Predicting Advanced Endovascular Aneurysm Repair Complications Using 3D Analytical Tools

by

Sean Allen Crawford

A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy, Biomedical Engineering

Institute of Biomaterials & Biomedical Engineering (IBBME)
University of Toronto

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Abstract

Fenestrated and branched endovascular aneurysm repair [(F/B)EVAR] is a minimally-invasive method for the treatment of aortic aneurysms involving the visceral segment. These procedures involve the placement of a stent graft that incorporates fenestrations or branches with the goal of excluding the aneurysmal sac while preserving blood flow to the visceral arteries. These fenestrations or branches need to align precisely with the target arteries to maintain blood flow and prevent ischemia related adverse events. The objective of these studies is to provide a more comprehensive understanding of stent graft misalignment and to identify methods to predict and prevent stent graft misalignment with a long-term goal of making these procedures safer and more effective for patients.

Stent graft misalignment is a multifactorial process that includes stent graft planning, intraoperative positioning, and stent graft rotation. Greater than 50% of patients undergoing (F/B)EVAR had at least one misaligned renal fenestration and misalignment was associated with higher rates of procedural target vessel complications and severe post-operative adverse events. Similarly, intraoperative stent graft rotation (occurring in 37% of fenestrated procedures) was also associated with a 36% absolute increase in post-operative adverse events. In a multivariate
analysis, factors predictive of stent graft rotation included iliac artery torsion, iliac artery calcification, and device length. Insertion technique also plays an important role in the degree of stent graft rotation. In vivo correction for orientation which is commonly performed during the insertion of the device appears to increase the observed rotation and supports the concept of fully removing the device, adjusting the orientation, and subsequently reinserting. Finally, this thesis describes a finite element analysis-based method for predicting the final location of the delivery system and the resulting aortoiliac deformation.
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Chapter 1

Introduction
1 Introduction

1.1 Clinical Background and Study Rationale

An abdominal aortic aneurysm (AAA) is a focal dilatation of the abdominal aorta, the artery that is the primary supply of blood to the abdominal organs and lower extremities (Figure 1-1A). AAAs occur in 7.6% of men and 1.3% of women over the age of 65 and are the 14th leading cause of death in the United States with similar mortality rates in Canada.\(^1\)-\(^3\) The natural history of this disease is continued aneurysmal growth and ultimately aortic rupture, which carries a significant mortality of approximately 80%.\(^4\) Only 50% of patients with a ruptured AAA will survive to reach a hospital. Of those that make it to hospital, only 50% will survive the surgery to

Figure 1-1. (A) Diagrammatic representation of a normal aorta and an abdominal aortic aneurysm, (B) Standard infra-renal stent graft (Cook Medical), (C) Schematic of stent graft deployment within the aorta, and (D) Illustration of a fenestrated stent graft (Cook Medical).
repair the ruptured aneurysm. This high mortality rate associated with ruptured AAAs highlights the need for the surgical repair of aneurysms before they rupture.

Endovascular aneurysm repair (EVAR) is a minimally-invasive method for treatment of AAAs in which a stent graft is inserted via the femoral artery, through the iliac artery, and into position within the aorta (Figure 1-1B). Relative to the traditional open-surgical repair, infrarenal EVAR has a significantly lower perioperative mortality of ~1%, compared to the 3-5% perioperative mortality for an open repair.\(^5\text{-}^7\) The stent grafts are comprised of fabric tubes reinforced with metal stents (Figure 1-1C). To enable the delivery of the stent graft through the iliac artery into the aorta, it is compressed within a delivery sheath, which is removed during deployment. The expanded device is then anchored to the aortic wall through a combination of radial force and barbs at the proximal aspect of the device.\(^8\)

A standard bifurcated stent graft (Figure 1-1B) can be utilized if there is greater than 10 mm of non-aneurysmal aorta distal to the renal arteries; however, in approximately 15% of abdominal aortic aneurysms, there is insufficient non-aneurysmal aorta available and a custom-made stent graft is required.\(^9\) The primary component of a custom-made stent graft is the modular main body. This main body consists of a tubular stent graft with fenestrations or branches positioned for a patient’s specific anatomy (Figure 1-1D). This modular main body is then connected via these fenestrations to the target visceral artery with covered stents to maintain visceral artery perfusion. Currently, there are two commercial manufactures of custom-made stent grafts: Cook Medical (Bloomington IN, USA) and Vascutek (Inchinnan, UK). Currently, only the Cook Medical ZFEN device has regulatory approval in the USA; however, either manufacturer can be used in Canada via a special access request for devices that are not yet approved by Health Canada. Typically, these devices are employed in patients that would be unable to tolerate an open surgical repair. Other alternatives to using these custom devices can include physician modified grafts and/or the use of parallel stenting techniques.

One of the primary challenges in employing these custom-made devices is ensuring that the fenestrations align appropriately with their target arteries. Fenestration misalignment not only creates a more technically challenging procedure but can also potentially result in significant clinical sequelae. Misalignment can lead to branch stent occlusion or stenosis, which impairs blood flow to the involved visceral arteries (celiac, superior mesenteric, and renal arteries).
Ultimately, this impaired blood flow results in complications such as bowel ischemia or renal failure.\textsuperscript{10,11} We hypothesize that a significant number of the complications associated with misalignment occur secondary to the increased catheter and wire manipulation required to cannulate and stent the target artery, leading to injury of the arterial endothelium and/or microembolization.

Fenestration misalignment, while recognized clinically, is poorly understood and under-reported in the literature. Fenestration misalignment is thought to be a multifactorial process occurring through one or more of the following mechanisms: (1) errors in stent graft planning, (2) intraoperative stent graft rotation, and/or (3) inaccurate intraoperative positioning. This dissertation will focus primarily on mechanisms (1) and (2); however, it is important to note that inaccurate intraoperative positioning (3) can in part be mitigated through the use of an experienced multidisciplinary team and the incorporation of adjunctive imaging technologies such as CT/fluoroscopy fusion imaging.\textsuperscript{12,13}

Currently fenestrated or branched stent grafts are planned based on a preoperative CT angiogram (CTA). Multiplanar reconstructions of this three-dimensional CTA dataset are used to assess the position of each visceral artery and plan the location of the fenestrations accordingly. However, the limitation of this approach is that it suffers from high intra- and inter-operator variability.\textsuperscript{14} Depending on how the multiplanar reconstructions are created (i.e. whether it is based on the vessel centerline, a modified centerline, or the axial images) the relative positions of the four vessels can appear quite different. To further add to the complexity of the planning process the insertion of a stiff delivery system causes a relative straightening of the aortoiliac geometry and must be taken into consideration to create an accurate plan. Even if all the above described planning is successful, these stent grafts can rotate unpredictably during the unsheathing process in an estimated 30-40% of patients.\textsuperscript{15} This rotation potentially results in fenestration or branch misalignment and the underlying causes are not well understood.
1.2 Long Term Aim

The long-term aim of this research is to improve patient safety by increasing the precision of fenestrated stent graft creation and deployment. To achieve this aim, detailed patient-specific experimental and computational models of stent graft delivery and deployment will be developed. These models will be used to identify factors that cause stent graft rotation and subsequent misalignment. Patient-specific computational models can also be used by clinicians during pre-procedural planning to improve the accuracy of fenestrated stent graft planning.

1.3 Specific Objectives

1.3.1 Chapter 2 - Impact of Fenestrated Stent Graft Misalignment on Patient Outcomes

During fenestrated endovascular repair (FEVAR), accurate alignment of the fenestration and the target artery is necessary to prevent potential adverse events. While there are a small number of literature reports describing fenestration and/or branch misalignment, notably Park et al and Ullery et al, the clinical sequela of misalignment remains poorly described. The objective of Chapter 2 is to evaluate the clinical outcomes following fenestrated stent graft misalignment during FEVAR.

1.3.2 Chapter 3 - Prediction of Advanced Endovascular Stent Graft Rotation and its Associated Morbidity and Mortality

Advanced endovascular aneurysm repair with fenestrated and branched stent grafts are increasingly being used to repair complex aortic aneurysms; however, these devices can rotate unpredictably during deployment, leading to device misalignment. The objectives of Chapter 3 are (1) to quantify the short-term clinical outcomes in patients with intra-operative stent graft rotation and (2) to identify quantitative anatomical markers of the arterial geometry that can predict stent graft rotation preoperatively.

1.3.3 Chapter 4 - Surgical Technique and Intraoperative Stent Graft Rotation in Fenestrated Endovascular Aneurysm Repair

The objectives of Chapter 4 are (1) to develop a mechanically realistic aortoiliac model that can be used to evaluate specific anatomic variables that are linked to stent graft rotation, (2) to enable
realistic preoperative simulation of stent graft deployment, and (3) to evaluate aspects of stent graft deployment technique that may contribute to stent graft rotation.

1.3.4 Chapter 5 - Fenestrate and Branched Stent Graft Planning: An Objective Semi-Automated Approach

Current methods for stent graft planning rely on the planning surgeon to not only understand and visualize a complex three-dimensional vascular structure but also to anticipate how that vasculature will change in response to the insertion of stiff endovascular tools. The objective of Chapter 5 is to create an objective semi-automated stent graft planning method that incorporates the aortoiliac deformation caused by the insertion of the delivery system.
1.4 Overview of Existing Literature and Previous Work

Fenestration misalignment can be attributed to a combination of factors including errors in stent graft design, intraoperative stent graft rotation, and intraoperative positioning. The overall incidence of fenestrated stent graft misalignment is not well-reported in the literature. Park et al. reported a misalignment of >30° in 23.2% of cases and a misalignment of >45° in 5.8% of cases in a cohort of 38 patients, but did not evaluate clinical outcomes. Similarly, Ullery et al reported shuttering (a form of misalignment occurring in unstented fenestration or scallops) in 50% of the evaluated SMA fenestrations/scallops in a cohort of 28 patients. However, despite the high incidence of shuttering in their cohort, no significant adverse events were noted. Finally, Lala et al looked at the influence of adverse events in stented vs unstented SMA fenestrations and saw an approximate 40% higher adverse event rate in the unstented fenestrations and hypothesized that these complications were secondary to fenestration misalignment.

While clinically it has been noted that stent graft rotation can occur during device deployment, the incidence and mechanisms underlying stent graft rotation were not previously known. Our laboratory retrospectively evaluated 42 FEVAR procedures and found that stent graft rotation was noted in the surgical records of 36% of cases. However, since this data relied on information extracted from operative notes, 36% may be an underestimation of the true incidence of stent graft rotation. The limitations of this retrospective study highlight the importance of a prospective evaluation of stent graft rotation. In standard infrarenal EVAR procedures, tortuous, calcified, and/or narrow iliac arteries can lead to increased perioperative complications (i.e. iliac artery rupture), but very little is known about the anatomic impact on fenestrated or branched EVAR procedures.

We hypothesize that local geometric variables including iliac artery torsion and rigidity and diameter interact to produce a net rotational torque on the device as it transits the iliac arteries. Based on data from our retrospective population, it is expected that torsion will be the most significant factor in stent graft rotation. We hypothesize that as the device transits the iliac artery, the accumulated torsion applies an effective torque to the exterior sheath of the device; however, because the stent graft is stiffer than the sheath, a rotational potential energy is generated. When the device is deployed, the stent graft is no longer constrained and the stored rotational potential energy results in rotation.
While vessel rigidity and diameter would not inherently create an applied torque on the device, they both contribute to the effective torque applied to the device by the torsion of the iliac artery. During the implantation of a stent graft, a stiff wire is placed within the arterial lumen to guide the device into position. In healthy compliant arteries, this stiff wire results in straightening of the artery and a reduction in net torsion. As vessel rigidity increases through atherosclerosis and calcification, the straightening induced by the stiff wire is lost, resulting in a relatively higher torsion and applied torque. Vessel rigidity, as approximated by its Young’s Modulus, ranges from 0.2 MPa in healthy vessels to 2 MPa in atherosclerotic vessels.

Finally, no comprehensive tools currently exist to aid surgeons in the planning of advanced endovascular procedures. Starnes et al recently published promising results on their investigational software platform for the creation of physician modified grafts; however, the effectiveness of this platform in predicting the interaction between the aorta and the delivery system is as of yet unclear. The use of finite element methods to predict aortoiliac deformation has been proposed by a number of groups but has primarily been limited to looking at the influence of a stiff guidewire and not the entire delivery system. Our laboratory recently reported on a computational stent graft deployment model that incorporates the complex contact structure between the iliac artery wall and the deployment device in an effort to predict stent graft rotation.
Chapter 2

Effects of Intraoperative Fenestration Misalignment in Fenestrated Endovascular Aneurysm Repair on Patient Outcomes.

Crawford, SA; Osman, E; Doyle MG; Lindsay, T; Amon, CH; Forbes, TL

During fenestrated endovascular repair (FEVAR), accurate alignment of the fenestration and the target artery is necessary to prevent potential adverse events. While there are a small number of literature reports describing fenestration and/or branch misalignment, notably Park et al and Ullery et al, the clinical sequelae of misalignment remains poorly described.10,16 The objective of Chapter 2 is to evaluate the clinical outcomes following fenestrated stent graft misalignment during FEVAR.

Contribution to the Literature

• Quantification of the incidence of intraoperative stent graft misalignment.
• Establishes for the first time a strong association between serious adverse events and stent graft misalignment, providing both short and long-term patient outcomes.

Author Contributions

• Crawford, SA: study design, data collection, data analysis, drafting manuscript
• Osman, E: data collection
• Doyle, MG: study design, critical review
• Lindsay, T: study design, critical review
• Amon, CH: study design, critical review
• Forbes, TL: study design, critical review
2 Impact of Fenestrated Stent Graft Misalignment on Patient Outcomes

2.1 Abstract

2.1.1 Objective

During fenestrated endovascular repair (FEVAR), accurate alignment of the fenestration and the target artery is necessary to prevent complications. This study’s objective is to determine the incidence of clinical outcomes following fenestration misalignment during fenestrated endovascular aneurysm repair.

2.1.2 Methods

A single center, retrospective chart review was performed for all FEVARs between January 2008 and April 2015. Data was gathered from patient records and intraoperative imaging. Native vessel angles were calculated using the vessel centerlines. Intraoperative stent graft orientation was determined by changing the angle of the image intensifier as the fenestration was profiled for cannulation. Vertical fenestration misalignment was defined as $\geq 4\text{ mm}$ and is the distance from the center of the fenestration markers to the center of the target vessel ostium at the time of cannulation. Horizontal stent graft misalignment was defined as a difference between the native vessel angle and the intraoperative fenestration angle of $\geq 15^\circ$. Native vessel angles were calculated using the vessel centerlines. Intraoperative stent graft orientation was determined from the angle of the image intensifier as the fenestration was profiled for cannulation. Early and late clinical outcomes were analyzed with respect to the presence of either vertical or horizontal misalignment of the renal artery fenestrations.

2.1.3 Results

The study cohort includes 65 patients who underwent FEVAR during this study period. A horizontal misalignment of $\geq 15^\circ$ occurred in 40% of patients (N=26) and $\geq 30^\circ$ in 9.2% of patients (N=6). A vertical misalignment of $\geq 4\text{ mm}$ occurred in 32.3% of patients (N=21). The incidence of severe postoperative complications, defined as any in-hospital end organ ischemia and/or death, was significantly higher for patients with stent graft misalignment, 31% (N=11) vs 3% (N=1) in the aligned group. There was a trend towards higher rates of target vessel cannulation failure in patients with stent graft misalignment 3% (N=99 fenestrations) vs 0%
(N=76 fenestrations). The combined incidence of any intraoperative target vessel complication was significantly higher in patients with misalignment, 8.1% [4, 15] vs 1.3% [0, 8]. Long-term survival was significantly lower in patients with stent graft misalignment, which was primarily driven by high intraoperative and in-hospital mortality rates (P<.05).

2.1.4 Conclusions

Intraoperative stent graft misalignment is associated with higher rates of procedural target vessel complications and severe post-operative adverse events. Patients with stent graft misalignment should be considered high-risk for early postoperative complications. These results highlight an important need for improved FEVAR planning.
2.2 Introduction

Fenestrated endovascular aneurysm repair (FEVAR) is a method for treating complex abdominal aortic aneurysms that are impossible to repair with conventional endovascular devices. These fenestrated devices can be custom made to the individual arterial anatomy of each patient by tailoring the position of each visceral fenestration based on data from a preoperative CT angiogram. In certain centers and regions around the world these devices can either be fully customizable or only partially customizable, as is the case with the ZFEN device (Cook Medical, Bloomington, IN). While this procedure represents a significant step forward in the evolution of endovascular aneurysm repair, these procedures still carry a significant risk of peri-operative morbidity (12-40%) and mortality (2-5%) with no reliable method of preoperative risk stratification.

FEVAR can be a technically demanding procedure, especially when the stent graft and its fenestrations are not precisely aligned with the intended target arteries. This misalignment can ultimately lead to branch vessel injury and visceral organ ischemia or malperfusion.

The cause of fenestration misalignment is not well described in the literature but is likely a multifactorial process that can occur through errors in stent graft planning, intraoperative positioning of the device and stent graft rotation during device deployment. One of the challenges in accurately designing these devices is anticipating how the device will deploy within the aorta as well as anticipating how the aortic anatomy may change with the introduction of a stiff guidewire and delivery system. Depending on the measurement technique used in device planning, the presence of severe aortic angulation poses a significant risk of fenestration misalignment. Even though several studies have reported on the shortcomings of centerline measurements in relation to EVAR/TEVAR planning, there are no reports, so far, on their role in stent graft misalignment in FEVAR. Stent graft planning and intraoperative positioning errors have been shown in part to be mitigated by the involvement of an experienced multidisciplinary team as well as by using adjunctive technologies such as hybrid fusion imaging. However, despite these technological advances, fenestration misalignment remains a problem.

Most studies evaluating fenestration or branch misalignment in the literature have failed to reliably link stent graft misalignment with any significant clinical sequelae. However, most of
these studies use postoperative CT angiograms to evaluate the incidence of fenestration misalignment.\textsuperscript{16, 39, 41} The primary limitation of this approach is that the deployment of a rigid bridging stent pulls the fenestration and the target artery into a better alignment, thereby lowering the sensitivity of detecting device misalignment at the time of cannulation. This approach fails to capture many of the iatrogenic sources of vessel injury including dissection and perforation that can lead to very significant clinical sequelae, such as bowel ischemia and renal failure. Additionally, the long-term consequences of the elevated stresses that the bridging stent applies to the branch artery in the case of an initial misalignment is not known.\textsuperscript{42, 43} We hypothesize that stent graft misalignment is a significant factor in the high early (<30 day) rates of postoperative morbidity and mortality associated with fenestrated endovascular aneurysm repair and may also contribute to an increased incidence of late re-intervention and mortality.
2.3 Methods

2.3.1 Patient Selection

Following research ethics approval, a retrospective review was conducted at a single institution of all patients who underwent FEVAR with a custom-made fenestrated device between January 2008 and April 2015. The only exclusion criterion was the absence of appropriate medical imaging, which included the absence of a thin-slice CTA (≤ 3 mm) and/or the absence of fluoroscopic images of sufficient quality to assess the fenestration orientation and position. All procedures were performed in one of two hybrid operating theatres with fixed imaging systems. The devices used during this study period were custom-made (Cook Medical, Bloomington, IN) fenestrated stent grafts.

2.3.2 Outcome Measures

Patient demographics and operative details including operative time, fluoroscopic time, contrast volume and any intraoperative complications or adjunctive maneuvers noted in the operative report were recorded. Any 30-day and/or in-hospital complications were also documented. The primary clinical outcome of this study was any end-organ ischemia and/or death during the 30-day/in-hospital period. This composite outcome includes postoperative ischemic events including bowel ischemia, kidney failure (requiring hemodialysis), and/or paraplegia. Long-term survival and freedom from re-intervention were also recorded and analyzed. Renal function was estimated using the CKD-EPI creatinine estimation of the glomerular filtration rate (eGFR).\textsuperscript{44, 45}

Patients were classified into two groups, based on the presence of misalignment in the renal fenestrations in either the horizontal or vertical direction. A subset analysis was also conducted evaluating the clinical outcomes in patients with both horizontal and vertical misalignment. The threshold for horizontal misalignment was ≥ 15°, which is equivalent to a 30-min change in clock position and is greater than 50% of the fenestration width. The threshold for vertical misalignment was ≥ 4 mm, which is equal to half of the largest fenestration diameter (8 mm).

2.3.3 Measurement of Fenestration Misalignment

Misalignment of the renal fenestrations was assessed following complete deployment of the main body device but prior to the insertion of any rigid guidewires or stents into the visceral branches that may improve the fenestration alignment. This did not consider adjunctive or corrective
movements made by the surgeon to attain improved alignment. Vertical misalignment was measured directly from the fluoroscopic image as the distance between the center of the vessel ostium and the center of the fenestration opening in the direction parallel to the stent graft (Figure 2-1). Horizontal misalignment is the difference in angles of the preoperative position of the vessel ostium on the planning CT angiogram and the orientation of the fenestration at the time of cannulation.

To determine the position of the visceral vessels the aorta was segmented from the mid-thoracic level to the level of the aortic bifurcation, including the origins of the visceral branches (celiac artery, superior mesenteric artery (SMA), left renal artery, and right renal artery) using the open source software The Vascular Modeling Toolkit as described previously. Briefly, the arterial volume described was initialized using a colliding fronts approach followed by a marching cubes algorithm to translate the segmented volume into a discrete vessel surface. The vessel was then smoothed using a Taubin smoothing algorithm. A representative arterial segmentation of the visceral segment is shown in Figure 2-2A. Once the geometry was extracted, the aortic and visceral vessel centerlines were calculated, smoothed, and resampled at 1 mm intervals. The origin of each visceral vessel was then automatically determined as the point at which that

![Figure 2-1. Representative image of the vertical misalignment measurement (\(\chi\)) on an intraoperative fluoroscopic image.](image)
**Figure 2-2.** (A) Representative segmentation of a visceral aortic segment. (B) Schematic representation of the calculation of the native visceral vessel angulation based on the aortic centerline, B and the vessel ostium, C. (C) Representative fluoroscopic image of a right renal fenestration viewed at 90°. (D) Schematic diagram of the calculation of the intraoperative fenestration angle (\(\alpha\)) using the angle of the image intensifier (\(\beta\)). Horizontal misalignment = \(\varepsilon - \alpha\)
vessel’s centerline exits the outer bounds of the aorta as determined by the maximally inscribed sphere radius of the aortic centerline. The angle of each visceral vessel ($\varepsilon$) was then computed in the plane perpendicular to the aortic centerline as the angle between the vector connecting the centerline and the vessel ostium ($\overrightarrow{BC}$) relative to the AP plane ($\overrightarrow{AB}$) (Figure 2-2B).

The intraoperative horizontal orientation of the fenestration ($\alpha$) was then determined by selecting a fluoroscopic image in which the angle of image intensifier ($\beta$) was set perpendicular to the fenestration of interest (Figure 2-2C). The angle of the fenestration can then be calculated as $\alpha = 90^\circ - \beta$ (Figure 2-2D). The horizontal misalignment of the fenestration was then calculated as the difference between the native vessel angle ($\varepsilon$) and the intraoperative fenestration angle ($\alpha$). This approach relies on the assumption that the native geometry remains unchanged with the insertion of the guidewire, delivery system, and stent graft. This assumption may lead to false positives in the categorization of patients into the misalignment group given the potential for anatomical changes following the insertion of stiff tools and devices.

2.3.4 Statistical Analyses

Continuous variables are presented as mean $\pm$ standard error of the mean, and discreet variables (i.e. comorbidities) are presented as the number of patients (percent of group total). Unpaired two-tailed t-tests and two-way ANOVAs were used for continuous variables and Fischer’s exact test was used for nominal variables, where appropriate. Statistical analysis was performed using GraphPad Prism 6.
2.4 Results

Eighty FEVARs were performed at our institution during the study period. Sixty-five of these cases had sufficient imaging data available to assess the misalignment of the renal fenestrations; 12 patients were excluded for insufficient fluoroscopic images and 3 patients were excluded for missing thin-slice preoperative CTAs. The mean patient age was 76 ± 1 years and 82% (N=53) were male. The primary indication for operative repair was aneurysmal size (N=63) followed by rapid aneurysmal expansion (N=2). The mean maximal aortic diameter for the entire cohort was 64 ± 1 mm (N=65).

A horizontal fenestration misalignment of greater than 15° (30 min clock position) was identified in 40% (N=26) of patients and greater than 30° (1-hour clock position) in 9.2% (N=6) of patients. The overall mean horizontal fenestration misalignment in this group was 23° (IQR 17-29, N=26). A vertical misalignment of greater than 4 mm was identified in 32.3% (N=21) of patients, with a mean vertical misalignment of 5.8 mm (IQR 4.5-6.7 mm, N=21). Representative images of horizontal and vertical misalignment are shown in Figure 2-3. The study cohort was analyzed with respect to two groups: patients with misaligned renal fenestrations in either the vertical or horizontal direction (misaligned) and patients with optimally positioned renal fenestrations (aligned). While this study categorized stent graft misalignment based only on the

![Figure 2-3](image_url)

**Figure 2-3.** (A) Representative fluoroscopic image of vertical misalignment in a left renal artery and (B) Representative CTA image of horizontal misalignment in a left renal artery.
renal arteries, it may be expected that in instances of renal artery misalignment the SMA and celiac artery would be more likely to be misaligned as well.

Patients with misaligned fenestrations were significantly older (78 ± 1 vs 74 ± 2 years, P=.02) and were more likely to be female with 28% (N=10) of the misaligned group being female versus only 7% (N=2) in the aligned group (P=.05). Most comorbidities were not statistically different except for a higher previous stroke rate in the aligned group (17% vs 0%, P=.01). While not statistically significant, it is worth noting that the incidence of peripheral arterial disease was 18% higher in patients with misaligned fenestrations (P=.18). Complete demographics and comorbidities are summarized in Table 2-1. There were no differences in the stent graft configurations or mean number of fenestrations between the two groups (Table 2-2).

The primary clinical outcome, which is a composite of any end-organ ischemia and/or death, was significantly higher in the misaligned group at 31% (N=11) versus 3% (N=1) in the aligned group. While this study is insufficiently powered to look at individual complications rates it is worth noting that all instances of bowel ischemia (N=4), renal failure requiring dialysis (N=1), and death (N=4) were in patients with fenestration misalignment (Table 2-3). Of the patients who died within the 30-day/in-hospital time frame, three died of complications related to bowel ischemia. Two of these patients underwent conversion to an open repair following failed cannulation and/or occlusion of the SMA intraoperatively and one required early re-operation for a thrombosed SMA on the second post-operative day. The fourth patient that died, developed toxic megacolon and required a left hemicolectomy before ultimately developing sepsis and multi-organ failure. The overall hospital length of stay was 5 days longer in patients with fenestration misalignment versus patients with optimal alignment (10 ± 1.5 days vs 5 ± 0.5 days, P=.005). There was no significant difference in the number of endoleaks between the two groups.

With respect to intraoperative details, patients with misaligned fenestrations had longer total procedural times (351 ± 25 min vs 262 ± 15 min, P=.007) and longer fluoroscopy times (106 ± 8 min vs 85 ± 6 min, P=.04) than patients with optimally positioned fenestrations. There was also a trend towards increased contrast usage in patients with misaligned fenestrations (239 ± 20 mL vs 193 ± 13 mL, P=.07). Intraoperative target vessel complications (including vessel dissection,
Table 2-1. Patient Demographics and Comorbidities [Mean ± SEM or No (%)]

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>74 ± 2</td>
<td>78 ± 1</td>
<td>.02</td>
</tr>
<tr>
<td>Male Gender</td>
<td>27 (93)</td>
<td>26 (72)</td>
<td>.05</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>29.8 ± 1.1</td>
<td>29.4 ± 1.2</td>
<td></td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>24 (82)</td>
<td>30 (83)</td>
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</tr>
<tr>
<td>Dyslipidemia</td>
<td>22 (76)</td>
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<td>.5</td>
</tr>
<tr>
<td>Chronic Renal Failure</td>
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<td>12 (33)</td>
<td>.6</td>
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<tr>
<td>Coronary Artery Disease</td>
<td>16 (55)</td>
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<tr>
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<tr>
<td>MI or Prior PCI/CABG</td>
<td>13 (45)</td>
<td>16 (44)</td>
<td>1.0</td>
</tr>
<tr>
<td>COPD</td>
<td>13 (45)</td>
<td>16 (44)</td>
<td>1.0</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>10 (34)</td>
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<td>Peripheral Vascular Disease</td>
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<td>15 (42)</td>
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</tr>
<tr>
<td>Tobacco use</td>
<td>25 (86)</td>
<td>28 (77)</td>
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</tr>
<tr>
<td>Pervious Abdominal Surgery</td>
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<td>4 (11)</td>
<td>.5</td>
</tr>
<tr>
<td>Previous Aortic Surgery</td>
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<td>0 (0)</td>
<td>.20</td>
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occlusion, and/or perforation) were higher in patients with misaligned fenestrations (8%, N=8) when compared to those with optimally aligned fenestrations (3%, N=1, P=.04). The overall target vessel patency at 30-days was 97% (171/175) with all the thrombosis/failure to cannulate events occurring in the misalignment group.

After a mean follow-up of 34 ± 4 months, there was one instance of aneurysm related mortality. In this case the patient/family elected for conservative management following the development of an iliac limb type 1b endoleak after progressive aneurysmal dilatation. The overall cohort survival was 90% and 86% at 1 and 3 years respectively. Patients with misalignment had significantly lower survival 82% vs 100% at 1 year and 78% vs 96% at 3 years (Figure 2-4A; P<.05). The overall freedom from re-intervention for the entire cohort was 81% and 79% at 1 and 3 years respectively. There were no significant differences between the two groups with respect to freedom from re-intervention (Figure 2-4B). Additionally, long-term renal outcomes were assessed at 1 and 3 years postoperatively in terms of eGFR and no significant differences were observed (Figure 2-5).

<table>
<thead>
<tr>
<th>Table 2-2. Device Specifications [Mean ± SEM or No (%)]</th>
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<tr>
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<tr>
<td><strong>Stent Graft Device</strong></td>
</tr>
<tr>
<td>2 Fen</td>
</tr>
<tr>
<td>2 Fen + Scallop</td>
</tr>
<tr>
<td>3 Fen</td>
</tr>
<tr>
<td>3 Fen + Scallop</td>
</tr>
<tr>
<td>4 Fen</td>
</tr>
<tr>
<td><strong>Mean No. Fenestrations</strong></td>
</tr>
<tr>
<td><strong>Total No. Fenestrations</strong></td>
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Table 2-3. Procedural details and 30-Day/In-hospital post-operative clinical outcomes

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<tr>
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<tr>
<td>Total Procedural Time (min)</td>
<td>262 ± 15</td>
<td>351 ± 25</td>
<td>.007</td>
</tr>
<tr>
<td>Mean Fluoroscopy Time (min)</td>
<td>85 ± 6</td>
<td>106 ± 8</td>
<td>.04</td>
</tr>
<tr>
<td>Mean Contrast Volume (ml)</td>
<td>193 ± 13</td>
<td>239 ± 20</td>
<td>.07</td>
</tr>
<tr>
<td>Hospital Length of Stay (days)</td>
<td>5 ± 0.5</td>
<td>10 ± 1.5</td>
<td>.005</td>
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30-day Complications

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<tr>
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<tr>
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<td>Paraplegia</td>
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<tr>
<td>Myocardial infarction</td>
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<td>1.0</td>
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<td>Ischemic Colitis</td>
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<td>.12</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0 (0)</td>
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<td>1.0</td>
</tr>
<tr>
<td>Death</td>
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<td>4 (11)</td>
<td>.12</td>
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No. of Endoleaks

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<tr>
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<tr>
<td>Type 2</td>
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<td>.39</td>
</tr>
<tr>
<td>Type 3</td>
<td>3 (10)</td>
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<td>.6</td>
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Intraoperative Target Vessel Cannulation Failure

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<tr>
<td></td>
<td>0 (0)</td>
<td>4 (11)</td>
<td>.12</td>
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Intraoperative Target Vessel Complication

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<tr>
<td></td>
<td>1 (3)</td>
<td>8 (8)</td>
<td>.04</td>
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End-organ Ischemia and/or Death

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<tr>
<td></td>
<td>1 (3)</td>
<td>11 (31)</td>
<td>.008</td>
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¹ Target vessel dissection, occlusion, or perforation
Figure 2-4. Kaplan-Meier analysis of (A) survival in patients with intraoperative misalignment vs patients with appropriate alignment (P<.05) and (B) freedom from re-intervention in patients with intraoperative misalignment vs patients with appropriate alignment.
A subset analysis was performed to evaluate the clinical outcomes of patients with both horizontal and vertical misalignment (N=7). These patients accounted for 5 of the 11 cases of the primary composite outcome of any end-organ ischemia and/or death (71% event rate). Specifically, one patient had early occlusion of their SMA, one had early occlusion of a renal artery, one had transient paraplegia, and two patients died. Notably these patients also had long lengths of hospital stay at 15 ± 6 days.

**Figure 2-5.** Estimated eGFR (CKD-EPI) in the preoperative period, 48 hours post-op, at time of discharge, and at one and three years of follow up.
2.5 Discussion

The use of fenestrated and branched stent grafts for the repair of complex aneurysms involving the visceral segment has enabled the treatment of patients who would otherwise not tolerate open repair.\textsuperscript{34-36} Despite the advances made over the last decade this procedure still carries very significant morbidity and mortality rates.\textsuperscript{35, 37} This study reveals a very strong correlation between intraoperative renal fenestration misalignment and severe ischemic complications and death. It also demonstrates that patients who are older or female are more likely to have renal fenestration misalignment. While older patients may suffer from a greater burden of atherosclerosis and potentially have a more hostile aortoiliac anatomy, it is less clear why females are more likely to suffer from misalignment. This may be secondary to smaller access vessels or perhaps more tortuous access vessels, but more research is needed to fully assess this discrepancy. Finally, the hospital length of stay is twice as long in patients with renal fenestration misalignment compared to those with well aligned renal fenestrations (10 days vs 5 days). Performing a fenestrated endovascular procedure can be a relatively straightforward task or it can be a very technically challenging endeavor that can take many hours to complete.\textsuperscript{11} This spectrum of difficulty observed when performing this procedure is highly dependent on two factors: the patient’s anatomy and the alignment of the stent graft fenestrations. Cannulation of a renal artery or similarly, the superior mesenteric artery, which has been completely or partially blocked by a misaligned fenestration can lead to significantly increased cannulation times and subsequent difficulty in tracking a bridging stent into position.

We hypothesize that the increased catheter and wire manipulation required in patients with stent graft misalignment leads to iatrogenic vessel injury (i.e. perforation and dissection) as well as to an increased risk of microembolization, both of which can lead to potential ischemic complications. Most of the ischemic complications (i.e. bowel ischemia) and deaths occurred in the early post-operative period and can be linked directly to iatrogenic vessel injury and/or failed cannulation at the time of the initial procedure. The long-term data suggest that if patients with misalignment survive the perioperative period, they behave similarly to those without misalignment with respect to mortality, freedom from re-intervention, and renal outcomes. This is also consistent with work done by Ullery et al showing that anatomic alterations because of FEVAR are created at the time of the index procedure and don’t significantly change during the follow-up period.\textsuperscript{48}
The primary method for the assessment of misalignment in the literature is the evaluation of post-operative CT imaging.\textsuperscript{16, 39-41} The challenge of this approach in stented fenestrations is that the deployment of a rigid stent can mitigate a significant degree of misalignment, but does not negate the early complications that may arise from the increased manipulation required to place the stent. In contrast to this methodology, the current study evaluates intraoperative fenestration misalignment prior to the deployment of the bridging stent. While this approach potentially overestimates misalignment, it permits the identification of complications that would most likely arise from misaligned fenestrations.

This study highlights the importance of further evaluating the incidence and causes of stent graft misalignment as well as the utilization of adjunctive technologies and techniques that can improve alignment. One of the primary challenges in creating accurate stent graft plans, is the ability to accurately predict how the stent graft will lie within the aorta, particularly if the aorta is not straight, and more importantly how the aortic geometry will change in response to the insertion of a stiff delivery system. Maurel \textit{et al} evaluated the degree of visceral anatomy displacement following insertion of the delivery system and found median vessel ostium displacements of 6-7 mm which is greater than the width of a typical renal fenestration.\textsuperscript{39} A further challenge is the accurate deployment of the stent graft device within an aorta that may no longer conform to the preoperative planning CT. Several groups have shown that fusion imaging technologies can improve the accuracy of stent graft deployment, lower contrast use, and procedural times.\textsuperscript{12, 13, 49} A final issue in the deployment of fenestrated stent grafts is the unpredictable rotation of the fenestrated device during unsheathing and deployment which can result in stent graft rotation. Our institution recently reported on a predictive algorithm based on iliac artery torsion and calcification data that could enable an enhanced preoperative risk assessment for these patients.\textsuperscript{31, 47} Additionally, other groups have looked at methods to enhance stent graft planning through the use of 3D-printed geometries in the creation of physician-modified endografts.\textsuperscript{26, 50, 51}

One of the limitations of the current study is its retrospective nature and relatively small sample size, which makes it under-powered to assess individual patient complications. This patient cohort dating back to 2008 also includes our early experience with this procedure and the inherent learning curve.\textsuperscript{52} Finally, the methodology selected to assess horizontal rotation has two inherent limitations: 1) it relies on the fluoroscopic images, which are assumed to be at 90° to the
fenestration, to minimize parallax error and 2) it relies on the assumption that the aortic anatomy does not change with the insertion of the stiff devices. Both of these limitations may lead to an overestimation of fenestration misalignment; however, despite these limitations this methodology best allows for accurately capturing true intraoperative fenestration misalignment in a retrospective dataset.

2.6 Conclusion

Despite the patient specific and custom nature of fenestrated stent grafts, fenestration misalignment of greater than 15° (horizontal) and/or 4 mm (vertical) occurred in greater than 50% of the patients in the current study. More importantly, patients with stent graft misalignment are at a significantly elevated risk of early postoperative morbidity and mortality (31% vs 3%), which carries through to the long-term survival trends. Patients with misalignment also stayed in hospital twice as long as patients with aligned stent grafts. These results highlight the need for further research into methodologies and techniques to improve preoperative planning that will limit stent graft misalignment and facilitate the implantation of these devices.
Chapter 3

Prediction of Advanced Endovascular Stent Graft Rotation and its Associated Morbidity and Mortality

Crawford, SA; Sanford, RM; Doyle, MG; Wheatcroft, M; Amon, CH; Forbes, TL

Advanced endovascular aneurysm repair with fenestrated and branched stent grafts are increasingly being used to repair complex aortic aneurysms; however, these devices can rotate unpredictably during deployment, leading to device misalignment. The objectives of Chapter 3 are (1) to quantify the short-term clinical outcomes in patients with intra-operative stent graft rotation and (2) to identify quantitative anatomical markers of the arterial geometry that can predict stent graft rotation preoperatively.

Contribution to the literature

- Quantifies the incidence of intraoperative stent graft rotation.
- Establishes a strong association between intraoperative stent graft rotation and increased perioperative morbidity and mortality.
- Identifies anatomic and device variables associated with stent graft rotation and proposes a method for preoperative prediction of intraoperative rotation.

Author Contributions

- Crawford, SA: study design, data collection, data analysis, drafting manuscript
- Sanford, RM: study design, critical review
- Doyle, MG: study design, critical review
- Wheatcroft, M: study design, critical review
- Amon, CH: study design, critical review
- Forbes, TL: study design, critical review
3 Prediction of Advanced Endovascular Stent Graft Rotation and its Associated Morbidity and Mortality

3.1 Abstract:

3.1.1 Objective

Advanced endovascular aneurysm repair (EVAR) with fenestrated and branched stent grafts are increasingly being used to repair complex aortic aneurysms; however, these devices can rotate unpredictably during deployment, leading to device misalignment. The objectives of the current study are A) to quantify the short-term clinical outcomes in patients with intra-operative stent graft rotation and B) to identify quantitative anatomical markers of the arterial geometry that can predict stent graft rotation preoperatively.

3.1.2 Methods

A prospective study evaluating all patients undergoing advanced EVAR was conducted at two university affiliated hospitals between November 2015 and December 2016. Stent graft rotation (defined as ≥ 10°) was measured on intraoperative fluoroscopic video of the deployment sequence. Standard pre-operative CTA imaging was used to calculate the geometric properties of the arterial anatomy. Any in-hospital/30-day complications were prospectively documented, and a composite outcome of any end-organ ischemia and/or death was used as the primary endpoint.

3.1.3 Results

Thirty-nine patients undergoing advanced EVAR were enrolled in the study with a mean age of 75 (IQR, 71-80) and a mean aneurysm diameter of 64 mm (IQR, 59-65). The incidence of stent graft rotation was 37% (n=14) with a mean rotation of 25° (IQR, 21-28°). A nominal logistic regression model identified iliac artery torsion, volume of iliac artery calcification, and stent graft length as the primary predictive factors. The total net torsion and the total volume of calcific plaque was higher in patients with stent graft rotation, 8.9±0.8 mm⁻¹ vs 4.1±0.5 mm⁻¹ (P<0.0001) and 1054±144 mm³ vs 525±83 mm³ (P<0.01) respectively. The length of the implanted stent grafts was also higher in patients with intraoperative rotation, 172±9 mm vs 156±8 mm (P<0.01). The composite outcome of any end-organ ischemia and/or death was also substantially higher in patients with stent graft rotation, 36% vs 0% (P=0.004). Additionally,
patients with stent graft rotation had significantly higher combined rates of type 1b and type 3 endoleaks 43% vs 8% (p=0.03).

3.1.4 Conclusions:

Patients with intraoperative stent graft rotation have a significantly higher rate of severe postoperative complications and this is strongly associated with higher levels of iliac artery torsion, calcification, and stent graft length. These findings suggest that pre-operative quantitative analysis of iliac artery torsion and calcification may improve patient risk stratification prior to advanced EVAR.
3.2 Introduction

Fenestrated/branched endovascular aneurysm repair (f/b-EVAR) is a minimally invasive method for the repair of juxtarenal and thoracoabdominal aneurysms that cannot be repaired through conventional EVAR techniques. This can involve custom made devices that are manufactured to have fenestrations and/or branches that match each patient’s specific arterial anatomy. While these procedures have enabled the repair of aneurysms in patients that would otherwise not tolerate a major open procedure, they are not without significant morbidity and mortality. F/b-EVAR has a reported 30-day mortality of 3-5% and a reported 30-day morbidity of 12-40% including spinal and mesenteric ischemia and renal complications. The ability to identify preoperative risk factors for these severe postoperative complications is essential for safe surgical planning and decision making.

In standard infrarenal EVAR, it is well described that hostile arterial anatomy such as severe aortic neck angulation or conical morphology can lead to increased morbidity; however, with f/b-EVAR it is much less clear which preoperative factors may influence patient morbidity. Clinically, it has been noted that the branched/fenestrated main body component can rotate during deployment (unsheathing), resulting in misalignment of the stent graft fenestrations and/or branches. While it is known that misalignment increases the technical difficulty of the procedure, little is known about the effect of stent graft rotation on patient outcomes. Lala et al. reported shuttering of the superior mesenteric artery in 21% of cases, of these cases 50% required re-intervention for ischemic complications. Additionally, the misalignment of fenestrations has been shown to lead to a higher incidence of technical failure, which can necessitate open conversion or result in vessel occlusion resulting in potential kidney failure or bowel ischemia.

We hypothesize that as the stent graft is introduced through the iliac artery, regions of torsion, calcification and stenosis cause an accumulation of rotational energy in the stent graft. This energy is released when the stent graft is unsheathed, resulting in stent graft rotation. While iliac vessel calcification and stenosis are common parameters assessed clinically, torsion is difficult to assess qualitatively and is not commonly measured. Iliac artery torsion describes the twisting of the vessel out of its plane of curvature as it goes from the femoral artery to the aorta. The objectives of the current study are A) to quantify the short-term clinical outcomes in patients
with intra-operative stent graft rotation and B) to identify quantitative anatomical markers of the arterial geometry that can predict stent graft rotation preoperatively.
3.3 Methods

3.3.1 Patient Selection

Following research ethics approval, a prospective study evaluating all patients undergoing advanced endovascular aneurysm repair was conducted at two university affiliated hospitals between November 2015 and December 2016. Exclusion criteria included any previous aortic repair involving the iliac arteries and/or the use of an intraoperative iliac conduit. This study did not involve any modifications to the surgical standard of care for this procedure. All procedures were performed in a hybrid operating theatre with fixed-imaging systems. The use of fusion CT technologies was at the discretion of the operating surgeon. In addition, no additional information (i.e. calculations of torsion, curvature, etc.) were provided to the surgeon preoperatively.

3.3.2 Clinical Outcome Measures

Patient demographics, co-morbidities and pre- and postoperative bloodwork were collected. Operative details including operative time, fluoroscopy time, patient radiation dose, volume of contrast dye injected, and any intraoperative complications or adjunctive maneuvers were documented. Finally, any postoperative in-hospital and/or 30-day complications were prospectively documented, and a composite outcome of any end-organ ischemia and/or death was used as the primary clinical endpoint. This composite outcome includes any postoperative ischemic events including bowel ischemia, kidney failure (requiring hemodialysis), pancreatitis (with concurrent branch artery occlusion), and paraplegia.

Patients were classified into two groups: those with intraoperative stent graft rotation and those without (non-rotation). Stent graft rotation was defined as a change in the stent graft orientation of $\geq 10^\circ$ between the pre-deployment (sheathed) position and the post-deployment (unsheathed) position of each stent segment of interest. The pre-deployment position is the aligned position of the compressed stent graft segment within the aorta immediately prior to its unsheathing. The post-deployment position is the position following full expansion of the segment of interest, prior to any attempts to correct the orientation. The stent grafts were deployed in a segmental fashion to allow the surgeon to attempt to correct for any rotation or errors in positioning of the stent. Any operator dependent rotation of the delivery system was not included in the calculation of
rotation. The degree of rotation was calculated from the fluoroscopic video of the deployment sequence as the mean change in orientation of each fenestration or branch as well as the top (if present) and bottom vertical markers. These measurements were made using the Radiant DICOM viewer (Radiant DICOM Viewer, Poznan, Poland).

3.3.3 Geometric properties of the aorta and iliac arteries

The aortoiliac geometry was segmented and analyzed using the open source software The Vascular Modeling Toolkit.\textsuperscript{46} Briefly, the arterial volume was initialized from the preoperative CT angiograms using a threshold based colliding fronts approach. A marching cubes algorithm was then used to translate the segmented volume into a discrete vessel surface. The surface of the vessel was then smoothed using a Taubin smoothing algorithm. Finally, a vessel centerline was calculated, smoothed, and resampled at 1 mm intervals. Using this centerline, the geometry of the iliac artery through which the device was delivered was quantified using three parameters: vessel curvature, torsion, and diameter. Curvature ($\kappa$) and torsion ($\tau$) are local variables of the centerline ($c$) and are defined as:\textsuperscript{58}

$$\kappa(s) = \frac{|c'(s)xc''(s)|}{|c'(s)|^3}$$

$$\tau(s) = \frac{[c'(s)xc''(s)] \cdot c''''(s)}{|c'(s)xc''(s)|^2}$$

where $s$ is the curvilinear abscissa along the vessel centerline. Curvature represents the degree of deviation of a curve from a straight line (which has zero curvature) and can be defined as the inverse of the radius of an osculating circle at a given point (P) along the centerline (Figure 3-1). Torsion represents the rate at which the plane containing the osculating circle changes, or in simpler terms, it is the degree to which a curve deviates from being in a single plane at any given point. Unlike tortuosity, a global variable, that describes the overall deviation of the centerline from a straight line, torsion and curvature are local variables that are calculated at each point along the centerline and then summed along the length of the centerline. The vessel diameter is calculated as the maximum inscribed sphere diameter. The maximum inscribed sphere diameter is the diameter of the largest sphere that can be drawn within the vessel at a point along the vessel centerline. This measurement is representative of the minimum vessel diameter.\textsuperscript{59}
Maximal aortic neck angulation was calculated in the infrarenal and suprarenal positions. This angle was calculated as the maximal angle that could be formed along the aortic centerline between 3 equivalently spaced points (≤60 mm apart) in the coronal and sagittal projections as well as the maximum angle in 3D space.

The volume of iliac artery calcification was quantified using a custom, automated MATLAB script (MathWorks, Natick, MA). The iliac artery was segmented in each DICOM image using the previously calculated centerline and a threshold-based method. The number of voxels within 5 mm of the external boundary of the segmented image set with an intensity greater than 700 HU was then quantified to capture any wall calcification. The number of calcified voxels was then converted to a volume of calcium (mm$^3$) using the known resolution and slice thickness of the DICOM images. The resulting calcium segmentation was then manually inspected to ensure accuracy.

### 3.3.4 Statistical Analysis

Continuous variables are presented as mean ± standard error of the mean, and discreet variables (i.e. comorbidities) are presented as the number of patients (percent of group total). Unpaired two-tailed t-tests were used for continuous variables and Fischer’s exact test was used for
nominal variables where appropriate. A nominal logistic regression model with stepwise variable selection (minimum BIC) was used to identify significant predictors of stent graft rotation and to create a linear predictive model. Standard analyses of model residuals and lack of fit tests were performed. Univariate statistics were performed using Graphpad Prism 6 and multivariate statistics were performed using JMP Pro 13.
3.4 Results

Thirty-nine patients underwent advanced EVAR at two university affiliated hospitals during the study period. One patient was excluded from the analysis following an aborted procedure in which the stent graft could not be implanted. The mean patient age was 75±1 years (IQR, 71-80) and the mean aneurysm diameter was 63.5±0.9 mm (IQR, 59-65). The indications for surgical repair were aneurysm size (n=37) and rapid aneurysm growth (n=1). Devices were either Zenith Fenestrated AAA Endovascular Grafts (n=3), Zenith t-Branch (n=1), or custom medical devices manufactured by Cook Medical (n=34) (Cook Medical, Bloomington, IN). The stent grafts were inserted via the right femoral artery in 87% of patients (n=33) and were inserted percutaneously in 11% of patients (n=4). The median number of fenestrations/branches was three. The overall incidence of 30-day/in-hospital severe complications, defined as any end-organ ischemia and/or death, was 13% (n=5) and the overall in-hospital/30-day mortality was 5% (n=2). The incidence

| Table 3-1. Patient demographics and co-morbidities. |
|----------------------------------|-----------|------------|----------------|---------|
|                                  | Non-rotation (n=24) | Rotation (n=14) | Overall (n=36) | P-Value |
| Age (years)                     | 74 ± 1.2            | 77 ± 1.7             | 75 ± 1.1       | 0.2     |
| No. of Males                    | 17 (71%)            | 8 (57%)              | 25 (66%)       | > 0.5   |
| Aneurysm Size (mm)              | 62 ± 2              | 63 ± 1               | 62 ± 1.4       | > 0.5   |
| Co-morbidities                  |                      |                       |                |         |
| Hypertension                    | 19 (79%)            | 14 (100%)            | 33 (86%)       | 0.14    |
| Dyslipidemia                    | 14 (58%)            | 9 (64%)              | 23 (61%)       | > 0.5   |
| Chronic Renal Failure           | 4 (17%)             | 2 (14%)              | 6 (16%)        | > 0.5   |
| Coronary Artery Disease         | 10 (42%)            | 5 (36%)              | 15 (39%)       | > 0.5   |
| COPD                             | 5 (21%)             | 5 (36%)              | 10 (26%)       | > 0.5   |
| Peripheral Vascular Disease     | 3 (13%)             | 2 (14%)              | 5 (13%)        | > 0.5   |
| Cerebrovascular Accident        | 1 (4%)              | 1 (7%)               | 2 (5%)         | > 0.5   |
| Previous Abdominal Surgery      | 9 (38%)             | 4 (29%)              | 13 (34%)       | > 0.5   |
| Smoking History                 | 19 (79%)            | 9 (64%)              | 28 (78%)       | 0.4     |
The measured intraoperative stent graft rotation only considers rotation during the unsheathing phase of deployment and does not consider any rotation of the delivery system during introduction of the device into position within the aorta. Figure 3-2 shows a representative series of fluoroscopic images depicting the stent graft rotation during device deployment. There were no significant differences in patient age, aneurysm size or preoperative co-morbidities between the rotation and non-rotation groups (Table 3-1). The composite outcome of any end-organ ischemia and/or death was significantly higher in patients with stent graft rotation, 36% vs 0% in the non-rotation group (P=0.004). The full complication profile is described in Table 3-2. Briefly, the ischemic complications in patients with stent graft rotation included paraplegia, myocardial infarction, ischemic colitis, pancreatitis, and branch stent occlusion. Patients with stent graft rotation also had a higher combined rate of type 1b and type 3 endoleaks, 43% vs 8% (P=0.03). Finally, there was a statistically insignificant trend towards

**Figure 3-2.** Representative images of severe stent graft rotation during device deployment within the abdominal aorta in a patient. (A) Prior to deployment (B) Mid deployment and (C) Deployment completion. The top and bottom vertical positional markers are highlighted in red.
Table 3-2. Perioperative surgical details and 30-day/in-hospital postoperative complications.

<table>
<thead>
<tr>
<th></th>
<th>Non-rotation (n=24)</th>
<th>Rotation (n=14)</th>
<th>Overall (n=38)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Rotation (°)</strong></td>
<td>4.4 ± 0.5</td>
<td>25.4 ± 3.0</td>
<td>12.3 ± 2.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td><strong>Mean Fluoroscopy Time (min)</strong></td>
<td>96 ± 6.2</td>
<td>117 ± 9.6</td>
<td>104 ± 5.5</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Mean Contrast Volume (mL)</strong></td>
<td>160 ± 12</td>
<td>159 ± 16</td>
<td>158 ± 10</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td><strong>Radiation Entrance Dose (µSv)</strong></td>
<td>5178 ± 587</td>
<td>7347 ± 1266</td>
<td>5699 ± 613</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Hospital Length of Stay (days)</strong></td>
<td>5.5 ± 0.9</td>
<td>7.7 ± 1.8</td>
<td>6.2 ± 0.9</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>No. of Re-interventions</strong></td>
<td>3 (13%)</td>
<td>4 (29%)</td>
<td>7 (18%)</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Branch Stent Occlusion</strong></td>
<td>0 (0%)</td>
<td>2 (14%)</td>
<td>2 (6%)</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>30-day Complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>0 (0%)</td>
<td>2 (14%)</td>
<td>2 (5%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (4%)</td>
<td>1 (7%)</td>
<td>2 (5%)</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Ischemic Colitis</td>
<td>0 (0%)</td>
<td>1 (7%)</td>
<td>1 (3%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0 (0%)</td>
<td>1 (7%)</td>
<td>1 (3%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0%)</td>
<td>2 (14%)</td>
<td>2 (5%)</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>No. of Endoleaks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1b</td>
<td>0 (0%)</td>
<td>2 (14%)</td>
<td>2 (5%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Type 2</td>
<td>7 (29%)</td>
<td>3 (21%)</td>
<td>10 (26%)</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Type 3</td>
<td>2 (8%)</td>
<td>4 (29%)</td>
<td>6 (16%)</td>
<td>0.17</td>
</tr>
<tr>
<td><strong>End-organ Ischemia and/or Death</strong></td>
<td>0 (0%)</td>
<td>5 (36%)</td>
<td>5 (13%)</td>
<td>0.004</td>
</tr>
</tbody>
</table>
higher fluoroscopic times and higher total radiation dose in patients with stent graft rotation
(P=0.06 and P=0.08 respectively).

The nominal regression model identified iliac artery torsion, volume of arterial calcification, and
device length as the primary predictive factors of stent graft rotation. The prediction formula for
stent graft rotation generated by this model is:

\[
R = 6.03 \left( \sum Torsion (\text{mm}^{-1}) \right) + 0.0276(\text{Calcium Volume} \ (\text{mm}^3)) \\
+ 0.221(\text{Device Length} \ (\text{mm})) - 101.4
\]

A value of R greater than 0 is predictive of significant stent graft rotation (defined as greater than
10°). On the present data set, this model has a sensitivity and specificity of 95%. Figure 3-3
illustrates this model as a function of the degree of stent graft rotation.

The total net torsion of the iliac arteries was significantly higher in patients with stent graft
rotation, 8.9±0.8 mm\(^{-1}\) vs 4.1±0.5 mm\(^{-1}\) (Figure 3-4A, P<0.0001), the total volume of calcific
plaque in the iliac arteries was also significantly higher in patients with stent graft rotation,
1054±144 mm\(^3\) vs 525±83 mm\(^3\) (Figure 3-4D, P<0.001). Finally, the devices in patients with
stent graft rotation were significantly longer, 172.3±8.5 mm vs 156.0±8.2 mm (Table 3-3,
P<0.01). A summary of all device specifications is presented in Table 3-3. There were no
significant differences in aortic neck angulation between the two groups (Table 3-4).

There was no significant difference in mean torsion between the left and right iliac arteries,
6.5±0.7 mm\(^{-1}\) vs 6.0±0.6 mm\(^{-1}\), and there was no significant difference between mean volume of
calcific plaque between the left and right iliac arteries, 719±94 mm\(^3\) vs 702±84 mm\(^3\). However,
using the multivariate model above, a different result (rotation vs no rotation) would have been
predicted in 34% (n=12) of cases by using the opposite iliac artery.
Figure 3-3. Nominal logistic regression fit presented as a function of stent graft rotation.

Figure 3-4. (A) Total iliac torsion (B) Mean Iliac Curvature (C) Mean iliac diameter, and (D) Iliac calcium volume in patients with stent graft rotation or without (non-rotation). Mean ± SEM, ***P<0.0001
Table 3-3. Delivery system and stent graft specifications.

<table>
<thead>
<tr>
<th>Stent Graft Configuration</th>
<th>Non-rotation (n=24)</th>
<th>Rotation (n=14)</th>
<th>Overall (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Fenestrations</td>
<td>3 (13%)</td>
<td>0 (0%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>2 Fenestrations + Scallop</td>
<td>5 (21%)</td>
<td>1 (7%)</td>
<td>6 (16%)</td>
</tr>
<tr>
<td>3 Fenestrations</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>3 Fenestrations + Scallop</td>
<td>7 (29%)</td>
<td>5 (36%)</td>
<td>12 (32%)</td>
</tr>
<tr>
<td>4 Fenestrations</td>
<td>5 (21%)</td>
<td>5 (36%)</td>
<td>10 (26%)</td>
</tr>
<tr>
<td>4 Branches</td>
<td>3 (13%)</td>
<td>2 (14%)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>2 Fenestrations + 2 Branches</td>
<td>0 (0%)</td>
<td>1 (7%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Mean No. Fenestrations/Branches</td>
<td>3.0 ± 0.2</td>
<td>3.4 ± 0.2</td>
<td>3.1 ± 0.1</td>
</tr>
<tr>
<td>Total No. Fenestrations/Branches</td>
<td>64</td>
<td>49</td>
<td>113</td>
</tr>
</tbody>
</table>

Table 3-4. Aortic neck angulation.

<table>
<thead>
<tr>
<th></th>
<th>Non-rotation (n=24)</th>
<th>Rotation (n=14)</th>
<th>Overall (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Suprarenal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronal (°)</td>
<td>26 ± 1</td>
<td>28 ± 3</td>
<td>26 ± 2</td>
</tr>
<tr>
<td>AP (°)</td>
<td>20 ± 1</td>
<td>24 ± 2</td>
<td>21 ± 1</td>
</tr>
<tr>
<td>3D (°)</td>
<td>29 ± 2</td>
<td>30 ± 2</td>
<td>29 ± 2</td>
</tr>
<tr>
<td><strong>Infrarenal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronal (°)</td>
<td>36 ± 4</td>
<td>41 ± 5</td>
<td>38 ± 3</td>
</tr>
<tr>
<td>AP (°)</td>
<td>32 ± 3</td>
<td>36 ± 3</td>
<td>34 ± 2</td>
</tr>
<tr>
<td>3D (°)</td>
<td>43 ± 4</td>
<td>48 ± 3</td>
<td>45 ± 3</td>
</tr>
</tbody>
</table>
3.5 Discussion

This prospective study on the implantation of fenestrated and branched stent grafts reveals that patients with a high burden of calcific disease and high torsion within the iliac arteries are at a significantly higher risk for intraoperative stent graft rotation and that this, in turn, is associated with severe perioperative complications. While this study does not causally link iliac artery torsion and calcification to stent graft rotation, it strongly suggests a mechanism by which these complications might arise. This is the first study to prospectively evaluate the clinical complications and predictive factors of advanced endovascular stent graft rotation. In addition, this study provides a predictive model which could be used preoperatively by clinicians to predict intraoperative stent graft rotation following prospective validation.

Successful insertion of a stent graft requires both an adequate conduit (the iliac artery) and a tract (an extra-stiff guide wire) to allow the stent graft to be appropriately positioned within the aorta. In healthy and compliant arteries, the stiff guide wire facilitates the insertion of the delivery system by partially straightening the iliac artery. However, as the burden of atherosclerotic disease increases, the iliac artery becomes less compliant. As a result, the artery retains higher levels of torsion which would normally be negated by the extra-stiff guide wire. This theory explains the requirement for both a high level of torsion and a high volume of calcific plaque to induce stent graft rotation that was found in the current study. The observed contribution of device length on stent graft rotation may be secondary to the increased freedom of movement of the stent graft within the sheath. The point of greatest fixation of the stent graft within the delivery system is the most proximal stent, which is constrained by the friction of the top cap, the friction of the sheath, and the attached trigger wires. As you progress more distally on the stent graft, only the friction of the sheath and the flexibility of the fabric limit its rotation. The longer devices typically have increased coverage above the visceral arteries, which places the target fenestrations further from the proximal fixation within the delivery system and may result in a greater potential to rotate.

The end result of intraoperative stent graft rotation is the misalignment of the fenestrations and branches with the intended target arteries. This misalignment increases the technical difficulty of placing the bridging stents into the target arteries; however, technical success was still achieved in 98% of the target arteries which is comparable to the 95-100% reported in the literature.
We hypothesize that despite the high rates of reported technical success, the misalignment of the stent graft leads to both longer cannulation times as well as the potential for compression or dislodgment of the bridging stent from the persistent rotational forces experienced by the stent graft throughout the cardiac cycle. Additionally, increased catheter and wire manipulation can lead to prolonged ischemia, distal emboli, and/or vessel dissection. Many of the ischemic complications that were found in this study (i.e. bowel ischemia, and pancreatitis, and even lower limb paralysis) can be linked to one of these two mechanisms. However, it is also important to consider that the increased rate of complications seen in this patient group may be reflective of the increased burden of atherosclerotic disease and may in fact not be caused directly by stent graft rotation. Future interventional studies would be required to establish a definitive causal relationship between stent graft rotation and the poor clinical outcomes.

The primary limitation of the current study is its relatively small sample size. While adequately powered for the primary composite endpoint and geometric analysis, the study is underpowered to assess the highly variable parameters such as fluoroscopy time, radiation exposure, and the low individual complication rate. Additionally, due to the prospective nature of this study, long term data on patient survival and complications (i.e. bridging stent occlusion) is not yet available. Finally, this study only evaluated endografts from Cook Medical and devices from other manufacturers may respond differently to the factors evaluated by this manuscript. Due to the low number of advanced endovascular repairs performed relative to conventional EVAR, future studies will need to utilize ex-vivo models such as mechanically realistic aortic phantoms or numerical finite element simulations to further evaluate the importance of arterial stiffness and torsion on the deployment of advanced stent grafts.

Once prospectively validated, this predictive model could provide important preoperative information for both the clinician and patient. At the simplest level, this model could be used to augment the current preoperative risk assessment to allow patients and clinicians to make a more informed decision about the treatment of their aneurysm. Additionally, it may allow clinicians to modify their operative plan if stent graft rotation is predicted. These modifications could include insertion of the device through the opposing iliac artery, the use of a common iliac conduit to minimize the impact of arterial torsion on the stent graft delivery system or a redesign of a fenestrated stent graft to a branched device to help facilitate cannulation. We hypothesize that branched devices may be more forgiving to stent graft rotation as the origin of the branch is
designed to be deployed above the artery and typically allows for an easier cannulation of the target vessel when misalignment is present.

3.6 Conclusions

Iliac artery torsion, calcification and stent graft length are strongly associated with stent graft rotation, and patients who experience intraoperative stent graft rotation have significantly higher rates of severe post-operative complications. These findings also suggest that preoperative quantitative analysis of iliac artery torsion and calcification is important for patient risk stratification prior to advanced EVAR.

3.7 Acknowledgments

The authors would like to thank Naomi Eisenberg for her administrative support and assistance with patient recruitment. The authors would also like to acknowledge the financial support for this study provided by the PSI Research Foundation and the Ontario Graduate Scholarship Foundation.
Chapter 4

Impact of Insertion Technique and Iliac Anatomy on Fenestrated Endovascular Aneurysm Repair

Crawford, SA; Doyle, MG; Amon, CH; Forbes, TL

The objectives of Chapter 4 are (1) to develop a mechanically realistic aortoiliac model that can be used to evaluate specific anatomic variables that are linked to stent graft rotation, (2) to enable realistic preoperative simulation of stent graft deployment, and (3) to evaluate aspects of stent graft deployment technique that may contribute to stent graft rotation.

Contribution to the Literature

- Development of a mechanically realistic aortoiliac phantom model that accurately models intraoperative stent graft rotation
- Demonstrates for the first time that iliac artery torsion and rigidity are direct causes of stent graft rotation
- Identification of operator insertion techniques that exacerbate stent graft rotation.

Author Contributions

- Crawford, SA: study design, data collection, data analysis, drafting manuscript
- Doyle, MG: study design, critical review
- Amon, CH: study design, critical review
- Forbes, TL: study design, critical review
4  Impact of Insertion Technique and Iliac Torsion on Fenestrated Endovascular Aneurysm Repair

4.1  Abstract

4.1.1  Objective

The objective of this study is to develop a mechanically realistic aortoiliac bench-top model to evaluate specific anatomic variables associated with stent graft rotation, to enable realistic preoperative simulation of stent graft deployment, and to evaluate aspects of stent graft deployment technique that may contribute to stent graft rotation.

4.1.2  Methods

Idealized aortoiliac geometries were constructed using polylactic acid for rigid geometries or polyvinyl alcohol cryogel for flexible geometries. The rigid geometries were directly 3D-printed on a Taz 6 FDM printer at 0.2 mm resolution, while the flexible geometries were cast in 3D-printed molds (15% polyvinyl alcohol, four freeze-thaw cycles). Idealized geometries were structured with varying amounts of net torsion and rigidity. Cook Medical ZFEN devices or infra-renal bifurcated devices were evaluated in this study. Deployments were performed under fluoroscopy in a 37°C water bath and models were pressurized to 100 mmHg with normal saline. Rotation was then calculated by tracking the positional change of gold markers affixed to the devices. Three patient-specific models were also created from preoperative CT angiograms and evaluated.

4.1.3  Results

In the rigid iliac artery models, the stent graft rotation during deployment increased with increasing torsion; torsion levels of 1.6, 2.6, and 3.6 mm$^{-1}$ had mean rotations of 5.2±0.02°, 11.2±2.8°, and 27.6±2.1° (P<.001). In the flexible models, the most significant rotation was observed in the models with the highest net torsion and rigidity, 58 ± 2.1° (7.5 mm$^{-1}$ net torsion and 254 N·m² flexural rigidity). No rotation was observed in either the low rigidity or zero torsion models. Applying torque to the proximal aspect of the device during insertion, which is often required to compensate for iliac torsion, significantly increased stent graft rotation by an average of 28° across all levels of torsion (P<.01). Multiple device insertions prior to deployment
did not change the observed device rotation. The patient specific models accurately predicted the degree of rotation seen intraoperatively to within 5°.

4.1.4 Conclusions

Insertion technique plays an important role in the degree of stent graft rotation during deployment of the device. Our model suggests that in vivo correction of device orientation which is commonly performed during the insertion of the device can increase the observed rotation and supports the concept of fully removing the device, adjusting the orientation, and subsequently reinserting. Additionally, increasing iliac artery torsion in the presence of increased vessel rigidity directly results in increased stent graft rotation.

4.2 Introduction

Fenestrated endovascular aneurysm repair (FEVAR) is a minimally invasive method to repair abdominal aortic aneurysms that involve the visceral aortic branches. This procedure involves the placement of a fenestrated stent graft such that the fenestrations align with the visceral vessels. These devices can be custom-made for each patient, with the positions of the fenestrations tailored to each patient’s individual anatomy. Misalignment is a recognized clinical problem of this procedure in which one or more of these fenestrations is misaligned with its target vessel. This misalignment can increase the technical difficulty of the procedure and lead to an increase in target vessel complications, including target vessel dissection, occlusion, and/or end organ ischemia.

Stent graft misalignment is a multifactorial problem that involves three primary components: stent graft design, stent graft placement, and intraoperative stent graft rotation. Intraoperative stent graft rotation, the focus of this manuscript, refers to a twisting of the stent graft away from the pre-deployment position during the unsheathing process. This rotation results in a misalignment of the fenestration and the target artery and has been associated with a 36% increase in severe clinical complications in a prospectively followed cohort. Dowson et al and Gallitto et al have also both previously shown that ‘hostile’ iliac artery anatomy is linked to poor patient outcomes. Additionally, it has been shown that iliac artery torsion and iliac artery calcium volume are strongly associated with and predictive of stent graft rotation, but a direct causative link has not been established.
Despite these studies outlining the association between hostile iliac anatomy and poor patient outcomes, surgeons can still only use these predictive algorithms and simulations as a method for preoperative risk stratification. The objective of this study was to develop a mechanically realistic aortoiliac model that can be used to evaluate specific anatomic variables linked to stent graft rotation, enable realistic preoperative simulation of stent graft deployment, and evaluate aspects of stent graft deployment technique. Both rigid and flexible idealized models as well as flexible patient-specific models will be used to evaluate these objectives. We hypothesize that increasing iliac artery torsion and iliac artery stiffness will result in increased stent graft rotation and that manipulation of the delivery system in vivo is a direct contributor to the observed degree of stent graft rotation.
4.3 Methods

4.3.1 Polyvinyl alcohol cryogel preparation

The Young’s modulus of the polyvinyl alcohol cryogel (PVA-c) material is dependent on the polymer concentration, the number of freeze-thaw cycles, and the conditions of the polymerization.$^{66-68}$ The PVA-c used in this study was synthesized by dissolving polyvinyl alcohol (P1763, Sigma-Aldrich, MO, USA) in dH$_2$O at 90°C for 2 hours with continuous agitation. The resulting PVA solution is then maintained (covered) at room temperature for 24 hours to allow any entrapped air bubbles to come out of solution. The PVA solution was then injected into the appropriate mold, frozen at -20°C for 4 hours, and subsequently thawed at 10°C for four hours. The average thaw rate under these conditions was measured to be approximately 0.3°C/min.

4.3.2 Uniaxial tensile testing

The uniaxial tensile testing apparatus was equipped with a 5 kg load cell (Test Resources, MN, USA). PVA-c samples were prepared as described above with 10%, 15%, and 20% concentrations of PVA and each subjected to 2, 4, and 6 freeze-thaw cycles. The stress-strain curves are then generated using 10 x 50 x 2 mm cast strips of the PVA-c. The strips are subjected to a strain rate of 10% per min and the resulting forces are measured. The cross-sectional area of the test pieces is measured using digital calipers and the Young’s modulus ($E$) is estimated in the linear region using the equation:

$$E = \frac{\sigma(\varepsilon)}{\varepsilon} = \frac{F/A}{\Delta L/L_0}$$

(1)

where $F$ is the force exerted, $A$ is the cross-sectional area, $\Delta L$ is change in length, $L_0$ is the initial length, $\sigma$ is the tensile stress and $\varepsilon$ is the extensional strain.$^{69}$

4.3.3 Idealized models

Idealized iliac artery geometries were constructed in SolidWorks (Dassault Systèmes, Waltham, MA, USA) to assess the impact of torsion and vessel rigidity on stent graft rotation during deployment. All idealized iliac models were constructed to have a centerline length that was representative of the approximate centerline length of actual iliac vessels, ranging from 160 mm
to 180mm. Vessel torsion in these models was created using a helically structured iliac artery. The pitch and radius of the helix were modified to generate a specified level of torsion. Torsion represents the degree to which a curve deviates from being in a single plane at any given point and is measured using the open source software VMTK (Orobix, Italy). Unlike tortuosity, a global variable that describes the overall deviation of the centerline from a straight line, torsion is a local variable that is calculated at 1 mm intervals and then summed along the length of the centerline.

Rigid geometries were directly 3D-printed out of polylactic acid (PLA) using a Taz 6 FDM printer (Aleph Objects, CO, USA) at a 0.2 mm resolution. Three rigid geometries with net torsions of 1.6 mm⁻¹, 2.6 mm⁻¹, and 3.6 mm⁻¹ were constructed. While these torsional values are below the clinical threshold that typically results in stent graft rotation, experimentally it was determined that, in a rigid system, higher levels of torsion result in fracture of the distal aspect of the deployment system.

Flexible geometries were created by casting a 15% PVA solution in 3D-printed PLA molds (0.3 mm resolution; Taz 6) and subsequently polymerizing the models with four freeze-thaw cycles. Flexible geometries were created with net torsions of 0 mm⁻¹, 5 mm⁻¹, 6.25 mm⁻¹ and 7.5 mm⁻¹. Varying wall thicknesses of 2, 3, 4, and 5 mm were selected to evaluate the impact of vessel rigidity. For the purposes of comparison, the chosen wall thicknesses have flexural rigidities (Young’s modulus × second moment of area) of 63, 115, 170, and 254 N·m², which is equivalent to a Young’s modulus of 230, 420, 620, and 925 kPa in a native iliac artery, assuming a wall thickness of 1.5 mm and an inner diameter of 8 mm. For reference, healthy, non-atherosclerotic common iliac arteries have a Young’s modulus of approximately 200 kPa, whereas severely atherosclerotic arteries which can have Young’s moduli ranging from 700 kPa to upwards of 1600 kPa. A representative idealized iliac artery mold is pictured in Figure 4-1A.

### 4.3.4 Patient specific models

Following institutional research ethics approval, three patients were selected from a prospectively maintained advanced EVAR database, two patients who experienced stent graft rotation and one patient who did not. Aortoiliac geometries were segmented from preoperative CT angiograms from the level of the distal thoracic aorta to the common femoral artery as described previously.
Figure 4-1. CAD renderings of representative molds for (A) the flexible idealized models and (B) patient-specific models.
Briefly, a colliding fronts approach is used to segment the initial geometry followed by a marching cubes algorithm to translate the segmented geometry into a discrete surface model and finally a Taubin smoothing algorithm is applied. An outer mold is generated by first offsetting the vessel surface by 3 mm in the normal direction and subsequently decimating the number of triangular elements to ~25,000 (Meshmixer, Autodesk, CA, USA). The offset geometry is then imported into SolidWorks, modified appropriately and Boolean subtracted from the mold body. A modified vessel centerline is then used as the parting line for the mold. A representative patient-specific mold is illustrated in Figure 4-1B.

A lost-core casting technique was used to create the patient specific models. The outer body of the mold was 3D-printed at a resolution of 0.3 mm out of a flexible thermoplastic polyurethane material (NinjaFlex, Ninjatek, PA, USA). The inner core of the mold is printed from a water-soluble thermoplastic polyvinyl alcohol (eSUN, Shenzhen, China) at a resolution of 0.2 mm. The model is then cast with a 15% PVA solution as described for the idealized models and subjected to four freeze-thaw cycles. Once polymerized the model is immersed in 37°C distilled water until the inner core is fully dissolved. The reported iliac artery torsion and calcium volume for the respective patients were calculated as described previously.65

4.3.5 Experimental apparatus and stent graft deployment

An experimental apparatus was constructed consisting of a plexiglass (PMMA) enclosure, a recirculation pump, and a heating element. The enclosure was filled with water and maintained at 37°C, while the arterial anatomy was pressurized with 0.9% normal saline to 100 mmHg. The models were fixed at the proximal aortic and distal iliac ends as well as at the aortic bifurcation. Infra-renal bifurcated grafts were used for the rigid models and ZFEN stent grafts were used for all flexible models (Cook Medical, Bloomington, IN). The infra-renal stent grafts were modified with a linear array of gold markers to enable visualization of the orientation along the entire length of the graft during experimentation. Stent grafts were re-sheathed between deployments and used multiple times until visible degradation of the outer sheath was observed.71 All deployments were performed by a vascular surgery resident using a portable C-arm (Philips, The Netherlands). The degree of stent graft rotation was calculated from the fluoroscopic video of the deployment sequence as the relative change in orientation of the vertical positional markers from
pre- to post-deployment. These measurements were made using the Radiant DICOM Viewer (Radiant DICOM Viewer, Poznan, Poland).23

Three specific techniques for device insertion and alignment of the positional markers were evaluated in this study:

**Straight insertion:** The orientation of the vertical markers was assessed pre-insertion, but no operator correction was applied for any observed twisting of the device during insertion.

**Corrected insertion:** The orientation of the vertical markers was assessed pre-insertion and the operator maintains the orientation of the positional markers throughout the insertion of the device by applying corrective torque at the distal end of the sheath while ensuring that torque is applied to both the inner cannula and the outer sheath.

**Multiple straight insertions:** The orientation of the vertical markers was assessed pre-insertion. The device was then inserted without applying any correction to compensate for observed twisting of the device. Once the device was fully in position, the relative position of the vertical markers was assessed, the device was then fully removed and offset by the corresponding amount and re-inserted without any operator correction of the observed twisting. This procedure was repeated a second time if necessary to obtain appropriate alignment.

4.3.6 Statistical Analysis

Continuous variables are presented as mean ± standard error of the mean. Unpaired two-tailed t-tests and two-way ANOVAs were used for continuous variables, where appropriate. Multiple comparison tests were performed with a post-hoc Tukey test. Univariate analyses were performed using Graphpad Prism 6 (Graphpad Software Inc, CA, USA). Multivariate analysis and modeling of the torsion, stiffness, and rotation was performed with a standard least squares regression algorithm (JMP 14; NC, USA).
4.4 Results

4.4.1 PVA-c tensile properties

The mechanical properties of PVA-c are dependent in part on the initial polymer concentration, the number of freeze-thaw cycles, and the rate of thawing. To ensure the appropriate tensile properties of the generated PVA models, we evaluated the stress-strain curves for PVA concentrations of 10%, 15%, and 20% each at 2, 4, and 6 freeze-thaw cycles. The corresponding stress-stretch curves are shown in Figure 4-2A-D. A PVA concentration of 15% and 4 freeze-thaw cycles was selected for the use in this study, which corresponds to a Young’s modulus of 160 kPa. These parameters were selected to maximize the Young’s modulus, while minimizing the material viscosity and preparation time. The thickness of the models was then modulated to attain an equivalent flexural rigidity.

4.4.2 Idealized PVA-c models – Vessel torsion and rigidity

In the rigid iliac artery models, the stent graft rotation during deployment increased with increasing torsion. Torsion levels of 1.6, 2.6, and 3.6 mm⁻¹ had respective mean rotations of 5.2±0.02°, 11.2±2.8°, and 32.5 ± 2.1° (P<.001).

Rotation in the flexible idealized iliac artery models was evaluated using a 4-level partial factorial design with respect to its equivalent flexural rigidity (63, 115, 170, 254 N·m²) and vessel torsion (0, 5, 6.25, and 7 mm⁻¹). Both the flexural rigidity and the vessel torsion significantly increased the observed rotation (Figure 4-3; P<.0001). There was also a strong positive interaction between the vessel torsion and the model rigidity (i.e. torsion more strongly impacts rotation when the vessel is stiffer; P<.01). The highest rotation measured in the evaluated models was 58 ± 2.1° with a torsion of 7 mm⁻¹ and a flexural rigidity of 254 N·m² (representing atherosclerotic iliac arteries). Additionally, no significant rotation was observed in either the flexible models representing healthy arterial properties (63 N·m²) or in the models with no torsion.⁷⁰
Figure 4-2. Representative stress-stretch curves for polyvinyl alcohol cryogel samples prepared with initial polymer concentration of 10%, 15%, or 20% and subjected to (A) 2, (B) 4, or (C) 6 freeze-thaw cycles. (D) Summarized Young’s moduli with respect to number of freeze-thaw cycles and polymer concentration as calculated from the physiologic region of the stress-strain curves.
Figure 4-3. Prediction surface of a multivariate analysis of stent graft rotation in response to increasing vessel rigidity and torsion. The table below summarizes the mean ± SEM for rotation in each tested model.

<table>
<thead>
<tr>
<th>Flexural Rigidity (N•m²)</th>
<th>Torsion (mm²)</th>
<th>63</th>
<th>115</th>
<th>170</th>
<th>254</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>1.1 ± 0.1°</td>
<td>-</td>
<td>-</td>
<td>1.2 ± 0.1°</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>-</td>
<td>13 ± 3.6°</td>
<td>14 ± 4.3°</td>
<td>20 ± 4.5°</td>
</tr>
<tr>
<td>6.25</td>
<td>-</td>
<td>-</td>
<td>15 ± 4.3°</td>
<td>28 ± 1.0°</td>
<td>47 ± 4.7°</td>
</tr>
<tr>
<td>7</td>
<td>1.2 ± 0.2°</td>
<td>20 ± 4.5°</td>
<td>37 ± 1.0°</td>
<td>58 ± 2.1°</td>
<td></td>
</tr>
</tbody>
</table>
4.4.3 Influence of operator technique

Operator technique was tested in the rigid iliac artery models and subsequently confirmed in the flexible idealized models. Three techniques were evaluated: straight insertion, corrected insertion, and multiple straight insertions.

There was no difference in the measured rotation amount between the straight insertion technique and the multiple straight insertion technique. However, the corrected insertion technique increased stent graft rotation by 27°, 37°, and 20° at 1.6, 2.6, and 3.6 mm⁻¹ of vessel torsion in the rigid models respectively (Figure 4-4; P<0.01). This phenomenon was also observed in the flexible idealized models. Using the corrective insertion technique increased the rotation from 20 ± 4.5° (straight insertion) to 56 ± 7.3° (corrected insertion; P=.05) in the low torsion (5 mm⁻¹), high flexural rigidity (254 N·m²) model.

4.4.4 Patient-specific PVA-c models

Three patient-specific models were selected from a prospectively maintained advanced EVAR database, two patients with significant rotation and one patient with minimal rotation. CAD renderings of the selected aneurysms are shown in Figure 4-5. These models were created with a vessel wall thickness of 3 mm which equates to an approximate flexural rigidity of 115 N·m². The corrective insertion technique, which is the prevailing clinically used technique, was used for all patient-specific deployments. Interestingly, despite not using patient specific material properties, the observed rotation was very similar to that seen intraoperatively. The respective model rotation, intraoperative rotation, and iliac characteristics are presented in Table 4-1. Notably, the absolute error in rotation in the model vs the actual measured intraoperative rotation was less than 5° in all three patients.

While the corrective rotation technique was shown to increase rotation in the idealized models, device rotation can be minimized if the operator starts with the device substantially offset in a direction opposite to that of the iliac torsion and rotates the device into position during insertion. For example, if the device rotated 30° clockwise during deployment, the operator starts with the device offset in the counterclockwise direction and rotates it clockwise into position during insertion. Using this method, the relative amount of rotation can be substantially reduced. Through a process of trial and error, the observed rotation in patient 1 could be reduced from 34°
to only 7° by initially offsetting the delivery system by 45° counter-clockwise and rotating it clockwise into alignment during insertion. Similarly, the observed rotation in patient 2 could be reduced from 27° to 3° but required an initial offset of 90°.

Figure 4-4. Evaluation of the effect of operator insertion technique in rigid idealized models at varying levels of torsion. **Straight**: No correction of device orientation during insertion. **Multiple**: Insert the device, note orientation, fully remove the device, correct the orientation accordingly, and re-insert. **Corrected**: Gradually correct the orientation of the device as needed during insertion.
Figure 4-5. CAD renderings of the three patient-specific aortic geometries evaluated.

Table 4-1. Measured rotation during ZFEN deployment in patient specific aortoiliac phantoms compared with the observed intraoperative rotation during patient deployment.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Model Rotation (°)</th>
<th>Intraoperative Rotation (°)</th>
<th>Absolute Error (°)</th>
<th>Iliac Torsion (mm³)</th>
<th>Iliac Calcium Volume (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.3</td>
<td>0.2</td>
<td>2.1</td>
<td>5.2</td>
<td>413</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>29</td>
<td>2</td>
<td>13.1</td>
<td>1352</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>30</td>
<td>4</td>
<td>8.2</td>
<td>1244</td>
</tr>
</tbody>
</table>
4.5 Discussion

Fenestrated endovascular aneurysm repair represents a substantial step forward in the minimally invasive treatment of complex aortic aneurysms; however, it still carries a substantial risk of perioperative morbidity (12-40%) and mortality (3-5%). This relatively high complication rate for a minimally invasive procedure, highlights the need for a thorough investigation into the underlying anatomical and surgical factors that are causing these complications. In the current study, through the development of a mechanically realistic aortoiliac phantom model, we demonstrate a direct link between iliac artery torsion/stiffness and intraoperative stent graft rotation. We also demonstrate that one the most common surgical techniques used for inserting these devices, referred to here as the corrected insertion technique, directly contributes to increasing stent graft rotation. Finally, this model could serve as a method to preoperatively evaluate rotation in particularly high-risk patients to help mitigate stent graft rotation entirely.

Previously we have shown that the high perioperative risk associated with FEVAR is concentrated predominantly in patients who have fenestration misalignment or in patients who experience significant intraoperative stent graft rotation. Both of these complications can be linked to hostile aortoiliac anatomy. In the current study, iliac vessel torsion and rigidity both significantly contribute to stent graft rotation, and there is a significant positive interaction between these two variables such that patients with high iliac torsion and rigidity have substantially more device rotation. This closely matches the trends seen in our previously reported prospective clinical study, in which a multivariate model predicted the significant factors to be iliac artery torsion, volume of calcium (a marker of vessel rigidity), and device length. Similarly, Gallitto et al. demonstrated that the presence of severe iliac angulation, calcification, or vessel narrowing increased late mortality in advanced EVAR. The strong interaction between torsion and calcification is the result of a relative straightening of the iliac artery in response to the insertion of a stiff guidewire and the stiff device itself. Severely atherosclerotic iliac arteries, which are stiffer, straighten less and retain more of the measured torsion and thus impart more torque onto the delivery system.

The FEVAR procedure involves the advancement of the delivery system over a stiff guidewire through the iliac arteries and into position within the aorta. As the device is inserted, torsion in iliac arteries causes the tip or distal end of the delivery system to twist in the same direction as
the iliac torsion. We hypothesize that because the inner cannula of the device (typically stainless steel) is more rigid than the flexible outer sheath, the torsion results in differential amounts of rotation between the sheath and the stent graft itself creating a rotational potential energy within the device. This hypothesis is supported by the fact that if the operator applies torque in the direction of the iliac torsion during insertion, stent graft rotation is reduced; however, if the operator applies torque in the opposite direction to that of the iliac torsion during insertion, stent graft rotation is increased. Respectively, this application of torque is either mitigating (former) or exacerbating (latter) the differential rotation between the inner and outer components of the delivery system.

The corrected insertion technique is the most common technique used at our institution, but significantly increased the measured stent graft rotation. This technique involves the gradual insertion of the stent graft under fluoroscopic guidance, with the surgeon making rotational adjustments to maintain the correct orientation of the positional markers. This torque applied by the surgeon, is in the direction opposite to the measured iliac torsion. We hypothesize that this amplifies the differential rotation between the inner and outer components of the device, building up a greater potential energy, and resulting in increased stent graft rotation. However, if the operator inserts the device fully, notes the alignment of the fenestrations, and fully removes the device before adjusting the alignment (multiple insertion technique) the amount of torsion observed in the idealized models was substantially lower. It is important to note that this technique may not be applicable in all patients, especially those with narrow or circumferentially calcified iliac arteries, as there is the potential to damage the arterial anatomy by transiting the relatively large device multiple times.

The patient-specific models tested in this study were accurate in terms of their ability to predict the amount of observed intraoperative stent graft rotation, with an absolute error of less than 5° in the test cases. Given the absence of patient specific material properties and the known importance of iliac artery rigidity it was anticipated that several iterations of the model stiffness would be required for each patient to achieve accurate results; however, in these patients this appeared not to be the case. Further validation will be required to assess if this holds true through a broader range of patient-specific models. Additionally, both patients 2 and 3 had a similar measured stent graft rotation despite differing amounts of iliac torsion. This may reflect the influence of the patient-specific geometry on the degree of observed iliac straightening. This
PVA-c phantom model could be an important component of preoperative surgical simulation in patients identified to be at high-risk for significant stent graft rotation. This model would allow the surgeon to identify how much to offset the device prior to insertion to minimize the observed stent graft rotation.

There are several limitations to the patient-specific models described in this manuscript. These models assume uniform material properties and a uniform wall thickness throughout. Patient specific properties such as localized calcifications may have a significant impact on the stent graft rotation in some patients. Other properties such as the natural anisotropy of the vessel wall is also neglected in this study. Finally, these patient-specific models only evaluate the patent luminal area of the aneurysmal aorta and do not include the intraluminal thrombus. Despite these limitations, these models enabled a very accurate prediction of stent graft rotation (within an absolute error of only 4°).

4.6 Conclusions

Insertion technique plays an important role in the degree of stent graft rotation during deployment of a fenestrated stent graft. Our model suggests that in vivo correction for orientation, which is commonly performed during the insertion of the device increases the observed rotation and supports the concept of fully removing the device, adjusting the orientation, and subsequently reinserting. While this technique may not be applicable to all patients, it has the potential to reduce fenestration misalignment and its clinical sequelae. Additionally, this model supports our hypothesis that iliac artery rigidity and torsion are the primary causes of intraoperative stent graft rotation.

4.7 Acknowledgements

This work was funded by a grant from the Physician Services Incorporated (PSI) Foundation as well as the Canadian Society for Vascular Surgery Cook Research Award. We would also like to acknowledge Cook Medical for their in-kind contribution of the stent grafts used in this study.
Chapter 5

Fenestrated and Branched Endovascular Stent Graft Planning: A Finite Element Analysis Approach

Crawford, SA; Genis, H Doyle, MG; Amon, CH; Forbes, TL

Current methods for stent graft planning rely on the planning surgeon to not only understand and visualize a complex three-dimensional vascular structure but also to anticipate how that vasculature will change in response to the insertion of stiff endovascular tools. The objective of Chapter 5 is to create an objective semi-automated stent graft planning method that incorporates the aortoiliac deformation caused by the insertion of the delivery system.

Contribution to the Literature
- Demonstrated an effective method for accurately simulating the delivery system position within the aorta.
- Implemented an automated 2D active contouring approach to predict the final position of the stent graft and to generate a stent graft plan

Author Contributions
- Crawford, SA: study design, data collection, data analysis, drafting manuscript
- Genis, H: study design, data collection, data analysis
- Doyle, MG: study design, critical review
- Lindsay, T: study design, critical review
- Amon, CH: study design, critical review
- Forbes, TL: study design, critical review
5 Advanced Endovascular Aneurysm Repair Planning: A Finite Element Analysis Approach

5.1 Abstract

5.1.1 Objective:

To create a stent graft planning tool that incorporates the aortoiliac deformation caused by the insertion of the delivery system in order to reduce the occurrence of fenestration misalignment and its associated complications.

5.1.2 Methods:

Preoperative CT angiograms, stent graft plans, and clinical data for 38 advanced endovascular procedures were obtained from a prospectively maintained clinical database. Vascular deformation in response to the insertion of the delivery system was modeled using the finite element solver LS-DYNA. The simulated delivery system was initialized inside the aorta using the vessel centerline and the simulation was terminated when the delivery system and vessel reached an equilibrium position. The position of the delivery system was validated through a rigid 2D-3D image registration of the spine in the simulations and intraoperative fluoroscopic images. A custom algorithm then simulated stent graft expansion within the deformed geometry using an active contour technique and calculated the relative fenestration positions. The angle and vertical position of the fenestrations in the simulated stent graft plans were then compared with the original clinical stent graft plans.

5.1.3 Results:

Simulated stent graft plans were generated for thirty-eight patients. The mean discrepancy between the simulated and actual delivery system positions was 2.8 ± 0.3 mm. Sixty-one percent of the simulated plans had at least one fenestration that was at least 15° or 4 mm different from the clinical plan. When compared to the original clinical plans, patients with discrepant plans had a median [range] difference in the angle of the fenestrations of 0° [0 - 45°], 7.5° [0 - 30°], 7.5° [0 - 30°], and 15° [0 - 52°] for the celiac, superior mesenteric, left renal, and right renal arteries respectively. The median [range] differences in the vertical positions of the fenestrations were 2.5 mm [0 - 7.2 mm], 2.4 mm [0.2 - 13.2 mm], and 3.2 mm [1.4 - 13 mm] for the celiac, left
renal, and right renal arteries, respectively. When clinical information was reviewed, patients with discrepant stent graft plans had longer lengths of hospital stay, 8.5 vs 2.8 days (P<0.001), and had a trend towards an increased incidence of severe complications, 22% (N=5) vs 0% (N=0; P=0.06).

5.1.4 Conclusions:

One of the factors contributing to complications in advanced endovascular aneurysm repair is fenestration misalignment. This study proposes an objective method for fenestrated stent graft planning that incorporates the intraoperative deformation of the arterial tree and the simulated position of the device within the aorta.
5.2 Introduction

Endovascular aneurysm repair (EVAR) is a minimally invasive surgical technique for repairing abdominal aortic aneurysms through the placement of a stent graft to exclude the diseased aneurysmal segment from the systemic blood flow.\textsuperscript{73} A standard bifurcated stent graft can be utilized if there is greater than 10 mm of non-aneurysmal aorta distal to the renal arteries; however, in ~15\% of abdominal aortic aneurysms, the stent graft would need to cover one or more of the visceral vessels (celiac, superior mesenteric, and renal arteries) in order to obtain an appropriate seal.\textsuperscript{9,74} The development of fenestrated and branched stent grafts, which have either nitinol reinforced holes or stented branches for one or more of the visceral vessels, has expanded the scope of EVAR to include aortic aneurysms involving the visceral segment. Once deployed, the fenestrated/branched main body is then connected via these fenestrations/branches to their target vessels \textit{in vivo} with bridging stents, thus preserving blood flow while still excluding the aneurysmal sac.

Currently, fenestrated and branched stent grafts are designed using measurements from a preoperative CT angiogram (CTA). One of the challenges associated with this approach is the difficulty in predicting where the stent graft will ultimately lie within the aneurysmal aorta. Currently, surgeons typically create multiplanar reconstructions of the CTA images along a modified vessel centerline using experience to guide the positioning; however, \textit{Koleilat et al} have shown that it required an average of 6 measurements from independent expert operators to achieve an accurate measurement of the fenestration position.\textsuperscript{14} To further complicate the issue of fenestration alignment, the stiff tools that are used to implant the stent graft cause the intraoperative vascular anatomy to straighten resulting in altered positions of the vessel ostia.\textsuperscript{22-24} \textit{Maurel et al.} showed that the vessel ostia of branching arteries were displaced 6.4 mm on average following the insertion of the delivery system.\textsuperscript{39,40} The high variability associated with CTA measurements along with the intraoperative changes to vessel anatomy contribute substantially to fenestration misalignment. We have previously shown that fenestrations are misaligned with their target arteries in greater than 50\% of patients undergoing this procedure. In this cohort, misalignment was associated with a significant increase in severe perioperative morbidity and mortality; 31\% of patients with misalignment had the composite outcome of any end-organ ischemia and/or death versus only 3\% of patients who were not misaligned.\textsuperscript{64} Additionally, the misalignment of these custom-made fenestrations has been shown to lead to a
higher incidence of technical failure, which can result in occlusion of important visceral vessels leading to potential kidney failure or bowel ischemia.\textsuperscript{10, 11}

While this problem is multifactorial, stent graft design is an important contributor to fenestration misalignment, which in turn has been associated with a high rate of severe patient complications. The aim of this study is to develop a method to simulate the position of the stent graft within the aorta and to determine the corresponding change to the vascular anatomy to enable the creation of a more accurate stent graft plan.
5.3 Methods

5.3.1 Patient data

Thirty-eight consecutive patients who underwent a fenestrated or branched endovascular aneurysm repair [(F/B)EVAR] between November 2015 and December 2016 were selected from a prospectively maintained advanced EVAR database. The only exclusion criterion was previous aortoiliac surgery involving the placement of a Dacron graft. This study was approved by the institutional research ethics board. Clinical data presented in this study represent complications seen prior to either 30-days or discharge from hospital. The primary clinical outcome was a composite of any complications resulting in end organ ischemia and/or death, including events such as bowel ischemia, paraplegia, and pancreatitis. Iliac artery torsion and calcification were calculated as described previously. Torsion $\tau$ is a local variable that represents the degree to which the centerline deviates from being in a single plane at any given point and is defined as:

$$\tau(s) = \frac{[c'(s) \times c''(s)] \times c'''(s)}{|c'(s) \times c''(s)|^2}, \quad (5-1)$$

where $s$ is the curvilinear abscissa along the vessel centerline $c$. The vessel centerline is sampled at 1 mm intervals and the torsion is summed. The volume of iliac calcification is measured using an automated MATLAB script that detects calcific plaques using the vessel centerline, radius, and a threshold of 700 HU (MathWorks, Natick, MA).

5.3.2 Mechanical aortoiliac model

Using the preoperative CT angiogram, the aortoiliac vasculature was segmented as previously described. Briefly, the aortoiliac vasculature and the visceral branches were segmented from the mid-thoracic aorta to the bifurcation of the common femoral artery using the open source software, The Vascular Modelling Toolkit (VMTK). A colliding fronts segmentation approach was used, followed by a marching cubes algorithm to translate the 3D volume into a discrete surface mesh. Only the luminal volume was segmented in this process and intraluminal thrombus was not considered in this study. The resulting segmented vessel was meshed with triangular shell elements with a target element size of 1.5 mm producing meshes with ~35,000 elements (HyperWorks, Altair, MI, USA). A representative mesh of the visceral segment is shown in Figure 5-1.
The following hyper-elastic isotropic material model is used for the vessel wall and is based on a simplification of the 5-parameter Mooney-Rivlin model:

\[ W = C_{10}(I_1 - 3) + C_{20}(I_1 - 3)^2, \]  

where \( C_{10} \) and \( C_{20} \) are 17.4 N/cm\(^2\) and 188.1 N/cm\(^2\) respectively.\(^7\) An assumed uniform wall thickness of 1.5 mm was used throughout.\(^7\) The stent graft delivery system is represented as a linear array of beam elements 2 mm in length with a diameter of 7.8 mm (corresponding to the width of the device delivery system).\(^2\) For the delivery system, a linear elastic material model was used with a Young’s modulus of 0.6 GPa, a density of 6850 kg/m\(^3\), and a Poisson’s ratio of 0.3.\(^2\)

### 5.3.3 Simulation process

The initial stress of the blood pressure on the vascular geometry is calculated through an iterative process.\(^7\) Briefly, this approach first pressurizes the initial geometry and then incrementally subtracts the nodal displacements from the initial geometry until the residual difference between

![Figure 5-1. Representative aortic mesh](image)
the new zero-stress geometry and the initial CTA geometry is minimized. The pressurized zero-stress geometry is then used for the subsequent simulations.

The simulation is initialized by rigidly deforming the delivery system to the vessel centerline (calculated using VMTK). The delivery system is then released, and the simulation runs until an equilibrium is reached. An initial damping factor of 20% of critical is applied to both the vessel and guidewire to dampen the unrealistically high potential energy created by deforming the simulated delivery system to the tortuous vessel centerline. The dampening factor was then incrementally reduced to 0.1% for the guidewire and 10% for the vessel. The simulation was then allowed to come to equilibrium over the course of 200 ms.

Rigid boundary conditions were imposed on the nodes comprising the proximal aortic edge as well as the distal external iliac edges. The internal iliac arteries were constrained translationally in the anterior posterior direction but were allowed rotate freely. The anterior surface of the spine is also included in the simulation as a fixed rigid body. This was achieved by creating a series of smoothed spline curves along the anterior surface of the spine and lofting them into a surface mesh using LS pre-post (Livermore Software Technology Corporation, CA, USA). These boundary conditions are set to mimic the continuation of the vasculature and the influence of external structures such as the abdominal and pelvic organs, retroperitoneum, spine, and pelvis, which limit the movement of the arteries. To simulate fixation of the proximal end of the delivery system by the operator, the proximal 10 mm of the simulated delivery system is also rigidly fixed. All simulations are performed with LS-Dyna (Livermore Software Technology Corporation, CA, USA) using 16 cores on a high-performance computing server with an approximate simulation time of 45 minutes.

### 5.3.4 Automated stent graft planning

A custom algorithm was used to calculate the appropriate placement of the desired fenestrations and/or branches using the simulated, deformed aortic geometry and the simulated delivery system. This algorithm reformats the input 3D dataset into a series of 2D images perpendicular to the delivery system and spaced at 0.5 mm intervals. An active contour technique was then applied to simulate the expansion of the stent graft within the arterial lumen. Specifically, the graft was initialized in the pre-determined position of the delivery system and a balloon force was applied to expand the contour of the graft. This balloon force was opposed by (1) a gradient
based penalty factor at the boundary of the vessel lumen and (2) a rigidity constraint that serves to limit the extent to which the graft can deviate from its natural circular shape. This expansion proceeds until either an equilibrium state was reached or until the uncompressed graft diameter was reached. The position of each vessel origin was then determined relative to the centroid of the newly expanded stent graft. The horizontal fenestration position was defined as the angle between the vector connecting the vessel origin and the graft centroid relative to the anterior-posterior plane. The vertical position was determined relative to the superior mesenteric artery (SMA) as the distance between the image plane containing the vessel origin of interest and the image plane containing the SMA origin. For the purposes of comparing the branched stent graft plans, in which the branch is typically placed 15-20 mm cranial to the vessel origin, this study only compares the anticipated position of the vessel origin as marked on the clinical stent graft plan to the simulated vessel origin. The threshold used for assessing whether a simulated plan matched the actual clinical plan was 15° in the horizontal/rotational direction and 4 mm in the vertical direction. This threshold has been shown to have clinical significance with respect to perioperative adverse events.64

5.3.5 Validation

The position of the delivery system is validated using fluoroscopic images obtained at the time of the procedure in which the delivery system is positioned appropriately within the aorta just prior to deployment. A 2D-3D rigid registration technique is used to register the 2D fluoroscopic image to the 3D simulation data. Specifically, the spine is segmented from the preoperative CT angiogram using a threshold-based technique and incorporated into the 3D simulation space. The bony processes of the spine are then registered with the 2D fluoroscopic image. The mean Euclidean distance between the simulated delivery system and the actual delivery system was then calculated.

5.3.6 Statistical Analysis

Continuous variables are presented as mean ± standard error of the mean, and discreet variables (i.e. comorbidities) are presented as the number of patients (percent of group total). Unpaired two-tailed t-tests were used for continuous variables and Fischer’s exact test was used for nominal variables where appropriate (Graphpad Prism 6).
5.4 Results

5.4.1 Model Calibration and Validation

All calibration and sensitivity studies were performed on patients 2-10. The Young’s modulus of the delivery system, the part damping profiles, and the mesh size were tuned to minimize the residual error using an average of ten of the 38 patients. The optimal material averaged Young’s modulus of the delivery system was found to be 0.6 GPa (Figure 5-2B), which corresponds well to the reported literature values ranging from 0.3 – 1.1 GPa for the Cook Medical infrarenal bifurcated stent grafts.22 The material model appeared to be relatively insensitive to changes in the material properties of the vessel wall (Figure 5-2A). The damping profile of the vessel wall was tuned to minimize the numerical instabilities associated with the large initial contact forces observed during the initial release of the delivery system from its rigid constraint as well as the instabilities associated with the large resultant mesh deformations from the straightening of the iliac artery. The damping profile of the delivery system was tuned to minimize oscillation within the vessel. The results of the mesh independence analysis are presented in Figure 5-2C. The optimal target mesh size was found to be 1.5 mm which equates to approximately 35,000 elements. Further, refinements in mesh size beyond 50,000 elements resulted in numerical instabilities secondary to the large initial contact forces created by rigidly deforming the delivery system to the vessel centerline.

![Figure 5-2](image-url).

Figure 5-2. Sensitivity analyses for (A) aortoiliac vessel material properties and (B) elastic modulus of the delivery system. (C) Mesh independence study for increasing element densities.
Thirty-eight patients were simulated in this study with a mean registration error of 2.8 ± 0.3 mm and a range of 0.8 - 9.7 mm. The complete list of patient registration errors is presented in Table 5-1 and representative registered images are shown in Figure 5-3. Fifty-eight percent of patients (N=21) had a mean registration error of less than 3 mm and only two patients had a mean registration error greater than 5 mm. The two patients with registration errors greater than 5 mm (Patients 10 and 15) both had staged procedures in which a thoracic stent was placed after the CT angiogram but prior to the deployment of the fenestrated or branched device that altered the final position of the delivery system within the aorta.

5.4.2 Automated stent graft planning

New simulated stent graft plans were generated for all thirty-eight patients included in the study. The simulated stent graft plans were then compared to the actual clinical plans of the implanted stent grafts. Patients were divided into two groups based on whether the simulated plans matched the original clinical plan (Matching Plans) or had at least one fenestration that was significantly different (Discrepant Plans). Sixty-one percent of patients (N=23) were found to have at least one fenestration that was predicted to be at least 15° and/or 4 mm different from the clinical plan. The most common discrepant fenestration was the right renal artery followed by the left renal artery. In patients with discrepant plans, the median [range] difference in vertical position relative to the SMA between the two plans was 2.5 mm [0 - 7.2 mm], 2.4 mm [0.2 - 13.2 mm], and 3.2 mm [1.4 - 13 mm] for the celiac, left renal, and right renal arteries, respectively. The median [range] difference in horizontal position between the two plans was 0° [0 - 45°], 7.5° [0 - 30°], 7.5° [0 - 30°], and 15° [0 - 52°] for the celiac, superior mesenteric, left renal and right renal arteries, respectively.

Figure 5-4 and Figure 5-5 are representative of a discrepant plan (Patient 19) and highlight how measurement technique can have a significant impact on fenestration positioning. As shown in Figure 5-4C-F if the graft plan is created based on the vessel centerline the right renal artery is predicted to be lower than the left renal artery by 7 mm, and this is in fact how the stent graft was designed clinically (Figure 5-5A). However, based on the deformed aortic geometry shown in Figure 5-4A, the simulated stent graft plan predicts the right renal artery to be higher than the left renal artery by 4 mm (Figure 5-4G-J).
Table 5-1. Mean error in simulated delivery system position relative to intraoperative fluoroscopic images.

<table>
<thead>
<tr>
<th>No.</th>
<th>Side</th>
<th>Registration Error (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Right</td>
<td>NA&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>Right</td>
<td>1.0</td>
</tr>
<tr>
<td>3</td>
<td>Right</td>
<td>1.3</td>
</tr>
<tr>
<td>4</td>
<td>Right</td>
<td>2.0</td>
</tr>
<tr>
<td>5</td>
<td>Right</td>
<td>1.2</td>
</tr>
<tr>
<td>6</td>
<td>Right</td>
<td>2.9</td>
</tr>
<tr>
<td>7</td>
<td>Right</td>
<td>1.1</td>
</tr>
<tr>
<td>8</td>
<td>Right</td>
<td>3.1</td>
</tr>
<tr>
<td>9</td>
<td>Right</td>
<td>1.4</td>
</tr>
<tr>
<td>10</td>
<td>Left</td>
<td>5.4</td>
</tr>
<tr>
<td>11</td>
<td>Left</td>
<td>2.3</td>
</tr>
<tr>
<td>12</td>
<td>Right</td>
<td>1.4</td>
</tr>
<tr>
<td>13</td>
<td>Right</td>
<td>4.3</td>
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<tr>
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<td>2.7</td>
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<tr>
<td>15</td>
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<td>9.7</td>
</tr>
<tr>
<td>16</td>
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<td>Right</td>
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<td>Right</td>
<td>0.8</td>
</tr>
<tr>
<td>20</td>
<td>Right</td>
<td>3.4</td>
</tr>
<tr>
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<td>Right</td>
<td>2.9</td>
</tr>
<tr>
<td>22</td>
<td>Right</td>
<td>2.2</td>
</tr>
<tr>
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<td>Right</td>
<td>2.3</td>
</tr>
<tr>
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</tr>
<tr>
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<td>Right</td>
<td>NA&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
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<td>3.2</td>
</tr>
<tr>
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</tr>
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</tr>
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<tr>
<td>37</td>
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<tr>
<td>38</td>
<td>Right</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Mean ± SEM 2.8 ± 0.3

<sup>1</sup>Insufficient fluoroscopic image for registration
From the intraoperative fluoroscopic images shown in Figure 5-5B, we can see that measured parallel to the stent graft, the right renal artery is in fact higher than the left by several millimeters. This discrepancy resulted in a slight overlap of the main body stents at the level of the right renal artery fenestration and a subsequent kinking of the main body below.

5.4.3 In-hospital / 30-day clinical outcomes

For the overall cohort the mean age was 75 ± 1 years and the mean maximal aneurysm diameter was 62 ± 1 mm. There were no significant differences in patient demographics between the two groups (Table 5-2). Patients with discrepant plans had longer lengths of hospital stay relative to patients with matching plans, 8.5 vs 2.8 days respectively (P<0.001). Additionally, there was trend towards a higher incidence of end-organ ischemia and/or death in patients with discrepant plans, 22% (N=5) vs 0% (N=0; P=0.6). The complete list of complications is listed in Table 5-3.
Figure 5.3. (A-I) Representative images of the rigid 2D-3D registration of the bony spine to validate the simulated position of the delivery system (orange) against the true intraoperative position of the delivery system (blue) for patients 2-10 respectively.
Figure 5-4. Patient 19 - (A) Initial deformation of the delivery system to the aortic centerline. (B) Position of the delivery system and aortoiliac deformation post-simulation. (C-F) Calculations of fenestration position based on preoperative vessel centerline and (G-J) based on the deformed geometry and delivery system for the celiac, superior mesenteric, left renal and right renal arteries respectively.
Figure 5-5. Patient 19 - (A) Clinical stent graft plan showing the right renal artery (1) to be the lowest and (B) intraoperative fluoroscopic images of the same patient showing the left renal artery (2) to be the lowest post deployment. This discrepancy results in slight overlap of the stents at the level of the right renal and corresponding kink in the main body below the fenestration (red arrow).
Table 5-2. Patient demographic and anatomic data

<table>
<thead>
<tr>
<th></th>
<th>Matching Plans (N=15)</th>
<th>Discrepant Plans (N=23)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>76 ± 2</td>
<td>74 ± 1</td>
<td>0.3</td>
</tr>
<tr>
<td>No. Males</td>
<td>73% (N=11)</td>
<td>61% (N=14)</td>
<td></td>
</tr>
<tr>
<td>Aneurysm size (mm)</td>
<td>62 ± 3.1</td>
<td>62 ± 1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Maximal aortic angulation (°)</td>
<td>45 ± 12</td>
<td>48 ± 10</td>
<td>0.8</td>
</tr>
<tr>
<td>Iliac artery torsion (mm⁻¹)</td>
<td>5.7 ± 0.9</td>
<td>6.3 ± 0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Iliac calcium volume (mm³)</td>
<td>646 ± 117</td>
<td>764 ± 117</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 5-3. Clinical patient outcomes (30 Day / In-hospital)

<table>
<thead>
<tr>
<th></th>
<th>Matching Plans (N=15)</th>
<th>Discrepant Plans (N=23)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Length of Stay (days)</td>
<td>2.8 ± 0.6</td>
<td>8.5 ± 1.1</td>
<td>0.0004</td>
</tr>
<tr>
<td>Intraoperative fluoroscopy time</td>
<td>92 ± 8</td>
<td>112 ± 7</td>
<td>0.07</td>
</tr>
<tr>
<td>Radiation entrance dose (µSv)</td>
<td>5399 ± 797</td>
<td>6188 ± 839</td>
<td>0.5</td>
</tr>
<tr>
<td>Contrast volume (mL)</td>
<td>145 ± 15</td>
<td>168 ± 12</td>
<td>0.2</td>
</tr>
<tr>
<td>No. of Re-interventions</td>
<td>6.7% (N=1)</td>
<td>26% (N=6)</td>
<td>0.2</td>
</tr>
<tr>
<td>Branch stent occlusion</td>
<td>6.7% (N=1)</td>
<td>4.3% (N=1)</td>
<td>1.0</td>
</tr>
<tr>
<td>30 Day/ In-hospital Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paraplegia</td>
<td>0</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Ischemic Colitis</td>
<td>0</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>End organ ischemia and/or Death</td>
<td>0% (N=0)</td>
<td>22% (N=5)</td>
<td>0.06</td>
</tr>
</tbody>
</table>
5.5 Discussion

Fenestration misalignment in advanced endovascular aneurysm repair has been shown to be significantly associated with a very high incidence of complications (31% incidence of end-organ ischemia and/or death). This is a multifactorial problem which involves many aspects including device design, deployment position, and/or intraoperative stent graft rotation. Despite advances in these areas, stent graft plans are still being created using methods that have high intra- and inter-operator variability as well as relying on 3D-reconstructions that don’t reflect the actual intraoperative aortic geometry. This study proposes an objective, operator independent methodology for the development of stent graft plans that incorporates a preoperative finite element analysis of the aortic deformation.

While the importance of incorporating the interaction between the stiff delivery system and an angulated aorta in device planning has been reported previously, the current methodology available to most vascular surgeons relies primarily on experience to obtain the correct modification of the vessel centerline. The failure to incorporate this interaction, as shown in patient 19, can lead to significant fenestration misalignment. But even with expert and experienced operators, Koleilat et al, have demonstrated poor intra- and inter-operator reliability of these measurements. This study presents an accurate, objective, and operator independent method for measuring the aortic deformation and determining the position of the delivery system within the aorta. Additionally, with a total run time of only 45 min, these simulations could easily fit within the current planning workflow of these devices.

The largest discrepancies observed in this study between the simulated position of the delivery system and the intraoperative position were in two patients who underwent a staged procedure prior the placement of the fenestrated/branched component without an interval CT angiogram. This highlights the importance of accurate initial geometry in determining the ultimate position of the stent graft. Despite these anomalies, the high degree of accuracy (2.8 ± 0.3 mm) to which the simulated delivery system matched the position of the intraoperative delivery system in this study demonstrates that the proposed methodology can be highly reliable for predicting where the device will be positioned within the aorta pre-deployment.

Sixty-one percent of the enhanced stent graft plans had at least one vessel that was greater than 15° or 4 mm different from the clinical plans created by the surgeons. This indicates that
incorporation of the deformed aortic geometry and an objective multiplanar reconstruction (based on the simulated insertion of the device) may have a significant impact on the accuracy of device design going forward. Given the increased challenge an angulated aortic neck poses when planning a custom stent graft, we had anticipated that patients with discrepant stent graft plans would have greater aortic angulation but no difference in aortic angulation was found between the groups. Similarly, neither the iliac artery torsion or volume of calcium was significantly different in patients with discrepant plans. The high variability found in these anatomical variables highlights the diversity of challenges that currently hinder the accuracy of advanced EVAR planning.

While this study was not powered to evaluate the relatively infrequent complications observed with (F/B)EVAR, a strong trend was still observed towards a higher incidence of severe complications in patients with discrepant plans. Consistent with this, patients with discrepant plans stayed in hospital on average 5 days longer then patients with matching plans. We hypothesize that these early complications arise primarily due to the excessive catheter and wire manipulation required to cannulate the target vessel in the presence of fenestration misalignment as well as the potential for subsequent kinking of the bridging stent at the fenestration-vessel interface.

The primary limitation of the current study is the relatively small sample size. While sufficient for the assessment and validation of the finite element model, it is underpowered to assess the infrequent clinical outcomes associated with (F/B)EVAR. This study also does not consider the impact of diameter reducing ties on stent graft design. Diameter reducing times are affixed to the posterior of the stent graft and temporarily reduce the diameter of the device by 4 mm. These ties can affect the positioning of posterior renal artery fenestrations during the cannulation phase and surgeons will often account for this when planning these devices. Additionally, this study neglects the potential influence of intraluminal thrombus on the deformation of the aorta. While the intraluminal thrombus may play a role in dampening the observed aortic deformation, we believe this influence to be small, which is in part corroborated by the accuracy of the validation data. Finally, this study validates the simulated position of the delivery system within the aorta, but it does not validate the change in position of the visceral vessel origins. Such validation would be required prior to the implementation of this technique in a prospective study cohort.
5.6 Conclusions

Despite the tremendous impact that these devices have had on minimally invasive vascular surgery and personalized vascular medicine, they still carry a very significant rate of morbidity and mortality. Enhanced methods for stent graft planning have the potential to significantly improve the safety of this procedure by reducing the incidence of intraoperative and postoperative complications caused by stent graft misalignment. This study also demonstrates the utility of finite element analysis methods for the preoperative simulation of surgical procedures and demonstrates the impact that they can have on surgical planning.
Chapter 6

Discussion
6 Discussion

The development of fenestrated and branched endovascular stent grafts for the repair of complex visceral aortic segment aneurysms was a significant advancement in minimally invasive vascular surgery. However, the complexity of these devices and their in vivo modular assembly has led to a unique set of challenges. The morbidity of fenestrated or branched endovascular aneurysm repair (F/B)EVAR is reported in the literature to range from 12-40% with a mortality of 2-5%.\textsuperscript{33-38} Despite being performed on higher risk patients, this complication rate is still superior to that of open repair; however, it leaves significant room for improvement.\textsuperscript{80} The overall complication profile seen in our center matches closely to the literature with a morbidity rate of 18% and a mortality rate of 6%. However, patients with stent graft misalignment incur a disproportionate number of these complications, 33% morbidity and 11% mortality.

6.1 Stent graft misalignment

While several studies have looked at stent graft misalignment, they have not found a conclusive link between misalignment and clinical complication profiles.\textsuperscript{10,16,17} In these studies, stent graft misalignment was measured based on post-operative CT scans, which underestimates the true degree of misalignment at the time of cannulation. As the bridging stent is deployed, the forces are distributed across the target artery, the main fenestrated body, and the bridging stent itself. This distribution of force tends to pull the fenestration into a better alignment with the target artery, as seen on the postoperative CT angiogram. The challenge with this approach is that it neglects (1) the increased potential stresses on the artery and (2) the increased catheter and wire manipulation that is required to achieve the deployment of the bridging stent.

We hypothesize that it is not necessarily the misalignment itself but rather it is the increased catheter and wire manipulation that causes a substantial number of the perioperative adverse events. In situations of ideal fenestration alignment, cannulation of the fenestration and target artery generally requires very little catheter and wire manipulation; however, in the setting of misalignment, the target fenestration and artery are often cannulated multiple times. The suboptimal positioning of the wire can often result in the wire ‘kicking’ out of the target vessel back into the aorta as the surgeon attempts to track a catheter or stent into position. It is this increase in catheter and wire manipulation that increases the risk for distal microembolization, dissection, and/or occlusion of the target artery. In addition to the potential for iatrogenic vessel
injury, the lengthened time required for cannulation also leads to longer ischemic times for the visceral organs and the spinal cord. With respect to the spinal cord, the internal iliac artery (an important spinal cord collateral) is often occluded by the large caliber of the delivery system (7.8 – 8.6 mm) until the target arteries are cannulated and the device deployment can be completed.

Interestingly, there was also a significantly higher proportion of women among the patients with stent graft misalignment. We hypothesize that this could be potentially related to narrower and/or more tortuous iliac arteries. While we did not necessarily see a significant difference in the prospective study evaluating stent graft rotation (Chapter 3), qualitatively there was a larger proportion of women in the rotation group (43%) vs the non-rotation group (29%). A dedicated study on the potential gender disparity in misalignment of advanced stent grafts would be required to fully evaluate for potential gender based anatomical differences.

The cause of stent graft misalignment has not been previously evaluated in the literature to any significant extent. Stent graft misalignment is a complex, multi-factorial problem with many potential contributing causes including: (1) the packaging of the stent graft, (2) the accuracy of the deployment position, (3) the positioning of the fenestration or branches within the stent graft, and (4) the unpredictable rotation of the stent graft during deployment. The packaging of the stent graft and/or the shipping process can potentially result in the graft being twisted within the sheath prior to insertion or deployment, which is on occasion seen clinically (especially in longer devices). With respect to intraoperative stent graft positing, accuracy has shown to be improved with fusion imaging technologies. This technology involves the rigid registration of the fluoroscopic images with a preoperative CT angiogram during the procedure to enhance the visualization of the aortic anatomy.\textsuperscript{12,13}

### 6.2 Stent graft rotation

In a prospectively followed cohort of 39 patients who underwent (F/B)EVAR, 37% had a stent graft rotation greater than 10° and the incidence of severe complications and/or death in patients with rotation was 36% relative to the complete absence of severe complications in patients without rotation. This data supports the concept that stent graft misalignment is strongly associated with severe perioperative complications. We hypothesize that the torsion of the iliac arteries imparts a torque onto the delivery system as it is advanced into position within the aorta. The amount of torque imparted on to the device is influenced by the degree of iliac artery
straightening caused by the stiff endovascular tools. In this context, the volume of iliac artery calcium is likely serving as a proxy measure for arterial stiffness. Ultimately, the applied torque results in the creation of a rotational potential energy through the differential rotation of the rigid inner cannula and the flexible outer sheath of the device. This potential energy is then released when the sheath is pulled back, causing the stent graft to rotate. The bench-top experiments in the rigid and flexible models also supported this hypothesis, demonstrating a significant positive interaction between vessel rigidity and torsion.

In a multivariate analysis, we demonstrate that iliac artery torsion, volume of iliac artery calcium, and device length are significant predictive factors of intraoperative stent graft rotation. Interestingly, when this model was applied retroactively to the opposing iliac artery, a different result (i.e. rotation vs no rotation) would have been predicted in 34% of cases. Pending future validation, the application of this predictive model to future patients could enable a more effective method of patient risk stratification.

While this data is informative on the potential causes of stent graft rotation, it still does not enable a precise prediction as to the exact amount of rotation to expect intraoperatively, nor does it explain the degree of observed variation in the clinical study. However, this variation can be explained in part by the effect of the insertion technique used. During the insertion of the delivery system through a high torsion artery, the stent graft twists in the direction of the torsion. In this situation, the operator typically applies a counter torque at the proximal end of the device to maintain the orientation of the fenestrations. However, as we have shown in Chapter 4, this counter torque significantly increases the measured stent graft rotation. On the other hand, the multiple insertion technique (insert the device, assess the orientation, completely remove the device, correct the orientation ex vivo, and reinsert the device) has a significantly lower measured rotation. Multiple insertions might not be feasible in all patients, but where applicable it may help to reduce the degree of intraoperative rotation observed.

Through the development of mechanically realistic patient-specific models, we were able to accurately simulate the degree of stent graft rotation observed intraoperatively. Interestingly, this did not require the incorporation of patient specific material properties, only patient-specific anatomical structure. While this appears to contradict the importance of vessel rigidity, it may be secondary to the small number of patients evaluated. Further validation with a broader range of
patients will be required to better understand the importance of vessel rigidity in this model. We also demonstrated the potential to eliminate rotation in the patient-specific models by starting with the device offset in the direction opposite to the measured iliac artery torsion and subsequently rotating the device into alignment during insertion. The amount of rotation required to eliminate the observed rotation was determined through trial and error and was not consistent between the two patients. This model has the potential to be an effective tool for the preoperative surgical simulation of high risk cases; however, due to the technical expertise required to create these models, wide spread adoption would be limited without commercial adoption. Such adoption is not without precedent however, currently Vascutek provides a rigid aortic model with the Anaconda device to help assess the appropriateness of the fenestration positions. In our laboratory, we also recently demonstrated a reasonably accurate prediction of stent graft rotation using a finite element analysis based model. This model consistently under predicted the observed device rotation. The straight insertion technique used in this model could potentially account for the observed underprediction.

6.3 Stent graft planning

One of the most important aspects in ensuring proper fenestration alignment is an accurate initial device plan. Currently, this process involves the creation of an aortoiliac centerline that is modified manually based on clinical experience and judgment. In theory, this manual modification should consider both the path that the device is likely to take within the aorta as well as any deformation that might occur secondary to the insertion of the rigid guidewire and delivery system. However, in practice, there is significant variability in these measurements.

Chapter 5 proposes a semi-automated, objective method for the design of fenestrated/branched stent grafts that uses finite element analysis and a custom 2D active contour algorithm to predict the final position of the stent graft. This approach was very accurate at predicting the final position of the delivery system, with a mean registration error of only $2.8 \pm 0.3$ mm. Future validation of this model in a prospective study will use intraoperative cone beam CT which will allow for an assessment of the aortic deformation accuracy. When these simulated plans were compared to the actual clinical plans, it was found that patients with discrepant plans stayed in hospital longer and had a trend towards an increased number of severe complications. This data
suggests that in this cohort, inaccurate fenestration planning may be resulting in fenestration misalignment and subsequent clinical sequelae. We hypothesize that this potential misalignment is in part due to the deformation of the aorta by the delivery system and in part due to an inaccurate estimation of the final position of the delivery system. Future work will involve the validation of not only the position of the delivery system but also the positional change of the branch vessels origins using intraoperative cone beam CT imaging.

6.4 Limitations

Complex endovascular aneurysm repair is a relatively uncommon procedure with only 30-40 procedures being performed at our institution each year. This presents challenges in data analysis when attempting to evaluate relatively rare outcomes or complications and is thus a primary limitation of the presented studies. Throughout the works presented in this thesis, simplified models that achieved a clinically relevant level of accuracy were preferred over more complicated models. For example, uniform material properties and an arterial wall thickness of 1.5 mm was assumed throughout. While this assumption has inherent limitations when predicting the mechanical interactions between the delivery system and the aortic wall it allowed for a reduced computational cost and a reduced simulation set-up time. Additionally, the presence of intraluminal thrombus was not considered in either the patient specific models or the finite element simulations, which has the potential to influence the deformation of the aorta seen in the presented models; however, the high level of accuracy achieved despite not incorporating the intraluminal thrombus suggests that its impact on aortic deformation is low. Finally, the calculation of misalignment in this thesis relies on the assumption that the native arterial geometry remains unchanged with the insertion of the delivery system. This assumption likely results in the overestimation of stent graft misalignment; however, it also enables the capture of misalignment related complications that might otherwise be missed by using a post-operative CT scan alone.
7 Conclusions

Misalignment is a multifactorial process that occurs to some extent in greater than 50% of patients and is associated with higher rates of morbidity and mortality. Intraoperative stent graft rotation, a significant source of misalignment, is also associated with significantly higher rates of end-organ ischemia and/or death. The underlying mechanism for stent graft rotation is most likely the accumulation of torque in the device from elevated levels of iliac torsion and atherosclerotic disease. Additionally, operator technique has been shown to play a significant role in potentially worsening the problem of stent graft rotation and we recommend that surgeons completely remove the device prior to adjusting the device orientation, if not clinically contraindicated. Finally, operator independent methods for stent graft planning have the potential to improve fenestration and branch alignment as well as the potential to reduce hospital length of stay and the incidence of severe adverse events.

This research represents an important first step towards the prevention of fenestration and branch misalignment. Future research will be required to independently validate the proposed predictive algorithm stemming from the multivariate analysis in Chapter 3. Additionally, future research will also need to evaluate a larger number of patient-specific models to fully understand the impact of vessel rigidity in a patient-specific context. Models (both benchtop and finite element analysis) incorporating patient specific calcifications and material properties may also play an important future role in augmenting the predictive models proposed in this thesis. The techniques developed in this manuscript could also be used to evaluate other vascular procedures such as the implantation of custom arch grafts. Finally, while the position of the delivery system was validated against intraoperative images, validation of change in vessel position using intraoperative cone-beam CT will provide a more definitive validation of the newly proposed stent graft planning method.
8 References


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