Evaluation of robotic catheter technology in complex endovascular intervention

MD (Res) Thesis

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Abstract

The past four decades have witnessed tremendous strides in the evolution of endovascular devices and techniques. Catheter-based intervention has revolutionized the management of arterial disease allowing treatment of aortic and peripheral pathologies via a minimally invasive approach. Despite the exponential advances in endovascular equipment, devices and techniques, catheter-based endovascular intervention has certain morphological and technological constraints. Complex patient anatomy, technological impediments and suboptimal fluoroscopic imaging, can make endovascular intervention challenging using traditional endovascular means. Conventional endovascular catheters lack active manoeuvrability of the tip. Manual control can hinder overall stability and control at key target areas, leading to significantly prolonged overall procedure and fluoroscopic times. Repeated instrumentation increases the risk of vessel trauma and distal embolization. More importantly, guidewire-catheter skills are not necessarily intuitive but must be developed and are highly dependent on operator skill with long training pathways as a result.

Recognizing the pressing need to address some of the limitations of standard catheter technology this thesis aims to evaluate the role of advanced robotic endovascular catheters in the aortic arch and the visceral segment. Clinical use of this technology is currently limited to transvenous cardiac mapping and ablation procedures. A comprehensive pre-clinical comparison and analysis of robotic versus manual catheter techniques is presented to reveal both their advantages and limitations, with particular
emphasis on the potential of robotic catheter technology to reduce the manual skill required for complex tasks, improve stability at key target areas, reduce the risk of vessel trauma, embolization and radiation exposure, whilst improving overall operator performance. The world’s first clinical report of robot-assisted aortic aneurysm repair, a “proof-of-concept” resulting from this research, is also presented, and the potential for future advanced applications in order to increase the applicability of endovascular therapy to a larger cohort of patients discussed.

**Declaration of originality**

I hereby declare that I am the sole author of this thesis and that all the work within is my own, except where work was carried out in collaboration with other individuals, who are appropriately credited. I was responsible for designing all the *in vitro* and *in vivo* studies with guidance from my supervisors as well as Colin Bicknell and Mo Hamady. I was also responsible for the system and model set-up, and operator recruitment for all simulated procedures. I created and maintained the relevant databases and performed the data extraction as well as the quantitative and qualitative analyses. Priya Chadha, Pasha Normahani, Frederic Cochennec and Melvinder Basra contributed to the data collection and analysis for the learning curves and in-situ fenestration chapters. I authorise the Imperial College Library to lend this thesis to other institutions or individuals for the purpose of research.
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I am also indebted to Mo Hamady for his invaluable input and endovascular expertise, and all the staff in the angiography suite of St Mary’s Hospital for accommodating me during the long hours of data collection for the in vitro experiments. I would also like to thank Yuval Sabari and Shaun Bowden for their continuing technical and industry support, and all the staff in Mountain View for making the in-vivo studies possible. A special thank you to Dan Wallace for his creativity and input; a truly inspirational engineer. My deepest gratitude goes to all the endovascular specialists and medical students who took part in the simulated cannulation procedures, Priya, Pasha, Fred, Mel and George for their contributions. It is also a pleasure to thank Erik Mayer, my office companion during the late night data analysis sessions for providing advice as well as entertainment; Sejal Jiwan and Trisha Bourke whose resourcefulness and dedication has been invaluable. Finally, this thesis would not have been possible without the input and support of Colin Bicknell, who has often had to bear the brunt of my frustration and rages against the world, but nonetheless has taught me to approach the most challenging clinical and research scenarios with enthusiasm, integrity and determination.
Dedication

This work is dedicated to Effie, Dimitris, Haris and Colin

“Σά βγαίσε στὸν πηγαίνο γιά τὴν ίδιακη,
νά εὖχεσαι νά ’ναι μακρύς ο δρόμος,
γεμάτος περιπέτειες, γεμάτος γνώσεις.”

And Leonidas (1914 – 2011)

“Τιμή πρέπει σ’ εκείνους όπου στὴν ζωή των ώρισαν να φυλάγουν Θηρμοπύλες.
Πότε από το χρέος μη κινούντες, δίκαιοι κ’ ίσοι, σ’όλες των τες πράξεις”

«Κ.Π. Καβάφης»
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# Abbreviations

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<th>Full Form</th>
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<tbody>
<tr>
<td>AAA</td>
<td>Abdominal Aortic Aneurysm</td>
</tr>
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<td>ACAS</td>
<td>Asymptomatic Carotid Atherosclerosis Study</td>
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<tr>
<td>ACST</td>
<td>Asymptomatic Carotid Surgery Trial</td>
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<tr>
<td>CAS</td>
<td>Carotid Artery Stenting</td>
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<tr>
<td>CCA</td>
<td>Common Carotid Artery</td>
</tr>
<tr>
<td>CEA</td>
<td>Carotid endarterectomy</td>
</tr>
<tr>
<td>CREST</td>
<td>Carotid Revascularization Endarterectomy Versus Stenting Trial</td>
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<tr>
<td>CSF</td>
<td>Cerebrospinal Fluid</td>
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<tr>
<td>CT</td>
<td>Computer Tomography</td>
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<tr>
<td>DREAM</td>
<td>Dutch Randomized Endovascular Aneurysm Management</td>
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<tr>
<td>DW-MRI</td>
<td>Diffusion-weighted Magnetic Resonance Imaging</td>
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<tr>
<td>ECST</td>
<td>European Carotid Surgery Trial</td>
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<tr>
<td>EVAR</td>
<td>Endovascular Aortic aneurysm Repair</td>
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<td>ICA</td>
<td>Internal Carotid Artery</td>
</tr>
<tr>
<td>IC3ST</td>
<td>Imperial College Complex Cannulation Scoring Tool</td>
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<tr>
<td>IQR</td>
<td>Interquartile range</td>
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<tr>
<td>IRAAA</td>
<td>Infra-renal abdominal aortic aneurysm</td>
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<tr>
<td>LOA</td>
<td>Loss of access</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>NASCET</td>
<td>North American Symptomatic Carotid Endarterectomy Trial</td>
</tr>
<tr>
<td>NNT</td>
<td>Number needed to treat</td>
</tr>
<tr>
<td>OSATS</td>
<td>Objective Structured Assessment of Technical Skills</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized controlled trial</td>
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<tr>
<td>RF</td>
<td>Radio frequency</td>
</tr>
<tr>
<td>SMA</td>
<td>Superior Mesenteric Artery</td>
</tr>
<tr>
<td>TAAA</td>
<td>Thoraco-abdominal Aortic Aneurysm</td>
</tr>
<tr>
<td>TCD</td>
<td>Transcranial Doppler</td>
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<tr>
<td>TEVAR</td>
<td>Thoracic Endovascular Aortic Repair</td>
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Chapter 1.

Endovascular Intervention

1.1. The evolution of Endovascular Therapy

Vascular Surgery is a rapidly evolving speciality driven largely by new advances in technology and a desire to perform less invasive procedures for patients that have significant co-morbidities. The advent of endovascular therapy has revolutionized the management of arterial disease allowing treatment of aortic and peripheral pathologies via a minimally invasive approach. It has also allowed treatment of patients whose respiratory and cardiovascular co-morbidities would have rendered them unsuitable and high risk for surgery. In a population with atherosclerosis, the number of minimally invasive catheter-based endovascular procedures has steadily risen as a result of increased operator experience, the availability of more sophisticated and versatile endovascular tools, and advances in imaging modalities [EVEM data, 2010].

The past four decades have witnessed tremendous strides in the evolution of endovascular devices and techniques. Early pioneering efforts provide a valuable insight into the technical complexities vascular specialists face in their pursuit of minimally invasive therapies for the aorta and its branches. In 1953, Ivan Seldinger made the first step from diagnostic to therapeutic angiography by describing the use of a guidewire technique to establish arterial access [Edholm P et al, 1956]. A decade
later, *Thomas Fogarty* developed the first balloon-tip catheter for peripheral arterial embolectomy [Fogarty TJ et al, 1965], and on the same principle, *Charles Dotter* first described the use of endovascular dilating catheters to treat an atherosclerotic stenosis [Dotter CT et al, 1964]. The concept of catheter-based intervention adopted by *Greenfield et al* led to the development of vena cava filters that have revolutionized the treatment of pulmonary thromboembolism [Greenfield LJ et al, 1973]. Further advances in catheter technology and manufacture provided *Andreas Gruentzig* with low-profile co-axial balloon systems; in 1974 he performed the first coronary artery balloon angioplasty, the most commonly performed endovascular intervention to date [Grüntzig A, 1979]. The adoption of balloon angioplasty catheters subsequently led to the introduction of the first intravascular balloon-expandable stent by *Palmaz et al* in 1985 [Palmaz JC et al, 1985]. Endovascular therapy has been described as a form of disruptive technology: “*a new technology that displaces the standard old method for performing certain functions because the new method is so clearly better than the old*” - *Frank Veith* [Veith FJ, 2008]. The use of endovascular technology to treat aneurysmal and occlusive arterial disease has produced results comparable if not improved, to those that can be achieved with conventional open surgical approaches in certain vascular beds. This has led to an overall increase in the vascular practice volume due to the broader applicability of these minimally invasive techniques to a larger patient population that would otherwise be deemed unsuitable for surgery. This thesis will investigate the potential role of endovascular robotic technology in complex vascular intervention focusing on two of the most challenging and disruptive applications of endovascular therapy: aneurysmal disease of the aorta and carotid artery disease.
1.1.1. Aneurysmal disease of the aorta

Aneurysmal disease of the aorta continues to be a major cause of death worldwide and the incidence increases with age, with 85% of all cases occurring in patients aged 65 and above [National Center for Health Statistics, 2007]. Aneurysm size, growth rate and smoking appear to be the most significant predictors of aneurysm rupture. Eighty percent of all aneurysms are thought to be degenerative and atherosclerotic in nature, with a further 15% due to dissection and the remainder secondary to connective tissue disorders, arteritis and trauma [Griep RB et al, 1999].

Since the first reported case by Dubost et al in 1952 [Dubost C et al, 1952] and subsequent modifications to the original technique, conventional open aneurysm repair became the mainstay of treatment for the next 30 years. Open infra-renal aortic aneurysm (IRAAA) repair requires general anaesthesia, a large abdominal incision, and cross clamping of the aorta in order to sew in a new prosthetic graft to replace the diseased segment. For thoraco-abdominal aortic aneurysms (TAAAs), defined by the involvement of the coeliac, superior mesenteric, renal and arch vessel origins, open repair represents an even more formidable task. Access to the aorta is gained through a thoraco-abdominal incision dictated by TAAA extent proximally, and division of the diaphragm. The clamp and sew technique with revascularization of major aortic branches, often requiring cardiopulmonary bypass with hypothermic circulatory arrest, single-lung ventilation, and cerebrospinal fluid (CSF) drainage/ epidural cooling, resulting in long operative times, significant blood loss, volume shifts, and prolonged recovery times. Despite significant advances in surgical technique and peri-operative critical care the traditional open repair, even in the most experienced
centres, is still associated with high morbidity and mortality rates: 1.4–6.5% for non-ruptured and 23–69% mortality for ruptured IRAAs [Ernst CB, 1993; McPhee J et al, 2009], and 8-30% for non-ruptured and 50–80% for ruptured, more extensive TAAAs, with a paraplegia incidence of up to 16% [Svensson LG et al, 1993; Safi HJ et al, 1998; Rigberg DA et al, 2006; Coselli JS et al, 2007; Schepens MA et al, 2007].

In 1991, Parodi et al combined both Dacron graft and balloon-expandable stent technology to create the first endovascular stent-graft for an infra-renal abdominal aortic aneurysm and introduced the concept of endovascular aneurysm exclusion [Parodi JC et al, 1991]. By 1994, Dake et al had published the first series of successful endovascular stent-grafting for isolated descending thoracic aortic aneurysms with no reported paraplegia [Dake MD et al, 1994]. Rapid advances in stent-graft technology and availability of improved devices have revolutionized the treatment of aneurysmal disease of the abdominal and thoracic aorta via a minimally invasive approach. In contrast to the traditional open repair, endovascular stent-grafting utilizes small groin incisions or a percutaneous approach for femoral artery access. It can be performed using regional or even local anaesthesia. The device is introduced through the femoral arteries and deployed under fluoroscopic guidance. The diseased aortic segment is relined, rather than replaced, with the endovascular stentgraft. This technique obviates the need for a large abdominal incision and aortic cross-clamping and hence minimizes blood loss and the physiological insult to the patient.
Infra-renal aortic segment - EVAR:

Several retrospective reviews, registries and prospective clinical trials have compared outcomes of endovascular aortic aneurysm repair (EVAR) for IRAAAs with those of conventional open repair [Zarins CK et al, 1999; Harris PL et al, 2000; Lee WA et al, 2001; Matsumura JS et al, 2003; Moore WS et al, 2003; Bush RL et al, 2006] and demonstrated reduced morbidity rates, reduced blood loss, shortened hospital stay, faster recovery times and encouraging short-term outcomes. The two large randomized controlled trials (RCTs) that followed, the Dutch Randomised Endovascular Aneurysm Management trial (DREAM) and EVAR-1 trials, confirmed the benefits of the less-invasive nature of endovascular repair and concluded that peri-operative mortality is lower following endovascular repair than with open repair (1.2% versus 4.6% in DREAM and 1.7% versus 4.7% in EVAR-1) [Prinssen M et al, DREAM 2004; Greenhalgh RM et al, EVAR-1 2004, Greenhalgh RM et al, 2010]. Data from both trials showed that all-cause mortality was similar in the endovascular repair and open repair groups (at approximately 11%-DREAM and 28%-EVAR-1), although there were persistently fewer aneurysm-related deaths in the endovascular group than in the open repair group (5.7% versus 2.1%-DREAM and 4% versus 7%-EVAR-1); the 3% operative mortality benefit from EVAR in terms of AAA-related deaths, was maintained at four years [Blankensteijn JD et al, 2005; De Bruin JL et al, 2010, Greenhalgh RM et al, 2010]. Both the EVAR and DREAM trials reported a higher rate of re-intervention over time following endovascular repair than open repair (20% versus 6% in the EVAR-1 trial). In the EVAR-1 trial, which enrolled patients between 1999 and 2004 from 37 hospitals in the United Kingdom, all-cause mortality curves in the two groups converged at two years and aneurysm-related
mortality curves converged at six years. However, between 30 days and 4 years after aneurysm repair, the majority of deaths in each group were due to either cancer or ischemic heart disease, and the all-cause and aneurysm-related mortality curves remained equivalent out to 8 years. The EVAR-2 trial which compared stenting to no intervention in those unfit for open aneurysm repair, showed that EVAR had a considerable 30-day operative mortality in patients already unfit for open repair, however it was associated with a significantly lower rate of aneurysm-related mortality than no repair [Greenhalgh RM et al, 2010, Brown LC et al, 2010]. The US-led Open Versus Endovascular Repair (OVER) RCT that compared post-operative outcomes up to 2 years after endovascular versus open elective AAA repair showed that peri-operative mortality was low for both approaches but lower for endovascular than open repair; the early advantage of endovascular repair was not offset by increased morbidity or mortality in the first 2 years on follow-up [Lederle FA et al, 2009].

These RCT trials have fuelled considerable debate among the vascular community. Both the EVAR-1 and EVAR-2 trials were limited by long delays between randomization and treatment, with 14 patients dying while awaiting EVAR. Moreover, 27% of patients in EVAR-2 crossed over from non-operative to endovascular repair, and these patients had a lower procedure mortality from EVAR than those originally assigned to it (2% v 9%). The results from these RCTs are also inherently linked to early devices and imaging technology, limited experience and outdated secondary treatment. The EVAR-1 trial was designed before the 2002 Society for Vascular Surgery reporting standards on EVAR were published [Chaikof EL et al, 2002]. Complications therefore reported in EVAR-1, especially with regards
to endoleaks and subsequent interventions are not applicable to current practice. Endoleaks, defined as persistent blood flow outside the lumen of an stent-graft but within an aneurysm sac or adjacent vascular segment, result from incomplete sealing or exclusion of the aneurysm sac, and thus cause reflux of blood flow and continued pressurization into the sac, leaving the patient at risk of aneurysm rupture [Cao P et al, 2010]. There are three main endoleak types: type I is a proximal (Type Ia) or distal Type (Ib) leak at the endograft ends resulting from inadequate seal at the corresponding landing zones, Type II endoleaks result from sac filling via collateral branch vessels (e.g. lumbers or the inferior mesenteric artery), and Type III endoleaks results from a leak through a defect in the graft fabric or ineffective sealing of overlapping graft joints. The EVAR Investigators defined all endoleaks as complications; there were a total of 288 patients with complications in the EVAR group versus 72 patients in the open group. Among all patients with complications, 156 were type II endoleaks (in 108 EVAR patients and and 3 open repair patients). Current practice in accordance with the Society for Vascular Surgery reporting standards, states that Type II endoleaks are often benign and may result in spontaneous resolution. The majority require observation, with intervention being reserved for patients with persistent endoleaks and aneurysm sac expansion. In terms of other complications and re-interventions, earlier stentgraft devices, which had an increased incidence of migration and late failure, are now rarely used. The concept of “freedom from re-intervention” after open repair is now also challenged: recent population-based studies show that patients undergoing open aneurysm repair are 12 times as likely to undergo laparotomy and adhesiolysis for small bowel obstruction in the future and that re-admission for non-operative management of bowel obstruction
that occurs more frequently after open repair is associated with a 30-day mortality of 10.9%. [Schermerhorn ML et al, 2010].

In recent years, with advances in device technology and increasing operator experience, criteria for treatment as well as for re-interventions are now better understood. Considerable emphasis is shifted towards improving patient fitness prior to treatment, particularly in terms of cardiac, respiratory and renal co-morbidities, and EVAR has become a durable and reliable option for those that are anatomically suitable. In addition to elective repair, after the initial report of successful endovascular repair of a ruptured abdominal aortic aneurysm (AAA) in 1994 [Yusuf SW et al, 1994], the use of endovascular stent-grafts for ruptured AAAs has been increasing, and several prospective trials and retrospective case series have shown reduced peri-operative morbidity and mortality rates as well as length of hospital stay especially in the high-risk group of patients [Ohki T et al, 1999; Hinchliffe RJ et al, 2001; Lee WA et al, 2004; Alsac JM et al, 2005; Dillavou ED et al, 2006; Dillon M et al, 2007]. A randomized controlled trial is currently underway [Powell JT et al, 2009].
Thoracic aortic segment-TEVAR:

It is in the thoracic aorta that endovascular stent grafting is having its greatest impact in terms of its perceived advantage, where it has rapidly become the first line therapy for much thoracic aortic pathology with defined indications for therapeutic intervention. Comparison of endovascular and conventional surgical techniques has shown a clear mortality advantage to the endovascular option (25% versus 5–10%) and a reduction in the incidence of paraplegia of less than 5%, not only for thoracic aneurysms but also for other aortic pathologies such as transections, acute aortic syndromes, complicated type-B aortic dissections, fistulae and other thoracic catastrophes [Leurs LJ et al, 2004; Makaroun MS et al, 2005; Cambria RP et al, 2009; Chiesa R et al, 2010; Ullery BW et al, 2011; Jonker FH et al, 2011, Patel HJ et al, 2011]. Endovascular reconstruction of the true lumen for acute complicated type-B dissections in particular, is becoming increasingly popular. Cumulative extraction of currently available outcomes data and meta-analytic interpretation of the available observational evidence suggest that endovascular stent grafts provide improved survival compared with the open surgical approach in these complicated type-B dissection cases presenting with organ malperfusion, impending rupture, ongoing pain, and resistant hypertension [Nienaber CA et al, 2011; White RA et al, 2011; Steuer J et al, 2011]. The absolute benefit of thoracic endovascular aneurysm repair (TEVAR) over alternative treatments for chronic uncomplicated Type-B dissections, however, remains uncertain. A single RCT, the INSTEAD (Investigation of Stentgrafts in Aortic Dissection) trial, demonstrated that in the setting of uncomplicated type-B aortic dissections, elective stentgraft placement in conjunction with optimized medical management fails to improve survival and adverse events
within an observation period of 2 years, despite favorable aortic remodelling [Nienaber CA et al, 2009]. The lack of natural history data and the significant heterogeneity in case selection in published reports, constitute significant obstructions to interpreting mid-term results for these cases [Thrumurthy SG et al, 2011]. The less invasive nature of endovascular stent grafting in the thoracic aorta, however, and the encouraging outcomes for specific pathologies have led many investigators to speculate that the technique may expand the applicability of endovascular intervention. High-quality data from registries such as the International Registry of Acute Aortic Dissection [Trimarchi S et al, 2011] and randomized control trials are required to define consensus; the ADSORB (Acute Uncomplicated Aortic Dissection Type B: Evaluating Stent-Graft Placement or Best Medical Treatment Alone) trial, a randomized controlled trial investigating the role of TEVAR in acute dissections, is currently underway [Tang DG et al, 2009, Brunkwall JS, 2011].
Thoraco-abdominal aortic segment:

The Hybrid approach

Although the use of endovascular stent grafts for isolated infra-renal or thoracic aortic aneurysms has shown significant promise, their use for extensive TAAAs is limited by the presence of the aortic arch vessels proximally and the visceral and renal vessels distally. In 1999, Quinones-Baldrich et al were the first to report a combined endovascular and open surgical approach for a type-IV TAAA, involving retrograde visceral bypass revascularization followed by successful completion endo-grafting and TAAA exclusion [Quinones-Baldrich WJ et al, 1999]. In 2003, the St Mary’s Vascular Unit at Imperial College independently developed a retrograde extra-anatomical visceral/renal debranching technique with completion endo-grafting for extensive TAAAs [Rimmer J et al, 2003]. Extra-anatomical bypass grafts from the aorta or iliac artery - depending on the distal extent of the TAAA - provide retrograde flow into each visceral and renal vessel allowing end-organ perfusion; the proximal artery is ligated to eliminate the risk of back bleeding into the aneurysmal sac. This approach limits the physiological derangements associated with proximal aortic cross-clamping, thoracotomy and single-lung ventilation in the traditional open repair. Our unit has reported the largest published series of these repairs for high-risk patients, with a 30-day mortality rate of 14.95% and a paraplegia rate of 8.4% [Black SA et al, 2006; Drinkwater SL et al, 2009], and the technique has now been adopted by various centres worldwide [Resch TA et al, 2006; Zhou W et al, 2006; Chiesa R et al, 2007]. Aneurysms that involve the more proximal descending thoracic aorta or the aortic arch may also require extra-anatomic bypasses of the subclavian, brachiocephalic and

The wholly endovascular approach:

fenestrated and branch stent-graft technology

Further advances in stent-graft technology in recent years, have allowed the treatment of more extensive aneurysm pathology, via an even less invasive, wholly endovascular approach, avoiding extensive aortic exposure whilst maintaining visceral branch perfusion, especially in patients unable to withstand the traditional surgical approach due to significant co-morbidities. New-generation custom-made fenestrated and branched devices were designed to extend the proximal sealing zone from the infra-renal segment to the supra-renal and thoraco-abdominal aorta by incorporating the visceral and supra-aortic branches. These sophisticated devices require fenestrations (windows) or formal directional branches to be made into the grafts according to individual patient anatomy, to maintain vital aortic branch perfusion.

Having gained access through the groin or via an iliac conduit, the fenestrated device is placed at the level of the target vessels under fluoroscopic imaging aligning the fenestrations with the target vessel ostia to allow cannulation, subsequent side-branch stenting and overall exclusion of the aneurysm. With branched devices, the aortic main body is deployed well above the target vessel, the branches are cannulated from
a brachial approach, and self-expanding stentgrafts are deployed to join the branch vessels with the main aortic body endograft.

In 1999 Browne et al first reported the use of a custom-made device in canine models [Browne TF et al, 1999]. Initial clinical experiences with these devices in a combined series of 16 patients with short-necked infra-renal aneurysms and no incidence of acute vessel loss or death were later described [Anderson JL et al, 2001; Stanley BM et al, 2001]. Several clinical reports have followed early experiences [Greenberg RK et al, 2004; Verhoeven EL et al, 2004] and recent reviews on fenestrated endografting for the juxta-renal segment demonstrated a peri-operative mortality of 1.1%, with 97% of the target vessels patency [Sun Z et al, 2006; O’Neill S et al, 2006]. Extrapolating fenestrated technology above the infra-renal segment to treat aneurysms involving the visceral arteries, was initially described by Anderson et al in 2005 [Anderson JL et al, 2005]. The first reported case of TAAA repair involved a homemade device with longitudinally oriented branches [Chuter TA et al, 2001]. Subsequently, a number of series have been published describing the results of endovascular repair of complex aneurysms with technical success range ranging from 90-98%, with 5-9% mortality, a paraplegia rate of 3% and significantly reduced length of hospital stay to a median of 9 days [Greenberg RK et al, 2006; Muhs BE et al, 2006; Roselli EE et al, 2007; Bicknell et al, 2009; Haulon S et al, 2010].

In selected patients, fenestrated and branched stent-grafting appears to be a safe and effective alternative to open and hybrid surgery for juxtarenal and thoracoabdominal aneurysms, with encouraging short and intermediate-term results [Greenberg RK et
al, 2008]. The procedure is currently developing and gaining acceptance; its long-term durability, however, is yet to be proven.
1.1.2 Carotid artery disease

Carotid artery stenosis, almost invariably atherosclerotic, is a frequent clinical problem. It can be asymptomatic or symptomatic presenting as one or more transient ischemic attacks relating to embolization of thrombus from stenotic lesions, hypoperfusion, or less commonly, as an ischemic stroke. Stroke is the third leading cause of death and the leading cause of serious, long-term disability. Approximately 15 million people suffer a stroke worldwide each year [Lloyd-Jones D et al, 2010]. Carotid endarterectomy (CEA) is currently the gold standard of treatment for the management of carotid artery disease for the prevention of stroke. Felix Eastcott is credited with the first carotid revascularisation in a symptomatic patient, performed in 1954 at St Mary’s Hospital [Eastcott HHG et al, 1954], whereas Michael De-Bakey, at the Methodist Hospital in Houston, developed and established the technique worldwide [DeBakey ME et al, 1975]. Six decades on, the management of carotid artery disease has been the subject of much controversy with regards to indication for treatment, diagnostic modalities, patient selection, treatment options, technical skill and operator experience.

There is strong evidence from high-quality prospective RCTs that surgical intervention is beneficial for carotid artery disease in symptomatic patients with an internal carotid artery stenosis of greater than 70%; the risk of stroke in such high-grade cases when treated with medical therapy alone, can be as high as 26% [Mayberg MR et al, 1991; ECST Collaborators 1991; NASCET Collaborators 1991; Rothwell PM et al, 2003]. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) demonstrated a 17% reduction in absolute stroke risk by two years
after CEA i.e. for every six patients treated, one major stroke can be prevented (number needed to treat (NNT)=6). Symptomatic patients with moderate stenoses (50 – 69%) have a smaller benefit, with a NNT of 22 at five years. In symptomatic patients with less than 50% stenosis, medical therapy is superior to surgical treatment.

The role of surgery for asymptomatic stenosis remains controversial. Another two high-quality trials estimated the average annual risk of stroke to be approximately 2% in asymptomatic patients with 60–99% stenosis treated with best medical therapy, versus 1% with surgical intervention [ACAS Committee, 1995; ACST Collaborators, 2004]. However, a recent systematic review and a number of natural history studies argue that with improvements in medical therapy in recent years, the average annual rate of ipsilateral stroke with best medical therapy alone can be as low as 0.34% [Abbott AL, 2009; Marquardt L et al, 2010]. Although the indications for surgical treatment of asymptomatic carotid disease are not clearly defined, identification of patients at risk of suffering a stroke is crucial so that interventions can be targeted and tailored to individual patient characteristics. It is important, therefore, to emphasize at this point, that risk stratification should not merely reflect stenosis severity and the presence or absence of symptoms. More sophisticated parameters such as plaque morphology, plasma biomarkers, stenosis progression, embolisation on transcranial Doppler and infarction on CT/MRI imaging should also be taken into account [Bladin C et al, 2010, Naylor AR 2011].
Carotid Artery Stenting

Over the past decade, carotid artery stenting (CAS) has emerged as a less invasive alternative to CEA. It is assumed that, by stent implantation, carotid plaque composition is modified such that the lesion becomes less vulnerable to rupture and embolisation. Given the widespread adoption and success of endovascular therapy in other vascular beds, there are several potential advantages of minimally invasive intervention especially in patients with cardiac co-morbidities, those with high-grade re-stenosis, hostile necks following radiation or radical neck surgery, or patients with inaccessible high cervical lesions. Overall, a minimally invasive endoluminal procedure is less dependent on patient co-morbidities and eliminates the risk of cranial nerve injury and may reduce hospital stay. Carotid balloon angioplasty was first performed in 1980 [Mathias K, 1981; Bockenheimer SA et al, 1983], and an endovascular stent was first used in 1989 to treat an intimal flap lesion following angioplasty [Théron J, 1992]. Since then, there has been a series of non-randomised and randomised trials as well as registries to assess the safety and efficacy of percutaneous carotid intervention.

Although there are substantial variations in procedural protocol and technique amongst endovascular specialists, the standard technique for CAS is described below. The procedure is performed in the angiography suite under fluoroscopic guidance. Under local anaesthesia, access is obtained via the femoral artery or in some cases via the brachial approach. The target carotid artery is cannulated using a 5F catheter in combination with a 0.035 inch guide wire. Standard angiographic projections to demonstrate the carotid bifurcation are obtained, along with intracranial views to assess the collateral circulation for any evidence of intracranial stenotic lesions. With
the catheter positioned in the common carotid artery (CCA), an exchange-length 0.035 inch wire is advanced into the external carotid artery (ECA). The catheter is exchanged over the wire for a guiding catheter or a long sheath that is then advanced into the CCA below the carotid bifurcation. Depending on the severity of the stenosis, the lesion in the internal carotid artery (ICA) is firstly crossed by an embolic protection device (EPD) – a specifically designed umbrella-shaped device that is used to capture debris and emboli. Balloon predilation may also be necessary if the stenosis is very severe. Once the lesion in crossed, a sheath-covered self-expanding stent is introduced and positioned in the stenotic portion of the ICA artery. Following stent deployment, an angiogram is obtained to confirm the increase in diameter of the artery. In severe cases of stenosis, the stent itself may only reduce the occlusion mildly. To overcome any residual stenosis, a balloon catheter may be placed within the stent and expanded to allow for greater augmentation of the vessel diameter, and after successful postdilation the EPD is removed, using a retrieval catheter. The technique has evolved with great contributions from industry providing lower profile systems, improved stents, and a variety of EPDs.

Data from isolated experienced centres, registries and one RCT indicate that CAS can be as effective as CEA in the prevention of ipsilateral stroke [Wholey MH et al, 2003; Yadav JS et al, 2004; Theiss W et al, 2008; Zahn R et al, 2008; SAPHIRE Investigators, 2008; Gray WA et al, 2009]. All other RCTs, however, including the recent CREST trial – the largest RCT to date – have demonstrated increased rates of cerebral embolization for CAS in comparison to CEA for symptomatic disease [Eckstein HH et al, 2008; Mas JL et al, 2008; CAVATAS Investigators, 2009; Ederle J et al, 2009; International Carotid Stenting Study Investigators, 2010; Mantese VA et
Compared with the surgical approach, the endovascular procedure is associated with a significant cerebral embolic burden [Bonati LH et al, 2010]. The excess risk of peri-procedural neurological complications observed in CAS seems to be multifactorial: poor patient selection, plaque morphology, tortuosity, angulation and complex aortic arch anatomy (bovine or Type III arch variants), device technology and operator experience, all play an important role. The low adverse event rates observed when CAS was performed extensively in registries in the early part of the century, led some CAS enthusiasts to believe that carotid surgery was to become obsolete and that CAS would replace the old gold standard, CEA. Since the appearance of the unacceptably high stroke rates reported in some RCTs and the controversy that followed, many of the original CAS enthusiasts went on to express a note of caution and the need for improved technology, experienced CAS operators and careful patient selection, avoiding those with complex anatomy or high-grade calcified lesions (Macdonald S et al, 2009; Naylor AR 2011).
1.2. Current Endovascular Tools

Stent-graft technology, from the early infra-renal devices to the more sophisticated fenestrated and branched endografts as illustrated above, is rapidly evolving, allowing more complex aortic pathology to be treated via the minimally invasive route. Endovascular guidewires, catheters and sheaths comprise the foundation of endovascular therapy both technically and conceptually and are essential for safe stentgraft deployment.

Guidewires

Whether diagnostic or interventional, current endovascular devices are rarely sufficiently manoeuvrable without the use of a guidewire. Guidewires are used to introduce, position and exchange catheters and other endovascular tools (Fig 1.2.1). They serve the purpose of creating a pathway through the vascular system, whilst achieving and maintaining critical access across target areas.

All guidewires are composed of a stiff inner core and an outer tightly coiled spring, which allows a catheter to track over the guidewire. The guidewire tip may be pre-formed into a straight, angled or J-curved tip, and “floppy” to minimize vessel wall trauma. Most commonly used wires are coated with a hydrophilic polymer similar to silicone, which facilitates passage through vessels and catheter exchanges. External torque devices can be employed to increase control of these wires (rotational movement of the ex vivo portion results in rotation of the in vivo portion). For access
to a specific target within a vessel, branch cannulation, or lesion crossing, a standard 
guidewire length of 145 to 180 cm is usually adequate. Exchange-length guidewires 
function to provide support and trackability to various catheters introduced over them. 
To facilitate exchange of catheters while maintaining a lesion crossing therefore, 
stiffer and longer (260–300 cm) exchange-length guidewires are used to minimize 
kinking. The standard guidewire diameter for peripheral interventions is 0.035 inch, 
and more recently due to improved guidewire construction, an increasing number of 
endoluminal procedures can be performed using 0.014 or 0.018 inch wires, to 
minimize vessel wall trauma.

**Fig 1.2.1 A range of endovascular guidewires**

A range of commonly used endovascular guidewires, essential for the introduction, positioning and exchange of 
catheters and other endovascular tools.
Conventional Catheters

A broad range of endovascular catheters is currently available, that vary in their preformed distal ends, hydrophilic nature, torquability, pushability, and flexibility. The majority of catheters manufactured today are composites, with a stiffer material for the main catheter body and a more flexible material for the soft tip. They have a diameter of 4 to 6F - with 5F catheters being by far the most common - and lengths ranging from 65 cm to 150 cm. Most catheters are advanced over a wire to minimize intimal injury, and can be non-selective or selective. Non-selective catheters are designed to rapidly infuse large volumes of contrast agent without causing injury to the vessel. Their distal portion contains multiple side-holes in addition to the standard end-hole and is preformed into a shape (usually a ‘pigtail’) that assists in the dispersion of contrast. These catheters have a high tensile strength - yet a low coefficient of friction, to be able to resist high burst pressures associated with high injection rates, and still maintain their predetermined shape in order to advance through tortuous vessels. They must also have low thrombogenicity.

Selective catheters with a single end-hole are designed for cannulation of branch vessels. A wide range of preformed distal ends is available to assist in selective cannulation of various anatomical targets (Fig 1.2.2). Catheters with curved distal ends are usually introduced over a guidewire with a floppy tip, so that they may assume their preformed shape when the guidewire is withdrawn with its distal tip within the catheter lumen. In catheterization of branch vessels with an acute angulation from the direction of approach such as a left subclavian or left carotid artery, reverse curve catheters or catheters with a secondary curve are designed for
engaging the vessel lumen. These double-curved catheters are first advanced past the target branch vessel and require manual re-shaping involving interaction with the vessel wall in the aorta proximal to the area of interest before the catheter is withdrawn back with the catheter tip directed toward the access site. To reshape, the catheter is advanced until the tip and primary curve are no longer supported by the guidewire. Then with the tip engaged in a side branch, the main body of the catheter is either advanced or rotated, reforming the catheter into its native shape. Alternatively, a catheter may be reformed by reflection off the aortic valve when cannulating branches in the aortic arch such as the carotid arteries.

**Fig 1.2.2 A range of conventional selective catheters**

A range of conventional, selective endovascular catheters with preformed distal ends to assist in selective cannulation of various anatomical targets.
**Sheaths**

Introducer sheaths are essential for catheter/guidewire exchanges and the introduction of endografts and other endovascular tools; they are designed to minimize vessel trauma and extravasation of blood while maintaining vascular access. Sheaths are inserted over a primary access guidewire after cannulation of the access vessel (usually the common femoral artery) using the Seldinger technique (Fig 1.2.3). Appropriately sized dilators aid the insertion of the larger sheath into the small puncture made by the puncture needle. Subsequent to insertion, all exchanges or introduction of guidewires, catheters, and devices takes place through the sheath lumen. Sheaths and dilators are usually constructed of Teflon (tetrafluoroethylene), a material of low coefficient of friction that is very torquable. Nearly all sheaths feature a haemostatic valve and a side infusion port.

Large-diameter sheaths (20–24 F) are available for deployment of aortic endografts and often these sheaths are included into the endograft delivery system. Sheath lengths range from 10 cm to 65 cm. The 10 to 15cm length is standard for most peripheral vascular interventions. Longer length sheaths are usually only needed for endograft placement or access to the contralateral side of the main aortic body. When the common femoral artery is either undersized or too diseased to facilitate access, creation of an iliac conduit using a 10mm Dacron graft is indicated to allow the introduction of necessary sheaths. Brachial or radial access may also be required in some procedures; these sites will usually accommodate insertion of a 4F sheath.
Fig 1.2.3 An endovascular sheath

Sheaths are designed to minimize vessel trauma and extravasation of blood while maintaining vascular access. They are inserted over a primary access guidewire using the Seldinger technique.
1.3. Limitations in endovascular intervention

Motivation and proposal

Despite the exponential advances in endovascular equipment, devices and techniques, endovascular intervention has certain morphological and technological constraints. Anatomical unsuitability due to complex patient anatomy, technological impediments as well as poor visualization of key regions of the arterial tree, can make endovascular intervention challenging using traditional endovascular means.

Radiation exposure and nephrotoxicity are other important factors that should be considered. All endovascular procedures are currently performed under fluoroscopic guidance. Technically complex cases inevitably take longer to perform and this increases both radiation exposure and contrast load. Recommendations to minimize radiation exposure for both of the patient and the operator include keeping fluoroscopic time to a minimum and maximizing working distance from the radiation source. Operators working 80cm from the radiation source receive 25% of the scatter dose received by those 40 cm from the source [Ho P et al, 2007]. Iodinated contrast agents are required to demonstrate the intravascular anatomy during these procedures, and they are nephrotoxic as they exacerbate the physiological hypoxia in the outer renal medulla leading to oxidative stress [Walsh SR et al, 2008]. Peri-operative renal failure is a key determinant of outcome for AAA repair, with significantly increased mortality rates in patients requiring renal replacement therapy [Wong GT et al, 2007];
measures therefore should be taken to limit the use of contrast load during endovascular repair.

Complications specific to endovascular intervention should also be taken into account. Both the EVAR and DREAM trials demonstrated a higher rate of re-interventions over time following endovascular repair than open repair (20% versus 6% in the EVAR-1 trial) [Greenhalgh RM et al, 2010]. Endograft migration with earlier devices, kinking and disruption of modular endograft components, and endoleak formation are all potential complications and therefore lifetime surveillance must be maintained [Chuter TA, 2009; Resch T et al, 2010]. Critics of endovascular technology often highlight its increasing costs. The EVAR-2 trial which compared stenting to no intervention in those unfit for open aneurysm repair, showed that the mean hospital cost per patient in the intervention group over four years was £13,632 (approx. $24,720 USD) compared with £4,983 (approx. $9,219 USD) in the non-intervention group [Greenhalgh RM et al, 2010]. The inherent cost for the custom-made branched and fenestrated devices in particular, also mandates careful consideration.

Current catheter technology has its own limitations. Conventional endovascular catheters have a limited repertoire of shapes and sizes, they are difficult to steer and lack active manoeuvrability at the tip. The delivery of torque at the distal end is also impeded by the unanticipated contact friction between the catheter and the access vessel at the proximal end. This manual control can hinder overall stability and control at key target areas. This necessitates frequent catheter changes, which can threaten the stable positioning of guidewires and result in loss of vessel access and
significantly prolonged overall procedure and fluoroscopic times. Access vessels can be tortuous and angulated; non-compliant rigid vessels increase the risks of iatrogenic vessel damage while making catheter control more challenging. Repeated instrumentation especially in the presence of vessel thrombus or calcification increases the risk vessel dissection, perforation and distal embolization. The latter is particularly pertinent in instrumentation within the aortic arch, where cerebral embolization may occur, resulting in stroke [Bonati LH et al, 2010]. Microembolisation of vessel plaques has been identified as a causative factor for spinal cord ischaemia [Berg P et al, 2001], renal impairment [Boules TN et al, 2007], and peripheral arterial ischaemia [Maldonado TS et al, 2004]. Iliac tortuosity can cause further problems with catheter control and manipulation. Graft rotation and misalignment of fenestrations/branches with the vessel ostia, due to angulation of the more proximal aortic segment in fenestrated and branched stent-grafting procedures, may further prevent easy and safe target vessel cannulation. More importantly, guidewire-catheter skills are not necessarily intuitive but must be developed; conventional catheter manipulation requires a high degree of technical performance, operator skill and long training pathways as a result [Neequaye SK et al, 2007]. Limitations specific to complex aneurysm repair and arch vessel intervention will be discussed in detail in later chapters.
Research Aims

Recognizing the pressing need to address some of the limitations of standard catheter technology this research aims to evaluate the role of advanced robotic endovascular catheters for complex arterial intervention in the aortic arch and the visceral segment. Clinical use of this technology is currently limited to transvenous cardiac mapping and ablation procedures. A comprehensive pre-clinical comparison and analysis of robotic versus manual catheter techniques is presented to reveal both their advantages and limitations, with particular emphasis on the potential of robotic catheter technology to reduce the manual skill required for complex tasks, improve stability at key target areas, reduce the risk of vessel trauma, embolization and radiation exposure, whilst improving overall operator performance. The world's first clinical report of robot-assisted aortic aneurysm repair, a “proof-of-concept” resulting from this research, is also presented and the potential for future advanced applications in order to increase the applicability of endovascular therapy to a larger cohort of patients discussed.
Chapter 2.

Robotic Technology

Robot-assisted surgery, surgical telemanipulation or computer-assisted surgery, are being developed to overcome human limitations and eliminate impediments associated with conventional surgical and interventional tools. Robotic technologies are increasingly being used by surgical disciplines to facilitate and improve performance of minimally invasive surgery and have been shown in many fields to significantly improve outcomes [Howe RD et al, 1999; Lanfranco AR et al, 2004]. Laparoscopic and endovascular techniques have both been introduced into the field of vascular surgery with specific advantages to patient outcomes [Ludemann R et al, 1999; Rouers A et al, 2005; Nio D et al, 2007; Lovegrove RE et al, 2008]. There has been an increasing interest in the application of robotic technology to enhance minimally invasive laparoscopic capabilities in the vascular tree.

In this chapter, a review of the current status of clinical applications and supporting evidence of robotics in vascular surgery is undertaken, followed by a description of the Hansen Sensei endovascular robotic system used in this research work.
2.1. Robotics in vascular surgery

Currently available laparoscopic robotic systems

Two advanced surgical robotic systems have been used in laparoscopic vascular surgery: the da Vinci (Intuitive Surgical Inc., Mountain View, CA) and Zeus (Computer Motion Inc., Santa Barbara, CA) systems [Martinez BD et al, 2004]. Of these, only the da Vinci system remains in current use for laparoscopic surgery, since the acquisition of Computer Motion by Intuitive Surgical and the corporate decision to stop production of the Zeus robot [Hanly EJ et al, 2004]. Both systems are comprehensive master-slave surgical robots with similar capabilities [Kim HL et al, 2004]. The da Vinci system consists of three components: the vision cart, the master surgeon console and the robotic platform. The vision system has a dual light source and cameras, which generate a stereoscopic image. The surgeon operates from a console, which is located away from the patient. The surgeon console contains an image-processing computer, which provides a 3-dimensional view of the operative field with adjustable magnification, a view port, instrument and camera arm clutches, and foot pedals for electrocautery. In addition, there is motion scaling, tremor elimination and an ergonomic working position for the surgeon. Using manipulators, the surgeon’s hand movements are digitally registered through sensors, and then transferred to the robotic instrument cart. Two or three robotic instrument arms and a camera arm are mounted on this mobile cart. The articulating laparoscopic instruments provide 7 degrees of freedom. The Zeus robotic system consisted of a surgeon control console and three separate robotic arms attached to the sidebars of the
operating table; two arms held surgical instruments and the third arm was a voice-integrated control endoscope for visualization.

**Clinical applications in laparoscopic vascular procedures**

The first report on robot-assisted laparoscopic aortic surgery was published in 2002; Wisselink et al used the Zeus robotic system to construct the proximal aortic anastomosis of an aorto-bifemoral bypass from a console remote from the operating table in two patients with aorto-iliac occlusive disease [Wisselink W et al, 2002]. A systematic literature search identified nine studies reporting on robot-assisted laparoscopic surgery for infra-renal aortic pathologies [Wisselink W et al, 2002; Desgranges P et al, 2004; Killewich LA et al, 2004; Kolvenbach R et al, 2004; Nio D et al, 2005; Stádler P et al, 2006; Diks J et al, 2007; Stádler P et al, 2008; Stádler P, 2009]. These are either case reports or case series, and after excluding publications with duplicate cases, four papers reporting on a total of 162 patients were analyzed (Table 2.1.1).
Table 2.1.1 Case series of robotically assisted laparoscopic vascular procedures

<table>
<thead>
<tr>
<th>Author</th>
<th>Kolvenbach et al</th>
<th>Desgranges et al</th>
<th>Diks et al</th>
<th>Städl er et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>2003</td>
<td>2004</td>
<td>2007</td>
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<tr>
<td>Number of patients</td>
<td>10</td>
<td>5</td>
<td>17</td>
<td>130</td>
</tr>
<tr>
<td>Robot</td>
<td>Zeus</td>
<td>Da Vinci</td>
<td>Zeus 5</td>
<td>Da Vinci</td>
</tr>
<tr>
<td>Operation</td>
<td>10 AAA</td>
<td>5 AOD</td>
<td>17 AOD</td>
<td>115 AOD, 11 AAA, 2 CIAA, 2 other</td>
</tr>
<tr>
<td>Conversion (n)</td>
<td>2 (hand-assisted)</td>
<td>1 (open)</td>
<td>3 (open)</td>
<td>3 (mini or full laparotomy)</td>
</tr>
<tr>
<td>Reason for conversion</td>
<td>NR</td>
<td>external conflicts between robotic arms</td>
<td>1 technical (robot) 1 bleeding lumbars 1 difficult dissection</td>
<td>1 difficulty excluding CIAA 2 bleeding (lumbars, anastomosis)</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>242 (mean)</td>
<td>188 (mean)</td>
<td>365 (median)</td>
<td>215 (median)</td>
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<tr>
<td>Clamping time (min)</td>
<td>96 (mean)</td>
<td>75 (mean)</td>
<td>86 (median)</td>
<td>43 (median)</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>NR</td>
<td>540 (mean)</td>
<td>1000 (median)</td>
<td>380 (median)</td>
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<tr>
<td>Morbidity (number[cause])</td>
<td>1 [ARF]</td>
<td>1 [ischaemic colitis]</td>
<td>1 [bleeding from prosthesis]</td>
<td>3 [MRSA 1 incisional hernia, 1 graft occlusion]</td>
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<tr>
<td>Mortality (number[cause])</td>
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<td>None</td>
<td>1 [MI]</td>
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<tr>
<td>Hospital stay (days)</td>
<td>7 (mean)</td>
<td>8 (mean)</td>
<td>4 (median)</td>
<td>5 (median)</td>
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<td>Follow up (months)</td>
<td>NR</td>
<td>8 (mean)</td>
<td>18 (median)</td>
<td>NR</td>
</tr>
</tbody>
</table>

AOD, aorto-iliac occlusive disease; AAA, abdominal aortic aneurysm; CIAA, common iliac artery aneurysm; ARF, acute renal failure; MI, myocardial infarction; NR, not reported
The Zeus and da Vinci system were used to perform the aortic anastomosis in 15 and 147 cases respectively. Of the 162 procedures, 137 were performed for aorto-iliac occlusive disease, 21 for abdominal aortic aneurysms and 2 for common iliac artery aneurysm repair; the type of operation was not clarified in two cases. The conversion rate ranged from 3% to 20%, with technical problems related to the robotic system and bleeding from the lumbar arteries being the most common reasons for conversion. Morbidity rates ranged from 3% to 20%. One peri-operative death from myocardial infarction was described, resulting in an overall mortality rate of 0.6%. Only one comparative study of conventional laparoscopic and robot-assisted aortic surgery was identified, which demonstrated shorter anastomosis time in the robotic group, even though the total operating time was longer due to the technical complexity of the robotic device [Kolvenbach R et al, 2004].

Recent reports have extended the application of robotic technology beyond the construction of the aortic anastomosis. A technique of using robotic surgery as a sole modality for repair of an abdominal aortic aneurysm with sac exclusion and obliteration has been described [Wu T et al, 2009]. Furthermore, robotic devices have been used in other complex reconstructive arterial procedures such as renal and splenic artery aneurysm reconstructions [Luke P et al, 2006; Pietrabissa A et al, 2010]. A further step in the applicability of robotic surgery was undertaken to complement and enhance endovascular procedures. Robotic ligation of an inferior mesenteric artery for the treatment of a persistent type II endoleak after endovascular aneurysm repair has been reported [Lin JC et al, 2009]. Computer-assisted robotic technology has also been used as an adjunct to hybrid surgical debranching and endovascular repair of a TAAA aneurysm [Wahlgren CM et al, 2008].
Supporting evidence for the use of robotic systems in laparoscopic vascular surgery

Robotic instrumentation was initially evaluated in animal models with the implantation of infrarenal aortic grafts [Martinez BD et al, 2004]. The results obtained from this study showed that both da Vinci and Zeus robotic systems were effective in performing aortic anastomoses with the surgeon operating from a console away from the operating table. Another animal study investigated the hypothesis that robotic systems, with improved imaging and surgeon dexterity, might facilitate aortic laparoscopic procedures [Ruurda JP et al, 2004]. Comparison of the performance of robot-assisted and standard laparoscopic surgery revealed the superiority of the former, as evidenced by shorter procedure, suturing and clamping times, and less blood loss. The feasibility of robotic-assisted aortic anastomosis has also been tested in the thoracic aorta of animal models using the closed-chest technique [Tozzi P et al, 2003; Smith JM et al, 2005]. Of interest, the anastomosis time and haemostasis were found to be comparable between running suture techniques using the da Vinci system and interrupted nitinol clips.
2.2. Endovascular Robotics

Currently available endovascular robotic systems

Two main types of endovascular robotic systems have been developed, with different mechanisms of action: magnetically controlled systems such as the Niobe magnetic navigation system (Stereotaxis, USA) and electromechanical-based systems such as the Hansen Sensei robotic navigation system (Hansen Medical, USA).

Magnetically controlled Systems

The function of the Niobe remote-controlled magnetic navigation system is based on a magnetic field created by two computer-controlled 0.08T permanent magnets. Adjustment of the orientation and intensity of these magnets and subsequently the magnetic field, results in deflection of the catheter, which is equipped with magnetic implants in its tip. A computer-controlled catheter advancing system allows the operation to be remotely performed. This system can be used with 7-8 F diagnostic and ablation catheters with up to 120 degree bend radius. Use of the system also requires a dedicated 0.014 inch coronary guidewire (Stereotaxis). The wire contains a magnet embedded in its tip that allows the tip to be deflected by the surrounding magnetic field, and is advanced manually. It is not hydrophilic and does not have "memory." The stiffness of the wire is less than most commonly used guidewires. The Niobe system also requires refurbishment of the interventional laboratory to accommodate for the applied magnetic field.
A more recent robotic system to be developed using the same magnetic principal is the Maxwell Catheter Guidance, Control and Imaging system (Engineered Magnetics, Inc., California, USA), which uses eight electromagnets to guide a magnetically tipped catheter. These are fixed magnets that can vary the direction of the magnetic field. This system is not hindered by the lag time associated with rotation of the magnet and has a focused magnetic field.
The Hansen Sensei System controls a guide catheter via a “master-slave” electromechanical mechanism by digitally translating the hand motion of the operator. It allows visualization and positioning of the catheter tip at a desired point, while enabling the operator to remain seated at a remote workstation. This steerable catheter control system consists of three main components.

**The workstation**

The workstation is located remotely and away from the radiation source. It consists of the central computerized “master” input device, an Instinctive Motion Controller (IMC), a 3D hand-operated joystick, and screens that display imaging and force sensing data (Fig 2.2.1). This allows for the guide catheter to replicate the hand movement of the operator via the IMC joystick, delivering control in three dimensions, with seven degrees of freedom and visual force-sensing quantification as well as haptic feedback. The main fluoroscopic control view also displays a superimposed icon of the guide catheter with vectors for planar orientation and navigation.
Fig 2.2.1 The remote robotic workstation

The workstation is located remotely and away from the radiation source. It consists of the central computerized “master” input device, an Instinctive Motion Controller (IMC), a 3D hand-operated joystick, and screens that display imaging and force sensing data.
The remote catheter manipulator (RCM)

The RCM is located at the patients’ bedside and delivers the robotically steerable guide catheter (Artisan™, Hansen Medical). It receives catheter position commands from the “master” input device at the workstation, as issued by the IMC. The RCM is controlled via motors and tension wires that ultimately determine the position of the catheter tip. The RCM also has the ability to insert the entire Artisan forward and rotate it with a 270-degree bend radius (Fig 2.2.2).
Fig 2.2.2 The remote catheter manipulator

The RCM is located at the patients’ bedside and delivers the robotically steerable guide catheter. It receives catheter position commands from the “master” input device at the workstation, as issued by the IMC.
The robotic catheter

The Artisan robotic catheter consists of a flexible, multidirectional inner guide (11 F outer diameter, 8.5 F inner diameter) within a unidirectional outer guide sheath (14 F outer diameter, 11F inner diameter) (Fig 2.2.3). The inner guide has four embedded pull wires that deflect the catheter via internal sensors in a multidirectional fashion through tension controlled by the main console. The outer guide sheath provides stability and allows the entire system to rotate. This catheter system creates a workspace defined by a bend of up to 270 degrees with 10 cm extension of the inner guide. The steerable catheter in the current Hansen Sensei system may be directed over an independent wire, but does not depend on that wire to manoeuvre within the vasculature. A force quantification system (Intellisense™ Technology, Hansen Medical) has also been developed, and involves the introduction of an impedance force sensor through the Artisan catheter that allows constant measurements of catheter-tissue contact.
The Artisan robotic catheter consists of a flexible, multidirectional inner guide (11 F outer diameter, 8.5 F inner diameter) within a unidirectional outer guide sheath (14 F outer diameter, 11F inner diameter). This creates a workspace defined by a bend of up to 270 degrees with 10 cm extension of the inner guide.
Clinical applications in endovascular therapy

Remotely controlled steerable catheter navigation and vessel cannulation in the arterial tree is a novel approach in the field of endovascular arterial intervention.

*Supporting evidence for the use of robotic endovascular catheters in the arterial tree*

Experience with computerized robotically controlled catheter systems was initially obtained in *transvenous* cardiac mapping and ablation procedures for the treatment of cardiac arrhythmias. Early investigations in animal models demonstrated the feasibility and safety of navigation within cardiac chambers and facilitation of transseptal puncture; no intracardiac damage associated with catheter manipulation occurred [Saliba W et al, 2006]. In another animal study, an electromechanical robotic catheter system was evaluated for its ability to navigate within the heart and precision in ablation as compared with conventional ablation catheters [Al-Ahmad A et al, 2005]. This study demonstrated reduced navigation time and precision targeting associated with the use of the robotically controlled system. The transition from pre-clinical to clinical application of the Hansen Sensei robotic catheter system was associated with promising results. Preliminary experience of remote navigation for catheter ablation for the treatment of a variety of cardiac arrhythmias demonstrated its safety and clinical efficacy, as well as reduction in radiation exposure; the results were similar to conventional approaches for cardiac ablation [Kanagaratnam P et al, 2008; Saliba W et al, 2008, Di Biase L et al, 2009].
2.3. Conclusions

Robotic technology has the potential to enhance surgical intervention by extending human capabilities. Robotic systems can manipulate tools more accurately and steadily, by incorporating hardware and software filters, which eliminate physiological tremor. With remote manipulation, the comfort and ergonomics of the operator is significantly increased, with reduced fluoroscopic exposure for the operator in cases of x-ray guided interventions. These systems can also be integrated with more advanced 3-D imaging modalities with depth perception and adjustable magnification. The enhancement of laparoscopic vascular surgery with robotic systems has not been widely adopted by vascular communities and its role is not fully established. Experience is restricted to a few centres worldwide, which have demonstrated technical feasibility with satisfactory results. Comparative trials will be required to assess the true value of robotic laparoscopic surgery compared with conventional laparoscopic and open aortic surgery to be able to quantify the advantage of robotic technology and aid in justifying its cost.

Endovascular robotic technology in the arterial tree currently represents a virgin field of study. Some of the key advantages of laparoscopic robotic technology and its applications in vascular surgery may apply to complex endovascular intervention. The adoption of this advanced telemanipulation systems may enhance precision and dexterity in performing complex endovascular tasks and may be of value in overcoming the long learning curves associated with minimally invasive intervention.
Chapter 3.

Endovascular robotics for fenestrated stent grafting

3.1. Background

Advances in stent-graft technology have allowed the treatment of complex TAAA disease via a less invasive, totally endovascular approach. Fenestrated and branched stent grafting of aneurysmal juxta-renal and TAAA aortic segments and aneurysms that involve the supra-aortic vessels using custom-made stent grafts is an appealing concept, given the high morbidity associated with this condition and especially in patients unable to withstand the traditional surgical approach due to significant co-morbidities. The procedure is currently developing and gaining acceptance with encouraging short and intermediate-term results [Chuter TA et al, 2001; Verhoeven EL et al, 2004; Anderson JL et al, 2005; Sun Z et al, 2006; O’Neill S et al, 2006; Greenberg RK et al, 2006; Muhs BE et al, 2006; Roselli EE et al, 2007; Bicknell CD et al, 2009].

Despite an accurate custom-made device design, however, target vessel cannulation can be technically challenging and time consuming, especially in the presence complex anatomy including tortuous iliac arteries and an angulated visceral aortic
segment, with long fluoroscopic exposure times as a result. Conventional pre-shaped selective catheters have limited maneuverability, and require a high degree of finesse by the operator in order to safely position the catheter tip at the vessel ostia and maintain stability at target sites during passage of stiff wires and endovascular tools [Moore R et al, 2007; Bicknell et al, 2008] (Fig 3.1.1).

The purpose of this study was to investigate whether this complex endovascular procedure can be enhanced by a remotely steerable robotic endovascular catheter system, which may overcome some of the difficulties described above. The study compares robotic and conventional endovascular catheter techniques with respect to time, accuracy, and overall performance scores for target vessel cannulation within a pulsatile silicone phantom model.
Fig 3.1.1 Difficulties with conventional catheter manipulation

Bridging the gap between the fenestration/target vessel ostium interface with conventional endovascular catheters can be challenging. Often, the catheter passes through the fenestration, however, due to limited manoeuvrability and torquability it fails to engage the target vessel ostium from the aneurysm sac, with repeated cannulation attempts and long fluoroscopic times as a result. An intra-aortic molding balloon can be used to prevent upward angulation and subsequent displacement of the wire from the target vessel when a less flexible catheter is passed, and facilitate therefore introduction of guiding catheters in fenestrated stent-graft procedures. This technique however, can be utilized when the fenestration is remote from the top cap of the main aortic body device.
3.2. Methodology

Aortic model

A silicone-based, transparent, computed tomography (CT)-reconstructed anthropomorphic phantom representing a TAAA aneurysm was used (Elastrat Sàrl, Geneva, Switzerland). The aorta was dilated throughout its length (5.2 cm visceral segment diameter) with marked aneurysmal dilatation of the infra-renal segment (8.1 cm maximum diameter). This model was chosen as infra-renal fixation would not be achievable due to lack of landing zone proximally, necessitating repair with fenestrated stent grafting of the visceral and supra-renal segment. The phantom was filled with a blood-mimicking water-glycerol mixture (60:40 by volume concentration) and circulated using a pulsatile blood pump providing physiologically realistic blood-flow waveforms (Fig 3.2.1).
A silicone-based, transparent, computed tomography (CT)-reconstructed anthropomorphic phantom representing a TAAA aneurysm was used, 5.2 cm in diameter at the visceral segment diameter, with marked aneurysmal dilatation of the infra-renal segment (8.1 cm maximum diameter). The phantom was filled with a blood-mimicking water-glycerol mixture (60:40 by volume concentration) and circulated using a pulsatile blood pump providing physiologically realistic blood-flow waveforms. A four-vessel fenestrated stent graft was constructed and deployed in fixed suspension via strings with each fenestration aligned to the corresponding vessel ostia.
A four-vessel fenestrated stent graft was constructed from a standard thoracic graft (42 mm x 10 mm, Medtronic, Santa Rosa, CA). The stent graft was initially deployed over the visceral segment (52 mm in diameter) of the transparent phantom; each fenestration point was marked in a retrograde fashion from the corresponding target vessel. The stent-graft was then removed and four fenestrations reinforced with a Prolene suture and radio-opaque markers were constructed in the laboratory: three large (12 mm) fenestrations for the right renal, celiac, and superior mesenteric arteries and one small (8 mm) fenestration for the left renal artery. The endograft was subsequently redeployed in fixed suspension via strings to simulate the partial deployment of the Zenith platform. The strings were adjusted to prevent misalignment prior to each procedure.

Operators

Fifteen operators (eight vascular surgeons, seven interventional radiologists) of varying endovascular experience were recruited to participate in the study. They were divided into three groups, based on their endovascular procedure experience. Four operators had performed 100 to 200 endovascular procedures and had some experience in fenestrated stent grafting (<5); (Group A); five operators had performed 200 to 300 endovascular procedures and had moderate experience in fenestrated stent grafting (5-15); (Group B); whereas six operators had performed over 300 endovascular procedures and had good experience in fenestrated stent grafting (>15), carotid stenting, and branch vessel cannulation; (Group C).
Study protocol

Each operator was asked to cannulate all four vessels in the fenestrated stent-graft aneurysm model, namely the renal arteries, coeliac and superior mesenteric (SMA) arteries, under fluoroscopic guidance, using conventional and robotic techniques. A range of ten 4 F to 5 F selective catheters and appropriate endovascular guidewires commonly used in fenestrated stent grafting were available to all operators. The Hansen Sensei System (Hansen Medical, Mountain View, CA) was used for robotic catheterization. Operators were randomly assigned to conventional or robotic techniques as the first procedure undertaken. Passive intraprocedural support was provided by an assistant and a radiographer. Appropriate endovascular tools and a range of conventional catheters were selected when asked for, and C-arm orientation was changed when requested.

The study protocol included a didactic teaching session regarding the robotic system prior to use by each operator. All operators were familiarized with the robotic system following a short but standardized training protocol, involving cannulation of the left subclavian artery in an aortic arch pulsatile silicon phantom. All procedures were performed in the angiography suite and recorded for video assessment. For analysis, video footage was blinded, with sound removed, and randomly ordered, identified only by an internal coding system. Data from video footage were collected for quantitative and qualitative metric analysis.
DATA COLLECTION

Quantitative metrics

Total procedure times and times for inserting the catheter into each target vessel from the time point the catheter entered the distal end of the graft were measured in minutes using a stopwatch. Vessel cannulation was considered satisfactory when the catheter was seen in a stable position and at least 3 cm into the target vessel. For those operators that were unable to catheterize the vessel in this manner, the final time to catheterization of the vessel with a wire was recorded, but not included in the cannulation time results. The absolute number of translational (linear displacement along a trajectory path) and rotational (circular displacement around a center axis) movements at the wire/catheter tip was counted in a binary fashion by two observers (C.R, C.B) using blinded-video recordings displaying 2-dimensional fluoroscopic data.

Qualitative metrics

Performance evaluation was carried out using procedure-specific scoring for vessel cannulation, on a 5-point scale: the Imperial College Complex Cannulation Scoring Tool (IC3ST), developed specifically for use in these experimental studies. The domains tested are specific to vessel cannulation but also rate the procedure as a whole and it is derived from the generic Objective Structured Assessment of Technical Skills (OSATS) scale validated by the University of Toronto Centre for Research in Education [Martin JA et al, 1997; Reznick R et al, 1997]. The IC3ST
scale was developed based on the established OSATS scale and previously validated and reliable procedure-specific scoring systems used in endovascular skills assessment [Hislop SJ et al, 2006; Van Herzeele I et al, 2008; Tedesco MM et al, 2008; Van Herzeele I et al, 2009] and other medical domains [Friedman Z et al, 2006; Aggarwal R et al, 2008].

The scale consists of seven domains with each attributed a score of 1 to 5, with 1 representing a poor performance, 3 representing a competent performance, and 5 representing an excellent performance. Descriptive comments for each technical domain are given at each of these anchoring points. It grades operators on catheter use and manipulation skills, instrumentation, embolization/dissection risk, successful vessel cannulation, and overall time, motion, and flow of the procedure. The minimum score for technical performance is 7. A score of 21 suggests competence and 35 is the maximum attainable score; the higher the score, the better the quality of performance. The marking sheet is shown in Fig 3.2.2. Qualitative performance rating was carried out by two blinded assessors (C.R and C.B) experienced in the use of rating scales.

Statistical analysis

Data were analyzed with the Statistical Package for the Social Sciences version 16.0 (SPSS, Chicago, Ill) using non-parametric tests. Differences between conventional and robotic vessel cannulation were compared using the Wilcoxon signed-rank test for related samples. Differences between operator groups based on endovascular experience using the IC3ST scoring scale (Groups A, B, and C) were assessed using
the Kruskal-Wallis test. A p value of less than 0.05 was considered to be statistically significant. Inter-observer reliability for blinded assessors was evaluated by determining a value for Cronbach’s alpha. It is suggested that for research purposes, a reliability coefficient of 0.6 to 0.8 is sufficient, and for a high-stakes assessment, this coefficient should be 0.8. The Spearman's rank test was used to correlate quantitative metrics (time, movements) with qualitative metrics (operator performance).
Fig 3.2.2 The Imperial College Complex Cannulation Scoring Tool (IC3ST)

The Imperial College Complex Endovascular Cannulation Scoring Tool (IC3ST)

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannulation</td>
<td>Inappropriate use of catheters, failure to change position (catheter unsuitability)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Improper catheter use initially, but recognized and rectified prior to successful return of equipment</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Correct catheter use with useful advantage</td>
<td>5</td>
</tr>
<tr>
<td>Wire &amp; catheter manipulation</td>
<td>Incorrect &amp; unsuccessful</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Multiple catheter tip drag on vessel wall</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Insufficient wire control</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>High degree of force</td>
<td>5</td>
</tr>
<tr>
<td>Contact with the vessel wall/vascular trauma &amp; dissection</td>
<td>Excessive force and multiple engagements of the catheter tip, dragging on vessel wall</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Scoring contact with the vessel wall and manipulation</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Minimal contact with the vessel wall, correct placement of wire and catheter</td>
<td>5</td>
</tr>
<tr>
<td>Areas of significant embolic potential</td>
<td>Scoring contact with areas of danger, embolization risk HIGH</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Recognition of potential areas of danger, embolization risk MODERATE</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Full awareness of areas of danger, embolization risk LOW</td>
<td>4</td>
</tr>
<tr>
<td>Vessel cannulation</td>
<td>Failure to control and maintain position, loss into the target vessel</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Successful wire control, no instability of the catheter, follow</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Successful cannulation with wire, guide catheter</td>
<td>5</td>
</tr>
<tr>
<td>Overall time &amp; motion</td>
<td>Slow, makes unnecessary movements</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Efficiently, score necessary movements</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Maximum efficiency, no unnecessary movement</td>
<td>5</td>
</tr>
<tr>
<td>Flow of procedure</td>
<td>One step, frequency, or need to discard the next step</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Two steps, error in understanding</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Error in planning, error in efficiency</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Successful planning, due to efficiency</td>
<td>5</td>
</tr>
<tr>
<td>General Score</td>
<td>Poor</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Competent</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Clearly superior</td>
<td>5</td>
</tr>
</tbody>
</table>

The minimum score for technical performance is 7, and 35 is the maximum attainable score. Operators were assessed on their ability to choose an appropriate catheter, the ability to recognize catheter unsuitability, use of their chosen catheter to its maximum advantage, and the ability to shape and torque the selected catheter with fine and controlled movements, as shown on the IC3ST scoring sheet. Embolization/dissection risk was assessed when looking at excessive force and multiple catheter tip dragings along the vessel wall and manipulation of the guiding catheter without the support of a guide wire, especially in areas of embolic potential, such as the ostia of the target vessels.
3.3. Results

3.3.1 Quantitative

*Whole procedure times:* For the whole procedure, median procedure time for cannulation of all four vessels was reduced using the robotic system [2.87 min (IQR; 2.20-3.90) versus 17.24 min (11.90-19.80); \( p < 0.001; \) Fig 3.3.1a]. These reductions were observed for each individual operator regardless of the level of endovascular experience (Fig 3.3.1b).

* Movements: * The total number of catheter tip movements for the whole procedure was also significantly reduced [38 IQR (29-57) versus 454 (283-687); \( p < 0.001; \) Fig 3.3.2a]. Again, reductions in overall procedure movements were observed for each individual operator (Fig 3.3.2b), regardless of the level of endovascular experience, with a high degree of inter-observer reliability (Cronbach’s \( \alpha = 0.94 \)).
**Fig 3.3.1 Whole procedure times**

**a.** Bar chart representing whole procedure time (minutes) with conventional versus robotic catheters. Median procedure times are shown on the y-axis. The error bars represent the interquartile ranges (Wilcoxon signed rank test). **b.** Line chart illustration of the data above showing reductions in median procedure time with the robotic system versus conventional techniques, for each individual operator. Each operator is represented as a marker on either side of the plot area.
Fig 3.3.2 Whole procedure movements

a. Bar chart representing whole procedure movements at the wire/catheter tip with conventional versus robotic catheters. Median number of movements is shown on the y-axis. The error bars represent the interquartile ranges (Wilcoxon signed rank test). b. Line chart illustration of the data above showing reductions in median number of wire/catheter movements with the robotic system versus conventional techniques, for each individual operator. Each operator is represented as a marker on either side of the plot area.
**Individual target vessel cannulation times:** The median times for catheterization of target vessels were 0.36 min IQR (0.20-0.60) for the left renal artery with robotic cannulation versus 7.13 min (2.50-8.00) using conventional catheters, 0.79 min (0.70-1.00) versus 2.76 min (1.90-3.90) for the right renal artery, 1.00 min (0.70-1.30) versus 2.26 min (1.30-3.30) for the coeliac artery, and 0.44 min (0.30-0.80) versus 2.06 min (0.98-6.40) for the SMA (Fig 3.3.3). All differences between conventional and robotic techniques were statistically significant (p < 0.001; Fig 3.3.4).

**Individual target vessel movements:** We observed a reduction in the median number of movements at the wire/catheter tip taken to complete individual target vessel cannulation using the robotic catheter: 5 IQR (3.5-8.5) versus 155 (57-292) for the left renal, 10 (7-18) versus 84 (47.5-152) for the right renal artery, 14 (6.5-21.5) versus 62 (35-100) for the coeliac artery, and 8 (7-14) versus 47 (36-134.5) for the SMA. All differences between conventional and robotic techniques were statistically significant (p < 0.001, Cronbach’s α 0.94; Fig 3.3.5).
Fluoroscopic images showing successful cannulation of the renal, SMA and celiac arteries using the robotic catheter system.
Fig 3.3.4 Target vessel cannulation times

Bar chart representing median individual target vessel cannulation times with conventional versus robotic catheters. The error bars represent the interquartile ranges (Wilcoxon signed rank test).

Fig 3.3.5 Individual target vessel cannulation movements

Bar chart representing the median number of wire/catheter tip movements for individual target vessel cannulation with conventional versus robotic catheters. The error bars represent the interquartile ranges (Wilcoxon signed rank test).
3.3.2 Qualitative

Validation of the IC3ST Scale

*Construct validity:* The IC3ST rating scale successfully differentiated between low (Group A: 100–200 endovascular procedures with some experience in fenestrated stent grafting, n = 4) and high (Group C: over 300 endovascular procedures with good experience in fenestrated stent grafting, carotid stenting, and branch vessel cannulation, n = 6) volume intervention groups of endovascular specialists. There were significant differences in performance with conventional vessel cannulation techniques between operator groups A and C: IC3ST score 15/35 versus 23/35, respectively, p = 0.04; Kruskal-Wallis test). There were no differences between groups using robotic techniques, demonstrating good construct validity of the IC3ST scale.

*Correlation between qualitative and quantitative metrics:* IC3ST scores showed inverse correlations with quantitative metrics (time and movements) for all variables but movements with robotic cannulation (Spearman's rank test r) (Table 3.3.1, Fig 3.3.6).
Table 3.3.1

<table>
<thead>
<tr>
<th>IC3ST Score</th>
<th>CORRELATIONS</th>
<th>Time (min)</th>
<th>Mvmts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional</td>
<td>( r )</td>
<td>-0.73</td>
<td>-0.62</td>
</tr>
<tr>
<td>( p ) value</td>
<td>0.002</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Robotic</td>
<td>( r )</td>
<td>-0.75</td>
<td>-0.42</td>
</tr>
<tr>
<td>( p ) value</td>
<td>0.001</td>
<td>0.12</td>
<td></td>
</tr>
</tbody>
</table>

Fig 3.3.6 Correlations between quantitative and qualitative metrics

IC3ST scores showed inverse correlations with quantitative metrics (time and movements) for all variables but movements with robotic cannulation (Spearman's rank test \( r \)).
Operator performance

Overall performance scores were significantly improved using the robotic system, despite minimal operator exposure to this technology [IC3ST score 29/35 IQR (22.8-30.7) versus 19/35 (13-24.3); p = 0.002, Cronbach’s α 0.85]. IC3ST scores ranged from 8 to 29 (maximum, 35) for conventional techniques, with 7 (47%) of the 15 operators displaying competent performance on this model (Fig 3.3.7). Using the robotic system, the IC3ST scores ranged from 19 to 34, with 14 (93%) of the 15 operators achieving competency, of which 10 (71%) demonstrated performance of a very high standard.
Fig 3.3.7 Overall operator performance

Line chart representing individual operator performance scores on the IC3ST scale with conventional and robotic cannulation techniques (Wilcoxon signed rank test). Each operator is represented as a marker on either side of the plot area.
Each group of operators with varying endovascular experience demonstrated an improvement in performance with robotic cannulation. For group A, median IC3ST score was 28/35 IQR (22-33) versus 15/35 (11-20); \( p = 0.04 \); for group B (200-300 endovascular procedures with moderate experience in fenestrated stent grafting, \( n = 5 \) ), median IC3ST score was 30/35 (27-31) versus 19/35(18-24); \( p = 0.07 \); and for group C, median IC3ST score was 28.8/35 (28.5-29) versus 22/35 (16-24); \( p = 0.06 \) (Fig 3.3.8). For groups B and C, these differences did not reach statistical significance using non-parametric test analysis for related samples (Wilcoxon signed-rank test). One operator in Group B scored 23/35 with robotic cannulation and 29/35 with conventional catheters, and one operator in the experienced group C showed no change in performance between the two techniques (IC3ST score of 29/35 for both conventional and robotic cannulation). All other operators improved their score using the robotic technique.
Fig 3.3.8 Performance scores according to endovascular experience

Bar chart representing operator performance scores between Groups A, B, and C using conventional and robotic techniques (Wilcoxon signed rank test).
3.4. Discussion

As endovascular procedures for the treatment of aortic disease develop and increase in complexity, there is a need to improve technical success, reduce procedure times, and minimize fluoroscopic exposure. Fenestrated and branched stent grafts were designed to extend the proximal sealing zone from the infrarenal segment to the suprarenal and thoraco-abdominal aorta by incorporating the visceral branches.

In recent years, there have been tremendous advancements in the development and technology of these devices, with results that compare favorably with those of open surgery. Successful results, however, require careful patient selection, appropriate custom-made device design, and technical expertise with endovascular grafting, as well as visceral vessel cannulation and stenting. The implantation procedure can be technically challenging even for experienced operators, especially in the presence of difficult anatomy. Vessel tortuosity can cause significant problems with catheter control and manipulation, while the presence of thrombus and calcification may lead to embolization or dissection with prolonged attempts at target vessel cannulation. Graft rotation and misalignment of fenestrations with vessel ostia, due to angulation of the more proximal aortic segment, may further prevent easy and safe target vessel cannulation. Long fluoroscopic times and radiation exposure to both patients and operators are also important concerns.

The success of tackling these adverse effects are largely dependent upon the skill and expertise of the operator using manually controlled conventional endovascular catheters that may be limited in their maneuverability and torqueability. Remotely
steerable robotic endovascular catheters technology may minimize some of these challenges by reducing the manual skill required and improving precision and stability while potentially reducing the operator’s learning curves.

In this study, robotic cannulation in a pulsatile aneurysm model was significantly faster than standard cannulation using conventional endovascular catheters for all target vessels. The number of movements at the catheter tip required to complete each task was also significantly reduced. This is likely a result of a greater range of motion with the robotic catheter and increased three-dimensional control of the catheter tip with seven degrees of freedom. With conventional catheters, the operator needs to make a series of movements that require adjusting the amount of manual torque in order to reach a given target. Some advocate, that during fenestrated endografting, the superior mesentery and coeliac arteries are more easily catheterized via a brachial approach. In this study, the femoral approach was used successfully in all catheterizations. Clearly, the current size of the robotic catheter would not be suitable for a brachial approach; however, the improved maneuverability and stability of the device may allow cannulation of visceral vessels through femoral access.

A limitation of other robotic and remote catheter control systems is the lack of mechanical feedback that the operator receives from manual catheter manipulation, and hence the ability to assess the amount of force that is being applied to the target tissues. With the Da Vinci robotic system in laparoscopic surgery, the operator is able to assess tissue deformation through direct visualization. One possible method of overcoming this in an endovascular setting reliant on fluoroscopic views is Intellisense Fine Force Technology incorporated within the Hansen robotic system,
which allows for visual and haptic feedback of the force applied to the catheter tip, thereby improving the safety of the device. Another limitation of the Hansen system is that it requires access via a 14 F sheath. If a four-vessel fenestrated stent graft procedure was to be undertaken via the femoral approach, four 7 F guide-sheaths would have to be inserted via a single common femoral artery. At present, simultaneous access to all four vessels can only be achieved by placing stiff guidewires using the robotic catheter and then subsequently placing guiding sheaths via the conventional approach. Further development of the robotic system is certainly mandated for optimal use in endovascular therapy.

Other factors such as operator and staff training, set-up times, overall cost, and system maintenance should also be taken into consideration. Set-up times in this study varied from 5 minutes to 15 minutes on average for each procedure. This can be seen as a drawback if one considers the set-up times for conventional catheters to be negligible; however, the potential advantage of faster target vessel cannulation and stability at sites of interest while accommodating other endovascular catheters, stiff wires, and side-branch stents may reduce procedure times as a whole, despite longer set-up times. The adoption of this new technology would certainly be more widespread if it can be shown to reduce procedure times, without significant increase in cost. An analysis regarding the cost-effectiveness of this system is beyond the remit of this thesis; cost can only be balanced out if this device is shown to reduce procedure times and improve accuracy in complex endovascular procedures such as fenestrated stent grafting in large patient series within a clinical setting.

Overall IC3ST performance scores were significantly improved using the robotic
system, and the majority of subjects demonstrated performance of a high standard, despite minimal exposure to this novel technology, demonstrating ease of use and its intuitive nature. Subgroup analysis revealed that, for the less experienced group A, performance scores were significantly improved with robotic cannulation. For groups B and C, these differences did not reach statistical significance using non-parametric test analysis for related samples (Wilcoxon signed-rank test), and this is not surprising, as, with any new device, there is a learning curve to its use. This may also be attributed to the relatively small sample size of the three groups. It is worth noting, however, that for highly experienced interventionalists (group C), IC3ST scores were high for conventional cannulation, and similar scores were attained using the robotic system even with short training times. Experienced operators may attain even higher scores with further training on the robotic system. The less experienced groups reached the same high standard as group C operators using robotic technology, which may impact on training and learning curves in the future.

One of the most obvious advantages of a remote-controlled catheter system is the negligible fluoroscopy exposure for the operator, as the workstation is located in the control room of the angiography suite and away from the radiation source. Although this study does not allow for a direct representation of the potential for this technology to reduce radiation exposure to patients, one can foresee the effect on patient exposure resulting from overall reduction in fluoroscopic times. The Hansen system is also compatible with existing non-fluoroscopic mapping systems such as CARTO (Biosense Webster Inc, Diamond Bar, CA) and NavX (St. Jude Medical, St. Paul, MIN). Enhanced integration of robotics with 3D navigation technology may further improve the accuracy of catheter positioning and manipulation that is of
paramount importance in fenestrated stent grafting. In addition, use of this system may limit the fatigue associated with prolonged complex endovascular procedures, as the operator can remain seated at the remote workstation, and thus further enhance operator performance.

This study is limited by the use of an in vitro pulsatile silicon phantom and does not totally reflect the challenges of navigating within the human aorta in a clinical setting. To explore this further, we have initiated a trial, approved by our Institution and the Regional Ethics Committee, to assess the feasibility of using this robotic technology in vivo and determine its safety and performance in clinical cases of fenestrated stent grafting.
3.5. Conclusions

These results demonstrate that robotic catheterization of target vessels during fenestrated stent grafting in a pulsatile flow model is feasible with negligible radiation exposure for the operator. Vessel cannulation times are reduced using robotic technology with significant reduction in the number of movements compared with conventional cannulation techniques. Steerable robotic catheters with intuitive control may overcome some of the limitations of standard catheter technology in the human vascular tree, enhance target vessel cannulation, reduce instrumentation, and improve overall performance scores. Further studies into the use of this technology in a clinical setting will be important in evaluating this system for use in complex endovascular procedures.
Chapter 4.

Endovascular robotics for arch vessel cannulation

4.1. Background

One of the major concerns of advanced endovascular carotid intervention as seen in carotid artery stenting (CAS) has been the potential to produce embolic particles that may manifest as neurologic deficits [DeMonte F et al, 1989; Ohki T et al, 1998; McPhee J et al, 2009]. Stroke resulting from cannulation of the great vessels during CAS cannot be prevented by current protection systems. In an analysis of 627 protected CAS procedures, Verzini et al documented 10 major strokes and 1 cardiac death; 4 major strokes occurred during the cannulation phase involving the arch vessel origin or the common carotid artery (CCA) itself [Verzini F et al, 2006]. There is considerable evidence, both experimental and clinical with Transcranial Doppler (TCD) and diffusion-weighted magnetic resonance imaging (DW-MRI), that microembolization during CAS takes place throughout all stages of the procedure [Coggia M et al, 2000; Bicknell CD et al, 2003; Blasel S et al, 2009; Vos JA et al, 2009; Bonati LH et al, 2010]. The excess risk of peri-procedural neurological complications observed during advanced endovascular intervention in the arch seems to be multifactorial: poor patient selection, carotid plaque morphology, tortuosity,
angulation and complex aortic arch anatomy (bovine or Type III arch variants), device technology and operator experience, all play an important role.

In order to improve clinical outcomes by reducing cerebral embolization rates and hence the risk of stroke, the above factors must be targeted. In recent years, improved patient selection and increased operator experience have facilitated complex intervention in the arch. Further technical refinements, however, may also be essential. Efficient stable sheath placement in the CCA is a crucial determinant of technical success, to avoid significant embolization from the aortic arch and the CCA as well as ensure a stable platform for introduction of endovascular tools into the internal carotid artery (ICA). The purpose of this study was to investigate whether arch vessel cannulation can be enhanced by a remotely-steerable robotic catheter system. The study compared robotic and conventional catheters with respect to time and accuracy of vessel cannulation, potential risk of embolization and overall operator performance using pulsatile silicone phantoms.
4.2. Methodology

**Aortic Arch models**

There are three types of aortic arches, based on the relationship of the innominate artery to the arch itself [Casserly IP et al, 2005; Bates ER et al, 2007]. The type I aortic arch is characterized by the origin of all 3 great vessels being in the same horizontal plane as the outer curvature of the aortic arch (Fig 4.2.1a). In the type II aortic arch, the innominate artery originates between the horizontal plane of the outer and inner curvatures of the arch. In the type III aortic arch, the innominate artery originates below the horizontal plane of the inner curvature of the arch (Fig 4.2.1b). The more inferior the origin of the target artery (i.e. type II or III aortic arch), the greater the difficulty in gaining access to the carotid artery with a higher the risk of distal embolization or dissection [Balzer JO, 2008].
Fig 4.2.1 Type I (A) and Type III (B) aortic arches

A: a type I arch is characterized by the origin of all 3 great vessels being in the same horizontal plane as the outer curvature of the aortic arch. B: a type III aortic arch, with the innominate artery originating below the horizontal plane of the inner curvature of the arch.
In addition to the type of arch, the configuration of the great vessels is also important. In the standard anatomical configuration, the innominate artery, the left CCA, and the left subclavian artery have separate origins from the arch. Two common anomalies are encountered in clinical practice, both of which have been termed ‘bovine arches’. The first variant involves a common origin to the innominate artery and the left CCA. The second common anomaly involves the left CCA arising as a branch of the innominate artery. Both of these variants can also cause access difficulties.

To assess the efficacy of robotic arch vessel cannulation, two silicone-based, transparent, CT-reconstructed anthropomorphic phantoms (Elastrat Sàrl, Geneva, Switzerland) were used representing:

a) A Type I aortic arch with bovine configuration of the left CCA
b) A Type III aortic arch

The phantoms were filled with a blood-mimicking water-glycerol mixture (60:40 by volume concentration) and circulated using a pulsatile blood pump providing physiologically realistic blood-flow waveforms (Fig 4.2.2). Arch vessel calibre varied between 6mm and 7 mm in diameter.
Fluoroscopic images of the two silicone-based, transparent, CT-reconstructed anthropomorphic phantoms representing the Type I and Type III aortic arches are shown. The phantoms were filled with a blood-mimicking water-glycerol mixture (60:40 by volume concentration) and circulated using a pulsatile blood pump providing physiologically realistic blood-flow waveforms.
Operators

Seventeen operators (nine vascular surgeons, seven interventional radiologists, one cardiologist) of varying endovascular experience were recruited to participate in the study. They were divided into three groups, according to their endovascular experience. Five operators had performed less than a 100 endovascular procedures and had minimal experience with CAS (0-2); (Group A), six operators had performed 100 - 300 endovascular procedures and had some experience with CAS (2-5); (Group B), whereas six operators had performed over 300 endovascular procedures and had moderate to extensive experience with CAS (5-70); (Group C).
Study protocol

Each operator was asked to cannulate the left subclavian (LSA), left common carotid (LCCA), right subclavian (RSA) and right common carotid (RCCA) arteries of the arch phantom, under fluoroscopic guidance, using conventional and robotic (Hansen Sensei) techniques. Operators were randomly assigned to conventional and robotic techniques, as well as the type of arch used as the first procedure undertaken. All operators underwent a short, standardized didactic teaching session on the robotic system before commencing the study followed by a practical demonstration and training session. Passive intra-procedural support was provided by an assistant and a radiographer. Appropriate endovascular tools, including wires and a range of ten conventional 4 F to 5 F shaped catheters commonly used in CAS were available and C-arm orientation was adjusted as requested by the operator. All procedures were performed in the angiography suite and recorded for blinded video assessment of quantitative and qualitative metrics.
DATA COLLECTION

Quantitative metrics

Ease of vessel cannulation - time and accuracy

Arch vessel cannulation times from the point the catheter entered the distal part of the descending aorta was measured in minutes using a stopwatch. Vessel cannulation was considered satisfactory when the catheter followed the wire at least 3 cm into the target vessel. For those operators that were unable to catheterize the vessel in this manner the end time to successful access to the vessel with a wire was recorded with a wire was recorded, but not included in the cannulation time results. The absolute number of translational (linear displacement along a trajectory path) and rotational (circular displacement around a center axis) movements at the wire/catheter tip was counted in a binary fashion by two observers (C.R and C.B) using blinded-video recordings displaying 2-dimensional fluoroscopic data.

Embolization risk

The number of times the catheter tip came into contact with the vessel wall (wall hits) at the ostium of the common carotid artery (CCA) and at the aortic arch from the aortic valve to the LCCA origin was also counted in a binary fashion by two observers (C.R and C.B) using blinded-video recordings displaying 2-dimensional fluoroscopic data displaying the outline of the aortic arch and the target vessels.
Qualitative metrics

Operator experience and performance

Performance evaluation was carried out using the IC3ST scale described in the last chapter (Chapter 3). Qualitative performance rating was carried out by two blinded assessors (C.R and C.B).

Statistical analysis

The Statistical Package for the Social Sciences version 16.0 (SPSS, Chicago, Ill., USA) was used for data analysis. The non-parametric distribution of the data necessitated the use of non-parametric tests for significance. Differences between conventional and robotic arch vessel cannulation were compared using the Wilcoxon signed-rank test for related samples.

Differences between operator groups based on endovascular experience using the IC3ST scoring scale (Groups A, B and C) were assessed using the Kruskal-Wallis test and post-hoc analysis with Mann-Whitney U test. The Spearman's rank test was used to correlate quantitative metrics (time, movements, wall hits) with qualitative metrics (operator performance). A p value of p < 0.05 was considered statistically significant. Inter-observer reliability for the blinded assessors was calculated with the Cronbach's alpha test statistic.
4.3. Results

4.3.1 Quantitative

Ease of vessel cannulation - time and accuracy

Arch vessel cannulation times (Fig 4.3.1) - 2/17 operators failed to cannulate the RCCA in the Type III arch using conventional catheters in a satisfactory manner as described in the methods section i.e. with the catheter following the wire at least 3 cm into the target vessel in a stable position. For the remaining 15 subjects median times for cannulation of the carotid arteries were significantly reduced using the robotic catheter system for both types of arches: Type I arch: LCCA 2.70min IQR (1.92-3.98) versus 0.80min IQR(0.30 -1.57) p=0.001, RCCA 1.70min (1.20-3.35) versus 0.69min (0.44-0.99) P=0.001; Type III arch: LCCA 3.78min (0.92-11.28) versus 1.02min (0.61-2.10) p=0.01, RCCA 6.2min (3.02-8.97) versus 1.81min (0.67-3.02) p=0.001. The median cannulation times for the LSA in the Type I arch were also significantly reduced LSA 0.76min (0.34-0.88) versus 0.25min (0.18-0.31) p=0.002.

Movements (Fig 4.3.2) - The median number of catheter tip movements for individual arch vessel cannulation was significantly reduced for all vessels with robotic catheterization techniques for both Type I and Type III arches: Type I arch: LSA 18 (14-31) versus 7 (6-10) p=0.001, LCCA 61 (51-165) versus 9 (7-25) p=0.001, RSA 22 (15-48) versus 11 (8-15) p=0.005, RCCA 48 (21-81) versus 9 (6-10) p=0.001; Type III arch: LSA 24 (17-38) versus 7 (6-11) p=0.001, LCCA 89 (45-284) versus 14
(12-21) p=0.001, RSA 69 (48-81) versus 31 (16-42) p=0.003, RCCA 209 (124-335) versus 30 (9-38) p=0.001. Inter-observer reliability between observers was calculated: Cronbach’s $\alpha$ =0.85, indicating a good degree of agreement.
Fig 4.3.1 Arch vessel cannulation times

Bar chart representing median individual arch vessel cannulation times with conventional versus robotic catheters, in the Type I (first two bars from left to right) and Type III (last two bars from left to right) arches. The error bars represent the interquartile ranges (Wilcoxon signed rank test).
Fig 4.3.2 Catheter movements in the arch model

Bar chart representing median number of movements for each individual arch vessel cannulation with conventional versus robotic catheters, in the Type I (first two bars from left to right) and Type III (last two bars from left to right) arches. The error bars represent the interquartile ranges (Wilcoxon signed rank test).
Embolization risk

Wall Hits (Fig 4.3.3) - Vessel wall contact with the aortic arch wall was reduced to a median of zero with robotic catheterizations. CCA ostium contact still took place, but was significantly reduced. Median catheter tip vessel wall hits were: Type I Arch: 2 IQR (1.5 – 13) versus 0(0-0); p=0.001 for the aortic arch and 4.5 (3.5 – 11.3) versus 2 (1.5 - 3.5); p=0.001 for the CCA origin, and Type III Arch: 13.8 (9.5 -19) versus 0.5 (0.3 – 1.5); p=0.001 for the aortic arch and 9 (5 -21.5) versus 5 (4 -9); p=0.04 for the CCA origin (inter-observer reliability: Cronbach’s α 0.82).
Fig 4.3.3 Wall hits during arch vessel cannulation

Bar chart representing median number of wall hits during carotid artery cannulations in the aortic arch proximal to the CCA and at the carotid ostium, with conventional versus robotic catheters, in the Type I (first two bars from left to right) and Type III (last two bars from left to right) arches. The error bars represent the interquartile ranges (Wilcoxon signed rank test).
4.3.2 Qualitative

The IC3ST rating scale successfully differentiated between low (Group A) and high (Group C) volume intervention groups of endovascular specialists in the Type I arch (IC3ST score 20/35 IQR (16 -28) versus 30.9/35 (27.6 -32.5) respectively; Mann-Whitney U test, p= 0.02), and between all three groups in the more technically challenging Type III arch (IC3ST score Group A: 14.5/35 (13 -16.5), Group B: 19.3/35 (16.9 – 22), Group C: 26.8/35 (25 -29.6); Kruskal-Wallis test, p=0.03). There were no differences between groups using the robotic system (inter-observer reliability: Cronbach’s α 0.94).

**Correlation between qualitative and quantitative metrics:** IC3ST scores showed inverse correlations with many of the quantitative metrics (times, movements, wall hits) (Spearman's rank test r) (Table 4.3.1, Fig 4.3.4).

<table>
<thead>
<tr>
<th>IC3ST Score</th>
<th>CORRELATIONS</th>
<th>Time (min)</th>
<th>Movmts</th>
<th>Wall Hits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional Type I Arch</td>
<td>r</td>
<td>-0.67</td>
<td>-0.57</td>
<td>-0.75</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>&lt;0.01</td>
<td>0.02</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Robotic Type I Arch</td>
<td>r</td>
<td>0.49</td>
<td>0.17</td>
<td>-0.59</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>0.04</td>
<td>0.52</td>
<td>0.01</td>
</tr>
<tr>
<td>Conventional Type III Arch</td>
<td>r</td>
<td>-0.63</td>
<td>-0.48</td>
<td>-0.85</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>&lt;0.01</td>
<td>0.04</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Robotic Type III Arch</td>
<td>r</td>
<td>-0.50</td>
<td>0.13</td>
<td>-0.49</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>0.04</td>
<td>0.63</td>
<td>0.04</td>
</tr>
</tbody>
</table>
IC3ST scores showed inverse correlations with many of the quantitative metrics (times, movements, wall hits) (Spearman's rank test r).
Operator performance

Overall performance scores were significantly improved using the robotic system:

*Type I Arch:* IC3ST score 26/35 IQR (20 -30.8) versus 33/35 (31 -34); p=0.001. 88.2% (15/17) of operators improved their scores using the robotic catheter system. With conventional cannulation, IC3ST scores ranged from 10 to 34, with 76.5% (13/17) of operators demonstrating competence in this model. Robotic cannulation scores ranged from 29 to 34.5, with all 17 operators achieving high-standard performance scores.

*Type III Arch:* IC3ST score 20.5/35 IQR (16.5-28.5) versus 26.5/35 (23.5 -28.8); p=0.001. 70.6% (12/17) of operators improved their scores using the robotic catheter system. Scores ranged from 12.5 to 34 with conventional techniques, and a mere 47% (8/17) of operators (8/17) demonstrated competence in the angulated aortic arch, whereas with robotic techniques, IC3ST scores ranged from 17 to 30, and 82.4% of the operators attained performance scores at the high-end of the IC3ST scale.

Low and medium volume interventionalists (Groups A and B) demonstrated an improvement in performance with robotic cannulation techniques. In the high volume intervention group (Group C), there was no statistically significant improvement in performance; however, all operators obtained high scores irrespective of the cannulation method used and completed the task faster, with fewer movements and wall hits using the robotic system. Operator performance results are shown in Figures 4.3.5 and 4.3.6.
Fig 4.3.5 Performance scores in the Type I Arch

Bar charts representing operator performance IC3ST scores in the Type I and Type III arches respectively between Groups A, B, and C using conventional and robotic techniques (Kruskal-Wallis and Wilcoxon signed rank tests). The line chart in the top right corner of each graph represents individual operator performance scores; each operator is represented as a marker on either side of the plot area.
4.4. Discussion

Accurate navigation through the aortic arch and stability of the wires and catheters during the procedure is of vital importance to reduce cerebral embolization and risk of stroke. Endovascular robotic technology may provide a useful adjunct to overcome some of the challenges of complex endovascular intervention in this setting. This chapter investigates whether use of a robotic catheter system can enhance the technical skill required in cannulation of the great vessels in complex arch anatomy, improve positional precision and stability, as well as operator performance.

Complex anatomy

Severe atherosclerosis of the aortic arch, tortuosity and extreme angulation of the great vessels (Type III arch) may prohibit straightforward catheterization, compromising catheter stability and the safety of the procedure, as highlighted in the Delphi Consensus statement [Macdonald S et al, 2009]. A very acute angle of the origin of the CCA off the aortic arch may result in unsuccessful vascular access, technical errors and overall technical failure. Vascular access may be even more challenging with bovine arch variants potentially exposing the patient to longer catheter manipulation and therefore potentially higher risk of embolization. The association between aortic arch anomalies and procedural risk has been explored in 214 consecutive patients; technical failure was higher and neurological complications occurred more frequently in the arch anomaly group (20% versus 5.3%, p=0.039); the type of aortic arch was the only variable independently associated with neurological complications (odds ratio=2.01, p=0.026) [Faggioli G et al, 2007]. In our study,
robotic cannulation of the CCAs was significantly faster than standard cannulation using conventional endovascular catheters. The number of movements at the catheter tip as well as the median catheter tip vessel wall hits were also significantly reduced. Although a degree of carotid ostium wall contact still takes place, use of the robotic catheter system virtually eliminates the number of wall hits in the arch, proximal to the CCAs. More importantly, the greatest differences were observed in the most challenging Type III arch and bovine configurations, which may reflect the improved maneuverability, torquability and stability of the robotic device.

Technological limitations of current techniques

The risk of embolization is thought to be proportional to the number of endovascular manipulations in the aortic arch and supra-aortic vessels; apart from complex anatomical factors, excessive instrumentation in the arch can also be due to suboptimal catheter selection or functionality [Schlüter M et al, 2003]. Conventional double-curve catheters pose an even greater risk of vessel wall trauma and embolization as they can be challenging to shape and rotate in the presence of a tortuous aortic arch or an unfavorable supra-aortic takeoff [Chang FC et al, 2009]. A general guideline to minimize excessive manipulation is the “3-15” rule: avoid using more than 3 catheters or spending more than 15 minutes in each cannulation attempt [Veerawamy RK et al, 2007]. A common strategy employed by many interventionalists especially in tortuous and angulated arches, involves advancing a curved endovascular catheter in the ascending aorta first before withdrawing the catheter along the outer wall of the aortic arch until it engages the target vessel origin.
This technique inevitably increases the risk of embolic sequelae especially in atherosclerotic arches. A robotic catheter system allows the operator to shape the catheter tip and follow the curve of the selected vessel or trajectory path with greater precision and accuracy, avoiding the need for the technique described above or repeated manipulations near the CCA origin whilst allowing for centerline navigation with minimal contact with the vessel wall. Furthermore, during robotic cannulations, we observed that the configuration of the robotic catheter remained unchanged on release of the 3D joystick, offering an additional functional advantage in terms of positional control and stability.

Operator Experience

With the introduction of CAS, a broad variety of "carotid interventionalists" has emerged. The Society for Vascular Surgery has published minimal catheter and guide wire skills performance guidelines for interventional procedures [White RA et al, 1999], but has not as yet defined the minimal requirements necessary for the performance of CAS, not only in terms of advanced technical skills but also clinical judgment in terms of patient selection and timing of intervention. The choice of technique in particular, is largely operator dependent and a number of clinical reports have highlighted the importance of the operator’s experience as a crucial factor in the clinical success [Ahmadi R et al, 2001; Lin PH et al, 2005; Verzini F et al, 2006; Theiss W et al, 2008]. A peri-procedural stroke-death rate of 5.9% is seen at centers with <50 interventions, whereas at centers with >150 cases, the stroke-death rate is significantly lower (3.0%) [Theiss W et al, 2008]. Verzini et al. observed a significant learning curve in operator experience: from a 3.1% 30-day major stroke-death rate
during the initial 195 protected CAS procedures to a 0.9% for 432 procedures over a 5 year period, along with reductions in procedure times and contrast volume used [Verzini F et al, 2006]. This learning curve effect has also been demonstrated by other centers [Lin PH et al, 2005] as well as RCTs such as the EVA-3S trial where the unacceptably high 9.6% 30-day stroke-death rate reported, may have been attributable to the fact that as few as five CAS procedures was the prerequisite for the participants [Mas JL et al, 2008].

In our study, despite minimal exposure of the operators to robotic endovascular technology and short training times, we observed a global improvement in quantitative metrics (times/movements/wall hits) and overall performance scores using the IC3ST scale with the robotic system irrespective of the operators endovascular experience, even in the more technically challenging tortuous aortic arch and bovine anatomy. Subgroup analysis revealed that the less experienced groups A and B, obtained scores at the high-end of the IC3ST scale, demonstrating the same high-standard performance as highly experienced interventionalists (group C). This may have important implications on training and learning curves for complex endovascular procedures in the clinical setting. In the high volume intervention group (Group C), there was no statistically significant improvement in performance; these operators obtained high performance scores irrespective of the cannulation method used but completed the task faster and with significantly fewer movements and wall hits. These findings highlight ease of use and the intuitive nature of this robotic technology. The scores obtained by experienced operators in our study reflect years of experience in using conventional endovascular catheters versus a short introductory session to the robotic system. These operators, therefore, may attain even higher
scores and improve their performance even further with subsequent training.

One of the most obvious advantages of remote-controlled robotic technology is the negligible fluoroscopic operator exposure, as the robotic workstation is located away from the radiation source. Although not directly represented in this study, radiation exposure for the patient may also be reduced from faster cannulation, secure vessel access and therefore overall reduction in fluoroscopic times.
Limitations

Wider access via the common femoral artery and alterations in the anatomy of the bifurcation are some of the disadvantages of using a co-axial system. Careless advancement of the sheath can also result in vessel dissection. Clearly the current size of the robotic catheter that requires access via a 14F sheath would not be suitable for a brachial approach, and the 11F inner guide is still too large to allow confident advancement into the CCA in a clinical setting. The ability, however, to place the robotic tip in a stable position just at the origin of the CCA is an obvious advantage. The current robotic device was manufactured for use in the heart via a transvenous approach. Further development of this robotic technology and a lower-profile device is certainly mandated for optimal use in advanced carotid and arch vessel intervention.

Other factors such as set-up times, overall cost and system maintenance must also be considered. No advantage was seen during simple tasks; cannulation of the subclavian arteries for instance and therefore routine use of the system for straightforward intervention would not be cost-effective. Finally, our study is limited by the use of *in-vitro* phantoms, as these experimental models do not reflect all the challenges of catheter navigation in atherosclerotic aortic arches and the carotid bifurcation within a clinical setting. In addition, the metrics used in this study are surrogate markers of embolization risk and technical performance, and are in no means a substitute to clinical endpoints; they do however provide us with a reliable estimate of technical skill in catheter and wire manipulations.
4.5. Conclusions

Cerebral embolic events and the risk of stroke constitute the most challenging problem in advanced endovascular intervention in the arch, and the predisposing factors have been discussed in this chapter. The results demonstrate that robotic technology has the potential to reduce the time, risk of embolization, radiation exposure and the manual skill required for carotid cannulation and stenting, whilst improving overall operator performance scores with minimal training. With advances in technology and imaging and the availability of dedicated equipment, better understanding of patient selection and timing of intervention current results are likely to be enhanced. Further studies utilizing this intuitive technology in the clinical environment are essential for evaluating its long-term safety and efficacy.
Chapter 5.

Endovascular catheter stability

5.1. Background

Mere target vessel catheterization does not necessarily reflect technical success in complex endovascular intervention. Equally important is the ability to advance stiff guidewires and other endovascular tools whilst maintaining stability at target sites. Stable catheter positioning is of paramount importance and particularly challenging when the path to the target vessel ostium consists of multiple bends in different planes. Exchanging a selective catheter over a stiff guidewire in a telescoping fashion is the standard maneuver to position a guide catheter into the target vessel. Tortuous and angulated arterial anatomy poses significant problems, and buckling or herniation of the guiding catheters back into the aorta frequently occurs threatening vessel access. This results in repeated cannulation attempts that contribute to the long fluoroscopic times seen in fenestrated endografting procedures and the increased risk of embolization during arch vessel intervention as highlighted in previous chapters.

In this chapter, we aimed to investigate the stability of the robotic catheter system during stiff-guidewire exchanges in the carotid and renal arteries in direct comparison with conventional endovascular catheter techniques.
5.2. Methodology

Aortic Model

A silicone-based, transparent, CT-reconstructed anthropomorphic phantom (Elastrat Sàrl, Geneva, Switzerland) was used, formed by combining two of the models described in previous chapters: the Type I aortic arch with bovine configuration of the LCCA (Chapter 4) and the TAAA aneurysm with a 5.2 cm dilatation of the visceral segment and a 8.1 cm dilatation of the infra-renal segment (Chapter 3). The phantom was filled with a blood-mimicking water-glycerol mixture (60:40 by volume concentration) and circulated using a pulsatile blood pump providing physiologically realistic blood-flow waveforms as previously described.

Study protocol

A single experienced operator cannulated the renal and carotid arteries (4 vessels in total) using standard-Terumo wires, which were then exchanged for 0.035-inch stiff-guidewires under fluoroscopy, using robotic and conventional catheters. Exchanges took place at 3 distinct points, with the catheter-tip at: 4 cm (Point-A), 2 cm (Point-B) and 0 cm (Point-C) from the target vessel ostium. Each task was repeated three times. Five commonly used, conventional catheters were tested. Two hundred and sixteen stiff-guidewire exchanges in total were recorded for video-assessment. Catheter tip deflection from each point during guidewire exchanges (distance in cm) was measured in a 2-dimensional plane using the recorded digital images.
Statistical analysis

The Statistical Package for the Social Sciences version 18.0 (SPSS, Chicago, Ill., USA) was used for data analysis. The degree of catheter tip deflection for robotic versus conventional techniques was analyzed using the Mann-Whitney U test.
5.3. Results

In 216 stiff guidewire exchanges studied, robotic endovascular catheters maintained stability at target sites with zero deflection during stiff guidewire exchanges, independent of the distance the catheter was introduced into the target vessel. Median conventional catheter deflection was as follows:

*Carotid arteries:* point-A (4cm into the vessel), 0cm IQR (0-0); point-B (2cm into vessel), 0cm(0-4.5) with complete loss of access (LOA) in 16.7% of cases; point-C (at the CCA origin), 7cm(1.3-9.8) with complete LOA in 50% of cases (Fig 5.3.1, Fig 5.3.2).

*Renal arteries:* point-A, 0cm(0-0.3); point-B, 4.5cm(1.8-7) with LOA in 25% of cases; point-C (the renal ostium), 5cm(4.3-5) with LOA in 62.5% of cases (Fig 5.3.3, Fig 5.3.4).

No statistically significant differences between robotic and conventional catheters were observed for point-A during renal cannulations (p=0.21) and points A and B during carotid cannulations (p=0.47). Robotic catheters however, demonstrated increased stability at points B for the renal arteries (p=0.005) and point C (i.e. the target vessel ostium) for both the renals and the CCAs (p=0.005 and p=0.03 respectively).
Fig 5.3.1

Catheter stability during stiff guidewire exchanges in the arch (LCCA)

Stiff guidewire exchanges during cannulation of the LCCA with conventional (bottom row) and robotic (top row) techniques are shown. Exchanges took place at 3 distinct points, with the catheter-tip at: 4cm (Point-A), 2cm (Point-B) and 0cm (Point-C) from the carotid artery ostium.

Fig 5.3.2 Loss of carotid artery access during stiff guidewire exchanges
Fig 5.3.3

Catheter stability during stiff guidewire exchanges in the visceral segment (R renal artery)

Stiff guidewire exchanges during cannulation of the right renal artery with conventional (top row) and robotic (bottom row) techniques are shown. Exchanges took place at 3 distinct points, with the catheter-tip at: 4cm (Point-A), 2cm (Point-B) and 0cm (Point-C) from the renal artery ostium.

Fig 5.3.4 Loss of renal artery access during stiff guidewire exchanges
5.4. Discussion

Adequate guide catheter positioning and support remains one of the leading challenges for peripheral arterial interventional procedures. Because of the unpredictable anatomy often encountered in complex cases, including excessive vessel tortuosity and acute angulation of the aortic bifurcation, which may not accommodate the use of conventional over-the-top guiding sheaths, suboptimal guide catheter support may contribute to prolonged instrumentation, unsatisfactory side-branch device deployment and embolicogenic sequelae [White CJ et al, 1991; Rundaback JH et al, 2001; Kandzari DE et al, 2003].

The use of either a guiding catheter or a long sheath is a prerequisite in arch vessel cannulation procedures and CAS; the inability to position a guiding catheter or a sheath near the carotid bifurcation is one of the main reasons for CAS failure. Exchanging a diagnostic catheter over a stiff guidewire in a telescoping fashion is the standard maneuver to position the guide catheter in the CCA. For tortuous vessels, the wire is positioned very distally in the external carotid artery (ECA), to allow a stable exchange. This technique may not be sufficient for a very acute angle of the CCA off the aortic arch and even when a 5F diagnostic catheter has been placed in the ECA, the introduction of a stiffer exchange guidewire usually pulls the catheter out of the vessel with the entire system herniating back into the arch. In cases that require a more aggressive guiding catheter shape and the tip of the guide cannot be positioned in the distal CCA, just below the carotid bifurcation, then it is usually positioned in the proximal CCA, which generally provides less support for the procedure, and may result in loss of access and multiple cannulation attempts.
To overcome some of these technical issues, several techniques and modifications have been proposed such as “steaming” the tip of the guiding catheter in order to reshape it [Houdart E et al, 2001], using microcatheters to stabilize the guidewire during manipulation [Van den Berg JC et al, 2002], and anchoring a stiff guidewire in the right brachial artery as support, in order to advance the guiding catheter up to the right subclavian artery and the CCA bifurcation [Gupta K et al, 2008]. If these maneuvers prove to be unsuccessful, then a direct carotid artery puncture or a transbrachial approach as a salvage technique can be considered if the patient's risks for CEA are unacceptably high. It has been proposed that up to 26% of CAS procedures require advanced technical skill and a modification in the standard technique for successful outcomes [Choi HM et al, 2004].

Conventional catheter instability can also compromise effective target vessel cannulation in the visceral segment in branched and fenestrated stent grafting procedures. Even small degrees of misalignment at the fenestration/target vessel ostium interface can make passing a catheter directly through the fenestration and into the target artery extremely challenging, with long fluoroscopic times as a result. In cases of marked aortic neck angulation, that necessitate the use of an extra stiff wire in the renal artery for sheath placement, renal perforation on sheath advancement has also been reported [Kristmundsson T et al, 2009]. Experienced operators have developed alternative techniques for dealing with such issues. For example, it may be easier to exit the fenestration and advance a wire up the aorta on the outer surface of the stent-graft, before turning back down the aorta to the orifice of the renal artery using a re-curved catheter. Alternatively, a catheter over a guidewire positioned
between the graft and the aneurysm sac can be used to gain retrograde access into the renal artery. From a left brachial access the guidewire is then snared and used to allow bridging stent deployment between the branch and the target vessel, thus completing the procedure [D'Elia P et al, 2010].

Despite recent advances in devices for catheter-based peripheral arterial revascularization procedures, the inadequacy of conventional catheters for the variable and often unpredictable anatomy of patients with complex arterial disease implies that alternative catheter designs are essential. The robotic catheter system is effectively a steerable sheath supporting a more flexible inner guide. Consequently, the catheter resists the tendency to herniate back into the aorta as wires and other endovascular tools are being advanced through its lumen. In the 216 stiff guidewire exchanges studied, robotic endovascular catheters maintained stability at target sites with zero deflection during stiff guidewire exchanges, independent of the distance the catheter was introduced into the target vessel and no loss of access. In contrast, conventional catheters required positioning at least 2cm into the target vessel in order to avoid catheter deflection and subsequent loss of access. Robotic catheters, demonstrated increased stability at point C, the target vessel ostium that may prove useful when tackling angulated aortic arches, aneurysm necks and tortuous branches.
5.5. Conclusions

As endovascular therapy is becoming more ambitious, there remains a need to develop new catheter designs that are more reliably suitable to complex peripheral arterial anatomy. Our results demonstrate that robotic endovascular catheters provide increased stability at target sites during stiff guidewire exchanges – a vital step for securing target vessel access in complex endovascular procedures involving the carotid and renal arteries. This enhanced positional control may offer a stable platform for future advanced applications involving device delivery or target intervention, such as in-situ fenestration, coil embolization and other therapeutic catheter-based interventions.
Chapter 6.

Iliac tortuosity: its effect on target vessel cannulation in the visceral segment

6.1. Background

The presence of hostile iliac anatomy is a challenge to successful endovascular intervention in the aorta and its branches. Adequate ilio-femoral access, endograft delivery and successful branch cannulation and stenting are all influenced by aortic and iliac tortuosity. Although not an absolute contraindication for standard endovascular aneurysm repair, unfavorable iliac anatomy can pose significant difficulties with endograft fixation and orientation, and may render some patients unsuitable for endovascular intervention [Wolf YG et al, 2001; Rodd CD et al, 2011]. It carries a 15-20% complication rate including hemorrhage, rupture, and dissection, which may necessitate conversion to open repair [Cuypers PW et al, 2000; Yano OJ et al, 2001; Millon A et al, 2009]. It has also been implicated as a cause of late complications and endograft failure through progressive distortion, limb retraction or occlusion, asymptomatic arterial dissection and endoleak formation [Tillich M et al, 2001; Hobo R et al, 2007; Hobo R et al, 2008; Millon A et al, 2009]. Severe iliac tortuosity can also be responsible for alterations in stent graft configuration before and after deployment, as demonstrated in a number of post-marketing trials for different manufacturers [Umscheid T et al, 1999; Makaroun MS et al, 2005; Moise
MA et al, 2006; Matsumura JS et al, 2008; Fairman RM et al, 2008]. Aortoiliac tortuosity is therefore an important factor in the selection, planning, conduct, and outcome of endovascular aortic intervention.

In complex endovascular procedures such as fenestrated and branched endografting, unfavourable iliac anatomy can impact not only on endograft delivery leading to misalignment between the fenestrations/branches and the target vessel ostia but also on the performance of the conventional endovascular catheters used for selective catheterization as an independent variable [Haulon S et al, 2007; Bicknell CD et al, 2009; Haulon S et al, 2010; Amiot S et al, 2010; Greenberg R et al, 2010]. Both these factors may subsequently compromise successful and safe target vessel cannulation. This study is the first report to date, attempting to quantify the effect of varying degrees of iliac tortuosity on the maneuverability and torquability of endovascular catheters during target vessel cannulation in the visceral segment in fenestrated endografting, comparing conventional and robotic techniques.
6.2. Methodology

Aortic Model

The pulsatile silicone CT-reconstructed anthropomorphic phantom (Elastrat Sàrl, Geneva, Switzerland) with the in-situ fenestrated stent graft described in Chapter 3 was used.

Tortuosity Index

To assess the effect of varying degrees of iliac tortuosity on the performance of conventional versus robotic endovascular cannulation of the renal arteries, three access vessels on the pulsatile phantom were chosen: the right external iliac artery (R EIA), the left external iliac artery (L EIA) and the left internal iliac artery (L IIA). The LIIA is of course not used as an access vessel in the clinical setting; it was chosen for the purposes of this study to reflect the different degrees of tortuosity. For each access vessel, the central luminal distance (L1) from the aortic bifurcation to the common femoral artery and the straight-line distance (L2) from the aortic bifurcation to the common femoral artery measured in a plane perpendicular to the central lumen line were calculated from volume-rendered CT reconstructions of the phantom. The L1/L2 ratio was used to calculate the iliac tortuosity index (τ) (Fig 6.2.1).

\[
\text{iliac tortuosity index (τ)} = \frac{L1}{L2}
\]
Fig 6.2.1 Calculation of the iliac tortuosity index

For each access vessel within the phantom, the central luminal distance (L1) from the aortic bifurcation to the common femoral artery and the straight-line distance (L2) from the aortic bifurcation to the common femoral artery measured in a plane perpendicular to the central lumen line were calculated from volume-rendered CT reconstructions of the phantom. The L1/L2 ratio was used to calculate the iliac tortuosity index, as shown here for the REIA.
The iliac tortuosity index (τ) was scored as follows specified in consensus reporting criteria and used in other publications [Chaikof EL et al, 2002; Karthikesalingam A et al, 2010; Rodd CD et al, 2011]; the corresponding values for the iliac angle (ϕ) are also shown:

<table>
<thead>
<tr>
<th>Severity</th>
<th>Tortuosity Index (τ)</th>
<th>Iliac Angle (ϕ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Absent</td>
<td>τ ≤ 1.25</td>
<td>160° &lt; ϕ &lt; 180°</td>
</tr>
<tr>
<td>1 Mild</td>
<td>1.25 &lt; τ ≤ 1.5</td>
<td>121° &lt; ϕ &lt; 159°</td>
</tr>
<tr>
<td>2 Moderate</td>
<td>1.5 &lt; τ ≤ 1.6</td>
<td>90° &lt; ϕ &lt; 120°</td>
</tr>
<tr>
<td>3 Severe</td>
<td>τ ≥ 1.6</td>
<td>ϕ &lt; 90°</td>
</tr>
</tbody>
</table>

The access vessel measurements are summarized in the following table (Table 6.2.1):

<table>
<thead>
<tr>
<th>Access Vessel</th>
<th>Tortuosity Index (τ)</th>
<th>Severity Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>REIA</td>
<td>1.36</td>
<td>1 = Mild</td>
</tr>
<tr>
<td>LEIA</td>
<td>1.56</td>
<td>2 = Moderate</td>
</tr>
<tr>
<td>LIIA</td>
<td>2.47</td>
<td>3 = Severe</td>
</tr>
</tbody>
</table>
Study protocol

Ten experienced operators (five vascular surgeons, five interventional radiologists) were recruited to participate in the study. Each operator was asked to cannulate the renal arteries within the phantom using the R EIA, L EIA or the L IIA as the access vessel, under fluoroscopic guidance, using conventional and robotic (Hansen Sensei) techniques in a randomized order. For conventional procedures, a range of ten 4F to 5F selective catheters and appropriate endovascular guidewires commonly used for renal artery cannulation were available to all operators. Passive intra-procedural support was provided by an assistant and a radiographer and C-arm orientation was adjusted accordingly, as requested by the operator. Operators were blinded as to the access vessel used and its corresponding tortuosity index. All procedures were performed in the angiography suite and recorded for blinded video assessment of quantitative and qualitative metrics.

DATA COLLECTION

Quantitative metrics

Cannulation times: Renal artery cannulation times from the point the catheter entered the aortic bifurcation was measured in minutes using a stopwatch. Vessel cannulation was considered satisfactory when the catheter followed the wire at least 3 cm into the target vessel.

Movements: The absolute number of translational (linear displacement along a trajectory path) and rotational (circular displacement around a centre axis) movements
at the wire/catheter tip was counted in a binary fashion by two independent observers using blinded-video recordings displaying 2-dimensional fluoroscopic data.

**Qualitative metrics**

*Operator performance*: Performance evaluation was carried out using the Imperial College Complex Cannulation Scoring Tool (IC3ST) described in previous chapters (Chapters 3 and 4). Performance scoring was evaluated by two blinded assessors (C.R and C.B), experienced in the use of rating scales.

**Statistical analysis**

The Statistical Package for the Social Sciences version 18.0 (SPSS, Chicago, Ill., USA) was used for data analysis. The absence of a normal distribution of the data necessitated the use of non-parametric tests for significance. Differences between conventional and robotic cannulation were compared using the Wilcoxon signed-rank test for related samples. A p value of less than 0.05 was considered statistically significant. Inter-observer reliability for the blinded assessors was calculated with the Cronbach's alpha test statistic.
6.3. Results

6.3.1 Quantitative

In total, 120 cannulations were observed. With increasing iliac tortuosity, time and catheter movements for renal artery cannulation using conventional techniques increased in a step-wise fashion: median times 7.6min IQR (4.6-9.3) versus 6.9min(4.2-11.4) versus 17.7min(13.3-22.6) and movements 184(110-351) versus 251(207-395) versus 569(409-616) for mild, moderate and severe tortuosity respectively; p=0.001 between low and high iliac tortuosity severity scores for time and movements. Renal cannulation times and movements were significantly reduced using the robotic system irrespective of iliac tortuosity severity scores: median times 1.4min(1.1-1.9) versus 3(2.3-3.3) versus 2.8(1.5-3.9) and movements 19(14-27) versus 46(43-58) versus 45(40-66). The greatest differences between conventional and robotic techniques were observed in cases of severe iliac tortuosity (severity score ≥3) for time: 17.7min IQR (13.3-22.6) versus 2.8min (1.5-3.9); p=0.005 and movements: 569 (409-616) versus 45 (40-66); p=0.005 (Fig 6.3.1, 6.3.2). Inter-observer reliability for measuring the number of movements was calculated with a Cronbach’s α of 0.94, indicating a high level of agreement.
Fig 6.3.1

Renal artery cannulation times and iliac tortuosity severity

Bar chart representing renal artery cannulation times with increasing iliac tortuosity severity, using conventional and robotic techniques (Wilcoxon signed rank test).
Bar chart representing the number of catheter tip movements for renal artery cannulation with increasing iliac tortuosity severity, using conventional and robotic techniques (Wilcoxon signed rank test).
6.3.2 Qualitative

Overall operator performance scores improved significantly using the robotic system, irrespective of iliac tortuosity severity. Median IC3ST scores were: 24/35 (19 – 28) versus 30/35 (29 – 31), 27/35 (22 – 30) versus 31/35 (30 – 33) and 21/35 (15 – 22) versus 33/35 (30 – 35) for mild, moderate and severe iliac tortuosity respectively (Fig 6.3.3). Reliability between assessors was calculated using Cronbach’s $\alpha$ was 0.85, indicating a high level of agreement.
Fig 6.3.3

Operator performance IC3ST and iliac tortuosity severity

Bar chart representing operator performance scores on the IC3ST scale for renal artery cannulation with increasing iliac tortuosity severity, using conventional and robotic techniques (Wilcoxon signed rank test).
6.4. Discussion

Despite continuing device and technical evolution, remote arterial access remains a significant challenge if access vessels are tortuous. Iliac artery tortuosity increases with age, is prevalent in aneurysmal disease and can be a limiting factor in endovascular intervention, directly impacting on the safe introduction of endovascular tools in the aorta and its branches [Wolf YG et al, 2001; Tillich M et al, 2001; Rodd CD et al, 2011]. This chapter examines the true effect of tortuosity in a pulsatile model and demonstrates the advantages of robotic catheters in this setting. Although this study has chosen to assess access vessel tortuosity in a fenestrated model, the effects of significant curvature in the iliac segment may be equally applicable to the majority of procedures performed through a femoral approach involving selective cannulation of target vessels. For fenestrated and branched endografting unfavorable iliac anatomy is particularly pertinent. One of the main challenges in these procedures is cannulation of the fenestration and visceral orifice via the introduction of guiding catheters and stents. With increasing iliac tortuosity as shown in our study, target vessel cannulation with conventional endovascular catheters becomes more technically demanding. Angulation at the access end of the path trajectory directly impacts on manipulation at the distal end of the wire/catheter interface, with limited torquability and buckling of the selective catheter, resulting in multiple cannulation attempts with frequent catheter changes. Even when the target vessel was successfully cannulated with a wire, advancing the less trackable catheters over hydrophilic guidewires proved to be difficult for a tortuosity severity score of 2 or above, and as a result, the catheter/wire often deviated upwards towards the thoracic aorta. These technological deficiencies in the presence of challenging iliac configurations
accounted for the observed increased length of time taken, number of movements to cannulate vessels; and suboptimal performance of the operators.

Many operators chose to exit the fenestration of the partially deployed endograft and advance the wire proximally in the aorta on the outer surface of the device, before turning back down to the orifice of the target vessel using a re-curved catheter; a technique for visceral artery cannulation used by some. As shown in our study, this maneuver may be sufficient for small to moderate degrees of iliac tortuosity, however in cases with a high tortuosity index control at the catheter tip is suboptimal and often the fabric lip of the fenestration or the stentgraft itself engaging the catheter results in repeated catheter manipulations and prolonged cannulation times [Moore R et al, 2007]. In this study overall, operators using the robotic catheter to cannulate vessels were faster, used less movements and with improved performance. This improvement in the studied metrics was not affected by changes in iliac tortuosity. Moreover, in contrast to the patterns seen with conventional catheters, functionality of the robotic catheter was unaffected by iliac tortuosity severity, with faster cannulation times, increased positional accuracy and control in terms of catheter tip movements and overall operator performance scores, that was particularly evident in the more tortuous cases.

Some of these issues are clearly device-specific. Access is primarily related to the flexibility, torquability, diameter, shape and stability of endovascular devices. Because of the unpredictable anatomy among patients undergoing catheter-based peripheral revascularization procedures, including excessive vessel tortuosity and extreme angulation at bifurcations, adequate guide catheter positioning and support
remain one of the leading challenges. It is often necessary to use catheters with complex distal shapes to successfully cannulate the branch vessels. These complex catheter shapes can act as a barrier to distal navigation at the target vessel ostia, and stability is frequently a problem. The use of larger catheters increases the stability; however, flexibility is often compromised. The robotic catheter acts as kink-resistant sheath providing support in key target regions despite severe degrees of iliac tortuosity. Enhanced control at the tip of the inner guide reduces the manual skill required for individual target vessel cannulations which are achieved faster, with fewer movements and increased positional precision protecting therefore the aorta and its branches from potentially embologenic and traumatic manipulations. One may argue that the differences between conventional and robotic techniques observed in our study may not be as clinically relevant for small degrees of iliac tortuosity, however, in cases with a high tortuosity index where catheter manipulation and control really becomes an issue, a more advanced catheter tool may indeed improve safety and efficacy.

Although not directly studied here, branch vessel stenting following successful cannulation of the target branch should also be taken into consideration. Even if a branch vessel with an acute downwardly oriented takeoff can be selectively engaged via the femoral approach, subsequent branch stent advancement still may not be possible. The presence of severe aorto-iliac tortuosity or occlusive disease may mandate approaching the vessel from an upper extremity approach, which in itself carries a significant embolic risk [Kessel DO et al, 2003]. The use of a catheter-guiding sheath is another alternative to allow tracking of extra-stiff wires and aid in overall stability [Rahimi SA et al, 2010]. The sheath is advanced until it is close to the
target vessel ostium, and with its support an angled glide catheter and glide wire combination can be used to cannulate the vessel [Moore R et al, 2007]; even with this approach however, perforation of the target vessel on sheath advancement has been reported [Kristmundsson T et al, 2009]. In contrast, as shown in the previous chapter (Chapter 5), the robotic device offers increased stability during stiff guidewire exchanges during target vessel cannulation both in the aortic arch and the visceral segment.

Various adjuncts may be utilized to assist with tortuous iliac anatomy. The most commonly used technique involves utilization of a longer sheath to support the catheter in the less tortuous aortic segment. Buddy wires, through and through wires from femoral to brachial access sites (the so-called "dental floss" technique) [D'Elia P et al, 2010], balloon angioplasty and stenting can all be attempted. These maneuvers can be useful for many non-calcified tortuous iliac vessels, however, when heavy calcification [Bowman JN et al, 2010] is present, vessel dissection and rupture are potential risks, and embolic sequelae may also occur when the brachial approach is used. Iliac conduits are used in 9.4 – 22% [Matsumura JS et al, 2008; Fairman RM et al, 2008] of anatomically challenging cases where iliac size is the main limiting factor. This technique requires a retroperitoneal incision and dissection, followed by placement of a 10 mm Dacron graft onto the common iliac bifurcation anastomosed in an end-to-side fashion. In our unit, we often tunnel the graft to the femoral region to avoid device entry into the native vessel at a steep angle. Although performed most often for introduction of stent grafts, this maneuver does reduce a number of curves in the ilio-femoral segment and in severely tortuous disease in patients that have multiple fenestrations to cannulate this technique may be useful. Upon completion of
the procedure, the graft can be transected and oversewn, leaving a small cuff of prosthetic on the iliac vessel, or it can be anastomosed to the common femoral artery forming an iliofemoral bypass. This technique has its advantages if there is a high likelihood of re-intervention. The morbidity of this approach, however, cannot be underestimated. The use of conduits via a retroperitoneal approach is associated with increased blood loss, operative time (by 82%) and median hospital length of stay as well as postoperative complications (up to 21%) [Lee WA et al, 2003; Fairman RM et al, 2008]. More recently, “internal endoconduit” techniques have been described, involving deployment of an iliac stent followed by angioplasty and controlled rupture of the iliac artery, to allow passage of the endograft delivery device; reports however are scarce and experience limited [Wu T et al, 2010; Peterson BG 2010].

Specifically for fenestrated stent grafting the problem may be compounded by graft related issues. Rotation of the custom-made endograft and subsequent misalignment between the fenestrations/branches and the target vessel ostia can lead to increased difficulty with target cannulation. In order to overcome some of the limitations of standard catheter technology and simplify the target vessel cannulation process, newer devices incorporating preloaded wires, catheters and sheaths have been developed. Preliminary results have shown that cannulation times are considerably shorter and access into the target vessel easier than with standard fenestrated or branched systems. Despite these important developments in stent graft design, however, it has become apparent that severe tortuosity of the iliac vessels can cause rotation of the device and twisting of the preloaded wires/catheters or sheaths which can lead to trauma and vessel loss [Manning BJ et al, 2010].
6.5. Conclusions

Despite recent advances in devices and techniques for catheter-based peripheral arterial revascularization procedures, there remains a need for the design of guide catheters capable of providing adequate support and maneuverability in patients with challenging anatomy. Although contemporary catheters may be sufficient for many revascularization procedures, the inadequacy of these tools for the variable and often unpredictable anatomy of patients with peripheral arterial disease implies that alternative catheter designs are essential.
Chapter 7.

Skill acquisition and learning curves for endovascular robotics

7.1. Background

Minimally invasive intervention coupled with the introduction of new technology creates new challenges in terms of clinical outcomes as well as training and credentialing. As seen in laparoscopic surgery, learning curves are steep [Lin JC et al, 2011; Ali MR et al, 2010; Staudacher C et al, 2010; Bagdasarian RW et al 2000]. The rate of skill acquisition often varies between surgeons and is influenced by patient selection and operative complexity, requiring therefore appropriate case-mix adjustment [Kayano H et al, 2011; Tekkis PP et al, 2005; Schauer P et al, 2003; Reissman P et al, 1996]. The steep learning curves are attributed to many aspects of current technologies utilized and mostly relate to the 2D imaging and instrument limitations as well as ergonomics [Bittner JG et al, 2008; Jordan JA et al, 2000]. Robotic assistance in laparoscopic surgery using the Da Vinci system allows for stereoscopic vision and improves dexterity, resulting in faster and more accurate performance of laparoscopic tasks; in terms of learning curves however, skill acquisition favors conventional laparoscopy with a flat-learning curve in experienced operators, suggesting that robotic assistance might be most beneficial in

In endovascular therapy, as seen with other fields of minimally invasive surgery, the level of procedural difficulty has increased in recent years, as its applicability extends to a more complex patient cohort. Catheter-based intervention requires a high degree of skill while manipulating intravascular devices often using counterintuitive hand movements. As case complexity increases and endovascular intervention becomes more ambitious, the mastering of endovascular skills can be challenging. This is highlighted by the extensive caseload, and the long mentoring and proctoring process required in order meet credentialing guidelines for endovascular procedures [White RA et al, 1999; Ahmadi R et al, 2001; Verzini F et al 2006].

The data presented in previous chapters suggests that robotic endovascular catheter technology has the potential to reduce the manual skill required for complex tasks. The impact of this technology however, on the skill acquisition for endovascular procedures has not been explored. This study aims to investigate the learning curve pattern in novice subjects for robotic endovascular catheters versus conventional techniques.
7.2. Methodology

Aortic Model

The pulsatile silicone CT-reconstructed anthropomorphic phantom (Elastrat Sàrl, Geneva, Switzerland) representing a Type I aortic arch with bovine configuration of the left CCA described in Chapter 4 was used.

Study protocol

Ten novice subjects (medical students) with no prior endovascular training were recruited and consented to participate in the study. All participants were given an information sheet followed by a standardized didactic teaching session that included endovascular techniques, apparatus being used, study purpose and assessment metrics. The subject’s understanding of this introductory course was then assessed using a questionnaire. Feedback was provided before progressing to the next stage. Prior to commencing the study, a short, practical demonstration of target vessel cannulation and equipment use was also provided. Participants were then allowed to practice cannulating the left subclavian artery (LSA) in the pulsatile aortic arch phantom.

Subjects were randomly assigned to conventional and robotic techniques as the first procedure undertaken, and were asked to sequentially cannulate four arch vessels namely the LSA, left common carotid artery (LCCA), right common carotid artery (RCCA) and right subclavian artery (RSA) via the femoral approach. A range of 4F to
5F selective catheters and appropriate endovascular guidewires, commonly used in arch vessel cannulation procedures, were available to all operators. The Hansen Sensei™ System (Hansen Medical, Mountain View, CA, USA) was used for all robotic cannulations.

All procedures took place in the Simulated Endovascular Suite (Fig 7.2.1 and 7.2.2) and were recorded for video assessment. Each task was repeated weekly over a 5-week period (10 sessions per subject, 100 procedures in total). At the end of the 5-week training programme, video recordings were analyzed for quantitative and qualitative metrics. Video footage was blinded and randomized, identifiable only by an internal coding system. Subjects were also sent a post-training self-report questionnaire on their overall experience with conventional and robotic endovascular techniques.
Fig 7.2.1 Conventional cannulation in the Simulated Endovascular Suite

The pulsatile aortic arch phantom is covered with surgical drapes, and video output of the real-time image is projected onto the LCD monitor screen.

Fig 7.2.2 Robotic cannulation in the Simulated Endovascular Suite

Workstation monitors display real-time images of the pulsatile phantom, and the operator manipulates the robotic catheter remotely via the hand-operated 3-dimensional joystick.
DATA COLLECTION

Quantitative metrics

Total procedure times and individual target vessel cannulation times were measured using a stopwatch. Times were recorded from the catheter entering the phantom at a fixed point of the descending aorta, and vessel cannulation was deemed satisfactory when the catheter was seen in a stable position over the guide wire and at least 3 cm into the target vessel. In addition, the absolute number of rotational and translational movements at the wire/catheter tip as well as wall hits during cannulation attempts were recorded in a binary fashion by two observers (P.C, P.N), who were blinded to individual operators and corresponding session.

Qualitative metrics

Performance evaluation was carried out using the Imperial College Complex Cannulation Scoring Tool (IC3ST) described in previous chapters. Performance scoring was analysed by two blinded assessors (C.R and F.C), experienced in the use of rating scales.
Statistical analysis

Data were analyzed with the Statistical Package for the Social Sciences version 18.0 (SPSS, Chicago, IL, USA). Learning curves were assessed using a Friedman (non-parametric repeated-measures analysis of variance) test. Sequential comparisons were made to identify plateau levels for all significant variables. The Wilcoxon signed rank test was used to determine both skill improvement from the first to fifth session and differences between conventional and robotic techniques. All tests were two-tailed and considered significant for $p < 0.05$. Inter-observer reliability for blinded assessors was evaluated using the Cronbach’s alpha coefficient (0.7-0.8 is considered to be significant, >0.09 for a high-stakes assessment).
7.3. Results

Skill acquisition

All study participants completed the 5-week training programme. Good interobserver reliability for blinded assessors was achieved for all metrics: total number of movements (Cronbach’s alpha = 0.99), wall hits (0.75) and IC3ST scores (0.87). Subjects exhibited statistically significant differences when comparing initial to final performance (week 1 versus week 5) for procedure times and catheter-tip movements. The 5-week training programme had no effect on wall hits. A flat learning curve was observed for robotic cannulation in terms of overall performance scores.

Sequential non-parametric comparisons identified a learning curve plateau level at week 3 for total procedure times and IC3ST scores using robotic technology; an earlier plateau at week 2 was seen for catheter-tip movements. With conventional catheterization, the plateau level was identified at week 3 for total number of movements and week 4 for total procedure times; no plateau was reached for total number of vessel wall hits and performance scores, which continued to improve throughout the training programme. Table 7.3.1 summarizes the results for weeks 1 and 5 including learning curve plateau levels for the different catheter types.
Table 7.3.1

<table>
<thead>
<tr>
<th>Metric</th>
<th>Catheter Type</th>
<th>Week 1 Median (IQR)</th>
<th>Week 5 Median (IQR)</th>
<th>p value</th>
<th>Plateau</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total time (min)</td>
<td>Conventional</td>
<td>6.4 (4.6-10.1)</td>
<td>4.2 (3.1-6.1)</td>
<td>0.022</td>
<td>Week 4</td>
</tr>
<tr>
<td></td>
<td>Robotic</td>
<td>12.4 (10.1-13.1)</td>
<td>5.3 (4.3-9.2)</td>
<td>0.007</td>
<td>Week 3</td>
</tr>
<tr>
<td>Movement</td>
<td>Conventional</td>
<td>205 (165-282)</td>
<td>74 (59-89)</td>
<td>0.005</td>
<td>Week 3</td>
</tr>
<tr>
<td></td>
<td>Robotic</td>
<td>124 (81-137)</td>
<td>33 (28-44)</td>
<td>0.005</td>
<td>Week 2</td>
</tr>
<tr>
<td>Wall hits</td>
<td>Conventional</td>
<td>47 (32-107)</td>
<td>29 (28-75)</td>
<td>0.139</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Robotic</td>
<td>5 (4-7)</td>
<td>7 (5-10)</td>
<td>0.200</td>
<td>N/A</td>
</tr>
<tr>
<td>IC3ST</td>
<td>Conventional</td>
<td>20/35 (14/35-22/35)</td>
<td>26/35 (19/35-27/35)</td>
<td>0.036</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Robotic</td>
<td>27/35 (25/35-28/35)</td>
<td>32/35 (30/35-33/35)</td>
<td>0.007</td>
<td>Week 3</td>
</tr>
</tbody>
</table>

**Comparison between catheter types**

Direct comparison between catheter types for median procedure times indicated that conventional catheterization was significantly faster for weeks 4 and 5 (Fig 7.3.1). Subjects, however, made significantly fewer catheter-tip movements using robotic technology every week throughout the programme (Fig 7.3.2). The robotic system virtually eliminated contact with the aortic arch proximal to the CCA origin and significantly reduced overall wall hits (Fig 7.3.3). It also resulted in significantly higher overall IC3ST performance scores (Fig 7.3.4).
Fig 7.3.1 Procedure times over the 5-week training programme

Bar chart representing median procedure times (min) with conventional versus robotic techniques over the 5-week training programme (Wilcoxon signed rank test). The learning curve pattern in the lower panes, for each individual operator is also shown.
Fig 7.3.2 Catheter movements over the 5-week training programme

Bar chart representing median number of catheter-tip movements with conventional versus robotic techniques over the 5-week training programme (Wilcoxon signed rank test). The learning curve pattern in the lower panes, for each individual operator is also shown.
Fig 7.3.3 Vessel wall hits over the 5-week training programme

Bar chart representing median number of vessel wall hits at the aortic arch proximal to the CCA and at the carotid vessel ostia with conventional versus robotic techniques, over the 5-week training programme (Wilcoxon signed rank test).
Fig 7.3.4 Overall performance scores during the 5-week training programme

Graph representation of the overall IC3ST performance with conventional versus robotic cannulation techniques during the 5-week training programme.
Self-report questionnaires

Eight out of 10 study participants scored the robotic system at 3 on a 3-point scale, indicating that the system was easy to learn on and steer, and was intuitive and responsive to operator commands. By contrast, 9/10 operators scored the conventional catheters at 2, on the same scale. Overall, participants preferred the robotic system and felt that it significantly enhanced their performance as a whole. The self-report questionnaire is shown below (Fig 7.3.5):

Fig 7.3.5 Participant Questionnaire
7.4. Discussion

The widespread adoption of endovascular therapy has important implications on the training and credentialing guidelines for vascular specialists. Advanced endovascular procedures are unique in that the risk posed to the patient as a result of the operator’s learning curve is significant and immediately apparent. Consequently, trainees are challenged by the prolonged learning curves associated with mastering complex techniques and the acquisition of essential generic skills [Gould D, 2010]. Although the apprenticeship model has stood the test of time, simulators dedicated to endovascular training are now available to offer trainees the opportunity to acquire basic skills and to undertake complex tasks outside the operating theatre with a view to allow for the early parts of the operators learning curve to take place within a safe environment [Ahmed K et al, 2010; Neequaye SK et al, 2007]. They do not however, reduce the operation requirements or the learning curve [Aggarwal R et al, 2006].

A further obstacle faced by the endovascular specialist trainee involves the limitations of current endovascular catheter technology. Any technological advancement that reduces the learning curve will have a significant impact on the length of endovascular training and importantly patient safety. There is a pressing need therefore, to improve endovascular catheter technology in order to shorten the learning curve and in turn improve patient outcomes.

A variety of advanced endovascular catheters have been developed in an attempt to reduce the technical burden to the endovascular specialist and have been widely adopted in transvenous cardiac mapping and ablation procedures [Arya A et al, 2010; Matsuo S et al, 2010; Saliba W et al, 2008; Kanagaratnam P et al, 2008]. The early
learning curve seen in transvenous mapping and ablation procedures using robotic technology through longer procedure times, although not formally assessed, is though to be mainly due to additional set-up times [Malcolme-Lawes L et al, 2010]. Pre-clinical testing of robotic endovascular catheters against conventional cannulation techniques in the hands of experienced operators has shown promise in enhancing target vessel cannulation, reducing instrumentation and improving operator performance as demonstrated in previous chapters. This chapter aimed to evaluate the learning curve pattern of endovascular robotics in novice subjects.

In this study, quantitative and qualitative metrics improved throughout the 5-week training programme (10 sessions for each subject), indicating that novices progressed through the learning curve with regards to basic endovascular skills. Evidence of improvement in performance is supported by the fact that subjects showed less variability in metrics during their training, as demonstrated by a reduction in the IQR. This is an important parameter to look for when evaluating skill acquisition and suggests consistency; the rate of improvement in performance seems to decelerate as the learning curve reaches a plateau.

Use of robotic technology resulted in significantly superior overall performance scores, with an earlier learning curve plateau. The clear advantages with regard to catheter movements and vessel wall hits observed indicate enhanced economy of movement and navigational accuracy. Although catheter-tip movements and vessel wall hits are surrogate measures for embolic risk, wall hits at the arch proximally to the CCA origin were virtually eliminated by the robotic system. This is likely to result from the greater range of motion that can be achieved with the RC and the increased
3D control at the catheter tip. Overall IC3ST performance scores were significantly improved using the robotic system over the 5-week period. During a total of 50 robotic cannulation procedures, 48 procedures scored between 21/35 and 34/35, indicating a competent performance and 2 procedures achieved a score of 35/35, indicating an excellent performance. Although a significant improvement over the 5-week study period was observed for the overall IC3ST performance scores with conventional cannulation techniques, 20 procedures achieved a score between 7/35 and 20/35 and 30 procedures scored between 21/35 and 34/35, with no operators achieving an excellent procedure score of 35. This illustrates the intuitive nature of the robotic technology as the majority of operators demonstrated a performance of a high standard at an earlier stage.

Although not directly quantified in this study, we observed that with experience, participants demonstrated a cognitive improvement in performance by developing different cannulation strategies using the robot and were able to keep the catheter low in the arch whilst directing the wire into the vessel by manipulating and steering its tip. By contrast, with conventional catheters, it was necessary to advance the catheter in closer proximity to the vessel ostium before guiding the wire through its lumen. Subcategory analysis of the IC3ST scores, revealed that participants demonstrated increased awareness of areas of significant embolic risk using the robotic catheter at week 2, most likely secondary to enhanced catheter control.

Surprisingly, subjects took significantly longer in cannulating all four arch vessels with robotic catheters. Novice subjects, however, often assume that faster completion of a technical task represents competence. Speed of task completion has been used
previously to assess competency during surgical procedures; a fast but unskilled operator, however, is less desirable than a slow, skilled operator. Faster completion of a procedure, therefore, is at best a crude measure of technical skill, and cannulation times alone do not reflect overall performance as demonstrated by IC3ST scores and all other metrics, especially for robotic cannulation techniques [Van Herzeele I et al, 2008; Johnson S et al, 2006; Moorthy K et al, 2003].

*Limitations*

This study is limited by the use of *in vitro* phantoms, as these experimental models do not reflect all the challenges of catheter navigation in atherosclerotic aortic arches and the carotid bifurcation within a clinical setting and even high-fidelity simulators can only replicate a subset of actual clinical scenarios. More importantly, catheter manipulation represents a specific but challenging part of many endovascular procedures; there are numerous factors contributing to the long learning curve of the endovascular specialist and they span technical skills as well as non-technical skills, such as patient selection, anatomical awareness and teamwork that have not been directly studied here. Nonetheless, robotic technology is perhaps the ideal platform whereby the integration of simulators for teaching purposes can occur. Our results are also reliant on the level of the subject’s motivation for performing well in a simulated environment with no perceived risk of adverse outcome, and therefore, may have been influenced by the individual subject’s attitude and aptitude for new skill acquisition.
7.5. Conclusions

Using this experimental model, novice subjects acquired rudimentary endovascular skills in a 5-week training programme utilizing both conventional and more advanced robotic endovascular catheter technologies. Robotic catheter techniques, although more intricate, do not seem to take longer to master and offer clear advantages with regard to positional control, at a faster rate. Robotic technology seems to be the intuitive and advanced skill acquisition occurs with minimal training. It may, therefore, have a significantly shorter path to proficiency allowing an increased number of trainees to attempt more complex endovascular procedures earlier and with a greater degree of safety.
Chapter 8.

Advanced applications:

In-situ Fenestration

8.1. Background

Diseases of the aorta involving arch and visceral branch vessels require challenging therapeutic maneuvers to ensure preservation of arterial flow within vital branches. Bespoke fenestrated and branch stent graft technology has shown encouraging short- and mid-term results in selected patients. Despite tremendous technological advances in this field however, factors such as the inherent delay in device manufacturing, anatomical and technical challenges, high degree of planning, and cost limit the uptake of this technology and render it unsuitable for urgent and emergency cases. In situ fenestration of aortic stent grafts is an attractive alternative that eliminates the need for preoperative custom tailoring with the potential to widen the therapeutic options available and to offer a bailout option after inadvertent side branch occlusion.

The concept of in situ fenestration involves intentionally covering aortic branches with an endograft and then reestablishing blood flow by fenestrating the fabric in vivo. Once the fabric has been breached, the fabric hole can then be dilated to a desired diameter and a branch stent is placed to maintain perfusion of the target
vessel. This technique can be performed in either a retrograde (from within the lumen of the side branch, therefore requiring downstream access) or an antegrade (from within the lumen of the stent graft) fashion and may be potentially applied to all major aortic side branches.

*Arch Vessels*

McWilliams et al first described retrograde in situ fenestration in bench and animal models [McWilliams RG et al, 2003], followed by the first successful clinical application in the left subclavian artery (LSA) via supraclavicular access using the back end of a 0.018-inch guidewire, a needle and serial cutting balloons in a modified Zenith thoracic endograft [McWilliams RG et al, 2004]. A similar approach was used to repair an aortic arch aneurysm by fenestrating the LSA with acute angulation of the vessel in relation to the arch, using through and through wire access, a precurved semirigid sheath and serial balloon dilatations [Manning BJ et al, 2010]. Retrograde fenestration via surgical isolation of the left common carotid artery by puncture and balloon dilatation of a thoracic endograft for endovascular exclusion of a descending thoracic aortic aneurysm, has also been reported [Eid-Lidt G et al, 2008]. The feasibility of complete aortic arch reconstruction using the retrograde approach and conduit implantation with cerebral circulatory support was first demonstrated in cadaveric and animal models; balloon-anchored needle dilators and radio frequency (RF) plasma electrode catheters followed by balloon dilatations were used to create fenestrations [Numan F et al, 2008]. Sonesson et al applied this concept in the emergency clinical setting to treat an acute aortic arch rupture; cerebral flow was
maintained using a temporary bypass from the left femoral artery to both carotids perfusing both the anterior and posterior cerebral circulation [Sonesson B et al, 2009]. Successful laser (Turbo Elite laser ablation catheter, Spectranetics, Colorado Springs, CO) in situ fenestration of a Talent thoracic endograft via percutaneous access was recently used to revascularize the LSA in a patient with acute traumatic aortic transection [Murphy EH et al, 2009].

**Visceral and Renal Vessels**

Retrograde in situ fenestration is difficult to apply to the abdominal aorta because of the lack of downstream branch artery access. Inadvertent coverage of target vessels below the diaphragm traditionally mandates conversion to laparotomy largely because of limitations in current device technology and imaging modalities. Percutaneous access to the visceral and renal vessels can be challenging without laparoscopic placements of sheaths, coil embolization, or endoscopic closure of the arterial puncture on completion. More recently the “chimney” technique has been proposed, which involves deployment of a covered or bare-metal stent outside and parallel to the aortic endograft, thereby creating a conduit for branch revascularization [Donas KP et al, 2011]; its long-term effectiveness and durability however is yet to be proven. Tse et al described *antebrade* fenestration of abdominal aortic stent grafts in canine models under fluoroscopic guidance using intravascular ultrasound (IVUS, Volcano Corporation, Rancho Cordova, CA) as an adjunct; renal artery stents were inserted bilaterally prior to fenestration and used as fluoroscopic landmarks [Tse LW et al, 2007]. The same group recently published a similar experiment in canine models, using RF probes for endograft perforation having marked the renal arteries bilaterally.
with detachable coils [Tse LW et al, 2010].

Although the technical feasibility of retrograde in situ fenestration techniques in the arch has been established, clinical reports are scarce and its applicability to the visceral segment is limited. The antegrade approach, remains at the experimental phase and the optimum method for fashioning the fenestrations is yet to be determined. This chapter aims to examine different methods of graft puncture and dilatation and assess the feasibility of robot-assisted antegrade in situ fenestration in vivo.
8.2. Methodology

8.2.1 Preliminary phase

*Fashioning of the fenestrations*

Current endografts are not specifically designed for the purpose of fabric perforation and fashioning fenestrations. Modified needles are mostly used to create the fenestration, which is then dilated with either a cutting balloon or ordinary percutaneous transluminal angioplasty balloons. Tear propagation is greatly affected by changes in yarn and fabric geometry [Primentas A, 2001] and therefore different fabrics react differently to perforation and subsequent dilatation. Tearing occurs due to breakage of fabric cross-yarns as a result of lateral applied tension; in fabrics with low yarn mobility, such as the high-density fabrics used for endovascular grafts, high stress concentrations are found to develop at the deformation or tear initiation site [Hamkins CP et al, 1980]. Consequently graft fenestration is one of the areas of greatest concern as longitudinal propagation of the fabric tear extending beyond the ostium of the target vessel may result in significant periostial endoleaks and aneurysm rupture.

The purpose of this experimental study was to assess the effect of needle perforation and sequential dilatation with either standard or cutting angioplasty balloons on various commercially available stent grafts *in vitro*. The specific aim was to identify the optimal fenestration technique via quantitative and qualitative assessment.
Graft fenestration techniques were tested on three different commercially available stent grafts:

- **Talent** monofilament twill woven polyester (Dacron) (Medtronic Inc., Minneapolis, Minnesota, USA); ~0.09 mm thickness.
- **Zenith** multifilament tubular woven polyester (Dacron) (Cook Vascular Inc., Brisbane, Australia); ~0.15 mm thickness.
- **Endofit** thin-walled expanded polytetrafluoroethylene (ePTFE) (LeMaitre Vascular Inc., Massachusetts, Burlington, USA).

Fabric punctures were made using a 20-gauge needle and fenestrations were sequentially dilated at 30°, 60° and 90° angles using 6mm standard angioplasty (Sterling™ Monorail® Balloon, Boston Scientific, Natick, Mass, USA) or 7mm cutting balloons (Boston Scientific, Natick, Mass, USA) (Fig 8.2.1). With each balloon, the pressure was gradually increased to 10 atm until the balloon was fully open with no waist caused by the endograft; 137 fenestrations were fashioned in total.
Fig 8.2.1. Fenestration fashioning *in vitro*

Graft punctures using a 20-gauge needle and subsequent balloon dilatation of the fenestrations *in vitro* at 30°, 60° and 90° angles.
Quantitative and qualitative assessment

The fenestrations were evaluated using a Nikon Eclipse E400 microscope with a UV light source, Phase Contrast and a Nikon DXM 200 digital camera. Magnifications in the range of 2-100X were undertaken and images were captured using the microscope’s software. Specimens were examined to determine fenestration size, shape and margins specifically assessing the degree of fibre tears, aggregation and distortion using a scoring sheet (Table 8.2.1). Qualitative assessment was carried out by four blinded observers (C.R, C.B, M.H, N.C).

Statistical analysis

The Statistical Package for the Social Sciences version 18.0 (SPSS, Chicago, Ill., USA) was used for data analysis. The non-parametric distribution of the data necessitated the use of non-parametric tests for significance. Differences between fenestrations were compared using the Kruskal-Wallis test. A p value of p < 0.05 was considered statistically significant. Inter-observer reliability for the blinded assessors was calculated with the Cronbach's alpha test statistic.
Table 8.2.1. Qualitative scoring of the fenestrations *in vitro*

<table>
<thead>
<tr>
<th>SHAPE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Circular</td>
<td>4</td>
</tr>
<tr>
<td>Squared</td>
<td>3</td>
</tr>
<tr>
<td>Elliptical</td>
<td>2</td>
</tr>
<tr>
<td>Slit-like</td>
<td>1</td>
</tr>
<tr>
<td>Indefinable/highly distorted</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MARGINS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear, circumferential fibre aggregation (yarn) visible</td>
<td>4</td>
</tr>
<tr>
<td>Minimal number of fibres visible</td>
<td>3</td>
</tr>
<tr>
<td>Moderate number of fibres visible, fibre distortion/weakness beyond fenestration margins</td>
<td>2</td>
</tr>
<tr>
<td>Extensive degree of fibres visible, small fibre tear beyond fenestration margins</td>
<td>1</td>
</tr>
<tr>
<td>Extensive distortion, large fibre tear</td>
<td>0</td>
</tr>
</tbody>
</table>
8.2.2 Experimental phase

The purpose of this experimental study was to assess the feasibility of robot-assisted antegrade in situ fenestration of aortic endografts in the visceral segment in vivo. 17 aortic branches in total were targeted, namely: 16 renal arteries and 1 superior mesenteric artery, in 8 large (65-100kg), fully anesthetized and heparinized swines. All procedures were performed under fluoroscopic guidance in the angiography suite, in compliance with the Institutional Animal Care and Use Committee (IACUC) and Animal Welfare Act guidelines in an accredited animal care facility (Hansen Medical, Mountain View, CA).

Percutaneous access was gained via the common femoral vessels via 9F and 18F sheaths. Rotational angiography to create an arterial roadmap was used in 5/8 animal cases. For the remaining 3 cases, the position of the target vessels was marked on the fluoroscopy screen in an anteroposterior (AP) projection. Intravascular ultrasound (IVUS) technology was used as an adjunct in 2 cases. For each swine, 16-18mm iliac extension woven polyester endografts (Medtronic Inc, Minneapolis, Minnesota, USA) served as the main body device, and were introduced in the porcine aorta via the femoral access route. Under fluoroscopic control, the main aortic stent was positioned so that spaces between the metallic struts were located at the target vessel ostia and was then fully deployed across the visceral segment covering the target vessels. The Hansen Sensei™ System (Hansen Medical, Mountain View, CA, USA) was used for all cases and the Artisan robotic catheter was introduced via the common femoral artery using an 18F sheath. The virtual catheter on the robotic workstation monitor was aligned with the robotic catheter in AP, 40 degrees right anterior oblique and left
anterior oblique configurations to improve navigational accuracy. The robotic catheter tip was then positioned against the fabric of the main body device, adjacent to the ostium of the target vessel. The fabric was punctured with a 20-gauge customized flex-tip trans-septal needle (Hansen Medical, Mountain View, CA, USA) that was introduced and kept in place by the robotic arm to ensure that the fabric was perforated in the center of the ostium of the target vessel under continuous fluoroscopic monitoring. The position was confirmed by a small amount of contrast injected through the needle.

For each branch vessel targeted, a 0.014-mm guide wire (Cordis Corp., Miami, Florida, USA) was threaded through the needle and into the target vessel. The needle was exchanged for serial 4 x 20 mm and 5 x 20 mm angioplasty balloons (Boston Scientific, Natick, Mass, USA) over the wire and through the lumen of the robotic catheter for serial dilatations of the fenestration fashioned. A 6 x 12 mm balloon expandable bare metal stent (Formula 418® Biliary Balloon Expandable Stent, Cook Medical Inc., Bloomington, IN, USA) was then introduced via the robotic catheter into the target vessel. The robotic catheter was autoretracted and repositioned with fine movements to allow for balloon expansion, and the optimum angle was subsequently obtained to maintain stability during stent deployment.

Completion angiography was performed for all cases to assess patency of the target vessels. All animals were sacrificed according to Animal Welfare Act guidelines. Autopsy was performed in all cases the aorta, branch arteries and kidneys were harvested. The explanted endograft was subsequently analyzed with regards to the degree of fabric tear and seal adequacy.
8.3. Results

8.3.1 Preliminary phase

Compared to Dacron, PTFE grafts were easier to puncture and dilate with standard angioplasty balloons; Medtronic and Zenith Dacron grafts resisted low-pressure dilatation. The fabric of the Zenith stent graft was the most resilient and resulted in bursting of the balloon when the pressure exceeded 10 atm. Differences observed in the size of the fenestrations fashioned, also reflect the different tensile strengths of the fabrics tested. PTFE resulted in significantly larger diameter fenestrations: 5.2mm (4.5-6.6) versus 0.9mm (0.5-1.5) and 0.6mm (0.3-1.3) for Medtronic and Cook Dacron grafts respectively; p<0.001 (Fig 8.3.1).

In terms of descriptive and qualitative metrics following microscopic evaluation, there was good inter-observer reliability between assessors with a Cronbach’s α=0.89. PTFE graft puncture and dilatation resulted in elliptical fenestrations, oriented transversally along the endograft. Dacron fenestrations were mostly squared, however, in the Medtronic grafts, the fenestrations appeared circular when the needle/balloon was introduced at a 90° angle (Fig 8.3.2).
Fig 8.3.1 Endograft material and fenestration size

Bar chart representing mean fenestration dimensions post dilatation with standard angioplasty balloons at 30°, 60° and 90° angles. Fenestration resulted in significantly larger diameter defect in PTFE grafts versus Dacron fabrics, p<0.001 (Kruskal-Wallis test).

Fig 8.3.2 Endograft material and fenestration shape

Bar chart representing descriptive assessment with regards to fenestration shapes post dilatation with standard angioplasty balloons at 30°, 60° and 90° angles.
In Medtronic grafts, fenestration quality was significantly higher when the needle was introduced at 90° angles with clean, circumferential fibre aggregation (yarn) and minimal number of fibres and tears beyond the fenestration margin visible. PTFE graft puncture and dilatation also scored highly in terms of fenestration margins with smooth edges and no indication of fraying, especially at 90° angles; however a significant number of margin tears was observed with increasing balloon pressures. Cook grafts exhibited extensive fibre distortion at the fenestration margins and a large number tears were observed in 50% of specimens tested (Fig 8.3.3, Fig 8.3.4, Fig 8.3.5). Cutting balloon use resulted in significantly more fabric tears in all endograft types with extensive fibre distortion and fraying and poor overall quality fenestrations (Fig 8.3.6).
Fig 8.3.3 Endograft material and fenestration margin quality

Bar chart representing qualitative assessment scores for fenestration margins mean post dilatation with standard angioplasty balloons at 30°, 60° and 90° angles, where 4 represents the maximum attainable score.
Fig 8.3.4 Endograft material and fenestration margin tears

Chart representing percentage of fenestration margin tears observed post dilatation with standard angioplasty balloons for the three different endograft materials. Corresponding microscopic images (8X and 80X) of the fenestration margin tears are also shown.
Fig 8.3.5 Microscopic appearance of fenestrations *in vitro*

Microscopic images (8X) of the fenestrations *in situ* observed post dilatation with standard angioplasty balloons for the three different endograft materials at 30°, 60° and 90° angles.
Fig 8.3.6 Endograft material and fenestration margin tears using a cutting balloon

Chart representing percentage of fenestration margin tears observed post dilatation using cutting balloons for the three different endograft materials. Corresponding microscopic images (8X and 80X) of the fenestration margin tears are also shown.
8.3.2 Experimental phase

17 aortic branches in total were targeted, namely: 16 renal arteries and 1 superior mesenteric artery, in 8 large (65-100kg), fully anesthetized and heparinized swines. The results of the preliminary phase of the study indicated that Medtronic Dacron endografts responded well to needle puncture and subsequent balloon dilatation resulting in circular fenestrations with clean margins, good fibre aggregation and low incidence of fabric tears; they were therefore chosen to serve as the main body device for the in vivo experiments. The robotic catheter tip was positioned against the fabric of the main body device, adjacent to the ostium of the target vessel to facilitate needle puncture and serial dilatation at 90° angles, in order to produce high quality fenestrations as shown in the in vitro studies described earlier in this chapter. Stent-graft puncture and target-vessel cannulation with a guidewire was possible in 15/17 vessels attempted and subsequent branch-stent deployment was successful in 13/15 vessels. The technique is shown in Fig 8.3.7, 8.3.8 and 8.3.9. In 2 cases, attempts at needle puncture were unsuccessful due to insufficient angulation of the customized needle and the limited workspace within the small diameter porcine aorta (13 – 16mm). For the same reason, and despite the added support of the robotic catheter sheath, the angioplasty balloon could not be advanced across the graft to complete the fenestration in a further 2 cases. The wire exited in the retroperitoneal space in 3 cases and wire entrapment within the needle was observed in a further 2 cases.
A 16mm iliac extension Dacron endograft (Medtronic Inc, Minneapolis, Minnesota, USA) served as the main body device, and was introduced in the porcine aorta via the femoral access route. Under fluoroscopic control, the main aortic stent was positioned so that spaces between the metallic struts were located at the target vessel ostia and was then fully deployed across the visceral segment covering the target vessels.
With the main aortic body device fully deployed, the fabric of the endograft is punctured with a 20G customized needle that is introduced, guided and supported via the robotic catheter. A 0.014-mm guide wire was threaded through the needle to cannulate the R renal artery. A 4 x 20 mm angioplasty balloon advanced over the wire can also be seen. The robotic catheter has been autoretracted to allow for balloon expansion.
Fig 8.3.9 Balloon dilatation and branch vessel stenting *in vivo*

Following needle puncture and target vessel cannulation, serial angioplasty balloon dilatation of the fenestrations and subsequent branch vessel stenting is shown. The robotic catheter is autoretracted and repositioned with fine movements to allow for balloon expansion until the waist of the balloon disappears, aiming at 90° angles to the vessel ostium and maintaining stability during stent deployment.
Rotational angiography was used in 5/8 animal cases in order to create an arterial roadmap, improve navigation and target localization (Fig 8.3.10). For the remaining 3 cases, where rotational angiography technology was not available, the position of the target vessels was marked on the fluoroscopy screen in an anteroposterior (AP) projection. The 8F, 12MHz IVUS probe (In-Vision Gold; Volcano Corporation, Rancho Cordova, CA, USA) also used in 2 cases to enhance navigational accuracy, was inserted in the inferior vena cava and allowed visualization of the target vessel lumen, however, the aortic lumen could not be seen across the graft. A second IVUS probe positioned within the main aortic body could not clearly visualize outside the endograft, unless it was placed directly against the fabric of the device (Fig 8.3.11).

Completion angiography confirmed good flow in 15/17 vessels. Vasospasm as well as small filling defects was seen at the distal portion of the branch vessel stents for 8 vessels, suggesting a localized dissection; however, there was no evidence of flow limitation (Fig 8.3.12). Median procedure time was 75 min (IQR 60-90); median right renal artery coverage time was 17min (15-20) and median left renal artery coverage time was 23min (20-28). The median volume of contrast injected was 45ml (28-55). The estimated blood loss was less than 300mL. All swines tolerated the procedure well; blood pressure and heart rate remained stable throughout the procedure with no immediate complications.
Fig 8.3.10 Rotational angiography and arterial roadmapping

The three-dimensional (3D) reconstructed arterial road map obtained after a 240° rotation of the C-arm and a single injection of iodinated contrast, is superimposed on the real-time two-dimensional fluoroscopic image. The robotic catheter and fenestration needle can be seen aiming towards the right renal artery.

Fig 8.3.11 Intravascular ultrasound (IVUS)

The IVUS probe positioned within the main aortic body was used to confirm the position of the SMA prior to puncture and cannulation in this case. It could only visualize the SMA lumen across the graft provided that the probe was placed against the fabric of the aortic device. Bilateral renal stents following antegrade in situ fenestration are also shown.
Fig 8.3.12 Completion angiography

Completion angiography confirmed good flow in 15/17 vessels. Vasospasm as well as small filling defects were seen at the distal portion of the branch vessel stents in 8 cases, suggesting a localized dissection; however, there was no evidence of flow limitation.
The animals were sacrificed later for autopsy. Macroscopic examination showed evidence of a retroperitoneal hematoma in one swine. There were no visible perforations of the aorta or any of the target vessels in all but 3 cases. There was evidence of small, localized dissections in 8 cases; for the remaining specimens however the intima was healthy and intact.

The explanted endografts were subsequently analyzed with regards to the degree of fabric tear and seal adequacy. Specimen dissection confirmed fixation and sealing for all branch stents. Fabric evaluation revealed traces of puncture attempts and complete graft perforations, less than 0.3mm in size were observed in 3 cases.
8.4. Discussion

In-situ fenestration of aortic stent grafts utilizing a remotely controlled robotic steerable catheter system is an attractive alternative to custom-made fenestrated and branched stent grafts to overcome some of the inherent limitations associated with these manufactured devices. Although clinical reports are scarce, there is ongoing interest to improve current materials and techniques using advanced technology to make this exciting new concept a viable option for a wholly endovascular approach of aortic pathologies.

Current endografts are not specifically designed for the purpose of fashioning fenestrations and different fabrics react differently to perforation and subsequent dilatation. Consequently graft breaching and dilatation is one of the areas of greatest concern as longitudinal propagation of the fabric tear extending beyond the ostium of the target vessel may result in significant periostial endoleaks. The results of the preliminary in vitro experiment presented in this chapter suggest that compared with Dacron, PTFE is easier to perforate; the puncture can be readily dilated with a standard angioplasty balloon resulting in larger elliptical fenestrations. PTFE dilatation however, is more likely to result in propagating fabric tears at <90° dilatation angles. Microscopic analysis of 137 fenestrations revealed that fenestration quality is significantly higher when the needle is introduced at 90° angles and that angle is maintained during serial balloon dilatations. The highest fenestration quality in this bench qualitative and quantitative experiment was achieved in Medtronic Dacron stentgrafts showing circular fenestrations with clean margins, good fibre aggregation and low incidence of fabric tears; they were therefore chosen to serve as
the main body device for the *in vivo* part of this study. Cutting balloon use resulted in significantly more fabric-tears in all endograft types. Standard angioplasty balloons should therefore be preferred, as the number of ruptured fibers is limited in comparison, and the risk of arterial perforation is reduced.

The *antegrade* approach to in-situ fenestration in particular, requires accurate positioning of the instruments used to ensure precise puncturing of the endograft. Modified needles are mostly used to perforate the endograft; these can be difficult to direct especially through tortuous vessels, and the tip usually requires an acute angle in order to perforate the graft accurately, to ensure that the fabric is punctured in the center of the ostium of the branch vessel. Rigid sheaths can be used to direct the needle through the graft; this however would require through and through access between the target vessel and the access vessel to facilitate its delivery and to minimize the risk of arterial trauma. The Artisan robotic catheter acts as a flexible yet stable sheath, whereby a number of endovascular tools can be advanced through its lumen. The versatility of the robotic system, its precise positional orientation, minimum instrumentation of the vessel wall, and the ability to reproducibly and accurately return to sites of interest can facilitate in-situ fenestration of aortic stent grafts with minimal radiation exposure, as shown in the *in vivo* case series presented in this chapter. Stent-graft puncture and target-vessel cannulation with a guidewire was possible in 15/17 vessels attempted and subsequent branch-stent deployment was successful in 13/15 vessels. The robotic catheter tip was positioned against the fabric of the main body device, adjacent to the ostium of the target vessel to facilitate needle puncture and serial dilatation at 90° angles, in order to produce high quality fenestrations as shown in the *in vitro* phase of the study. Another important technical
aspect described in published reports of in situ fenestration techniques that may be overcome by use of the robotic system relates to the lack of control over where the fabric is punctured and dilated in relation to the endograft. The metallic struts of the graft endoskeleton should be avoided not only to ensure clean fenestration margins but also to minimize damage to the stent itself making it prone to early fatigue fractures.

This study demonstrates the feasibility of robot-assisted antegrade in situ fenestration in vivo. The use of robotic technology results in accurate and stable puncture dilatation of aortic endografts at 90° angles for optimum fenestration quality, whilst facilitating branch vessel cannulation and subsequent stent placement. Several important issues however, need to be addressed prior to wider clinical applications:

*Endograft Design and Seal Durability*

The in situ fenestration approach to aortic stent grafting will require significant developments in aortic graft as well as branch stent construction and design not only to facilitate the fenestration process but also to ensure its long-term efficacy. The main aortic stent will require further development to allow free flow into the visceral vessels before fenestration as in the case of standard custom-made devices. The seal durability between the fenestration margins and the bridging stent, given the challenging hemodynamic environment of the arch and the physiological movements of the renal ostia below the diaphragm, is yet to be proven. The current uncertainty regarding the fenestration margins and seal may be addressed by designing “reinforced patches” within the endograft to specific target areas. The incorporation
of modified fabric or deformable metallic threads that will condense around the fenestration to form a stable sealing ring against which the bridging stent can engage, resulting in a durable seal. The graft endoskeleton will also need to be modified, to avoid the presence of struts at the target areas. Partial deployment of the endograft itself, by maintaining attachment to its delivery system may offer some additional support by avoiding kinking of the graft material by the puncturing needle during the fenestration process.

**Imaging**

Although stent graft technology has evolved, the mainstay of image guidance in most endovascular treatment suites remains fluoroscopic, with its attendant radiation exposure to patient and staff and need for nephrotoxic contrast agents. Accurate visualization of key aortic regions preoperatively, but most important, in “real-time,” is essential for the efficacy and safety of the in situ fenestration process. Current fluoroscopic methods lead to loss of 3-dimensional information, which can result in difficulties in positioning of the guiding wires, catheter, and stents especially in the presence of complex anatomy. Fluoroscopic landmarks can be used prior to endograft deployment; however, these methods provide 2-dimensional information regarding a 3-dimensional object, the aorta.

IVUS probes placed either within the endograft or the inferior vena cava have the potential to offer useful anatomical information with regards to the position of the target vessel ostia especially below the coeliac axis where vessel access is challenging. In this study, IVUS guidance did not offer a significant advantage over
conventional imaging techniques mainly due to the limitations of current IVUS technology. Computer tomographic rotational angiography is another alternative, which in this case series enhanced navigational accuracy by providing a static 2D anatomical roadmap.

Both these imaging modalities, however, in their current form, do not offer reproducible, 3-dimensional, “real-time” navigation, which is essential for optimum accuracy and safety within the arterial tree. Ongoing research in our group is currently investigating advanced 3D navigational techniques involving impedance-based image registration systems and electromagnetic tracking of microposition sensors located at the tip of endovascular guidewires and catheters, which may enhance advanced endovascular applications such as in situ fenestration [Sidhu et al, 2010]. These technologies are currently widely applied in neurosurgery as well as cardiac mapping and ablation procedures [Harrisson SE et al, 2011; Steven D et al, 2010].

Fenestration Tools

More sophisticated endovascular tools, such as RF devices [Tse LW et al, 2010] and laser probes [Murphy EH et al, 2009] have recently been tested as adjuncts to improve fenestration quality and stability during the in situ process. RF ablation catheters are capable of creating full-size circular fenestrations with fused edges. Laser technology is promising especially with newer devices that burn a perfect circle through the wall of cerebral vessels using suction to hold on to the flap, preventing it from floating downstream and currently used for cerebral revascularization in neurosurgical procedures [Van Doormaal TP et al, 2008; Van Doormaal TP et al, 2010]. Current
devices, however, can be difficult to steer and control. Robotically steerable endovascular catheters provide an ideal platform for the introduction, manipulation and stability of endovascular tools and their compatibility with advanced navigation and imaging systems can further enhance the current and future methods of in situ fenestration.
8.5. Conclusions

The management of complex aortic pathologies remains a major challenge, particularly in the emergency setting. Extensive preoperative planning, cost of custom-made endografts, and the technical difficulties encountered in complex anatomical configurations hinder the wider applications of minimally invasive endovascular therapy. Hybrid techniques represent transitional options bridging to a complete endovascular approach. In situ fenestration is an attractive alternative and is clearly feasible. Optimization of the current method using advanced catheter and navigation technologies can potentially accelerate its development in the clinical setting. Further research, long-term follow-up data, and significant improvements in endograft design, materials, and imaging are required to make it a reliable and reproducible endovascular option.
Chapter 9.

First Clinical Application of Robotics in Endovascular Aneurysm Repair

9.1. Background

Prior to this research, clinical use of endovascular robotic technology was limited to transvenous cardiac mapping and ablation procedures [Kanagaratnam P et al, 2008; Saliba W et al, 2008, Di Biase L et al, 2009]. Following a comprehensive pre-clinical comparison and analysis of robotic versus manual catheter techniques in the arterial tree, this chapter reports the world’s first clinical application of endovascular robotics for endovascular aneurysm repair (EVAR), as a “proof - of - concept”, in order to assess this novel and innovative approach in the clinical setting.
9.2. Clinical Case

A 78-year-old man with chronic renal failure secondary to obstructive kidney disease (creatinine on admission 202 mmol/L) was admitted for elective repair of a 5.9-cm asymptomatic infrarenal abdominal aortic aneurysm (AAA), which had been under periodic ultrasound surveillance for 10 years. Following a standardized preoperative assessment protocol (dobutamine stress echocardiography, MAG-3 renal scanning, and lung function tests) and after discussion in our multidisciplinary forum, he was considered suitable for robot-assisted EVAR. Full, informed patient consent as well as approval by the Chairman of the Directors Board in our institution was obtained.

9.3. Technique

Following standardized training with the Hansen Sensei robotic system and after rehearsing the procedure in a laboratory environment, our group was able to undertake the first human case of robotically assisted endovascular infra-renal aneurysm repair. Under general anesthesia, the common femoral arteries were surgically exposed. After systemic heparinization (5000 units), a 28-316-mm-diameter 3 170-mm-long bifurcated Endurant stent (Medtronic Vascular, Santa Rosa, CA, USA) was introduced via the right groin over standard 0.035-inch stiff Meier wires (Boston Scientific Corp; Natick, MA, USA) and deployed under fluoroscopic control with an imaging catheter that was placed through the left femoral access. The 14F steerable robotic catheter was then introduced in the left femoral artery through
an 18F long access sheath. The virtual catheter image on the workstation screen was aligned with the robotic catheter in anteroposterior (AP) and 40° right and left anterior oblique configurations to improve navigational accuracy. The robotic catheter was driven into the aneurysm sac (Fig 9.3.1) utilizing the force-quantification system (Intellisense Technology).

The steerable tip of the robotic catheter was remotely driven adjacent to the distal end of the contralateral limb of the main bifurcated stent body under fluoroscopic guidance. The position was confirmed in AP and lateral projections. The contralateral limb was successfully cannulated using fine and controlled movements in less than 3min (Fig 9.3.2). The robotic catheter was then advanced to the level of the suprarenal aorta, and a 0.035-inch stiff Meier wire was passed through its lumen (Fig 9.3.3). The Artisan robotic catheter was autoretracted and removed through the 18F sheath. Completion angiography confirmed successful exclusion of the aneurysm with no immediate complications (Fig 9.3.4). No contrast was used during the robotic stage of the procedure; 38 mL of contrast used in total.

Postoperatively, the patient made an uneventful recovery with no deterioration of the renal function. Computed tomography prior to discharge, at three months and yearly thereafter confirmed that the stent-graft remained in good position, with no evidence of an endoleak and adequate sac shrinkage.
The robotic catheter is driven into the aneurysm sac. A force-quantification system (Intellisense Technology) represented visually as a graph on the workstation screen ensures safe manipulation of the robotic catheter tip. The steerable tip is positioned adjacent to the distal end of the contralateral limb of the main bifurcated stent body under fluoroscopic guidance. The virtual catheter is also seen.
Fig 9.3.2 Robotic cannulation of the contralateral limb

Successful cannulation of the contralateral EVAR limb. The inner guide of the Artisan catheter can be seen within the stentgraft, with the stiffer outer guide adding additional support for the passage of stiffwires.
Fig 9.3.3 Introduction of stiff guidewires through the robotic catheter

The robotic catheter is advanced and a 0.035-inch stiff Meier wire is passed through its lumen.
Completion angiography showing successful aneurysm exclusion with no evidence of vessel damage.
9.4. Discussion

With recent advances in endovascular technology, endovascular aneurysm repair has become an attractive alternative to open surgery for a range of aortic pathologies, with significantly reduced mortality and comparable long-term outcomes. Despite the exponential advances in endovascular equipment, devices and techniques, as discussed extensively in previous chapters, endovascular intervention has certain morphological and technological constraints.

A remote robotic catheter system may help overcome some of the anatomical and technical difficulties associated with endovascular aneurysm repair, especially when tackling complex anatomical configurations. A steerable multidirectional catheter with a tight bend radius that allows fine and controlled movements in multiple planes may be useful when dealing with difficult contralateral gates in infrarenal stents or anatomically challenging target vessel cannulation in fenestrated and branched stent grafting. The system also minimizes operator radiation exposure, as the workstation is located outside the endovascular suite and away from the radiation source (Fig 9.4.1).
Fig 9.4.1 Robot-assisted EVAR: first patient application

The operator manipulates the robotic catheter from the workstation outside the endovascular theatre suite, minimizing therefore radiation exposure.
This thesis has provided *in-vitro* and *in-vivo* evidence of the advantages of robotic catheter systems for endovascular intervention in terms of catheter maneuverability, stability, overcoming difficult anatomy, operator performance, safety, and skill acquisition. The world’s first robot-assisted endovascular aortic aneurysm repair presented in this chapter, received national and international press recognition (Smith R, 2008) and provided a proof-of-concept for robotic endovascular therapy in the arterial tree. Although the feasibility of robot-assisted aortic intervention in a clinical setting has been demonstrated, its role clearly lies in more complex endovascular procedures. To explore this further, we have initiated a trial, approved by our Institution and the Regional Ethics Committee, to assess and determine the safety and performance of endovascular robotic technology in the clinical setting with particular emphasis on fenestrated and branch endografting.
9.5. Conclusions

This initial clinical experience demonstrates that EVAR using robotically steerable catheters to cannulate the contralateral limb of an infrarenal stent-graft is technically feasible. Although these endografts are placed routinely without the need for such advanced technology, the authors believe that the steerable nature, flexibility, and stability of this robotic catheter system may be of benefit in more complex procedures, such as fenestrated stent-grafting, where fluoroscopic times are long and the anatomy more challenging. Further clinical evaluation of this promising technology is required in a randomized clinical trial setting.
Chapter 10.

Summary and future research

For over a decade, there has been a paradigm shift to an endovascular, minimally invasive approach whilst treating diseases of the aorta and its branches, with clear advantages in terms of morbidity and mortality in certain vascular beds, especially in patients with multiple co-morbidities that would otherwise be deemed unsuitable for traditional open surgical approaches. Endovascular intervention however, has certain morphological and anatomical constraints. Difficult anatomical targets may lead to prolonged endovascular instrumentation carrying significant risks to the patient such as distal embolization and vessel trauma, with increased fluoroscopic exposure and long overall procedure times. Furthermore, complex endovascular tasks require a refined set of operator skills and technical finesse that is usually acquired after years of experience and standardized training.

Conventional endovascular catheter technology contributes to these technical limitations; with a limited repertoire of shapes and sizes, they are difficult to steer and lack active maneuverability of the tip. This manual control can hinder overall stability and control at key target areas necessitating frequent catheter changes and risking loss of wire position in challenging cases. Catheter movement in itself consists of a series of interactions, which occur between the catheter, the guidewire and the vessel wall. Although effective, it is this wall interaction, which is responsible for many of the
complications reported, as repeated instrumentation especially in the presence of vessel thrombus or calcification, increases the risk vessel dissection, perforation and distal embolization. Endovascular flexible robotic technology presents itself as an attractive option, with enhanced active maneuverability, control at the catheter tip and the promise of “off the wall”, centerline navigation remotely and away from the radiation source.

This thesis examined the applicability of the Hansen Sensei system - originally designed for transvenous cardiac mapping and ablation procedures - in-vitro and in-vivo to evaluate its role in the arterial tree. Robotic endovascular catheters offer advantages for target vessel cannulation and effectiveness in reducing procedure times with greater accuracy and minimal contact with the vessel wall, in complex endovascular intervention. Robotic cannulation seems to be significantly faster than standard cannulation using conventional endovascular catheters in the visceral segment as well as the aortic arch. The data suggests that the time taken to access target vessels may be reduced by 83% using robotic technology, with important implications for fluoroscopic exposure, radiation dose and overall procedure times. The number of movements at the catheter tip required to complete successful target vessel cannulation is also significantly reduced. This is likely a result of a greater range of motion with the robotic catheter and increased three-dimensional control. With conventional catheters the operator is required to make a series of movements, adjusting the amount of manual torque in order to reach a given target. The benefits using robotic technology are particularly evident with the more challenging anatomical configurations, whereas one may argue that advantages during simplex endovascular tasks may be less clinically relevant.
Mere target vessel catheterization however, does not necessarily reflect technical success in complex arterial intervention. Equally important is the ability to advance stiff guidewires and other endovascular tools whilst maintaining stability at target sites. The robotic system is effectively a steerable sheath supporting a more flexible inner guide. Consequently, the catheter resists the tendency to herniate back into the aorta even with shallow cannulation, as wires and other endovascular tools are being advanced through its lumen. In 216 stiff guidewire exchanges studied, robotic endovascular catheters maintained stability at target sites with zero deflection during stiff guidewire exchanges, independent of the distance the catheter was introduced into the target vessel and no loss of access. In contrast, conventional catheters required positioning at least 2cm into the target vessel in order to avoid catheter deflection and subsequent loss of access. Robotic catheters, demonstrated increased stability at the target vessel osmium; this may prove useful when tackling angulated aortic arches, aneurysm necks and tortuous branches.

Tortuosity of the access vessels is another important factor to consider and constitutes a challenge to successful endovascular intervention. With increasing iliac tortuosity conventional catheter advancement and manipulation becomes more technically demanding. Angulation at the access end of the path trajectory directly impacts on manipulation at the distal end of the wire/catheter interface, with limited torquability and buckling of the selective catheter, resulting in multiple cannulation attempts with frequent catheter changes. Robotic catheter manipulation seems to be unaffected by iliac tortuosity severity with faster cannulation times, increased positional accuracy
and catheter control. Again these advantages were particularly evident in the more tortuous cases.

Investigating the system further, an overall improvement in operator performance whilst attempting complex endovascular tasks was observed. With robotic techniques, operator groups with varying experience in conventional endovascular procedures obtained equal scores indicating that skill using conventional catheters does not translate to robotic competence. However, the scores obtained using the robotic catheter were similar to those of highly experienced operators using the conventional approach, despite a short training period on the robotic system. The acquisition of rudimentary endovascular skills in novice subjects was also assessed in a 5-week training programme examining conventional versus robotic catheter techniques. Robotic catheters, although more intricate, do not seem to take longer to master and offer clear advantages with regard to positional control, at a faster rate, with shorter learning curves and an earlier plateau. Robotic technology seems to be the intuitive and advanced skill acquisition occurs with minimal training. It may, therefore, have a significantly shorter path to proficiency allowing an increased number of trainees to attempt more complex endovascular tasks earlier and with a greater degree of safety.

Endovascular robotic technology could be valuable for other advanced endovascular applications such as in-situ fenestration of aortic stent grafts, which would obviate the need for expensive, bespoke fenestrated stents that can take weeks to manufacture. The technique of robot-assisted in-situ fenestration may offer the option of total endovascular aneurysm repair to many patients who are either anatomically unsuitable for custom endovascular fenestrated stent grafting, those who require the
procedure on an urgent basis, or serve as a bail-out options during inadvertent branch coverage in standard endovascular repairs. To date, we have achieved antegrade, in-situ fenestration in porcine models using the Hansen system in conjunction with 3-dimensional rotational angiography and intravascular ultrasound. Accurate positioning of the catheter tip within the main aortic body, and adjacent to the vessel ostia is crucial in this procedure. Its position must also be stable, so as to allow precise puncture of the stent-graft and subsequent target vessel cannulation, serial balloon dilatations and stenting. This and other advanced applications may be further enhanced by 3D navigation technology and robotics seems to be the ideal platform for the integration of advanced “real-time” imaging techniques, localization, simulation and pre-procedure rehearsal; the Hansen system is compatible with existing non-fluoroscopic mapping systems such as NavX™ (St. Jude Medical, St. Paul, MN, USA). Integration of robotics with 3D navigation technology may further improve the accuracy of catheter positioning and manipulation, and is currently one of the main research focuses within our group [Sidhu R et al 2010, Lee SL et al 2011]; further work is currently underway in association with the department of Computing at Imperial College London.

The Hansen Sensei system is limited by the large 14F sheath (11F inner guide) size of the Artisan robotic catheter, which may not be suitable for certain branch vessels especially in the presence of significant atherosclerosis and calcification. Furthermore, although the Artisan outer sheath adds stability to the system, it is constrained to one-way fixed angulation as it was originally designed for access to the right atrium via the IVC. Our team has worked closely with our industry associates (Hansen Medical, USA) over the last 2 years to develop a smaller, more flexible and
adaptable catheter which has now received CE marking for use in the peripheral arterial vasculature. The development of this next-generation robotic system (Magellan) was based on the original platform of the Sensei system but with significant modifications, which afford enhanced maneuverability through a 6F inner guide platform with a 130° multi-directional articulation, and a 9.5F sheath with an additional 90° multi-directional articulation. The Remote Catheter Manipulator (RCM) allows retraction, insertion, rotation and catheter angulation of both the leader catheter and sheath, as well as providing 6 degrees of freedom. Furthermore, a robotic wire manipulator allows remote insertion, rotation and retraction of hydrophilic wires. The workstation is again located outside the angiographic suite and away from the radiation source, allowing catheter manipulation via a “master-slave” mechanism; the virtual catheter image projected on the workstation monitors identifies degrees of catheter flexion and rotation inside the vessel lumen, enhancing positional accuracy and catheter control. This specifically designed robotic catheter has a unique potential to simplify complex endovascular procedures.

The purchase, installation and maintenance costs of endovascular robotic technology, however, cannot be underestimated especially in the current financial climate of austerity. Our pre-clinical studies suggest that the time taken to access vessels may be reduced by 83% using robotic techniques, which for a complex four vessel fenestrated case in our institution in our earlier series would translate to an average 2hr 29 min reduction in operating time. Added benefits in terms of accuracy and radiation exposure make the use of flexible robotics an attractive option, however much will depend on the price of disposable components, clinical outcomes and the potential for
wider applicability. Clinical data and cost-effectiveness studies are essential for translation and wider adoption into healthcare.

Following standardized training with the robotic system and after rehearsing the procedure in a laboratory environment, in August 2008, we were able to undertake the first human case of robotically assisted endovascular infra-renal aneurysm repair worldwide, receiving national and international press attention and providing proof of the concept for robotic endovascular therapy. Experience with the robot has allowed our group to perform early clinical cases and design a trial to study the use of this technology for branch vessel cannulation in fenestrated stent grafting as well as challenging aorto-iliac cases. Refining the technical aspects of robotic endovascular robotic intervention using in-vivo and in-vitro models and studying clinical outcomes of the next-generation robotic catheter (Magellan) as part of our ongoing clinical trial we aim to further evaluate the clinical use of this technology in conjunction with advanced imaging and navigation techniques.
10.1. Conclusions

Despite recent advances in device technology for catheter-based peripheral arterial revascularization procedures, the inadequacy of conventional catheters for the variable and often unpredictable anatomy of patients with complex arterial disease implies that alternative catheter designs are essential. Complex endovascular procedures can be time consuming and require a high degree of technical performance and long training pathways as their success is determined largely by operator skill. This work suggests that in benchtop and *in-vivo* models, for most surgeons, complex endovascular procedures are easier to perform using the robotic steerable system. This translates into shorter fluoroscopic times, fewer catheter movements and vessel wall interactions, and less interference by complicating factors such as iliac tortuosity or shallow vessel catheterization. Integration of robotic technology into clinical practice may lead to improved catheter accuracy, stability and safety in comparison with conventional techniques whilst minimizing radiation exposure. Further development to optimize the use of endovascular robotics in the arterial tree and evaluation of this technology in the clinical setting is mandated prior to widespread applications. By refining and understanding the role of new technologies whilst developing new approaches to treating challenging cases, it is hoped that the applicability of minimally invasive endovascular intervention can be extended to a larger cohort of patients.


Brunkwall JS. Preliminary Results Of The ADSORB Trial Comparing TEVAR For Uncomplicated Type B Aortic Dissections With Medical Treatment, The Veith Symposium, Nov 2011, New York.


Dubost C, Allary M, Oeconomos N. Resection of an aneurysm of the abdominal aorta: reestablishment of the continuity by a preserved human arterial graft, with result after five months. AMA Arch Surg. 1952 Mar;64(3):405-8.


European Carotid Surgery Trialists Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-90%) or mild (0-29%) stenosis. Lancet. 1991;337:1235-1243.

European Vascular and Endovascular Monitor (EVEM), http://www.bibaresearch.com/services.htm


Publications & Prizes relating to this Thesis

Publications


15. Riga CV, Bicknell CD, Hamady MS, Cheshire NJW. Steerable catheters and their role in the visceral aortic segment. Vascular & Endovascular Consensus Update, BIBA publishing 2011


**Prizes**

Supervisors: CD Bicknell, CV Riga

Chadha P, Riga CV, Cochennec F, Normahani P, Kashef E, Hamady M, Cheshire NJW, Bicknell CD. : “Advanced catheter technology: is this the answer to overcoming the long learning curve in complex endovascular procedures?” The Royal College of Surgeons Undergraduate Research, Dec 2010 - 1st Prize
The National Undergraduate Surgical Conference - The Molnlycke Prize, March 2011
Supervisors: CD Bicknell, CV Riga

Riga CV, Cheshire NJW, Hamady M, Bicknell CD. “New horizons – endovascular robotics for complex vascular intervention”. Best multimedia presentation, Imperial College Research Excellence Award, Sept 2009 – 1st Prize
Riga CV, Bicknell CD, Hamady M, Cheshire NJW. “Endovascular robotic catheters as a useful adjunct to arch vessel cannulation”. The British Society of Endovascular Therapy (BSET), July 2009 – 1st Prize


Riga CV, Cheshire NJW, Hamady M, Bicknell CD. “Endovascular Robotics in advanced aortic intervention”. Imperial College Research Excellence Award, Dec 2008 – 2nd Prize

Riga CV, Bicknell CD, Cheshire NJW, Hamady M. "Robotic endovascular catheters improve accuracy, reduce time and minimize radiation exposure for visceral vessel and fenestrated stent cannulation". The British Society of Interventional Radiology (BSIR), Nov 2008 – 2nd Prize

Riga CV, Bicknell CD, Hamady M, Cheshire NJW. “The role of robotic endovascular catheters in target vessel cannulation”. The British Society of Endovascular Therapy (BSET), June 2008 – 1st Prize