7.9	1701.2	148.8	1552.3
8	22.5	9.2	13.7	5.5	17.7	7.2	1815.7	121.9	1693.8
Mean	21.7375	9.8625							1709.1cm ³

do – diameter of the pelvic outlet, di – diameter of the pelvic inlet, ht – Height, H – Height of large cone, h – height of small cone, L length of Large cone, l – length of small cone, LC – volume of large cone, sc – volume of small cone.

A further rectangular volume was placed within the cone representing the approximate position of the fallopian tubes in relation to the defined pelvic workspace and the robot access point; the rectovaginal recess. This rectangular volume measured 3cm (length), 1cm (width),

1cm (depth) was drawn 1 cm off the midline and 2 cm from the insertion point as a representation of the approximate relative position of the isthmus of the right fallopian tube; the anatomical target. The volume is representative of the variability in the position of the anatomy (*Figure 7.6*). The flexible robot was subsequently articulated as a computer simulated model to within these defined constraints.

7.3.2.2. Results

From this simulation, it was evident that the robot can be retroflexed and manoeuvred within the dimensional constraints of a human female pelvis. The estimated mean diameter of the female false pelvis was 217mm.

The robot is capable of retroflexion within a maximum radial arc of 108mm. For smaller pelvises it is likely that some initial lateral angulation into the peritoneal cavity from the insertion point, counter to the direction of desired retroflexion, will be required to ensure retroflexion can be performed without being interrupted by collision with the lateral side wall. The volume defined as the position of the isthmus of the fallopian tube, is capable of being covered by the robot using the distal tip with some variable lengths of insertion. Given the robots current dimensions and coupled with the endoscopic tools passed from the tip at various exteriorised lengths, the device is able to cover >90% of the represented volume. The simulations also indicate that to achieve this level of coverage the rigid section of the robot needs to be inserted into the pelvis to a length of 120 – 130mm and the endoscopic tool exteriorised to a length of between 2.5 and 4.5cm, a length which would be suitable to perform accurate and controlled intervention (*Table 7.2*). This may promote challenges in patients who have had previous abdominal procedures where the anatomical workspace may be reduced even slightly by the presence of scar tissue.

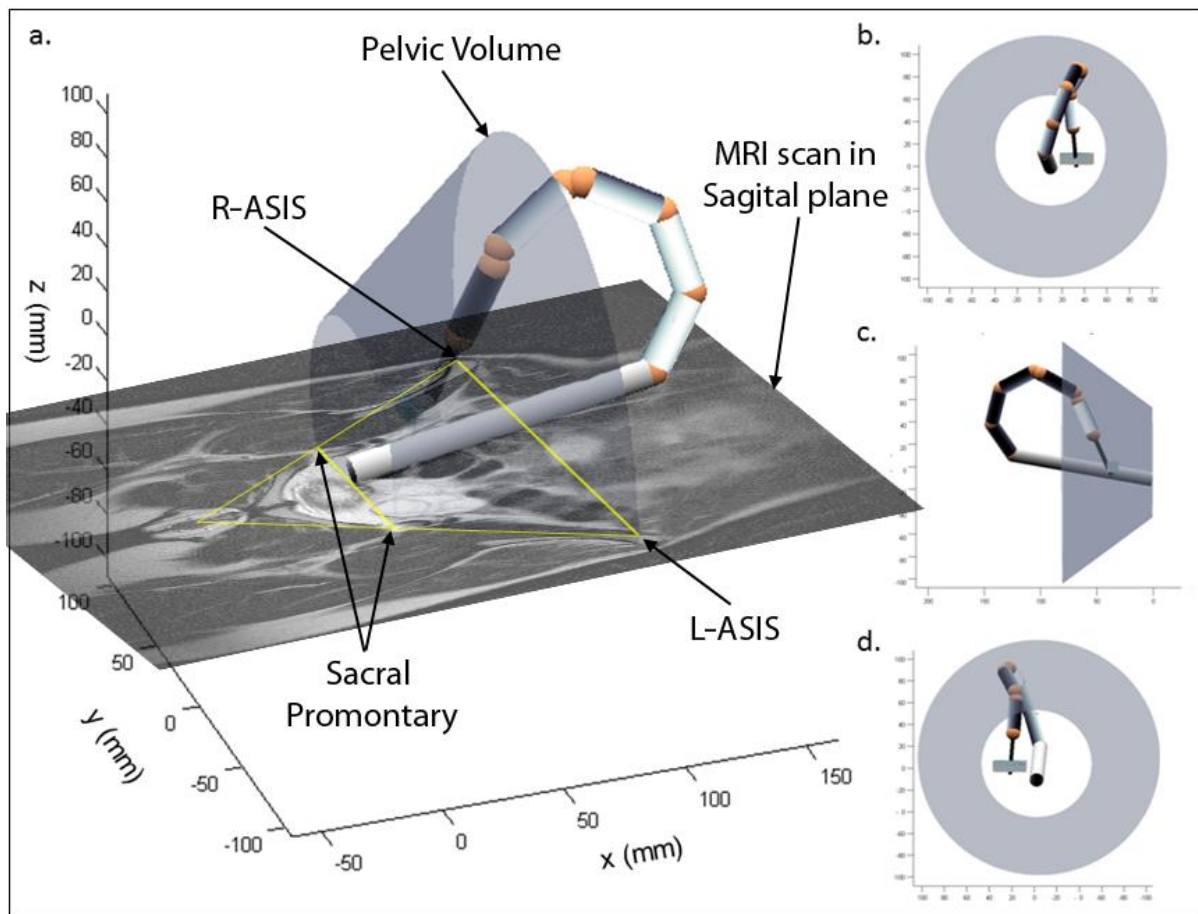


Figure 7.6: Constrained workspace analysis of a kinematically accurate computer generated model of the robot. The pelvic workspace is defined from female MRI images. ASIS – Anterior Superior Iliac Spine (L-left, R-Right)

Table 7.2; Optimum volume of the target (fallopian tube isthmus) covered by the movement of the distal segment of the articulated flexible access platform at specific insertion lengths of the robot into the pelvis and segmental extensions of the endoscopic tool from the head.
(The optimum coverage of the target is highlighted in red)

		Volume of target covered for each 2mm exteriorisation of endoscopic tool (mm ³)										
Increasing insertion of robot (mm)		120.00	121.00	122.00	123.00	124.00	125.00	126.00	127.00	128.00	129.00	130.00
Exteriorised length of Endoscopic tool (mm)												
24.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
26.00		73.52	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
28.00		311.26	230.27	159.65	109.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00
30.00		575.33	525.74	452.22	372.64	270.03	173.48	106.43	0.00	0.00	0.00	0.00
32.00		650.57	659.17	620.09	596.07	546.93	435.31	360.76	301.04	203.08	134.50	0.00
34.00		629.62	641.03	689.68	676.74	664.78	637.65	615.87	545.07	452.29	371.39	289.03
36.00		482.70	586.16	660.08	659.35	665.09	689.16	668.87	687.52	669.71	625.05	561.86
38.00		237.09	308.59	394.08	529.98	546.26	583.42	630.18	671.88	689.22	667.33	662.37
40.00		0.00	0.00	0.00	0.00	298.00	341.60	429.25	488.76	578.28	648.85	679.42
42.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00	236.81	302.14	382.94	462.59
44.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	202.14
46.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total volume of target covered (mm ³)		2960.1	2951	2975.8	2944.0	2991.1	2860.6	2811.4	2931.1	2894.7	2830.1	2857.4
% total volume of target covered		98.670	98.365	99.193	98.134	99.703	95.354	93.71	97.703	96.49	94.335	95.247

7.4. Results; The Bimanual instrument platform

7.4.1. Instrumental force application

The *in-vivo* trials highlighted that force requirements to manipulate tissue within the animal model were not easily met by the bimanual instruments. The aim of this trial was to ascertain the precise capabilities of the instrument arms and how re-design may improve the force transmission.

7.4.1.1. Material and Methods

A single instrument arm was setup, fixed to an optical table and driven to the fullest extent. A force torques sensor was fixed directly below the tip of the arm. The instrument arm was driven vertically down onto the sensor and the value recorded. The length of the articulating section of the instrument arm was incrementally reduced by drawing it into a fixed and rigid introducing shaft. This in effect increased the stiffness of the arm and the force was measured on each setting. (*Figure 7.7*)

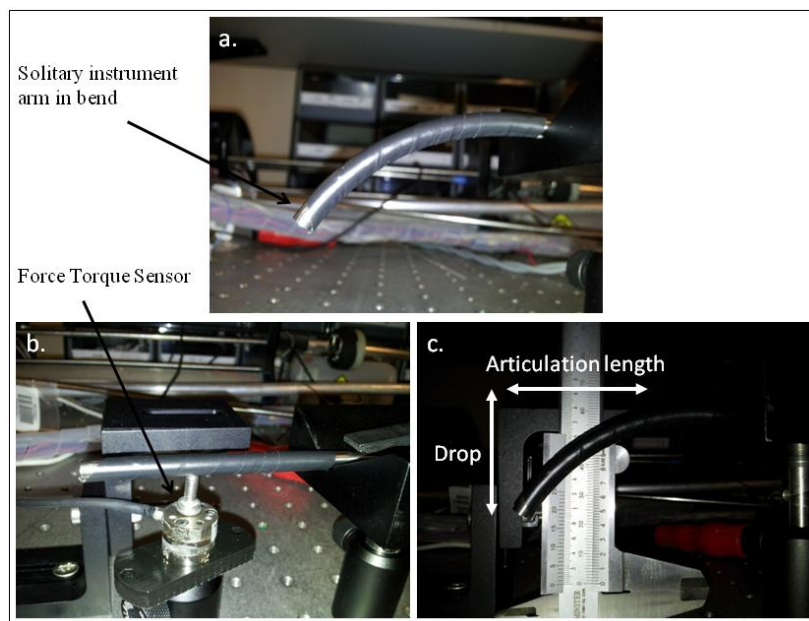


Figure 7.7; Images depicting the laboratory setup for determining the vertical force capabilities of the instrument arms.

7.4.1.2. Results

The initial outcomes from the force readings demonstrated forces of only 0.27N to 0.51N with a reduction in the articulating length of the arms ranging from 95mm to 150mm (Table 7.3). As would be expected as the length of the articulating arm is reduced to increase the force, the level of articulation and arm overlap, essential for any clinical procedure, would be reduced. As such it is a balance between articulating length and force. However, none of the force readings would meet the measured values for the force requirements within the *in-vivo* setting reported in Chapter 5; a redesign of the instrument arms will be essential.

Table 7.3; Arm lateral force versus arm length.

Arm length (mm)	150	135	110	95
Average Force (N)	0.27	0.35	0.44	0.51

The reduction in the length of the arm stiffened the whole arm enabling greater force to be delivered through the tendon to the instrument tip. As such, the redesign focused on stiffening the arm through two elements; shortening the arms to increase force for tissue manipulation and narrowing the individual slots in the hollow nitinol tubes to restrict the bending and increase the potential force delivery.

Further evaluation of the new design demonstrated that with an articulating length of 60mm the force transmission by the arms in the vertical plane was 1N. The force measured at 40mm was 1.3N which although closer to the requirements for clinical application as highlighted in Chapter 5, would no doubt inhibit the overlap and therefore the dexterity which the instruments could provide.

The challenge to meet the appropriate forces required for clinical application remains an evident problem. Ongoing design iterations are being evaluated which aim to better meet the force requirements for future iterations of the platform.

7.4.2. Instrumental workspace and its relevance to a focus clinical application.

The aim of this study was to evaluate the requirements of the bimanual instrument to meet the clinical workspace for a specific general surgical procedure. In doing so the limitations of the current instrumental design can be measured against these parameters to determine how the workspace of the instruments can be optimised.

7.4.2.1. Materials and methods

This study explored the workspace of the two main operating instruments, a grasper and a dissector for the purposes of determining the volume within which the tool tips operate to perform a specific surgical task. In this case the laparoscopic cholecystectomy for gallstones was chosen as it translates well into the ex-vivo setting where it could be trialled repeatedly and by multiple users with a broad range of surgical experiences. Furthermore, the procedure is routinely performed in clinical practice and could be a potential target for the robotic device in the future.

Subjects

Subjects were recruited to the study from Surgeons based at St Mary's Hospital, Imperial College Healthcare NHS trust, all of whom had some level of clinical experience. Their experience in laparoscopic cholecystectomy and general laparoscopic procedures was recorded using a five point questionnaire for each and an arbitrary score, weighted toward the number of laparoscopic cholecystectomies performed, stratified the subjects by experience for this procedure derived from these values.

Setup and task

The task was performed using whole pig livers with intact gallbladders fixed into a laparoscopic trainer (BTS300; Pharmabotics limited, Hampshire, UK). Each subject was provided with a laparoscopic grasper and laparoscopic scissors without diathermy. The lack of diathermy was an unfortunate requirement due to the interference with some of the sensors used during the trial never-the-less, the impact of this was minimal as the outcomes of the trial are to determine the workspace covered during the whole procedure by the instrument tips and with the quality of dissection moderately less important. However, the completion of gallbladder dissection, safely and as effectively as if it were performed within the clinical environment, was expected, though not formally assessed.

The cystic duct on each of the gallbladders was clipped with two clips prior to the commencement of each task. Each subject was required to dissect and free the cystic duct using the graspers and the scissors only. The cystic duct, once dissected with a clear window behind, was required to be demonstrated before dividing. Once the severed, the task required the dissection of the gallbladder from the gallbladder bed. The laparoscopic camera was held by the same person on all occasions and would take instruction from the subject as required for optimal viewing of the target field.

Instrument tracking

Both the laparoscopic instruments were fitted with a magnetic tracking marker on their shaft whose position within three dimensional space could be accurately recorded using a high powered magnetic field (Aurora Magnetic Tracker; NDI, Ontario, Canada). Before each task the position of the ports placed by each surgeon to their preference, was recorded in respect to the magnetic field. This was achieved by taking two reference points on either side of the port directly in contact with it, thereby enabling the central point to be calculated as the midway between the two. This acted as a fixed reference about which the instrument markers would move and from this coupled with knowing the length of the instrument and the distance between the marker and the tool tip, the instrument tip position for each recorded point in free space could be calculated. This particular tracking device records at a frequency of 40Hz.

Bimanual instrumental workspace

In a similar manner as a control the bimanual instrument was fitted with magnetic tracking markers on each of the arms. Each marker was placed at the distal tip of each instrument so that it could take advantage of measuring the 10mm linear translation that the prototype version 3 was capable of achieving. The prototype was positioned directly in front of the Aurora tracker enabling the position of the instrument arms in 3D space to be recorded. As would be expected for each single point of linear translation at the distal tip, so the arms would move producing a 2 dimensional concave area of coverage. As such the instrument arms were driven around to enable complete coverage of the potential area whilst the tips had no linear translation, 5mm of translation and the maximum 10mm translation. All the recorded

positions of the tracking marker were then coordinated to extrapolate what was in effect a volume of coverage which the instrument arms were able to meet. This assumes that the whole bimanual instrument device is fixed at the rear and is immobile which is of course not true. However, one of the other outcomes that this work will provide will be to determine how much translation of the device as a whole, will be needed to be undertaken to meet the requirements of a full cholecystectomy given the current format of the design and the range of workspace of the arms calculated.

Analysis

Each task was recorded, synchronised with the Aurora magnetic tracker and time stamped to ascertain the beginning and end of the procedure. This enabled the time points for events during the procedure seen on video to be accurately linked to the precise location of the instrument tip in 3D space. As a result, events that occurred during the procedural task which were not directly related to the operational workspace constraints for retraction and dissection such as when one of the measured instruments was removed from the referenced zone which may have occurred as a result of when a clip applicator was required to be used to control a bile leak from the gallbladder specimen hampering dissection. As a result only the workspace created by the instrument tips performing the task were recorded and analysed. Time sequences of the events considered irrelevant to the task were discarded.

The volumes for the bimanual instrument was calculated and aligned in a similar manner to the clinical workspace with the 6 degree of freedom trackers placed at the tip of each of the instruments. The instrument arms were driven continuously to map the entire workspace. This was performed with the linear tip translation at 0mm, 5mm and 10mm extensions to capture the true volume of coverage by the instrument tips.

Analysis of the instrumental workspace for both the clinical and bimanual platform instrumentation was undertaken using in-house developed Matlab™ (Mathworks Inc) software. All measurements were recorded in arbitrary units as derived from the aurora tracker ($1 \text{ AU}^3 = 1\text{mm}^3$). Once derived, the workspace of the instrument tips and the bimanual instruments could be compared. The quantification of the instrumental arm spread, workspace volume overlap and the translational requirements of the bimanual instrument

when aligned with the clinical workspace, as would be evident within the clinical setting, was evaluated.

Comparison was made to the position of the clinical instruments during each of the tasks. The position of each instrument in relation to one another was recorded at each given time point and the distance between them across 3D space measured. The results were then directly compared to the maximum spread of the instrument arms of the bimanual platform to determine the effectiveness to meet the requirements of a clinical procedure.

The Mann-Whitney U test for non-parametric data was used where statistical outcomes are quoted. A value of $p=0.05$ was taken as significant.

7.4.2.2. Results

Twelve surgeons were recruited to the trial. Their level of practical clinical experience in laparoscopic cholecystectomy ranged from 10 to over 2000 cases, with clinical seniority ranging from a year 5 surgical trainee to a practicing surgical consultant. Each subject completed the task as required, with the gallbladder removed on each occasion as a complete specimen.

Inter-Instrument tip distance

The maximum distance the arms on the bimanual instrument design can separate was measured at 90 mm. The distance between the two clinical instruments were measured at each referenced time point during the entire task. The minimum, maximum and mean inter-instrument tip distance across all the subjects was measured (*Table 7.4*). The mean inter-instrument distance was determined as 154mm (+/- 27.7). No significant difference was noted between experts, intermediates and novices when compared ($p=0.564$). The mean spread from the bimanual instrument was compared against the clinical values (*Figure 7.8*).

Table 7.4; Inter-instrumental distances measured during the laparoscopic cholecystectomy task for each subject.

Subject	Experience	Minimum (mm)	Maximum (mm)	Average (mm)
1	Junior	85.8209	165.913	127.4011
2	Intermediate	148.8135	214.3458	179.2955
3	Expert	145.3205	248.9445	199.0087
4	Intermediate	114.5535	181.4071	155.1256
5	Junior	117.8777	223.5826	148.3911
6	Intermediate	104.1113	188.3266	141.6329
7	Junior	120.5943	180.5908	154.6676
8	Expert	127.0026	206.1473	160.4111
9	Intermediate	114.3222	191.7025	149.298
10	Expert	79.2727	157.3863	107.8287
11	Expert	102.4133	176.4662	127.2384
12	Junior	165.8438	276.9125	198.5567
Mean		118.8288583	200.9771	154.0712833
StD (+/-)		25.33592994	35.10839168	27.72541694

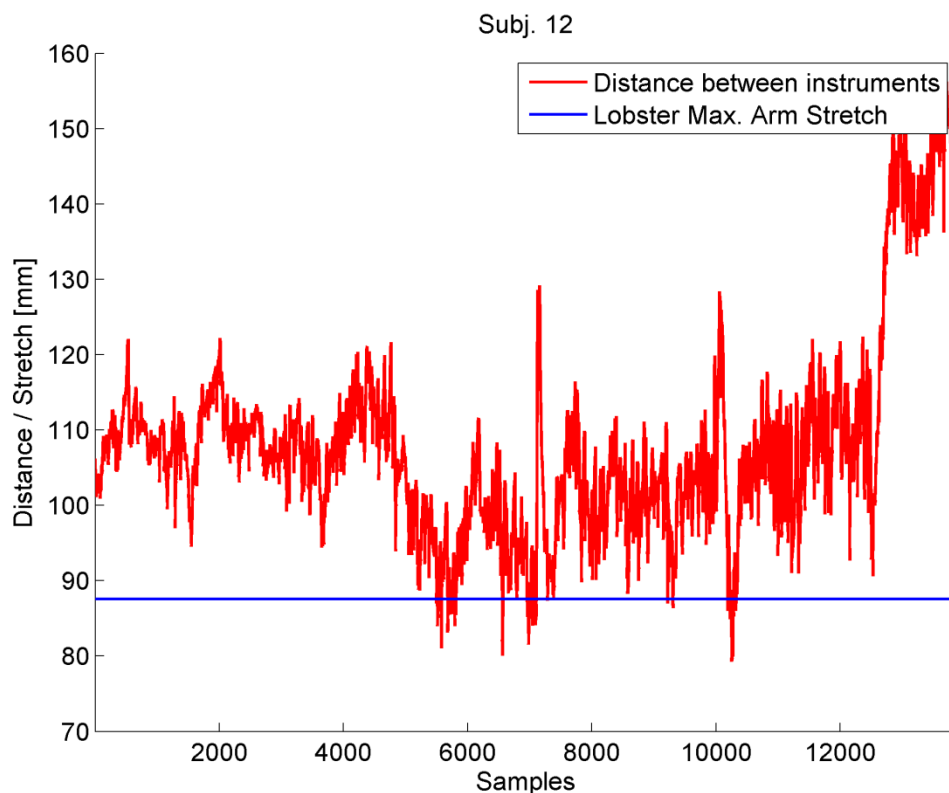


Figure 7.8; A graphical comparison of the inter-instrument tip distance measured during a laparoscopic cholecystectomy task (red line) with the maximum distance that the bimanual instrument tip can reach. (blue line)

This subject, displayed above, demonstrated the narrowest inter-instrument tip distance to complete the task out of all the 11 subjects.

Clinical workspace

The clinical workspace for each subject was determined and mapped for each individual subject. (Figure 7.9)

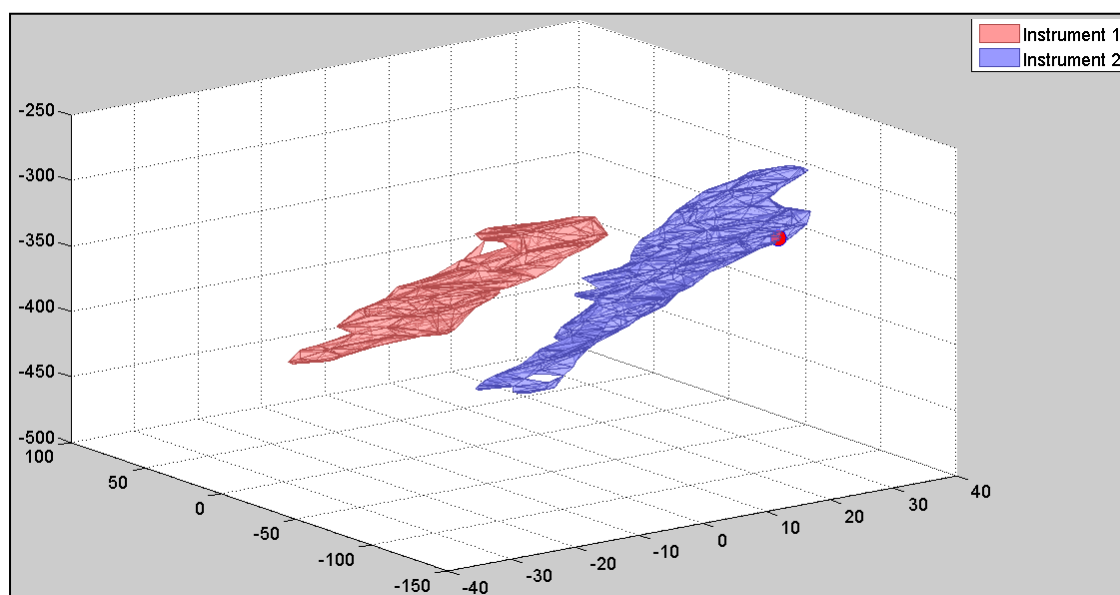


Figure 7.9; An example of the clinical workspace for an ex-vivo laparoscopic cholecystectomy when the retracting (Instrument 1 (red)) and dissecting (Instrument 2 (blue)) laparoscopic tool tips are mapped.

The volumes of the workspaces were determined from these derived models (Table 5). The total workspace volume defined by directly combining the volumes measured from each instrument tip was $43,742 (\pm 15,281) \text{ mm}^3$, a value found to show significant difference when the mean workspace derived by the junior trainees; $59,619 (\pm 14,702) \text{ mm}^3$, was compared against the experts $36,920 (\pm 5,563) \text{ mm}^3$; $p=0.014$, as well as the senior (intermediate) trainees $33,942 (\pm 19,419) \text{ mm}^3$; $p=0.034$. When the workspace from each instrument was independently evaluated a significant increase in the workspace for both instruments was noted in the hands of the junior trainee when compared against the experts. The dissecting tool showed the greatest difference $22,532 \text{ mm}^3$ versus $13,121 \text{ mm}^3$ ($p=0.027$) with the retracting instrument less so $37,087 \text{ mm}^3$ versus $28,573 \text{ mm}^3$ ($p=0.05$). (Figure 7.10)

Table 7.5; The independent instrument tip volumes as well as the combined volumes for the ex-vivo laparoscopic cholecystectomy task.

Subject	Experience	Retracting Instrument (mm ³)	Dissecting Instrument (mm ³)	Total instrumental volume (mm ³)	Combined task volume (mm ³)
1	Junior	14813	45165	59978	170495
2	Intermediate	7459	27565	35024	117195
3	Expert	11379	21866	33245	77860
4	Expert	10974	22949	33923	111135
5	Junior	36432	43856	80288	373158
6	Junior	24244	24795	49039	166127
7	Intermediate	4051	17828	21879	44499
8	Expert	21741	19574	41315	109419
9	Expert	10071	21689	31759	341796
10	Intermediate	4597	40326	44923	87840
11	Expert	11485	32874	44359	143334
12	Junior	14637	34533	49169	94033
Mean		14324	29418	43742	153074
<i>StD(+/-)</i>		<i>9224</i>	<i>9668</i>	<i>15281</i>	<i>102141</i>

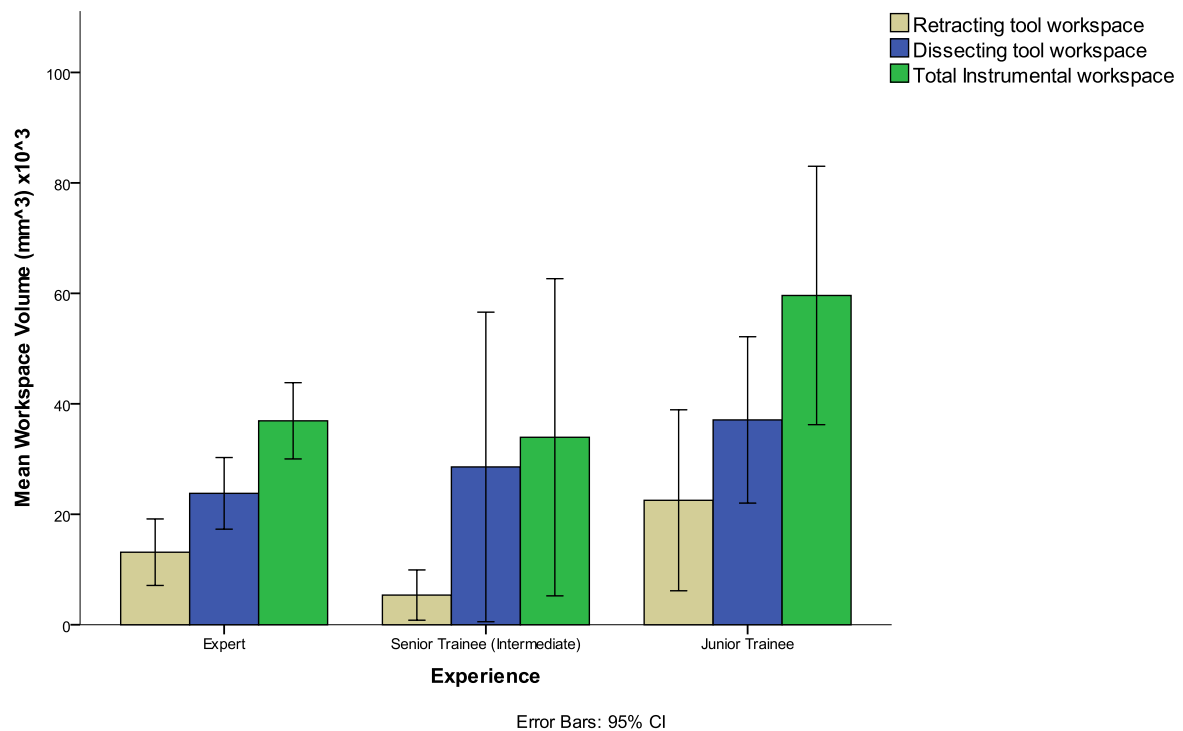


Figure 7.10; A graph demonstrating the mean workspace volume (mm³) measured across the various trainee levels for each tool independently and then combined.

The combined task volume included the sum of the volumes measured at the tip of each instrument i.e. the total instrumental volume, plus the space in-between. The total combined task volumes ranged from 44,499mm³ to 373,158mm³ with, perhaps expectantly, no strong statistical evidence to support a difference in the mean task volume between junior trainees and consultant surgeons (*Table 7.5*).

The combined task volume was derived as it was felt to be more broadly representative of the true surgical workspace requirement as it included the space in between the tools during the task. In a slightly different way, this space has already been evaluated with the instrumental arm distance defined by the distance between each instrument tip at each time point during the task. The marked variation in the inter-instrument spread was not shown to be related to the experience of the surgeons' trialled. With those findings it may suggest that this space is likely a result of factors unrelated to the experience of the surgeon. It would not therefore be inappropriate to suggest that one such factor may be related to the variation in the anatomy of the gallbladder size and shape. This would make the evaluation of the combined volume for comparison purposes with the bimanual instrument more relevant.

Workspace of the bimanual robot arms.

The workspace for the bimanual instrument arms was evaluated using the magnetic tracking marker as previously described. The volume recorded for each of the instrument arms was 12104mm³ for the left and 10605mm³ for the right. The total volume when combined was 22709mm³ with an overlap of the two arms measured as 9.8mm³; predominantly occurring when the instruments are extended using the linear tip translation to 5mm (*Figure 7.11*).

The entire volume covered by the instruments of the bimanual platform was compared like for like, to the clinical workspace volumes recorded from each subject. It was evident that a volume of 1.7 to 14.2 times that rendered by the platform was required to meet the volumetric needs of the clinical procedure; mean 5.8 ($\pm$ 3.9). However, these figures are arbitrary as they are based on a numerical evaluation and cannot necessarily be considered clinically relevant due to the discrepancy related to the orientation of bimanual platform relative to the gallbladder.

When approaching a gallbladder with the bimanual platform it would be expected that the device will be facing the gallbladder which is raised over the liver bed as may be seen in conventional laparoscopy. Although this assumes additional instrumentation or methods for gross gallbladder retraction, it would nevertheless be the most clinically relevant orientation for the purposes of evaluating the translational requirements of the current bimanual instrument design for this particular clinical example.

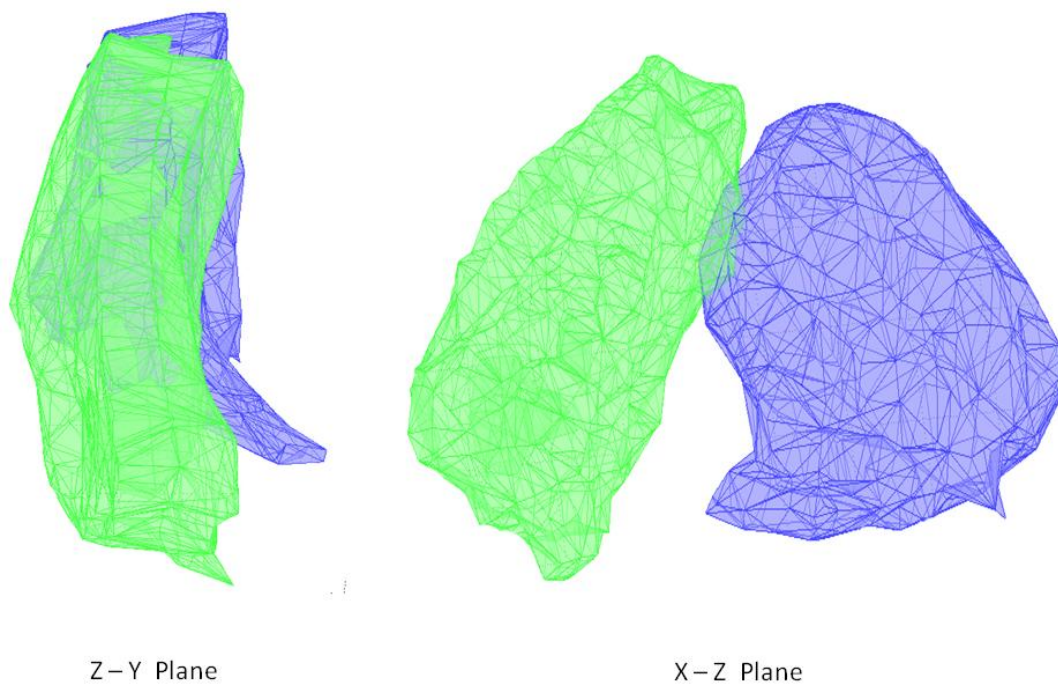


Figure 7.11; The workspace generated by the two arms from the bimanual instruments. Each instrument is colour coded for clarity. The different views highlight the concave areas covered which when combined with the linear translation generate a volume as shown. (Left image; as would be visualized with the bimanual platform facing right to left, Right image; facing forward)

Clinically Relevant Translational Requirements for the Bimanual Platform.

The requirement of the clinical workspace to be orientated with the alignment of the bimanual instrument as it would be presented to the target gallbladder is essential before formal true translational requirements can be drawn. Alignment of the clinical workspace was undertaken using principle component analysis technique to rotate the bimanual workspace to meet the appropriate alignment using in-house developed Matlab™ software (*Figure 7.12*).

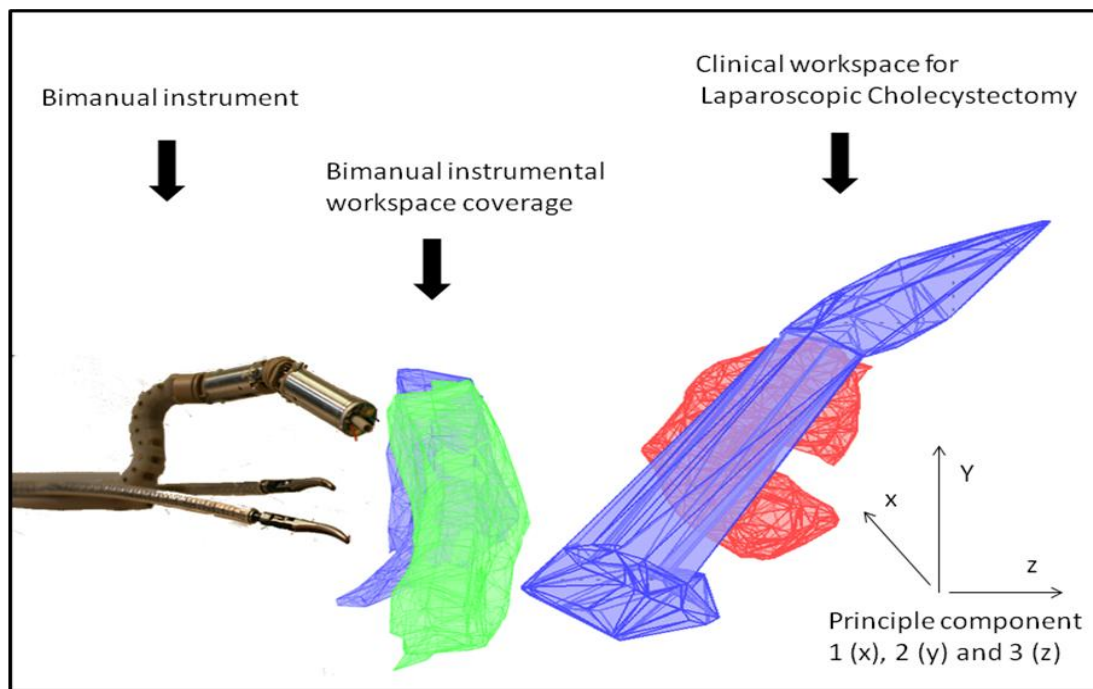


Figure 7.12; Image portraying the capabilities of the lobster to meet the clinical workspace requirements for a laparoscopic cholecystectomy when aligned.
When rotated the X, Y and Z axis are realigned as principle components 1, 2 and 3; or the new relative x, y and z

Table 7.6; Table highlighting the translational requirements of the bimanual instrument to meet the clinical requirements.

Subject	Principle Components		
	1 (x)	2 (y)	3 (z)
1	2.2	2.1	2.4
2	2.6	1.8	2.2
3	3.0	2.4	1.5
4	2.2	2.	2.0
5	2.8	2.2	2.5
6	2.4	2.0	1.8
7	2.2	1.6	1.8
8	2.5	1.9	1.9
9	2.4	2.9	1.7
10	1.9	1.7	1.9
11	2.3	2.1	2.0
12	3.3	2.6	1.5
Minimum	1.9	1.6	1.5
Maximum	3.3	2.9	2.5
Mean	2.5	2.1	1.9
(SD +/-)	0.4	0.4	0.3

The translation of the lobster across the PCA 1, 2 and 3 planes to meet the clinical requirements was assessed. The results indicated that the bimanual instrument, in its current configuration, requires translating 3.3 times in the PCA 1 (x) direction, 3.0 times along PCA 2 (y) and 2.5 times the PCA 3 (z) in order to meet the maximum clinical workspace volume documented from the series (*Table 7.6*).

This highlights the need for greater translation of the platform as a whole. This can be met both through increasing the translation of the instrument tips, which perhaps is more relevant with tissue manipulation than gross navigation, as well as and perhaps more relevantly, linear translation of the entire platform from the access point. This is perhaps the easiest to overcome from a design perspective when compared to the translation required in the X and Y direction. The need for greater articulation at this point is evident from this study which highlights the need for greater freedom of movement at the neck of the platform or upon the shaft to enable the instruments to cover greater volume in the X and Y planes. This presents an engineering challenge which may not be quite so easy to overcome that the linear translation of the Z –component. However, with the rigidity of the shaft associated with this design, use of the access point as a fulcrum could be utilised through more precise and broader external manipulation. Evidently, each clinical application will vary in terms of its translational requirements. Any further design iterations to the device must focus on a method of overcoming all the translational shortfalls. It is likely an external robotically controlled arm clamped to the device will be the method of choice to meet these needs.

With later designs which, if the system is being inserted through a distant access site, as demonstrated in Chapter 4, the ability to elevate the operative section of the platform may be more challenging as the reliance on an external arm and manipulation at a fulcrum point will not always be possible. Further design modification would therefore be required with potentially 1 or 2 degrees of freedom of motion added onto the shaft just behind the neck of the platform. This would enable the X and Y translational elements to be met but may be more challenging to integrate from an engineering perspective given the current design which relies upon the rigidity of the shaft.

Nevertheless, for each of the current designs, exemplar clinical applications were explored and the capabilities of the device towards clinical translation evaluated.

7.4. Defining Potential Clinical Applications

The most essential element to any novel surgical platform is to evaluate its potential for true clinical application. The theoretical potential for each surgical platform toward clinical effect has been discussed but the relevance to true application has yet to be explored. This requires not only the exploration of what will be the final disruptive clinical application for both platforms and given the early prototype designs that currently exist may still be difficult to pin-point, but also and perhaps more relevantly, define through a validation model where each platform fits in terms of the complexity of surgical applications which could be met once the flexible access surgical platforms is refined.

7.4.1. Materials and Methods

Ex-vivo laboratory based and live pre-clinical *in-vivo* trials were undertaken to explore the potential clinical applications where each of the developed platforms could be utilised. This was initially centred on the ability of the platforms to be objectively assessed using predefine criteria which acted as a guide upon which the complexity of the potential clinical applications could be based. The work has been directed at validating the robot through its ability to meet the surgical workflow requirements for each procedure. Validation is based upon confirming four specific aspects of the surgical pathway:

- 1) ***Access and diagnostics***; this explores the routes of access and ease of repeated access with maintenance of pneumoperitoneum. It also promotes the need for a rudimentary instrument channel for interventional and imaging purposes.
- 2) ***Tissue destruction and ablation***; this explores the need for the robot to be able to undertake tissue destruction for the purposes of dividing tissue.
- 3) ***Tissue dissection and resection***; this explores a more refined capability of more accurate division of tissue planes or large organ division.
- 4) ***Reconstruction***; this explores the ability of the device to reconstruct divided tissue.

As all the criteria are met so theoretically the device should be capable of a therapeutic surgical robot even if at a rudimentary stage of development. *Table 7.7* highlights these criteria and the potential clinical applications which could be achieved once met.

The idea was to develop a ground truth from which to trial and assess each of the robotic platforms, derive clinical procedures and focus future clinical trials to determine what further elements to the design would be required if it is to be clinically effective.

Table 7.7; The criteria used to objectively assess the clinical relevance of each of the developed iterations of the robot.

Functional Capability of the Robotic prototype	Exemplar of Operative Procedures achievable as each functional capability is reached.
Access & Diagnostics	<i>Transvaginal and single-incision pelvic exploration and focused energy delivery for treatment of ovarian cyst, endometriosis and sterilisation</i>
Tissue destruction / ablation	
Tissue dissection / resection	<i>Trans-thoracic procedural step illustration including vascular dissection and lymph node resection</i>
Reconstruction	<i>Transvaginal and single-incision sleeve gastrectomy, gastrojejunostomy and Roux-en-Y gastric bypass</i>



Increasing complexity of the surgical application

7.4.2. Procedural Validation

7.4.2.1. Achieving Access

Early trials were hampered significantly by the inability to secure a reliable and repeatable access route and one which would securely maintain full pneumoperitoneum throughout the procedure and therefore maintain the workspace required for the robot to manoeuvre.

These early challenges were met with initial frustration as the collapsing abdominal wall would damage the platform upon insertion (*Figure 7.13*) limiting the outcomes of the trial.

This was overcome with the sourcing of a 15mm, 150mm chimney bariatric trocar (Applied Medical, Rancho Santa Margarita, California, US) which was further extended with the addition of a custom made extension tube lengthening the chimney of the port to 400mm. This in effect, enabled access to the abdominal cavity to be undertaken in the normal manner using the bespoke port; establish pneumoperitoneum before safe insertion of the device. The delicate articulating segment of the platform would be safe inside the custom port, whilst pneumoperitoneum was re-established. This secure access technique enabled both the transabdominal and transvaginal NOTES access to be performed with equal repeatability and security for future trials.

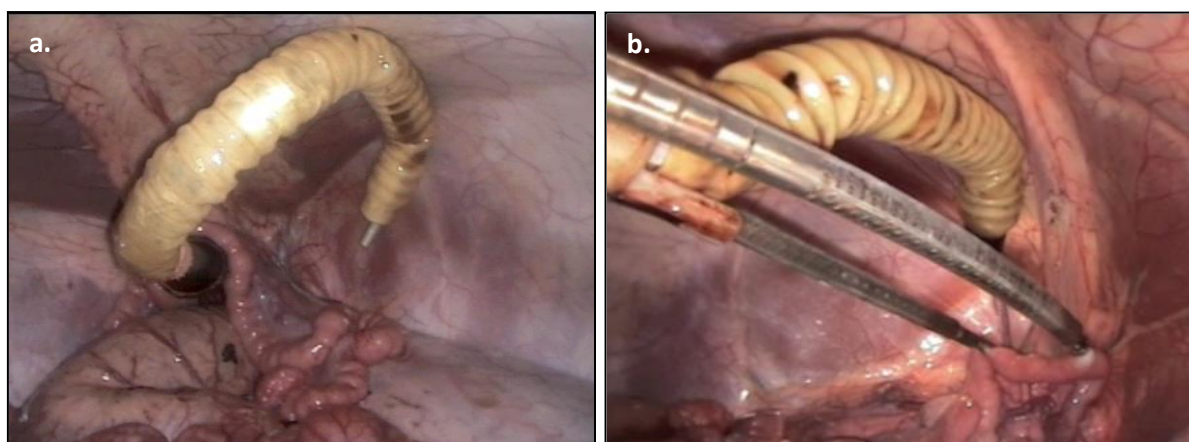


Figure 7.13: Articulated i-Snake (a) and with bimanual instrumentation (b); access assured through the transvaginal and transabdominal routes.

With the insertion of a device designed with a central channel dedicated to instrumentation, maintaining pneumoperitoneum during instrument interchange was noted to be a significant problem with air leak. With the early flexible designs the problem was highlighted and managed through a two course approach. The first was to increase the flow of carbon dioxide into the abdomen to overcome any small air leaks and the second was to ensure a flexible instrument was in the instrument channel whilst inserting the robot into the abdomen to reduce the aperture. This approach served two purposes particularly in the early trials. It enabled the pneumoperitoneum to remain consistent and therefore the workspace required to trial the device as well as ensuring an instrument could be used with the device, particularly in the period before a sheath was integrated into the internal channel to enable more efficient instrument interchange. Once the sheath was integrated, a small plug was inserted into the outlet of the channel at the proximal end which provided security and reliability of the pneumoperitoneum. With the design and testing of the bimanual instrument the issue of

pneumoperitoneum security became an issue once again. Early design trials were further hampered by this problem as the bimanual platform had two additional and significantly larger channels for the surgical instruments than the flexible design. The approach to this problem was the same as for the flexible design in principle with high flow and an attempt to maintain security of air loss from the proximal end of the robot initially with paraffin grease. This solution was overcome in subsequent trials with the redesign of the proximal section of the robot which integrated the instruments and central channels into a dual air tight sealed unit. Although air leak was still present this was more manageable with an elevated flow of carbon dioxide into the abdomen as before.

The techniques for maintaining pneumoperitoneum with high flow would not be clinically acceptable once translated due to the increased development of adhesions that has been demonstrated within the laparoscopic arena (132) A focused engineering solution will be needed to be integrated into the final design to formally overcome this problem before clinical translation.

7.4.2.2. Enabling Diagnostics

Camera visualisation is an essential requirement of any surgical robot, not only to enable safe navigation but also for diagnostic purposes. It became clear with ongoing trials that the visualisation of the whole abdominal cavity from the single 1.8mm camera alone was insignificant. The problem was not so much the camera size but the inadequacy of illumination. The large cavity space and the predominance of “red” throughout the visual field creates a darker image requiring a higher powered light source for optimal illumination. For the purposes of many of the initial trials the light source from a conventional laparoscope was used to overcome the problem whilst a permanent fix was sought. Multiple light sources were tested for both illumination capabilities (129) and objectively to determine the heat dissipation onto the tissue bed by macroscopic examination of the tissue post-mortem. The overall outcome from these trials was that the most appropriate illumination source currently available was white light emitting diodes (LEDs), heat sunk on to the platform tip (Chapter 6). Although illumination had been enabled, alternative cold light sources from external sources were nevertheless still being explored.

Further trials for the purposes of diagnostic intervention relied more on the ability to source diagnostic tools which could be integrated into the design such as the confocal

endomicroscope (pCLE); a flexible probe based endoscopic microscope capable of being passed through the internal channel of the flexible platform. The pCLE provides high powered histological images in real time when the tip is in contact with the tissue bed. With such an instrument given the high powered magnification, any small motion at the tip would be magnified into a significantly more extreme motion of the histological image which has a tendency to cause blurring of the image. The use of a more robotic platform enables the potential for greater control to be placed on the motion of the catheter tip enhancing the diagnostic capabilities of the pCLE (*Figure 7.14*). The enhanced workspace provided by the flexible access platform enabled the whole peritoneum to be explored from a single access point. Standard rigid laparoscopic instruments would not be able to provide the same cover from the single point than this flexible access device could achieve (133).

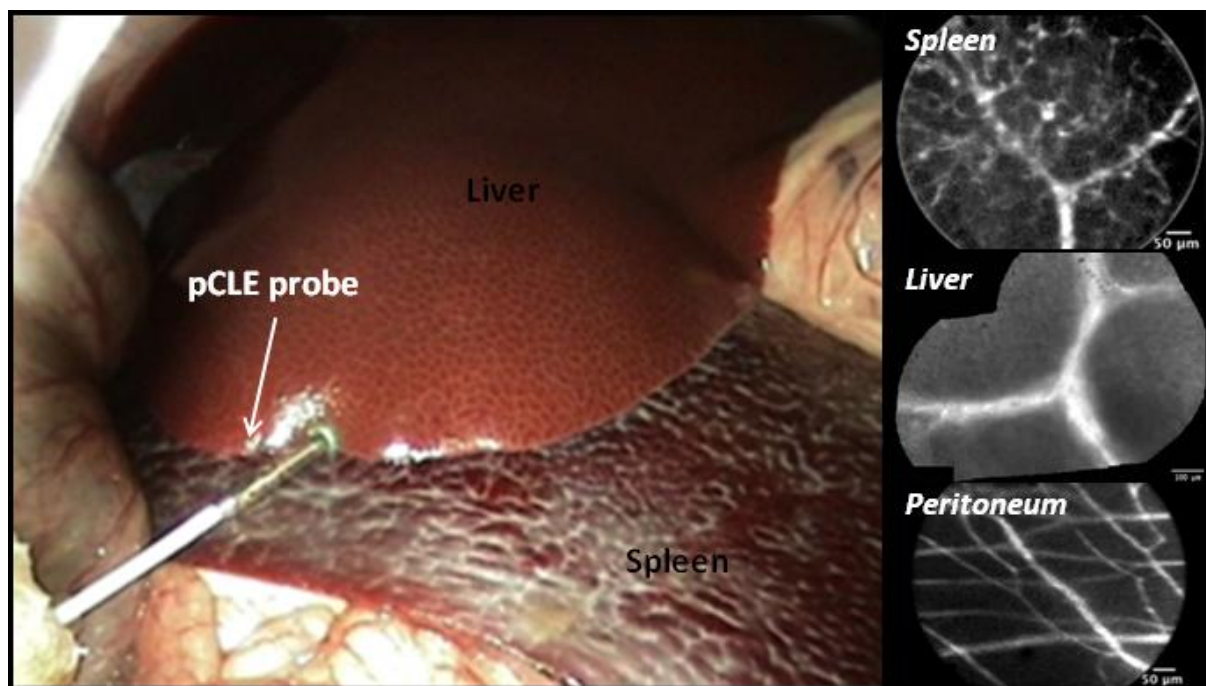


Figure 7.14; Images of the pCLE probe delivered through the flexible platform. The confocal images obtained with contact of the probe to the spleen, liver (showing hepatocytes) and the peritoneum are highlighted.

The bimanual instrument, by the same virtue, is also limited in its workspace capabilities. However, it has the capability of manipulating the tissue in such a way as to present it for diagnostic evaluation whether with the pCLE or potentially even an endoscopic balloon ultrasound probe delivered through the internal channel. This presents a unique advantage over any other minimally invasive intra-operative imaging tool available, which would be

challenging to use within the operative environment without the additional support of other surgical instruments.

7.4.2.3. Tissue destruction and ablation.

The requirement for any basic interventional device is to have the capabilities of performing some degree of tissue dissection or ablation of pathology. Although the flexible device is unable to undertake this independently, and to a point the bimanual instrument with the current design, the need was to explore and describe various externally developed instruments that would be suitable for use with this device and determine their suitability to be used with the internal 3.0mm channel.

As described, one of the most significant early challenges was enabling instruments to be passed through this central channel particularly whilst the individual joints were articulated at various angulations. The need for a sheath to secure the continuity of the internal channel lumen was evident. A bespoke custom designed internal channel was developed with an external company though a small compromise on articulation restriction was accepted evident particularly when undertaking tasks which required retroflexion but was more evident with some endoscopic instruments over others. The trialling of multiple flexible instruments for suitability, both in terms of size and reduced restriction on the articulation was undertaken.

Surgical procedures frequently rely on one or more focused energy delivery devices to facilitate tissue dissection and/or destruction. Energy modes such as electrical current, high-frequency ultrasound, laser and ionizing gases may be used in various settings. Equipping the flexible access platforms with interchangeable and compatible energy devices is essential if it is, bringing prototypes closer to a translatable clinical phase. Ex-vivo and *in-vivo* trials have been used to demonstrate usability and application for a toolbox of flexible energy devices (Table 7.8). Together, these devices now comprise a growing Focused Energy Delivery toolbox for the both the platforms (Figure 7.15). This toolbox accompanies existing endoscopic graspers, electrocautery scissors and biopsy instruments that have all been successfully deployed via the platforms internal channel during the early design phase trials.

Table 7.8; A selection of the flexible targeted energy delivery devices have undergone successful compatibility with the internal channel.

Energy mode	Device	Application
Monopolar electrical current	Endoscopic diathermy	<i>Tissue dissection</i>
Radiofrequency ablation	Habib EndoHBP	<i>Intra-paranchymal targeted ablation e.g. liver metastatic disease</i>
Ionising gas	ERBE Argon Plasma Coagulation (APC) probe	<i>Haemostasis Ablation of superficial lesions e.g. endometriosis, angiodysplasia</i>
Water-Jet	ERBE Hybrid Waterjet Knife	<i>Tissue dissection e.g. neurovascular bundle preserving dissection in prostatectomy</i>

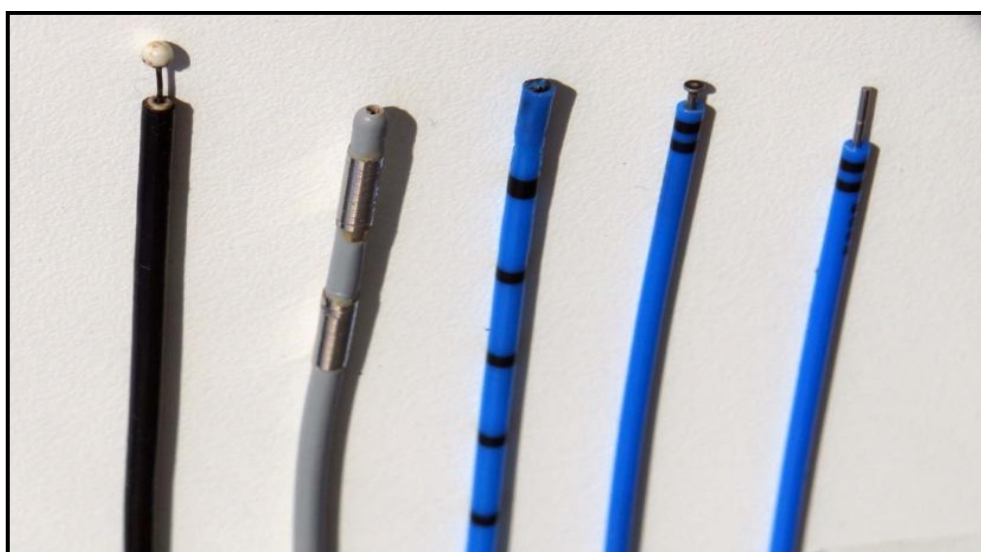


Figure 7.15; Distal ends of several toolbox targeted energy delivery devices are pictured above. These devices are (left-to-right) the Insulated-Tip (IT) diathermy knife (Olympus, UK), Habib EndoHBP radiofrequency (RF) ablation catheter (Habib, UK), argon plasma coagulation (APC) probe (ERBE,Germany) and both the T-type and I-type HybridKnife probes for water-jet assisted dissection (ERBE,Germany).

The potential for the use of many of these flexible endoscopic instruments have never been trialled outside the confines of the endoluminal environment. This includes the flexible ERBE argon plasma coagulation (APC) probe, which clinically is currently used within the investigative flexible endoscopy field for control of areas of bleeding within the colon particularly haemorrhagic proctitis or small bleeding angiomias. Within this setting it has had only limited use due to excessive excessive release of Argon gas produced during activation which can, in the pressure unmonitored bowel, potentially be a cause of perforation. However, its use within the broader surgical environment is novel with no clinical applications defined. Within this setting the problem of excess gas release is not of concern since in all circumstances of minimally invasive surgery, the pressure is continuously monitored and adjusted with some degree of automaticity, so reducing any associated pressure related risk.

The APC within the surgical setting was explored but more specifically for the ablation of superficial lesions or bleeding points on a liver surface (*Figure 7.16*). In addition to haemostasis, the APC probe may be deployed using the flexible platform for superficial ablation.

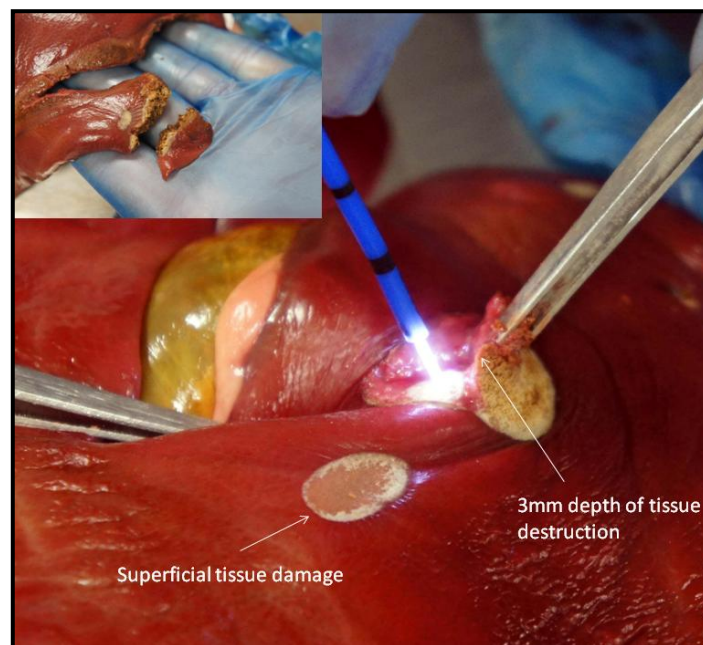


Figure 7.16; An ex-vivo liver cautery using the APC probe. The image highlights the ablative potential of the device together with the depth of tissue penetration on the liver. Inset shows its potential to undertake a liver resection.

Radiofrequency ablation, provided through a fine 3mm catheter has also been explored previously in laparoscopy, as well as percutaneously for the transhepatic destruction of liver metastasis with some success.

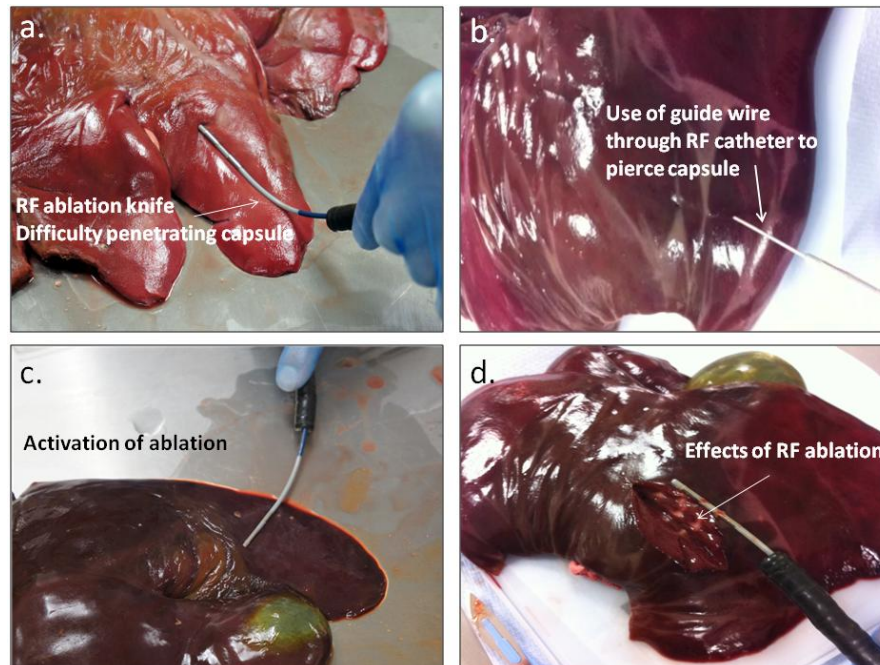


Figure 7.17 Ex-vivo Radio Frequency (RF) ablation of the liver. The problem of the flexibility of the catheter and the flexible endoscope as a delivery device is noted. The use of a guidewire to penetrate the liver capsule was essential.

The waterjet knife is another device which has clinically been trialled in the context of both liver diseases as a means to undertake liver resections within the open and laparoscopic setting, as well as within laparoscopic colorectal surgery, to dissect the hypogastric and sacral plexuses off the sacral promontory during an anterior resection.

Deployment of the HybridKnife via the flexible platform has demonstrated usability for non-anatomical wedge resection of the liver and gallbladder bed dissection for NOTES cholecystectomy. This has been repeated ex-vivo, with further roles explored for use in partial nephrectomy. With adjustable pressure settings, the water-jet knife can be calibrated to preserve nerves and blood vessels while dissecting surrounding soft tissue.

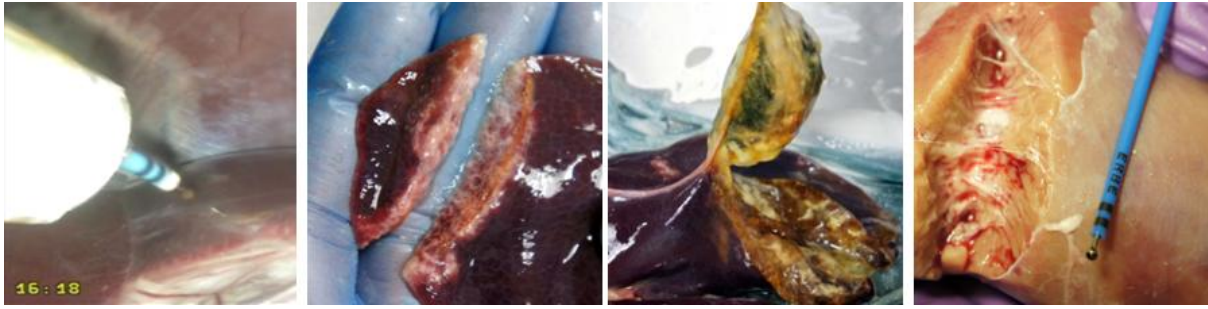


Figure 7.18 *In-vivo* and *ex-vivo* trials using hybrid-knife water-jet assisted dissection.

7.4.2.4. Tissue dissection and resection

Although some of the instruments trialled with the device could be loosely attributed to being capable of tissue dissection, such as the waterjet knife (ERBE Medical, Tübingen, Germany) or the flexible endoscopic scissors, the capabilities of which are inherently related to the ability of the tool rather than the design and engineering of the robot. Relevant tissue dissection and resection would require the formal retraction of the tissues to demonstrate the tissue planes adequately before dissecting. It implies a more precise tissue division. The design of the flexible access surgical platform up until this point has been a single channelled flexible device and although effective for some minor clinical applications relating to predominantly to focused energy delivery, its ability to undertake full surgical procedures independently is questionable even with the capabilities of some of the additional flexible instruments trialled. The platform would need to be designed to effectively impart enough force upon the tissue bed to enable dissection from a second and essentially a triangulating device, as indicated in the previous chapter.

Ex-vivo trials were undertaken to elicit whether the current configuration of the latest bimanual platform design (Chapter 6) was capable of undertaking precise dissection tasks. These tasks require effective translation between each of the arms as well as enough cross-over to enable tension to be maintained on the tissue bed whilst cutting. A simulated rig was erected using latex as the tissue material due to the restriction regarding the force capabilities of the current design. A pre-defined line was drawn on the latex to indicate the required path of dissection. With manual linear translation the bimanual platform successfully and repeatedly performed dissection along the pre-defined path (*Figure 7.19*).

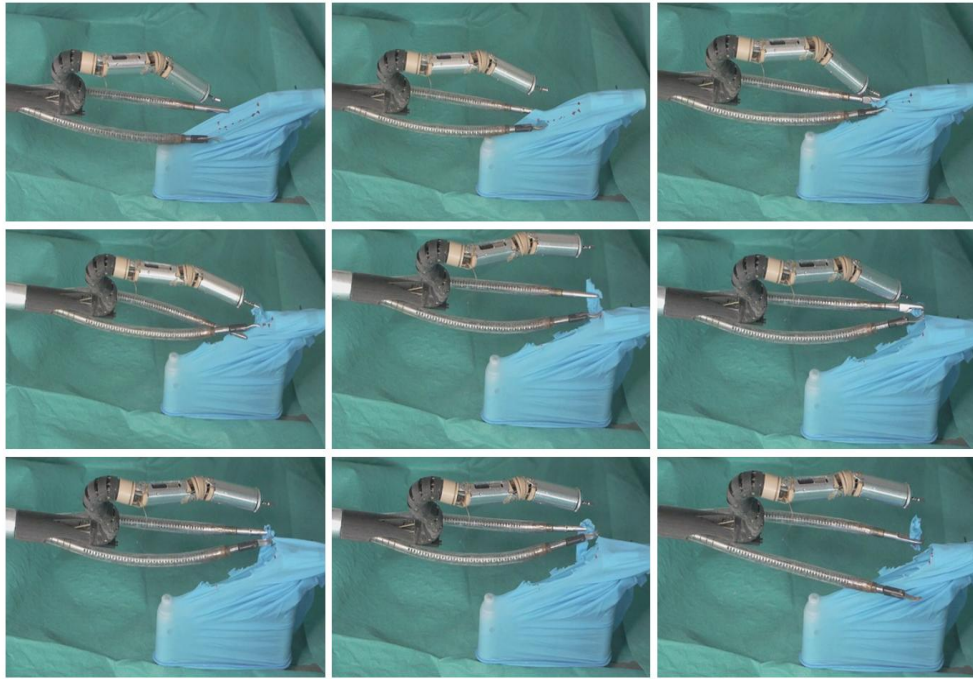


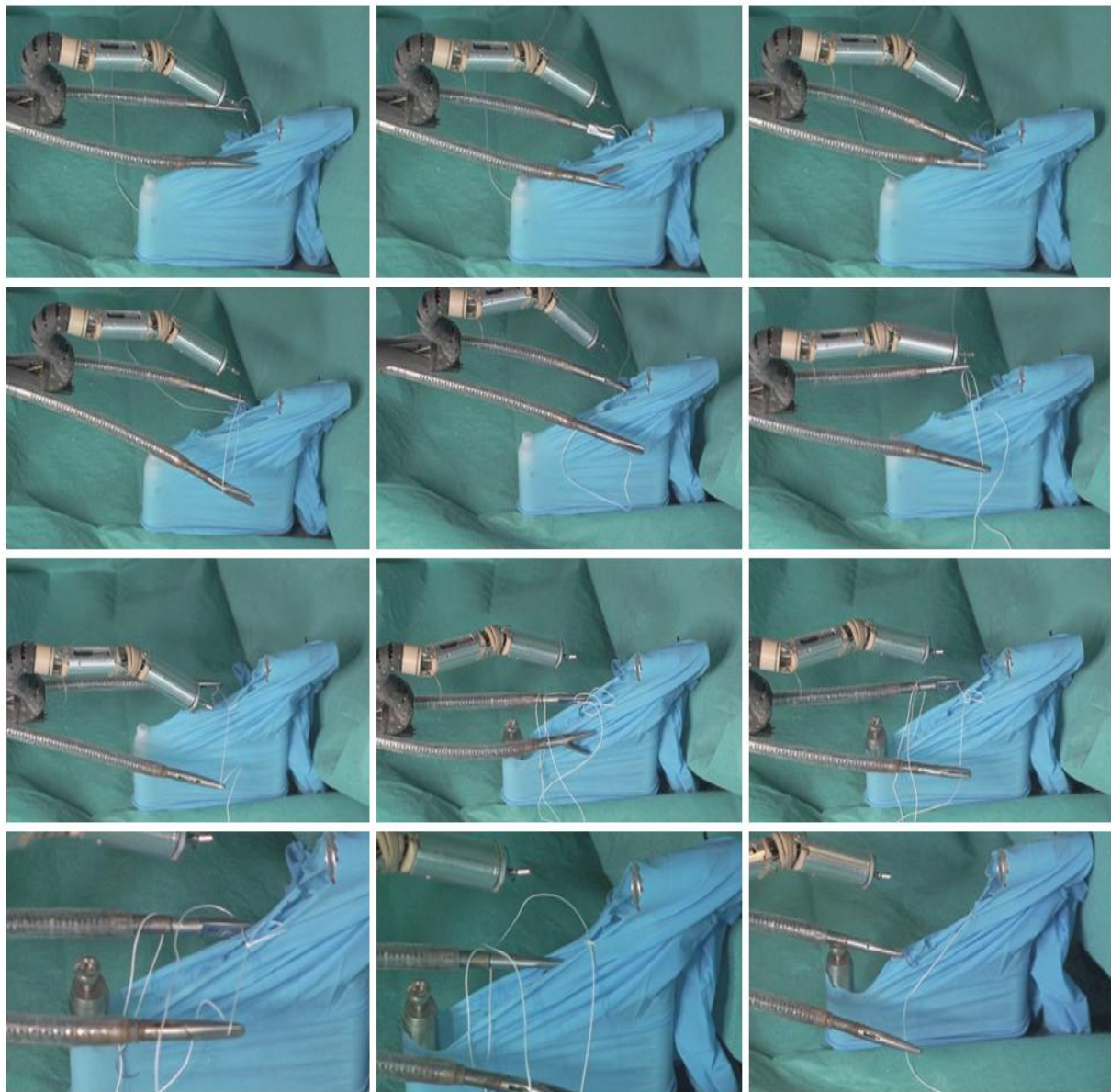
Figure 7.19; Image sequence demonstrating the capabilities of the bimanual instrument platform to undertake precise dissection. The dissection line is marked prior to resection so accuracy can be demonstrated. Note in image left-middle the instrument through the internal channel is assisting.

The potential of the device to expand the range of clinical applications for the robot has been greatly extended with the introduction of the bimanual instruments, with its ability to dissect and manipulate tissue significantly enhanced over the purely flexible design. Challenges in terms of the ability of the instruments to meet the force and to some extent the workspace requirements of surgical application are evident, however, the basic principles of dissection are demonstrated in this early prototype phase and with the elements of force and workspace refined, the ability to meet the more complex surgical procedures is achievable.

7.4.2.5. Reconstruction

Reconstruction of the tissue after dissection is complex and without any currently available flexible instrument available to ensure secure closure or approximation of any defect, the problem will require the use of the bimanual instrument.

Reconstruction in the existing format is a complex manoeuvre which requires triangulating instruments which have effective dexterity and bilateral tool tip overlap to enable needles to



**Figure 7.20; Image sequence of the bimanual instrument undertaking a suturing and knot tie task on a stretched latex glove. (Sequence runs left to right, top to bottom).
 Top row; Needle passed across the two leafs of the latex bridging the gap, Second row; first throw is undertaken, Third row, first throw secured and second throw made, Fourth row; double throw knot is secured.**

be passed from one instrument to the other. Initial trials explored the general requirements for an effective bimanual device to manipulate and transfer tissue between instruments. Accurate tool tip control, independent tool tip linear translation and independent tool tip rotation were early requirements for the design essential to meet the basic need of a collaborative instrumental design (*Figure 7.20*).

7.4.2.6. *Summary of the clinical design validation*

These trials have highlighted the potential of each device as effective clinical platforms. Both are capable of accessing the peritoneal cavity, undertaking diagnosis and ablating any noted lesions using focused energy devices or integrated instruments within the design. Precision resection is currently limited to the bimanual platform over the flexible design although with some further enhancements to the smoothness of the distal tip motion, greater precision may be imparted on the flexible design than currently exists which could broaden its capabilities within this area. Reconstruction is once again more limited to the bimanual instrument platform. The enhanced dexterity required for extracorporeal suturing is realised through the triangulated integrated design of the instrument arms coupled with both their wide and overlapping workspace volumes. Until tissue fusion capabilities or sub 3.0mm flexible suturing instruments become available the flexible platform is limited within this area, nevertheless, many clinical applications do not require the need for reconstruction and as such the wide range of workspace the flexible design can cover from its single incision access point may hold a significant advantage across a broad range of clinical forums.

7.4.3. Identification of Potential Applications for Future Clinical Translation

Evidently two platforms have been derived from the initial design trials, the flexible endoscopic platform and the bimanual instrument platform, each with their own defined strengths. The lack of instrumentation with the flexible endoscopic platform restricts the broad potential within the current surgical workflow for many current surgical procedures unlike the bimanual instrument which although is more restricted in terms of the flexibility in the site of access, has the potential to be able to perform a more complete and potential more complex procedure. However, the benefits of the flexible device are not so much in what it can achieve as a single entity, although not entirely limited in this capacity but in its ability to adjunct many existing and developing surgical techniques such as mini-laparoscopic or single

incision surgery. The ability to visualise beyond the straight path coupled with the delivery of flexible instruments exposes a unique platform which could be enhanced further by the use of mini-laparoscopic tools to overcome the lack of instrumental triangulation yet maintain cosmetic benefits. In addition this flexibility could also be advantageous as an adjunct to single incision surgery as it enables the surgical field to be viewed from any number of angles with the position of the camera placed out of the operative workspace of the tools, enhancing the capabilities of this technique.

With adjunctive tools such as mini-laparoscopy, the instruments can be placed in such a way as to expose the dissection plane enabling the flexible platform, with its flexible energy delivery tool box, to undertake precision dissection from any access site with a stable platform for instrument delivery. The potential applications for both these platforms when broadly considered are almost limitless (*Table 7.9*).

In general, the focus of all the trials have been based on specific procedures within the three agreed broad surgical specialties; pelvic, trans-abdominal and trans-thoracic, which will provide the basis for the exploration of clinical translatable applications for both the flexible access platform and the bimanual instrumental single incision platforms.

7.4.3.1. Pelvic applications

Within gynaecology three specific procedures have been highlighted as potential clinical targets for both platforms. These are:

1. Single incision / NOTES transvaginal tubal ligation for sterilisation.
2. Diagnosis and targeted ablation of pelvic endometriosis.
3. Ovarian Cystectomy.

All these procedures require confirmation of appropriate access, the ability to diagnose and treat appropriately either with tissue destruction and ablation or in the case of ovarian cystectomy a more precise dissection is required for which the bimanual platform may be more appropriate.

Table 7.9; Table listing the potential clinical applications which may play to the advantage of the flexible platform (Flex) alone (blue), when coupled with an adjunctive technique such as single incision or minilaparoscopic surgery (green) as well as those procedures that could be undertaken by the Bimanual platform in isolation (green and pink).

	Flexible Platform	Flex and Bimanual	Bimanual platform
Intra-abdominal	Peritoneoscopy		
	Adhesionlysis		
Liver	Abscess Drainage	Non-anatomical resection	
	Targeted ablation		
Pancreas	Pancreatic Head biopsy	Pancreatic pseudocyst drainage	
Gallbladder		Cholecystectomy	
Stomach		Gastric banding	
		Fundoplication	
		Sleeve Gastrectomy	
		Highly-selective vagotomy	
Small bowel		Roux-en-Y anastomosis	
		Ventral Hernia repair	
Large bowel		Right hemicolectomy	Colectomy
			Anterior resection
			AP resection
Pelvic	Tubal ligation	Hysterectomy	
	Endometriosis ablation	Salpingo-oophrectomy	
		Myomectomy	
Retroperitoneum			Partial nephrectomy
			Adrenalectomy
			Pyeloplasty
Intra-thoracic		Ablative pleurodesis	
		Thoracic Sympathectomy	
		Ablation of pleural plaques	
		Destruction of apical bullae	

Robotic assisted NOTES and Single Incision tubal ligation.

Tubal ligation, for permanent contraception, is a common surgical procedure worldwide with an estimated 650,000 performed annually in the United States alone (134). It is a preferred choice by many patients instead of other medical options available. Currently undertaken through the laparoscopic approach, the natural orifice transvaginal approach exposes attractive advantages. The lack of an abdominal scar or damage to the umbilicus, as may occur with the conventional laparoscopic approach, may prove for some patients to be the main consideration, particularly if both trans-vaginal and laparoscopic procedures offer similar morbidities. The introduction of a flexible hyper-redundant robotic platform to this approach may overcome some of the endoscopic challenges highlighted from previous NOTES tubal ligation cases (135) and promote the approach, with robotic assistance, as one that is safe, efficient and effective.

Ex-vivo trial tubal ligation

Ex-vivo trials were undertaken using a phantom simulator model (Limbs and Things Ltd Part 60283; Australia). Trials were conducted to explore the potential of the flexible device to articulate repeatedly, to meet the requirements for a human pelvis to reach the fallopian tubes and also to enable instruments to be passed through the central channel during this degree of articulation.

90 attempts to retroflex the articulating platform and strike the anatomical target from a straight alignment of the joints of the V5 flexible prototype was undertaken and successfully undertaken as part of a wider user trial; the results of which are discussed in Chapter 8. For each attempt the articulation was successfully performed and a flexible biopsy grasping instrument was passed down through the central channel to meet the target.

In-vivo trial tubal ligation

Under United Kingdom approved Home Office License (Appendix 1; number 80/2297) a 75kg female pig was used for the purposes of the trial. Due to differences in the pelvic and more specifically the uterine anatomy between the pig and the human, the uterine horns were used to represent the target fallopian tubes. The fallopian tubes in the pig model are shorter than those of the adult human and therefore do not adequately reflect the suitability of the

proposed clinical operation nor adequately demonstrate the capabilities of the robot. Prior to the procedure urinary catheterisation was undertaken and the bladder deflated.

Under direct vision a 10mm transumbilical port was inserted and pneumoperitoneum was established to maintain a pressure of between 12mmHg and 14mmHg. The transvaginal incision was subsequently made in the posterior fornix and a 15mm bariatric port (Applied Medical, CA. US) which had been customised in-house to a length of 400mm (in order to overcome the lengthy porcine pelvic anatomy) was inserted through the colpotomy and into the peritoneal cavity. The placement of the port was confirmed by the use of a 10mm laparoscope inserted transabdominally. This additionally enabled external visualisation of the robot to be undertaken during the task for recording purposes.

The uterine horns were exposed using a combination of external uterine manipulation with the animal placed in the Trendelenburg position. Due to the redundancy of the pelvic adnexa particularly the intra-peritoneal urinary bladder, within the pig model, assistance was also obtained from a 5mm laparoscopic grasper inserted through a 5mm trans-abdominal port. No further interventional assistance was obtained from the instrument once the robot was inserted.

The robot was inserted into the port and driven forward, retroflexed and rotated to target the right uterine horn. Once the tissue was visualised, guided by the on-board camera, the instrumental section of the procedure was undertaken. Two endoscopic clips (Boston Scientific, MA. US) were passed separately through the robot whilst in the retroflexed position and activated to lie side by side on the uterine horn. Once security of placement of the clips was confirmed through the elevation of the section using flexible endoscopic graspers, a needle endoscopic diathermy knife was inserted and, using the distal articulating segment of the robot, the uterine horn was divided between the 2 clips (*Figure 7.21*).

Robotic assisted ablation of pelvic endometriosis

To examine, diagnose and treat pelvic endometriosis it is essential to be able to manipulate and remove overlying tissue and bowel from the ovaries and pelvic adnexa prior to targeted

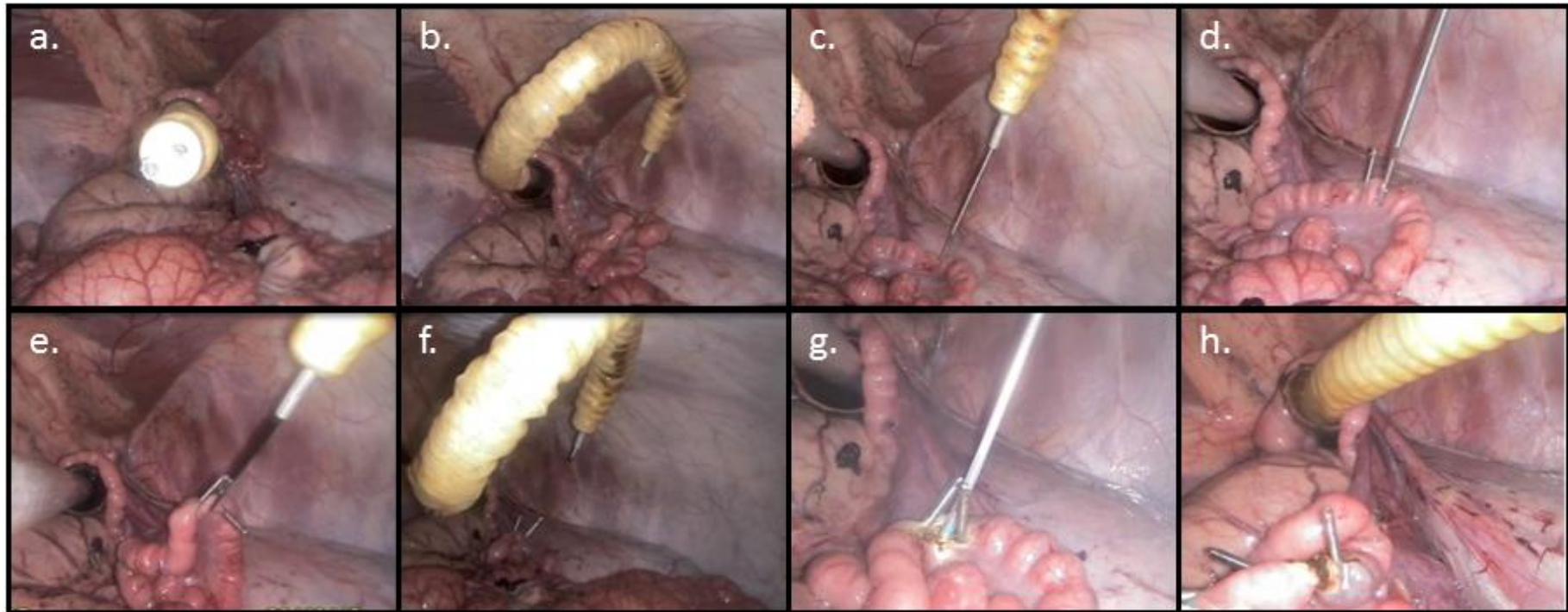


Figure 7.21; The sequence of events during the *in-vivo* trial for simulated tubal sterilization using the V5 prototype. Access via a posterior vaginal incision was undertaken enabling the V5 to be inserted into the pelvis (the extended trocar can be seen in all images) and which ended with the clipping and division of the right uterine horn.

ablation, more so than when considering the tubal ligation. However, placing the patient in the trendelenburg position will help significantly to clear the pelvis and expose the pouch of Douglas, the common site for pelvic endometriosis although deposits anywhere in the pelvis are possible.

The unique design of the bimanual platform is ideally suited for this. The arms are able to manoeuvre the bowel and tissue enough to visualise the deposits and using one of the focused energy delivery instrument passed through the central channel in the articulated head, ablate them. Focused laboratory trials were conducted using the simulated model to explore this potential. In addition, the use of the Argon plasma coagulation device was trialled with the flexible platform *in-vivo* to assess its capability to selectively target and ablate suspicious deposits.

Ex-vivo endometrial ablation

This trial was undertaken to assess and demonstrate the capabilities of the bimanual instrument to manipulate tissue overlying the ovaries on a simulated human pelvic mode. The model incorporated simulated endometrial deposits on the ovaries which were draped with a thin simulated peritoneal lining. The trial was used to assess whether the bimanual platform was able to lift and draw the lining away the ovaries to expose the endometrial deposits and ablate using a targeted instrument passed through the central channel (*Figure 7.22*).

Although the trial demonstrates the ability of the bimanual instrument to pass the tissue between arms as a means of drawing the tissue away, the true measure is the wide workspace that each instrument arm is able to cover and the overlap between each, which enables this application to be successful. The ability to pass tissue from one arm to the other with the recipient arm able to grip beyond the presenting arm so that the tissue can be drawn away from the target point is essential for this element of the application. The further benefit is once both arms are to one side of the central point gripping the tissue the articulating head is free to target each spot.

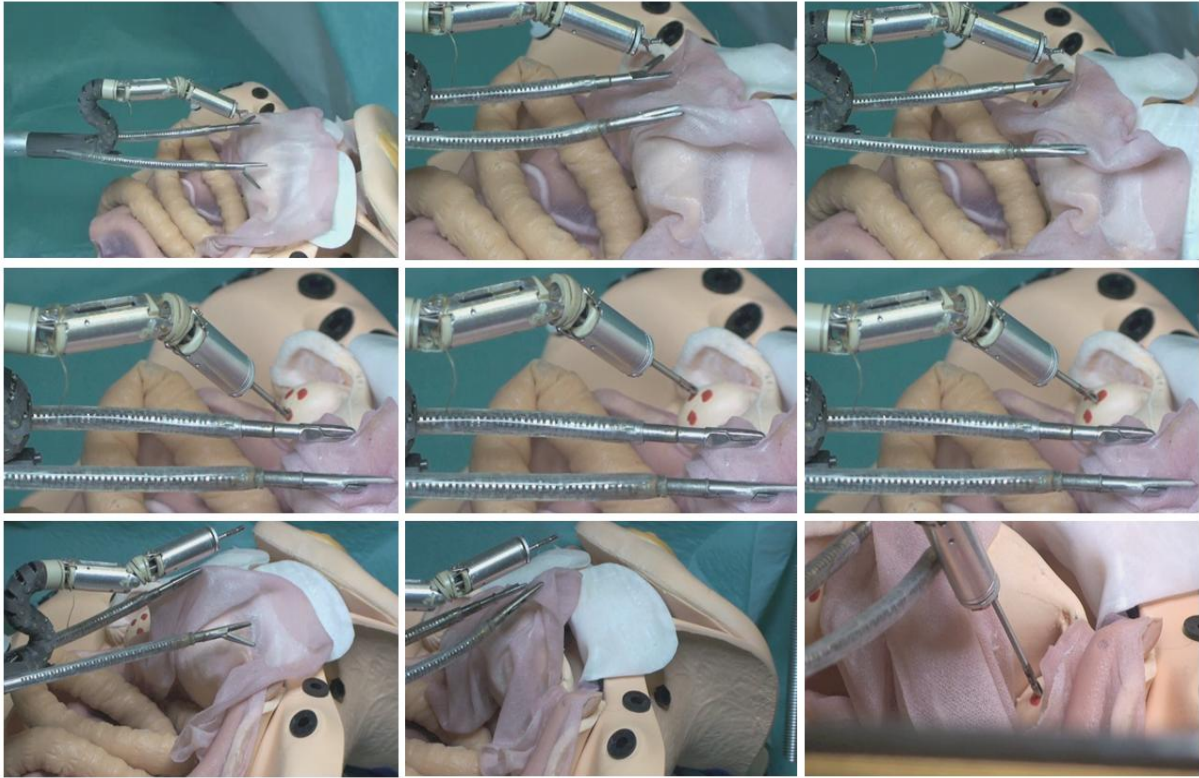


Figure 7.22; Image sequence of targeted endometrial ablation using bimanual instrument. The sequence (top left to bottom right) highlights the ability of the arms to manipulate tissue out of the proposed operative field enabling targeted ablation to take place using an instrument passed through the head. (Red spots on the Ovaries indicate endometriotic lesions)

In-vivo targeted endometrial ablation using flexible platform.

The demonstration of targeted ablation within the *in-vivo* environment was through the use of the flexible platform. The trial aimed to demonstrate the capabilities of the flexible platform to access common areas of endometrial deposits, peritoneal wall, floor and small bowel, targeting potential endometriosis lesions accurately with one of the flexible energy instruments passed through the internal channel.

For the purposes of the trial the Argon plasma coagulation (APC) instrument was used to ablate the targets once the flexible robot had identified the lesions. The trial demonstrated successful targeting of lesions using the flexible platform with the identified lesions successfully ablated using the APC. The most significant benefit was the wide area of articulation capable of being achieved by the flexible platform from the single incision point for the purposes of targeted ablation. The smooth control at the tip of the robot enabled precision targeting to be achieved (*Figure 7.23*)

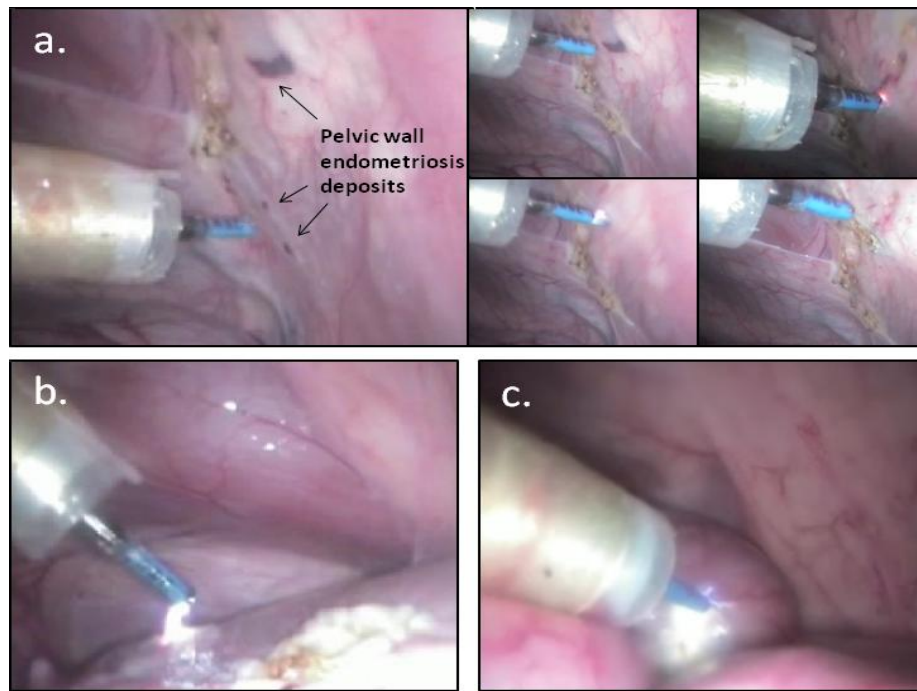


Figure 7.23; In-vivo target endometriosis ablation. The images demonstrate the use of the APC instrument and the precise control of the flexible platform to ablate the pelvic wall lesions (a) and from the same access site the ability to ablate targets on the floor of the pelvis (b) and the small bowel (c).

For the male patient, the clinical application which may be the most disruptive to current clinical practice is the prostatectomy. This procedure is the main marketing application of current robotic-assisted operating platforms. The precise dissection of the neurovascular bundles from the gland is promoted as enhancing surgical outcomes after the robotic-assisted prostatectomy. However, the ability of the current designs to undertake this procedure is limited by the lack of a suitable animal model or even the accessibility to an appropriate ex-vivo animal tissue model. Nevertheless, the design of the bimanual instrument exposes the greatest potential in being able to undertake this clinically as an on-demand device. Although much of the operation, particularly the placement of the posterior vesico-urethral stitch is still not possible with the current instrument tip design, the impact of a device capable of undertaking neurovascular bundle dissection will still be very disruptive to the current market.

7.4.3.2. Trans-abdominal applications.

One of the most accessible clinical targets for both flexible platforms is within the abdomen. The liver exposes the most significant potential clinical focus with the exploration of targeted ablation of metastatic disease using the Radiofrequency probe (RF). However, a significant proportion of this clinical field is undertaken by the interventional radiologists with image

guided probes inserted percutaneously. Nevertheless, there are areas, particularly the caudate lobe - segment I due to its posterior location as well as Segment VII of the liver which due to the costophrenic recess of the right lung prevents percutaneous access. As such an angulated path over the liver to access this segment using the flexible access platform could be performed under direct vision. For the caudate lobe both platforms may be able to pass beneath the liver and elevate it to expose it enough to deliver the RF probe. This may be possible with the addition of future software adjuncts such as augmented reality (136), which under pre-operative image guidance may better guide the RF probe to pin-point accuracy (Figure 7.24).

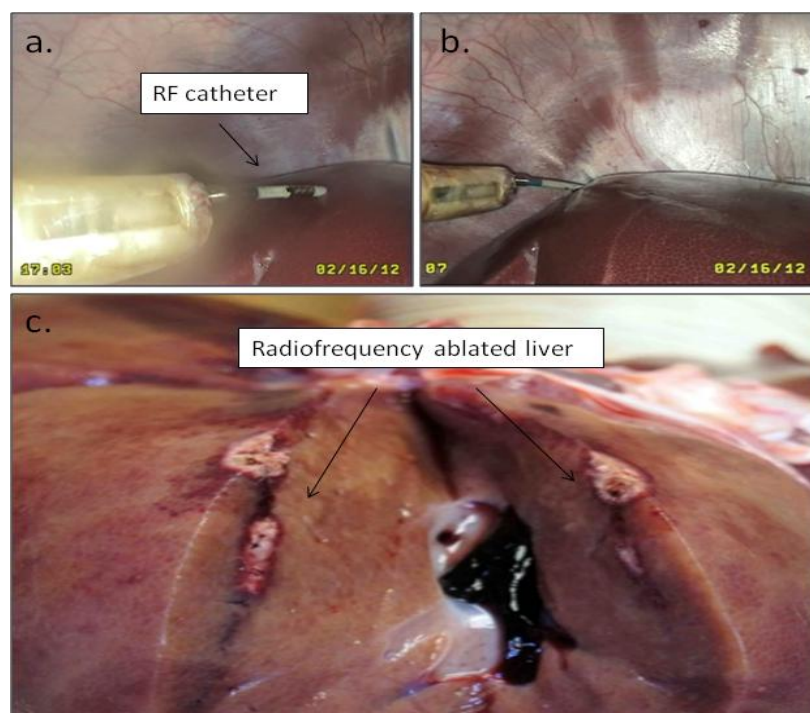


Figure 7.24; Validation of the flexible robotic platform *in-vivo* accessing the diaphragmatic region of the liver and inserting the RF probe. The outcomes at post-mortem of the effects of the RF probe activation.

The transabdominal approach may also expose a number of clinical exemplars which are difficult to explore using the porcine model. These include the Nissens Fundoplication for flexible access to demonstrate the left and right crus and create the window behind the oesophagus under direct vision. This is challenging in the animal model due to the large liver and spleen which tend to overlie this particular area and also restricts potential applications within the same area for the flexible design such as the highly selective vagotomy for significant dyspepsia.

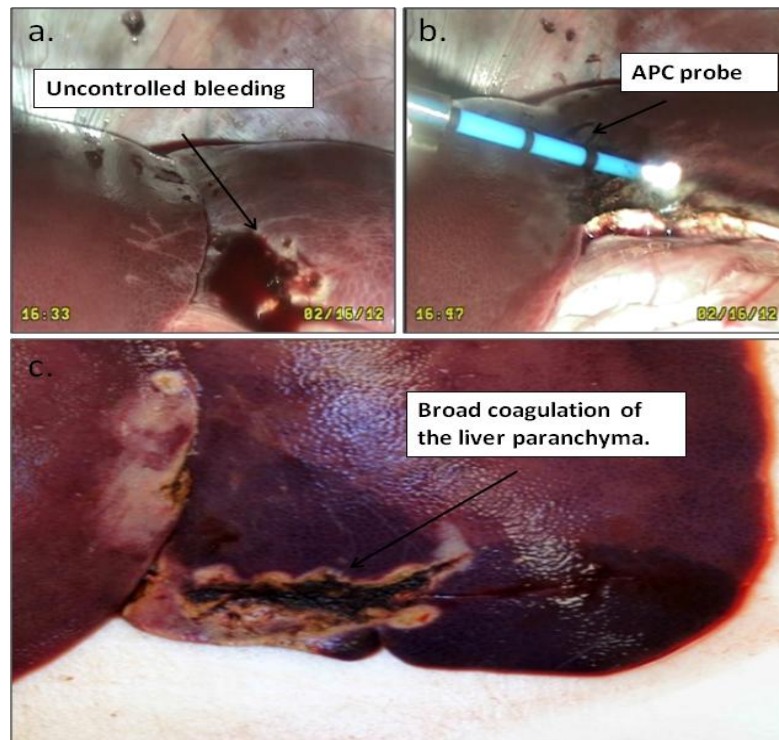


Figure 7.25; The APC utilized successfully for control of bleeding from the liver bed during an *in-vivo* trial.

The liver is a highly vascular organ prone to bleeding intra-operatively. To trial the effects of the APC probe for haemostasis injury to the liver bed was created. After application of the APC highly effective haemostasis was observed, with the precision and stability of the flexible platform aiding accurate delivery of targeted energy, avoiding iatrogenic damage to surrounding tissue (*Figure 7.25*). Due to the no-touching application of the APC probe to the tissue bed, minimal eschar was removed during haemostasis which often occurs when using standard electrocautery probes causing re-bleeding. The outcome was the confirmation of highly effective instrument for haemostasis.

7.4.3.3. *Trans-thoracic applications.*

Access to the thoracic cavity within the pig model has always proved challenging due to the narrow rib spacing (*Figure 7.26*) or the terminal event inevitably caused through accessing sub-diaphragmatically. Although, both of these access routes are theoretically possible given the dimensions of the robot no trial has been undertaken formally to confirm it.

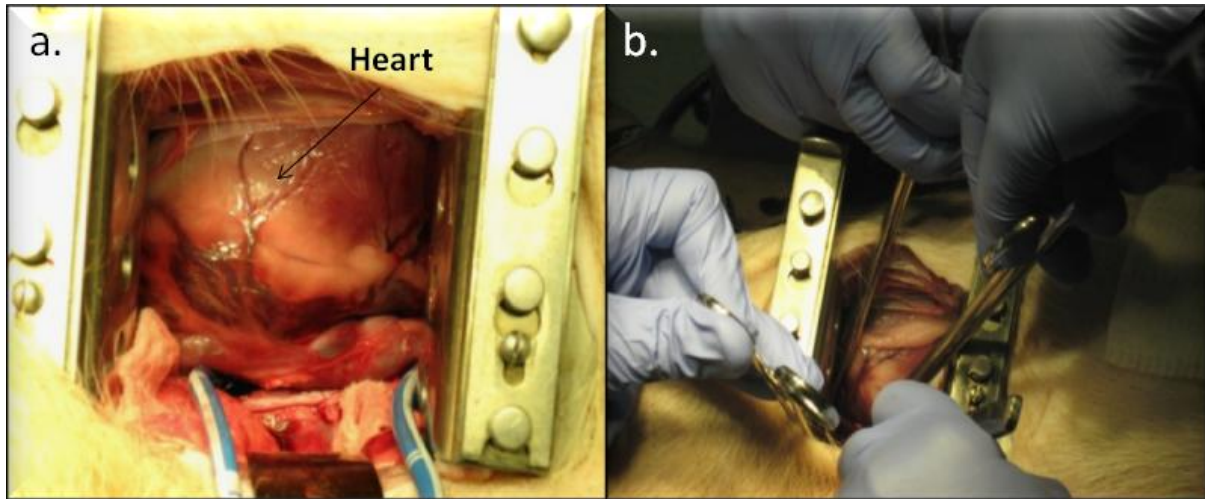


Figure 7.26; Image highlighting the minimal workspace within the pig thorax making access very challenging.

However, once access is confirmed it is likely that the challenges faced within the abdominal cavity relating to the loss of pneumoperitoneum would not be met in the thoracic cavity due to the rigidity of the thoracic cage so the prediction of getting it right in the abdomen first should prove accurate for advancing cardiac applications.

Once intra-thoracic, the procedure of dissecting and ligating the Internal Thoracic artery and exploring pulmonary intervention will follow the same surgical steps as laid out above for the gynaecological and gastrointestinal procedures. A firm focus on adequate dissection and reconstruction within the required workspace will be keys to successfully completing this procedural task.

To confirm access, a major hurdle in the expansion of the cardiac route, the decision to target the human cadaver as the most appropriate model for future trials would be the most sensible.

One potential application within the cardiothoracic remit is epicardial ablation for atrial fibrillation. A technique termed the maze procedure. This requires full thickness ablation of the muscle tissue to prevent aberrant electrical activities from re-circulating causing abnormal re-activation and the symptoms of palpitations and even the risk of strokes. This procedure is undertaken predominantly using a microwave catheter passed behind the heart circumventing the pulmonary veins although some epicardial ablation will be required to complete the maze. For this application it would be necessary for the platform to be capable of path following on a beating heart both visually and instrumentally.

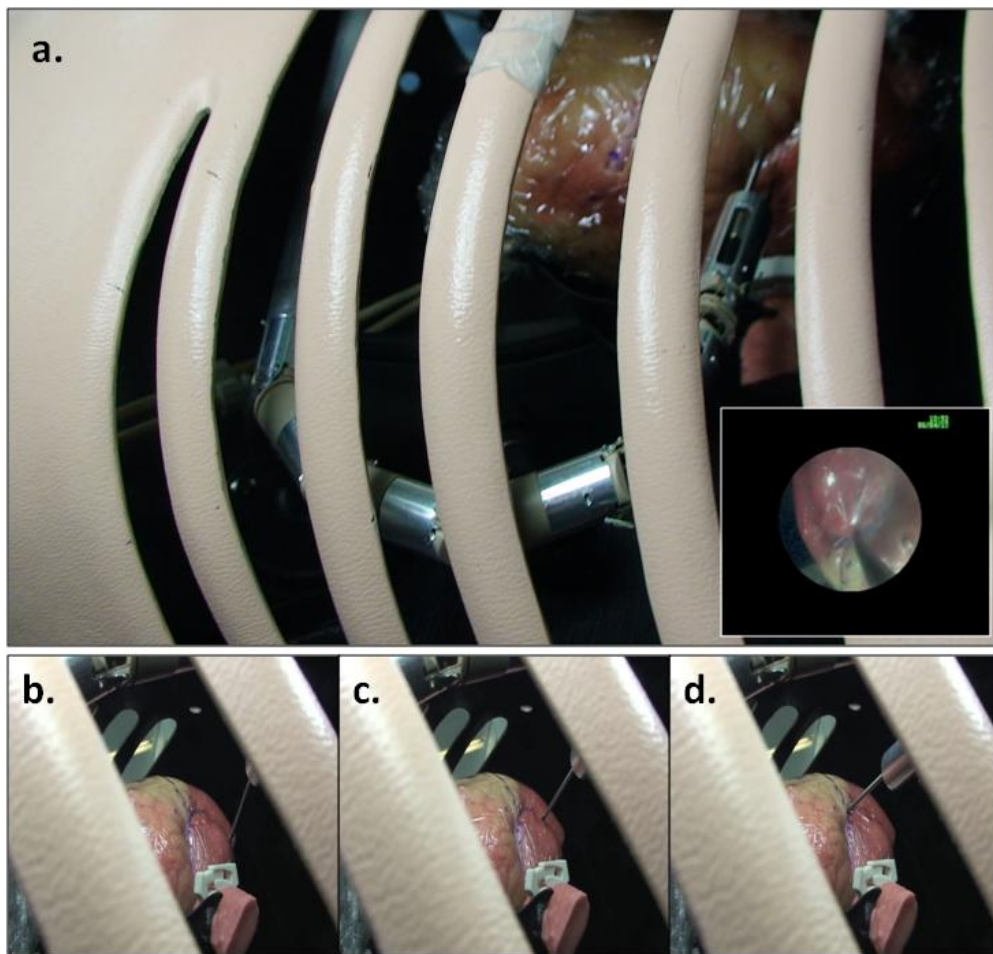


Figure 7.27; Images highlighting the precision motion of the flexible robot for epicardial ablation path (a) following with a sequence of *ex-vivo* path following trial (b, c and d). (Inset: view from on-board camera).

An *ex-vivo* trial was undertaken using a beating heart simulator within a simulated thoracic cage (*Figure 7.27*). The aim of the trial was to evaluate whether the precision at the tip of the flexible platform could enable an instrument to track a path on a beating heart. The smooth motion of the tip enabled the path to be successfully tracked. Further software adjuncts to the device to enable a more effective path following within the beating heart environment will enable greater precision and accuracy; these include the dynamic active constraints model (Ka-Wai et al) (126, 137).

7.5. Conclusion

These results demonstrate that even at this early prototype stage both platforms have clinical potential within the setting of minimally invasive surgery. The flexible platform has the capability to navigate to all areas within the abdominal cavity and be effective within the anatomical constraints of a human being. The device in its current form is already demonstrating usability and reliability in terms of control which will only improve further as joint position sensing and more unified control algorithms are integrated into the design.

Each platform has been trialled within the *in-vivo* model and demonstrates security of access and diagnostic capabilities. Each can repeatedly be used to access the peritoneal cavity from either a transvaginal or percutaneous incision reliably. Although the bimanual platform has limitations in terms of the flexibility of access sites when compared to the flexible design, the integration of the single user-controlled instrumentation defining a fully solo-operated single incision platform is unique and worthy of further development. The effect of which will ultimately lead to a robotic-assisted surgical operating platform which has a small operating theatre footprint capable of promoting on-demand image-guided precision surgery.

The focused development of an interventional articulated robotic platform has enabled a clinically relevant device to be developed. The feasibility of the flexible platform as a potential future robotic-assisted flexible endoscopic device through which diagnostic and interventional procedures can be carried out through a natural orifice or percutaneous approach safely and effectively has been confirmed. A clear surgical workflow has been defined to target the pelvic adnexa safely and effectively using the device. Further *in-vivo* studies, including pre-clinical survival studies will be required to refine and strengthen the design before formal clinical trials are undertaken with this model.

The bimanual instrument exposes a unique surgical platform. Its capability in terms of operative complexity far outweighs that of the flexible platform however, it remains in an early prototypal stage. Although, the workspace and dexterity achieved by the current design is close to that which is required for formal clinical application, it still falls short particularly in terms of force application by the instrument arms. This is profoundly restrictive in defining future clinical applications within the *in-vivo* setting however the device has demonstrated its capability to undertake collaborative tissue manipulation for precision dissection and reconstruction within the *in-vitro* environment. Greater refinement to the design of this platform is required before formal clinical translation can be considered. This includes, in

addition, an increase in the degrees of translation required at the instrument tips to meet the clinical workspace requirements both across the linear and vertical planes.

Each of the flexible access prototypes have been successfully trialled to determine their clinical potential and have been successfully tested across a range of potential focal clinical applications. Limitations common to each prototype design still exist; the camera and visualisation in particular coupled with some further considerations relating to spatial awareness and the need for an additional camera to widen the field of view particularly with the flexible design. Other elements such as the method and approach to sterilisation or disposability need also to be considered in-conjunction with the most appropriate material to be used for the sheath.

The design of an articulated robotic platform for diagnostic and therapeutic intervention even at the simplest level as defined by the flexible articulated platform, overcomes many of the challenges facing the conventional endoscope used to undertake single incision flexible access surgery. The simplicity in using the robot over the endoscope will undoubtedly promote wider dissemination of this technique and encourage more clinicians to explore the potential applications of the flexible access technique. The golden ticket will however come to fruition when the two designs are successfully amalgamated into a single entity promoting all the benefits of the flexible shaft for full flexible navigation to enable access to be achieved distant to the operative target and once at the site expand into the bimanual instrument capable of the performance required for enhanced complex surgery.

Chapter 8

Discussion and future work

This thesis defines and highlights the clinical relevance of flexible access surgery. The ergonomic considerations of the flexible endoscope as a surgical platform is explored with the shortfalls of its use highlighted through pre-clinical and clinical trials. The quantification of force as a requirement to be met before effective instrumentation can be developed is highlighted and explored, with a force map of the peritoneal cavity of the porcine model defined as an example of the ranges required. Methods to minimise these forces is discussed but the relevance of a more effective flexible access surgical platform is overwhelmingly evident if flexible access surgery is to be an acceptable clinical procedure. The inceptions of two novel flexible access platforms are presented in this thesis. Their design, shaped by the numerous clinical trials exposing the prototypes to the pressures and rigours of *in-vivo* use, is presented together with the theoretical validation of the platforms toward formal clinical translation.

Technological innovation is continuously reshaping the current practice of surgery through minimising the resulting physical and psychological impact on the patient. Thus far, laparoscopic surgery has been the fore-runner to the minimally invasive surgical revolution with the momentum maintained with the clinical introduction of the Single Incision Laparoscopic Surgery (SILS) technique and even more recently the introduction of the flexible endoscope as a surgical platform. Surgery using the flexible endoscope exposes a completely new avenue for surgical exploration. The flexibility of the instrument enables it to access any operative target through any incision; whether transcutaneously (138) or through the natural orifice approach (98). This in turn promotes greater choice to the patient as to the position of their scar; promoting a level of patient empowerment never previously seen in surgery. However, with current endoscopic equipment this new potential surgical freedom is being asphyxiated.

Limited by the size and position of the incision, surgery can only advance so far without the ergonomic challenges of instrument control and tissue manipulation impeding on the uptake and wider dissemination of the surgical technique in question; irrespective of the benefits to

the patient. Although training can overcome many of the ergonomic issues, the learning curve can be significantly protracted and will impede the introduction of any new technology. This was evident with the laparoscopic era which took nearly 20 years from inception to be considered acceptable. When the ergonomic challenges relevant to laparoscopy are compared to those related to the use of the flexible endoscope as a surgical platform, the ergonomic impediments associated with laparoscopy seem only minor.

The use of the flexible endoscope within surgery was first defined within the remit of Natural Orifice Transluminal Endoscopic Surgery. In its current form NOTES continues to be unable to present a clinically viable alternative to the laparoscopic approach which predominantly relates to the ergonomics of the flexible endoscope and instrumental control above all else. However, within the current clinical setting it does promote itself as a very promising adjunct; in the form of the hybrid NOTES-laparoscopic procedure (111). This approach has enabled the benefits of the flexible access technique to be examined without compromising on patient safety. Evidence from these trials has suggested modest improvements in terms of pain, and a reduction in the physiological impact from using the NOTES approach over the conventional (139). However, despite some feasibility studies undertaken internationally (140-142) suggesting that the pure NOTES approach will be a viable technique in the future it is unlikely, if true, that it will be in its current format. One element which despite the platform redesign which will block NOTES from wide clinical dissemination, is the required breach in the viscera within a natural orifice to access the relevant body cavity and the safety of closure. This will undoubtedly be overcome in time and with new designs of insertion techniques, instruments and operative platforms the current status of NOTES should not preclude the exploration of the flexible endoscopic technique from alternative sites such as the variety of transcutaneous approaches discussed in this thesis. The flexible access surgical approach embodies all the benefits that a flexible platform could bring to the surgical armamentarium. The ability to access target operative sites from distant incisions whether this is within a natural orifice or not. A concept which from simple population surveys appeared to be considered as acceptable. This thesis explored the challenges associated with flexible access surgery and probed into new platform designs which have the potential to meet the requirements essential to translate the concept into a safe and viable clinical reality.

The most significant problem relating to the technique is paradoxically, given the essential element to the flexible access technique, is the flexibility of the platform. The challenge

related to navigating an instrument which is only partially controllable at the tip within an unconstrained anatomical environment is evident and quantifiable through the work undertaken in Chapter 3. This chapter defined the challenge by demonstrating that a significant level of endoscopic experience is required to be obtained before the clinician can safely undertake even a straightforward navigational task; a level which would may not be acceptable for many surgeons should they wish to introduce the flexible access approach into their practice. This work also described the design and engineering of a novel flexible access simulator within which a unique method of quantifying endoscopic performance through mapping the motion of the user's wrist was developed. Chapter 4 explored the potential of the flexible access technique with clinical examples. It describes novel surgical applications within the human cadaver, animal and clinical human models which exposed the flexible access technique as a viable alternative to many common procedures undertaken using the open or laparoscopic technique. The description of using the subcutaneous planes to enable target operative sites, accessed from a distant incision point using a flexible endoscope has not previously been described and exposes a new avenue for technical surgical exploration. However, through the undertaking of these trials, a number of other significant challenges were highlighted which predominantly, and perhaps not unexpectedly, centred on the shortfalls of the flexible endoscope as a surgical platform and included in particular the lack of controlled instrumental delivery to the tissue. This device was developed in the 1960's for endoluminal investigation and has changed little in its design since that time. The core of the problem relating to instrumentation is due to three specific areas; the lack of a stable platform from which to undertake intervention and as a result provide the degree of force required to be delivered to the tissue bed essential for dissection or intervention. The final area is the lack of instrumental triangulation which although is an important area to address the essential requirement to instrumental triangulation is once again centred on the delivery of the appropriate force to the tissues to enable formal dissection and the triangulation aids in the performance once this has been met. Evidently from these trials, an alternative platform needed to become the main focus if flexible access surgery was to become reality.

The forces that would be required within the abdomen and methods to minimise force application was explored in Chapter 5. Formal and repeatable evaluations of the force requirements were undertaken within the in-vivo model as a means to quantify and reference the level of force requirements that the engineers would need to meet for the purposes of designing and constructing a flexible access platform. Force evaluation was undertaken using

a modified laparoscopic instrument adapted in-house with strain gauges, calibrated with weights to measure force through bend. This force instrument enabled accurate determination of the forces required to manipulate the various tissues within the abdominal cavity to be documented. It is hoped that this will act as a reference for medical engineers who are embarking on future flexible access robotic designs in the future. The work also explored methods to minimise the instrumental force requirement both through optimising tool tip triangulation as well as how more efficient placement of the instruments on the tissue bed affects the level of force is described. A further outcome to these trials was also noted. The quantification of tool-tissue interaction has not been previously described. As part of the workflow analysis of surgical procedures, the degree of tool tissue interaction was noted to be significantly different between junior trainees and senior experts using the laparoscopic technique. This method of assessing surgical skill within the clinical setting could play an important role for surgical training in the future or indeed in determining when challenging sections of an operation are being experienced by an otherwise competent surgeon; an area worthy of further exploration.

Chapter 6 described the inception, design and engineering of a novel flexible access surgical platform with an aim toward clinical translation. The evolution of the platform design is described based on the clinical challenges and achievements faced with each prototype stage. The final outcome from these trials was the development of two novel flexible access surgical platforms each promoting individual strengths. The flexible articulating platform is capable of full retroflexion within the abdominal cavity enabling pelvic intervention to be undertaken through a transvaginal access route and the bimanual instrument which in essence has the capabilities of being a robotic single-incision surgical operating system although lacks the hyper-redundancy affiliated to the flexible platform. The performance evaluation of both platforms is explored in Chapter 7 with the potential clinical applications for the individual designs discussed. It is evident that both designs hold significant promise yet the bimanual platform still needs some further engineering enhancements particularly in the area of force implementation through the instrument arms, although in reality both need to consider some of the more translational clinical requirements essential if either device is to be marketed. In particular the methods and effectiveness of sterilisation which includes determining the most appropriate material for the over-sheath, a problem not yet fully addressed.

It would be naive to believe that at present, the device currently trialled will realistically be able to complete a full clinical procedure to the levels defined by the royal colleges let alone exceed them, to provide a product with a clinical and therefore a market potential beyond that of its competitors. More realistically the need to define a clinical procedure and goal direct the platform for that specific unmet clinical need through a second round of engineering design and refinement, would be more reasonable to consider and ultimately more effective long term, although this attracts significant cost and significant time investment.

However, when considering time in terms of robotic design and translation for the healthcare industry the only comparison which is available, the daVinci™ should be considered. The original concept for the daVinci™ operating platform was born out of Stamford University in the early 1980's. It was nearly 15 years before full clinical translation. Despite having to meet the initial challenges of being the first general surgical robot to translate to clinical practice, it still serves as a benchmark for the time frame future robotic design for the healthcare industry should expect. The platform presented here is work born out over a four year period and represents only the initial concept prototypes. Future designs will become more sophisticated and clinically goal directed. There is no doubt that there is a niche in the clinical market place for such a product but maintaining motivation for this design, particularly at this early stage, and therefore maintaining funding will be the challenge.

The options to consider would be to consolidate the existing design and release it as a market ready Version 1 flexible therapeutic laparoscopic adjunctive tool for pelvic applications with incremental improvements as the design improves. The aim of which will move to support further development and potential future investment with a product that would be already sited within the operating theatre, to create a more clinically specific design that is more financially marketable in the long term. This option will promote the device but carries great risk as it could on the contrary cause derogation of the brand if unsuccessful and disparege further development altogether. The other drawback to this option is that the cost associated with marketing may be too high to consider at such an initial step.

The alternative may be to seek a different avenue for the device. The design of the joint is unique but the implications for their use in healthcare in terms of the engineering requirements are limited by the size of the device and the torque derived from the internalised motors. Other challenges such as sterilization of the device are also unique to the healthcare

industry and it is the combination of all of these factors which may direct exploration for future funding from alternative fields which do not require such demanding specifications. The aerospace industry and the nuclear power industry have both expressed interest in the use of flexible robotic platform designs. It would not be inconceivable to side step to a larger overall design of the device, provisionally driven by the healthcare industry but which could be demonstrated as effective when scaled up for the purposes defined by these alternative fields. Funding may be found from within these industries to secure the future of the design for flexible access surgery.

As an ongoing project significant refinement coupled with further in-vivo validation of the flexible access platforms with integrated joint position sensing has crystallised the potential roles of the these platforms in the surgical robotics market place. Distinction between the two platforms has become increasingly apparent during validation testing, with the flexible platform revealing itself principally as a sophisticated and intelligent adjunct device for laparo-endoscopic surgery, and the bimanual platform as an integrated and autonomous flexible robotic platform that holds great promise in redefining and advancing single access site intra-cavity surgery. The next step in terms of design needs to be on the integration of sensing. The difference between an enhanced mechatronic platform and a robotic platform is in the automaticity. As a result the need for sensing is essential to enable progression both clinically and from an engineering perspective to move onto the next phase of the project. An external autonomously controlled arm connected to the shaft of both platforms will be essential to enable automated linear translation but will be required to communicate with the articulated segment to enable gross navigation to target operative sites to be undertaken with fine manually controlled tip control integrated for operative targeting. With these elements in place both platforms truly become novel surgical robots.

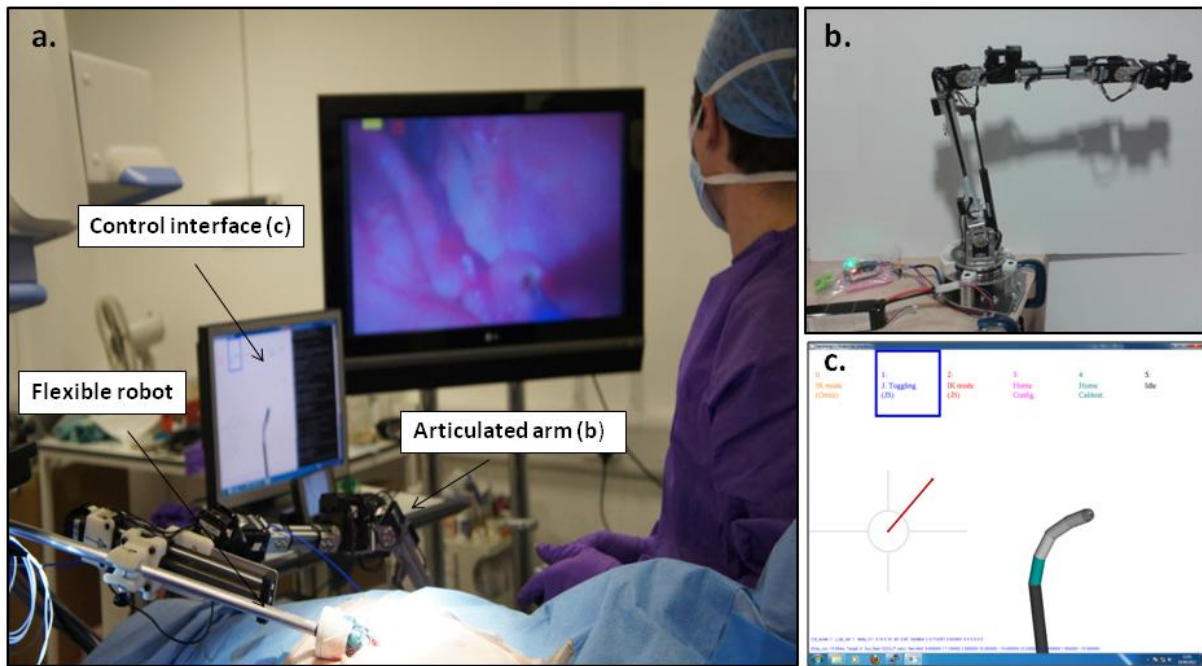


Figure 8.1; Ongoing in-vivo trials with an additional mechatronic external articulated arm (b) coupled with integrated joint position sensing which enables accurate positioning of the joints relative to one another (c). Sensing of the arm position and communication with the flexible platform internally will enable full robotic navigation technology to be realised.

The potential for each platform beyond this point extends to the capability of the device to offer all the possibilities affiliated to the integration of a computer aided platform within a clinical setting. The ability to link with pre-operative imaging as a means to enable personalised image guided navigation to be undertaken, guided by virtual constrained channels (143) to safely avoid dangerous anatomy, or the implementation of augmented reality (136) to highlight the position of a tumour deep within the parenchyma of an organ highlighted for organ preserving surgery to promote precision ablation or accurate biopsy.

It is evident that although the flexible platform may successfully perform a select surgical procedure independently; its design features endear it toward broader and flourishing clinical applications as an adjunct device in hybrid minimally invasive surgical procedures. These hybrid roles inclusively encompass laparoscopy, thoracoscopy, single incision (SILS) and extra-luminal natural orifice (NOTES) surgery. In these settings, the platform would be considered for introduction in place of a rigid laparoscope or flexible endoscope, facilitating improved access to target anatomy, precision, stability and control.

As of yet no mention of the flexible device within the endoluminal environment has been discussed. The challenge of the even greater flexibility beyond the seven degrees of freedom currently promoted for the device limits the extent to which the colon could be explored endoluminally. However, the oesophagus and stomach may offer greater promise. The straighter approach beyond the oropharynx into the oesophagus could enable a currently expansive clinical application to be realised. The per-oral endoscopic myotomy (POEM) for oesophageal achalasia (144) as well as submucosal dissection for gastric cancer (145), which is being explored across South-East Asia in particular, are being undertaken with some measurable success. The potential for the flexible design within this clinical setting could be of significant importance in terms of market placement. With some further modifications to the device, namely suction and wash channels, endoluminal surgery could be more precisely and effectively undertaken. Further trials within the animal and *ex-vivo* model will determine the design modifications required to meet this potential market gap.

With bimanual control, the instrumental platform remains poised to re-define the surgical landscape in minimally invasive surgery, principally single incision and natural orifice access surgery. In circumstances where the flexible platform may be used in hybrid procedures as an adjunct tool, the bimanual device will find autonomous use as an integrated platform for ‘pure’ single incision robotic procedures, streamlining surgical workflow and advancing minimally invasive surgery. Emergence of the flexible design into the surgical marketplace would be expected to provide a smoother and more step-wise introduction of flexible robotic platforms.

Reflection on the most prominent unique selling points for the flexible design and the bimanual design has facilitated clarity in defining the unmet clinical need in which each platform purposefully strives toward overcoming. The flexible access and stability of the flexible platform bridges technology gaps of both the rigid laparoscope and flexible endoscope, while preserving their benefits. By introducing a small footprint computer-assisted platform to the surgical environment it offers additional benefits of intuitive control and fine precision to enhance its role as an intelligent and sophisticated adjunct device for hybrid procedures.

Future trials need to be focused on head to head testing of the flexible design versus the rigid laparoscope and flexible endoscope within the *in-vivo* model. *In-vivo* validation of the

refined flexible prototype will be undertaken with integrated sensing for enhanced joint control as well as enabling problems relating to ensuring effective and reliable sterilisation to be undertaken. Local market evaluation amongst surgical subspecialties to evaluate the most appropriate focused clinical application for effective introduction will also need to be undertaken in conjunction with appropriate licensing body applications including Medicines and Healthcare products and Regulatory Agency (MHRA) as well as appropriate Conformité Européenne (CE-marking) and finally United States Food and Drug Association (FDA) approval for access to the United States market.

Successful commercialization of the flexible access platforms described will be almost entirely reliant upon defining the unmet clinical need and demonstrating that it can be achieved more efficiently through the use of the platform over the alternative commercialized tools. The choice of such a focused clinical application will be driven at least in part by current and future market forces coupled with the platforms unique featured capabilities of flexibility and control, and crystallising the design to meet the clinical requirements. Once defined, promotion of the device onto the venture capitalist market will be aimed at drawing upon both capital investment and advertising to drive commercialization.

A high profile launch at one of the regional scientific meetings will attract press coverage and exposure further promoting UK Innovation and providing a platform from which the benefits of what the device could provide to global healthcare. Once formal MHRA approval is gained, first in man trials will be undertaken and the results presented at high profile meetings and submitted for publication in high impact journals to maximise exposure.

The future is flexible! The future for surgery is flexible robotics.

Appendix 1: Copy of license to undertake *in-vivo* animal trials in the UK.



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Your Reference

Our Reference PPL 80/2297

Date 8 January 2009

Dear Dr Clark

ANIMALS (SCIENTIFIC PROCEDURES) ACT 1986

I am pleased to inform you that the Secretary of State has granted your application for a project licence. The enclosed licence number PPL 80/2297 will be valid until 8 January 2014.

Your attention is drawn to any endorsements on and any additional conditions attached to the licence. As project licence holder you must keep an up-to-date record of every personal licence holder working under the authority of the licence and must be satisfied that their personal licences are valid and are compatible with the procedures and animal types used on the project and with the conditions attached to the project.

Should you wish to vary the terms of this licence in any way, you must apply to the Home Office using the enclosed form and giving details of the changes requested and quoting the project licence number.

It is the responsibility of the holder of the Certificate of Designation to ensure that all scientific procedures conducted at the establishment are authorised by project and personal licences. You will wish, therefore, to copy the project licence to the holder of the certificate of designation at each establishment where the project is being undertaken and also to each deputy project licence holder.

Yours sincerely

Dawne Mansfield

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List of Abbreviations

APC	Argon Plasma Coagulator
AU	Arbitrary Units
AUC	Area Under the Curve
EUS	Endoscopic Ultrasound
FAS	Flexible Access Surgery
FDA	Food and Drug Administration (United States)
FT	Fouriers Transform
GB	Gallbladder
HF	High Frequency
ICU	Intensive Care Unit
LED	Light Emitting Diode
LF	Low Frequency
MF	Medium Frequency
MHRA	Medicines and Health Regulatory Authority (United Kingdom)
MiniLap	Mini-Laparoscopy
MIST	Minimally Invasive Surgical Techniques
MRI	Magnetic Resonance Imaging
NBM	Nil By Mouth
NOSsE	Natural Orifice Simulated Surgical Environment
NOTES	Natural Orifice Translumenal Endoscopic Surgery
PCA	Principle Component Analysis
pCLE	Probe based Confocal Endomicroscopy
PEG	Percutaneous Endoscopic Gastrostomy
RALP	Robotic Assisted Laparoscopic Prostatectomy
R-TME	Robotic Assisted Total Mesorectal Excision
RF	Radio-Frequency
SEMF	Submucosal endoscopic dissection with mucosal flap
SILS	Single Incision Laparoscopic Surgery
SSPD	Serial Self Propelled Decoupled joint
TME	Total Mesorectal Excision
TU	Transumbilical (as for Transumbilical approach)
TUBA	Transumbilical Breast Augmentation
US	United States of America
UK	United Kingdom
V _n	Prototype version (<i>n</i> =version number)
VATS	Video Assisted Thorascopic Surgery
VHF	Very High Frequency

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