

Thoracic Endograft Performance Evaluations

Insights shared at the 2007 Cleveland Clinic Stent Summit.

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The Cleveland Clinic hosted a summit August 30 through September 1, 2007 to discuss testing and clinical performance of endovascular devices with the goal of identifying measures to improve future testing and device design. The meeting brought together 107 representatives from the endovascular community, including engineers, physicians, regulators, and others involved in the design, development, and testing of endovascular devices. The conference focused on carotid artery stents and endovascular grafts used for the treatment of thoracic aortic aneurysms (TAAs). The first 2 days of the meeting involved a small number of focused presentations by keynote speakers followed by extensive working roundtable discussions by the summit participants. The final day was a consensus meeting to identify areas of potential improvement in current testing of these devices. This article summarizes the TAA endovascular graft discussions.

KEYNOTE SPEAKERS

The TAA day focused on the anatomy and physiology of the thoracic aorta in conjunction with clinical experience using endovascular grafts for aneurysmal disease in this environment. The following is a brief summary of the keynote presentations.

Overview of Anatomy and Imaging and Standards Update

By Mark Fillinger, MD, Dartmouth-Hitchcock Medical Center, and James F. McKinsey, MD, Columbia University Medical Center

Dr. Fillinger opened with an overview of the anatomical differences between abdominal and thoracic aortic anatomy. He noted that the thoracic aortic wall has more elastin and less collagen than the abdominal aortic wall and is therefore more compliant. He also high-

lighted the differences in locations of stable structures, with the thoracic aorta having only two stable points in contrast to many stable points in the abdominal aorta (Figure 1). Dr. Fillinger then related these differences to their effects on endovascular grafts. TAA endografts must resist migration toward the center from both the proximal and distal ends, span a longer segment of more compliant aorta, and anchor in a shorter distal zone than abdominal aortic aneurysm (AAA) endografts. Dr. Fillinger concluded by noting that forces acting on a TAA endograft are different from those on an AAA endograft, and the device design should take these differences into account.

Next, Dr. McKinsey gave an update on reporting standards for endovascular treatment of TAAs. He began by clarifying why good reporting standards are needed: Many familiar terms are used loosely in practice, and accurate definitions combined with consistent reporting standards will allow improved meta-analyses to better predict outcomes. The current effort is an update to the 2002 standard and addresses disease severity, detection, procedural technique, follow-up, and treatment

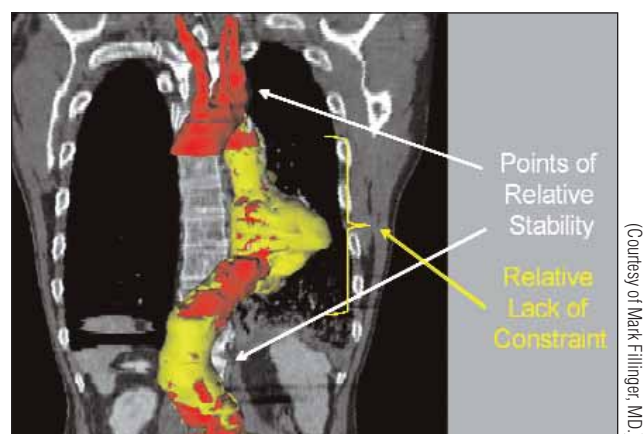


Figure 1. The thoracic aorta has fewer points of relative stability than the abdominal aorta.

(Courtesy of Hence J.M. Verhagen, MD, PhD.)



Figure 2. Dynamic CT images provided new insight into motion of the aortic arch and its branches during the cardiac cycle.

impact on quality of life. Dr. McKinsey concluded by emphasizing that the goal is to allow for better clinical investigation, trial design, and ultimately, improved quality of life for patients.

Overview of Physiology: Dynamics of the Thoracic Aorta

By Hence J.M. Verhagen, MD, PhD, Erasmus Medical Center, Rotterdam

Dr. Verhagen opened by stating that endovascular grafts are designed according to our current knowledge, which is limited and based in large part on static imaging. Changes in aortic diameter and conformation during the cardiac cycle are neglected when static imaging is used for endograft development and selection. He noted that dynamic imaging allows assessment of changes in the aortic diameter during the cardiac cycle (pulsatility) and assessment of the endograft's influence. Dr. Verhagen showed several dynamic CT sequences of TAA patients and highlighted both aortic diameter change, as well as significant movement of the arch vessels (Figure 2).

His study found pulsatility of approximately 10% throughout the descending thoracic aorta, and he observed that this value was not substantially changed by the deployment of an endograft, suggesting that 10% oversizing may not be enough. Dr. Verhagen concluded that the thoracic aortic physiology is "brutal" on an endovascular graft, and that new devices could benefit from insights gained with dynamic imaging techniques.

The Engineering Environment

By Robert G. Whirley, PhD, TriVascular2, Inc.

Dr. Whirley provided an overview of the TAA endograft environment from an engineering fundamentals perspective. He described and categorized the relative importance of loads arising from flow, pressure, and aortic motion interacting with anatomic angulation and device design. He reviewed the mechanisms that produce in vivo longitudinal loads on a TAA endograft and showed that the difference between aortic blood pressure and aneurysm sac pressure along with aortic angulation are the dominant factors that create longitudinal loads and that viscous blood flow drag was a negligible contribution (Figure 3). Dr. Whirley concluded with a comparison of the most significant engineering aspects of the thoracic and abdominal aorta.

Preclinical Evaluation (ISO 25539-1)

By Matthew S. Waninger, PhD, Cook Medical

Dr. Waninger began with a review of the merits of preclinical testing for endovascular grafts, including screening design flaws during development, ensuring all design requirements are met, characterizing long-term material integrity, and potentially helping to predict long-term clinical performance when long-term clinical data are absent. He then presented ISO 25539-1 as the primary tool for guiding preclinical testing and commented that such a standard is essentially, "A list of things to worry about." Dr. Waninger reviewed the major aspects of ISO 25539-1 as they apply to thoracic endografts. He noted that long update cycles can lead to the standard not fully addressing the requirements for evolving device designs and that the standard is intended to provide only general guidance rather than step-by-step instructions on conducting various tests. He concluded by highlighting the device risk analysis as a tool that can be used to determine what tests beyond those in the standard would be appropriate for a new device and illustrating some common mistakes in the testing of endovascular grafts.

Some interesting questions and answers followed this presentation. One participant asked if testing multiple devices with overlap was included in the standard, and it was explained that this testing is not explicitly required in the current ISO standard, but most manufacturers are doing it. Additional discussion focused on whether most clinical failures of thoracic endografts today are due to device shortcomings or due to disease progression. Dr. Greenberg commented that this question is difficult to answer today. Often, success depends

on the match of the graft to the patient, and the clinician may need to use other devices to supplement the endovascular graft. He commented, "As we get into more complicated situations, we are pushing the envelope—we have patients that need to be treated."

LESSONS LEARNED: CLINICAL ASPECTS

Other Uses Beyond TAA

By Michael D. Dake, MD, University of Virginia, and Roy K. Greenberg, MD, Cleveland Clinic

Dr. Dake presented a wide-ranging set of cases illustrating the use of thoracic endografts to treat various aortic pathologies, including traumatic injury, intramural hematoma, and acute dissection. He noted that we do not yet have devices focused on these various clinical applications. He showed two specific examples of pathologies for which no application-specific device was available: a hematoma with a penetrating ulcer and an aortic dissection. Dr. Dake concluded that, although currently available devices are a good start, the technology and the clinicians' desire to use devices for other applications are out of phase.

Dr. Greenberg also showed a spectrum of interesting uses for thoracic endovascular grafts, including treating an aortobronchial fistula and a combined ascending and descending aortic repair using a hybrid elephant trunk technique. He described how these devices can also be used for endovascular repair of the ascending aorta and commented that current technology allows devices to be placed very close to the left main coronary artery. Dr. Greenberg finished with a brief description of recent advances in CT imaging and showed several dynamic image sequences that clearly illustrated in vivo operation of normal and prosthetic aortic valves.

TAA Repair

By Mark Farber, MD, University of North Carolina Chapel Hill, and Rodney A. White, MD, Harbor UCLA Medical Center

Dr. Farber opened with the observation that, although there has been physician participation in device design and improvements for thoracic endovascular aneurysm repair over the last decade, significant challenges still exist with both devices and procedures. His list of major issues today included stroke, retrograde dissection, deployment accuracy, migration, device integrity, and implant malapposition in the arch or distal aorta. He then examined each of these issues in detail and presented data on the performance of various current devices in these areas. Dr. Farber concluded

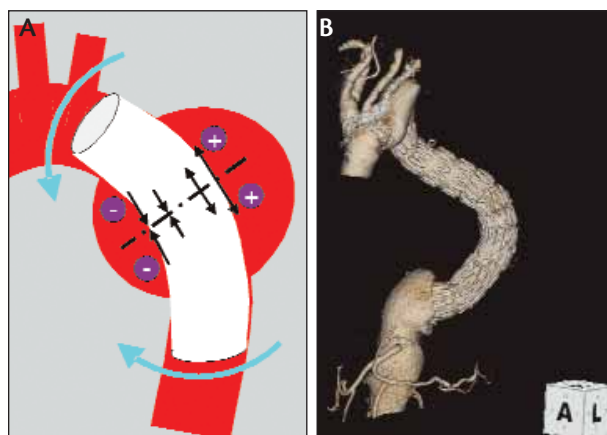


Figure 3. Diagram (A) and 12-month CT image (B) illustrating the effects of flexural loads on a thoracic endograft.

that although current devices are good, they have identifiable problems for which it is difficult to determine the root cause. Improvements can be made that will translate into better outcomes for patients.

Dr. White elaborated specifically on retrograde aortic dissection. He commented that it is an issue of endograft proximal construction and may well involve aspects of proximal bare-metal stent design. He showed four case illustrations and listed poor deployment technique and balloon dilatation as possible causes of retrograde dissection. Dr. White emphasized that adverse event reporting that we will rely on should be connected to an autopsy—it is too difficult to confidently establish the details of these cases from imaging alone.

These two presentations were followed by a lively discussion among the participants. Topics ranged from device design versus procedure as potential causes of retrograde dissections to the characteristics of an ideal thoracic endovascular graft. The group concluded that insufficient data exist today to answer their questions definitively, but some observations can be made. Regarding retrograde dissections, most participants believed that, although device design could play a role, it is likely more complicated than just the presence or absence of bare-metal stents. Some participants suggested that the way the device deploys could influence the risk of creating a dissection. One participant asked whether retrograde dissections were more common in dissection patients than aneurysm patients, and Dr. White commented that they have not seen a difference and have approximately a 2% incidence in each group. Dr. Greenberg commented that endoleaks can be significantly more difficult to see in the thoracic aorta than in the abdominal aorta, and treating them, especially in the arch, can be challenging.

TABLE 1. SUMMARY OF DISCUSSION ON THORACIC ENDOGRAFT ISSUES AND UNDERLYING ANATOMIC PARAMETERS

Device Issue	Potential Clinical Consequence	Underlying Anatomic Parameters
Malapposition or nonconformability in an angulated setting	<ul style="list-style-type: none"> • Retrograde dissection • Endoleak—type I • Endoleak—type III (component separation) • Aortic erosion 	<ul style="list-style-type: none"> • Aortic angulation/radii of curvature • Found from surface mapping/3D model
Deliverability/deployment accuracy/withdrawal	<ul style="list-style-type: none"> • Inaccurate placement • Implant dislodgement 	<ul style="list-style-type: none"> • Lesion length (focal vs long) • Access vessel tortuosity
Asymmetric radial force distribution (angulated setting)	<ul style="list-style-type: none"> • Retrograde dissection • Aortic erosion 	<ul style="list-style-type: none"> • Aortic angulation/radii of curvature
Implant integrity in presence of movement of the aorta (especially arch) and branch vessels	<ul style="list-style-type: none"> • Endoleak—type III (graft wear holes) 	<ul style="list-style-type: none"> • Aortic pulsatility >10% (change in diameter over diameter) • Aortic compliance—thoracic higher than abdominal

LESSONS LEARNED: ENGINEERING ASPECTS

After the clinical discussion, attention turned to engineering lessons learned from experience with thoracic endovascular grafts. Representatives from industry were invited to make a brief presentation sharing engineering insights, without cross-examination from the audience. Presentations were made by Robert Keller, PhD, and Roy Biran, PhD, from Gore & Associates (Flagstaff, AZ); Michael Moore from Bolton Medical, Inc. (Sunrise, FL); Ben Wolf from Medtronic Vascular (Santa Rosa, CA); and Brian Choules, PhD, from Cook Medical (Bloomington, IN). One presenter emphasized that the conditions in the instructions for use are those for which testing has been performed, and failure modes may exist if the device is used beyond those limits. Another speaker highlighted the important role of design inputs in designing preclinical tests and believed clinical shortcomings were related to inadequate design inputs in many cases (eg, poststent aortic compliance, static vs dynamic imaging data). The importance of using realistic anatomy for developing preclinical tests was echoed by another presenter. One participant shared a case history of anomalous graft wear during a pulsatile fatigue test that was traced to a test artifact. Collectively, these presentations offered insights derived from enormous engineering investments by multiple companies that should help all industry participants to more rapidly advance their thoracic endograft designs.

DISCUSSION

After the company presentations, the scientific committee led a workshop-style discussion among the participants. Participants were first asked the question, “What is the number one clinical issue that testing doesn’t address today?” Many clinicians highlighted the challenges of placing current-generation devices into the aortic arch. The group believed that these challenges often arise from device attributes that are poorly characterized or from inaccurate estimates of anatomic parameters in design inputs. Table 1 summarizes the device issues, associated clinical consequences, and underlying anatomic parameters from this discussion.

Participants were next asked to comment on additional issues that should be considered in the design of a thoracic endovascular graft but that may not be possible to incorporate into tests today. A dynamic discussion ensued, and this interchange surfaced issues that were too poorly identified or understood to incorporate into a test, as well as issues that were well understood but for which important anatomic parameters were unknown. A summary of the identified issues is presented in Table 2.

Finally, as a follow-up to earlier discussion on preclinical testing, participants were asked to identify and rank new and modified preclinical tests that should be considered for inclusion in the endovascular graft standard, ISO 25539-1. Surprisingly, there was a general consensus

TABLE 2. CHARACTERIZATIONS AND CONSIDERATIONS THAT MAY NOT BE POSSIBLE TO INCORPORATE INTO TESTS TODAY

Issues to Consider in Thoracic Endograft Design

- Aortic elongation/dilation over time
- Combinations of pathologies
- Should radial force vary by device size?
- What testing is needed for branched devices?
- Access site injury
- Implantation risks that are different from AAA (eg, stroke)
- Physiologic differences between young and old (eg, compliance)
- Thoracic aorta surface mapping

Information Needed

- How to define angulation
- Compliance of thoracic aorta

TABLE 3. NEW AND MODIFIED TESTS THAT PARTICIPANTS BELIEVED SHOULD BE CONSIDERED FOR INCLUSION IN ENDOVASCULAR GRAFT PRECLINICAL TESTING STANDARD, ISO 25539-1

New Preclinical Tests

- Graft wear/abrasion
- Axial fatigue
- Bending fatigue
- Computational fluid dynamics—for branch graft motion
- Fatigue to fracture/failure
- Component level test to address malapposition

Preclinical Tests to Be Modified

- Simulated use
- Pulsatile fatigue testing
- Increased delta-D
- Curved mock vessel
- Unsupported regions

on both aspects of the question. The resulting test update recommendations from the summit participants are listed in Table 3.

WRAP-UP

A wrap-up session was held Saturday morning to consolidate the previous day's conclusions and determine

the next steps. During this session, it was noted that more information was needed on pulsatility in the thoracic aorta. Drs. Greenberg and Verhagen agreed to collaborate on a statistically valid assessment of compliance in the thoracic aorta. There was also discussion on whether industry was ready to collaborate on advancing the use of computer simulation for thoracic endografts, although no consensus was reached. There was confirmation of the list of tests to be recommended for consideration by the ISO standards committee as shown in Table 3.

THE FUTURE

Although thoracic endovascular grafts are currently providing a good treatment option for many patients, there is significant room for improvement. Dynamic imaging studies of the thoracic aorta will improve our understanding of the environment in which thoracic endografts must function, and this understanding will in turn lead to better implant designs and improved pre-clinical tests. Continued clinical experience with current devices will shape future implant design efforts to broaden applicability and minimize complications. Ongoing collaboration among industry, clinicians, and regulators will be essential to improving thoracic endovascular grafts and broadening the range of pathologies that can be effectively treated with these devices. ■

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