Branch Technology: Innovation in the Development Process

Increasing AAA and TAA patient applicability while ensuring quality from design to market.

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The Thoracic Branch and Abdominal Branch Stent Grafts[a] are currently under development and are built on the Valiant® Thoracic and Endurant® Abdominal technologies (Medtronic, Inc., Minneapolis, MN). The Valiant Mona LSA Stent Graft, the clinical configuration of the Thoracic Branch Stent Graft, is currently under study in an FDA-approved feasibility study, and the Abdominal Branch Stent Graft is in development. These innovations are expected to expand applicability with an off-the-shelf device for patients whose aortic landing zone is insufficient for traditional endovascular aneurysm repair (EVAR)/thoracic endovascular aneurysm repair (TEVAR).

THE NEED FOR INNOVATIVE EVALUATION METHODS

The expectations with respect to quality, durability, and performance of branched stent grafts are unchanged from traditional (nonbranched) devices. As a result, these devices were designed and developed using industry standards similar to those for the development of traditional nonbranched devices. However, current industry standard requirements are not designed to specifically test the nuances of branched grafts, therefore requiring the development of new evaluation methods.[1]

A key aspect in developing these new evaluation methods was to fully understand the anatomical and physiological requirements of the intended patient population. Studies were carried out to understand the use requirements in animals and humans, which allowed engineering teams to develop the appropriate performance evaluation methods (including simulated use, durability, computational, and performance methods) tailored to the targeted patient population. This article focuses on two types of evaluation methods that were used to design these innovations—simulated-use evaluation and durability testing.

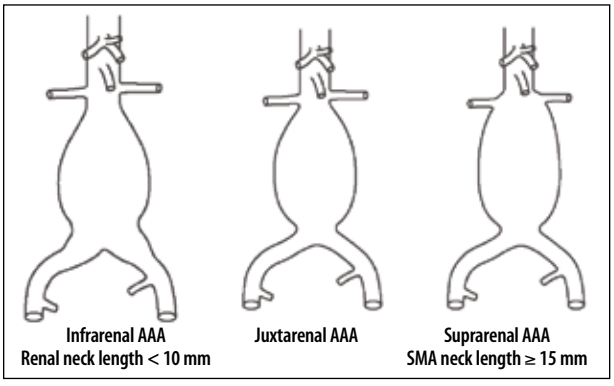

Figure 1. Anatomical scope for the Abdominal Branch Stent Graft system.

BRANCH TECHNOLOGY OVERVIEW

As described in detail in the previous article by Dr. Arko, the clinical configuration of the Thoracic Branch Stent Graft, Valiant Mona LSA Stent Graft system, is currently being evaluated in an early feasibility clinical trial. The Valiant Mona LSA Stent Graft is a modular system composed of two self-expanding stent grafts that are designed to perfuse the left subclavian artery (LSA) when the device is implanted in Zone 2 of the aorta for the exclusion of a thoracic aortic aneurysm (TAA). The main stent graft is built off of the commercially available Valiant Stent Graft but has been modified to incorporate a flexible cuff to accommodate a branch stent graft that extends into the LSA.

The Abdominal Branch Stent Graft system is designed to treat patients with short-neck infrarenal (< 10 mm), juxtarenal, and suprarenal aneurysms (Figure 1), which are estimated to comprise 20% to 30% of the total AAA population (data on file). These patients are currently being treated with the use of several methods, including custom devices, with off-label solutions, such as chimney configurations that have unproven durability;[2] or with open surgery.

[a]Technology under development, not approved commercially anywhere

The Abdominal Branch Stent Graft system is intended to treat these patients with a durable, off-the-shelf solution. The Abdominal Branch device is composed of a bifurcated aortic stent graft with a scallop for the superior mesenteric artery, two self-expanding, ePTFE-covered renal branch stent grafts, and Endurant® II limbs.

The bifurcated stent graft leverages features from the commercially available Endurant II Stent Graft. The graft material, suprarenal stent, iliac stents, and several of the markers are identical to those used in the Endurant II Stent Graft. The seal stent and body stents are unique to this device and are designed to maximize patient applicability while maintaining patency of the branch vessels. The renal branch cuffs were added to the bifurcated stent graft to allow mating with the renal branch stent graft. The renal branch stent graft was designed to be highly flexible in order to accommodate significant vessel tortuosity and motion.

SIMULATED-USE EVALUATIONS TO REFINE DEVICE DESIGN AND PROCEDURE

Thoracic Branch: Perfusing the LSA

The Valiant Mona LSA Stent Graft delivery system is built on the Captivia® delivery system platform (Medtronic, Inc., Minneapolis, MN), which incorporates tip capture to allow for controlled deployment, allowing the device to be placed accurately within the intended seal zone. Building off of this platform, the design team was faced with the challenge of how to provide rotational alignment of the system to ensure alignment of the cuff with the LSA. To optimize the procedure and hone the rotational alignment technique, the team utilized in vitro simulated-use testing and in vivo preclinical models to obtain physician and engineering feedback.

The goal of in vitro simulated-use testing was to evaluate the performance of the endovascular system in a clinically relevant environment that simulated the intended-use conditions, such as pressure, flow, and vessel compliance. To develop the test models, several geometric anatomical parameters were identified to aid in the quantification of aspects of the diseased anatomy. These parameters included tortuosity of the vessel, angulation at the landing zones, and the LSA take-off angle. To obtain these parameters, CT scans from several clinical studies and databases, including Valiant clinical trials, were analyzed and reconstructed. In total, the anatomic geometries of more than 600 patients were analyzed and quantified. Using these parameters, several clinically relevant simulated-use silicone models of the thoracic aorta and iliac arteries were created with varying degrees of tortuosity (Figure 2).

With anatomically relevant simulated-use models, the engineering team was able to partner with physicians to evaluate the use and performance of the device, as well as implement device and procedural refinements as needed to ensure deployment accuracy of the cuff and enhance ease of use. In addition to the simulated-use bench model testing, preclinical studies were performed with physicians, providing insights into the procedure and device not possible through simulated-use bench model testing alone. The preclinical models were able to evaluate the dynamic aortic motion, the translation of two-dimensional angiographic images to three-dimensional rotational alignment of the cuff, and the hemostasis management of a two-wire system. Both simulated-use and preclinical models advanced our understanding and appreciation for the methods and visual cues necessary for successful device deployment.

Figure 2. Example of Valiant Mona LSA simulated-use silicone model to evaluate the performance in a clinically relevant environment that simulates intended use conditions such as pressure, flow, and vessel compliance.

Abdominal Branch: Perfusing the Renal and SMA

Developing an off-the-shelf device is significantly more challenging in branch endovascular therapy than traditional EVAR. Physician input revealed the complexity of the procedures currently used to implant branched AAA stent grafts. This complexity is associated with long and unpredictable procedure durations, high fluoroscopy exposure, and the use of a large number of ancillary devices.[3,4] Based on this knowledge, the Abdominal Branch Stent Graft team first focused on developing a logical and repeatable procedure and then on designing delivery systems to facilitate that procedure. Clinically relevant simulated-use models were constructed by analyzing and quantifying real patient anatomies. Initial prototype devices were designed from predicate device components, allowing physicians to perform deployments and provide immediate procedural feedback. The feedback acquired from these initial deployments expedited our refinement of procedural and device concepts and led to significant improvements of the simulated-use model. Simulated-use evaluation by physicians continues to be a key driver for device refinements. The simulated-use model has evolved to a state-of-the-art setup, which utilizes fluoroscopic imaging, physiologic pressure and pulsatile flow, contrast injection, and challenging anatomic features.

TRANSLATING ANATOMIC MOTION INTO FATIGUE TESTING FOR ENSURED DURABILITY

Thoracic Branch: Ensuring Durability in the Relative Motions Between the LSA and the Aorta

In addition to accurately reaching the landing zone, perfusing the LSA, and excluding the aneurysm, the Valiant Mona LSA Stent Graft was designed to ensure robust durability and performance throughout the life of the patient. To define the use conditions, and because the published literature on thoracic aortic and LSA dynamics were limited, our research and development team leveraged the data sets of the more than 600 patient anatomies discussed previously in the simulated-use section. An initial design iteration of the stent graft system was evaluated as part of a chronic porcine model to assess acute performance and deliverability of the device, as well as chronic patency of the branch device. However, upon completion of the study, stent strut fractures were identified within the branch device, indicating that the extent of relative motion between the aorta and LSA exceed the capabilities of the device and that a new branch stent graft design would be required. As a result of these findings, a thorough evaluation and quantification of human aortic and LSA motion was conducted.

The magnitude of cardiac and respiratory motions of the LSA and the aorta was initially quantified from several multiphase CTAs and two-dimensional angiographic cines in porcine models and later analyzed for human subjects (Figure 3; Table 1). When comparing the porcine cardiac preoperative data to the combined porcine cardiac and respiratory data, the data demonstrated the majority of relative motion between the LSA and aorta was cardiac induced and located in the anterior/posterior plane. When comparing the cardiac preoperative data to the cardiac postoperative data, the relative motions are decreased in the stented patients. When comparing the porcine and human preoperative cardiac motions, the motion from the porcine model was greater. In addition, preliminary

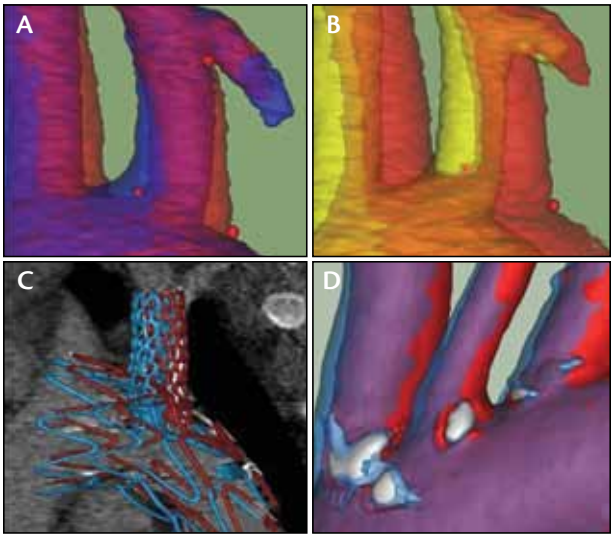

Figure 3. Valiant Mona LSA use conditions using multiphase CTA for porcine cardiac preoperative data throughout systole (purple) and diastole (orange) (A), porcine cardiac and respiratory preoperative data throughout systole inhale (yellow) and diastole exhale (red) (B), porcine cardiac postoperative data throughout systole (blue) and diastole (red) (C), and human cardiac preoperative data throughout systole (purple) and diastole (red) (D).

two-dimensional angiographic cine data of stented aneurysmal human aortas were captured from an approximate 30° left anterior oblique view angle and then analyzed to quantify respiratory and cardiac motions. From these human studies, the relative motion between the thoracic aorta and the LSA was minimal: 0.7 mm in the anterior/posterior plane and 0.7 mm in the caudocranial plane.

As these use conditions became better understood and defined, so did the benchtop fatigue tests and designs. These updated and new fatigue tests were able to identify and challenge the critical design features,

TABLE 1. CONTRIBUTIONS OF RELATIVE CARDIAC AND RESPIRATORY MOTIONS BETWEEN THE LSA AND THE AORTA

Maximum Relative Displacement Between the LSA and the Aorta Using Multiphase 4D CTAs (dimensions in mm)

Direction of Maximum Relative Displacement	Porcine			Human
	Cardiac Preoperative (n = 8)	Cardiac and Respiratory Preoperative (n = 5)	Cardiac Postoperative (n = 14)	Cardiac Preoperative (n = 7)
Left-Right	± 0.6	± 1.0	± 0.2	± 0.8
Anterior/Posterior	± 2.4	± 2.9	± 1.4	± 1.6
Caudocranial	± 0.7	± 0.7	± 1.0	± 1.0

Abbreviations: 4D, four-dimensional.

such as the cuff and branch graft flexibility, to ensure durability. The stent graft evolved into its current state through design loops as motion data were gathered and the system was challenged through more refined tests. In the end, it was evident a more flexible system was required. As a result, the stent graft transitioned from a stiff junction (both cuff and branch graft) into a flexible system able to dissipate the relative motions between the LSA and the aorta. This development culminated in the durability results found in both the preclinical model and benchtop fatigue tests.

Abdominal Branch: Ensuring Durability in the Relative Motions Between the Renals and the Aorta

The Abdominal Branch program is the first program at Medtronic to develop a stent graft that branches the renal arteries and the abdominal aorta. The Abdominal Branch program has leveraged best practices from the Thoracic Branch program. Specifically, the team partnered with Prof. Christopher Cheng at Stanford University to obtain data on renal tortuosity and motion. In a unique study published in the *Journal of Vascular and Interventional Radiology,* 16 AAA patients underwent three-dimensional gradient-echo MRA imaging before treatment.[5] The MRA data were used to reconstruct each patient's anatomy at inspiration and expiration (Figure 4). These reconstructions were utilized to extract values for maximum angulation, change in angulation, and radius of curvature both at the ostia and at the mid-renal arteries. These variables were adopted as boundary conditions in new fatigue tests to challenge the device in its anticipated clinical environment. Evaluations to date indicate the Abdominal Branch Stent Graft shows promise for a durable, off-the-shelf solution needed to treat these challenging patient anatomies.

ADVANCING TECHNOLOGY

With complex patient anatomies, a deeper understanding of the use conditions is required to develop a durable branched stent graft system. With increased emphasis on collecting and analyzing the use conditions of the in vivo environment, the Valiant Mona LSA Stent Graft and Abdominal Branch Stent Graft systems have been designed with ease of use and durability in mind. Through the implementation of innovative techniques to better understand the anatomy of the target populations, new bench tests were developed to advance the methods of endovascular device design. The encouraging results of these developments are evident in the two branch device programs. The Valiant® Mona LSA has been successfully implanted in seven patients in the United States as part of the Early Feasibility IDE, and the Abdominal Branch system is progressing toward its final design before clinical use. ■

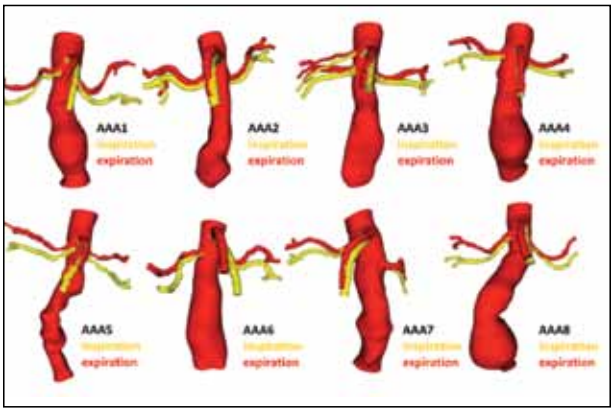

Figure 4. Abdominal Branch use conditions: renal artery and superior mesenteric artery motion at inspiration and expiration.

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