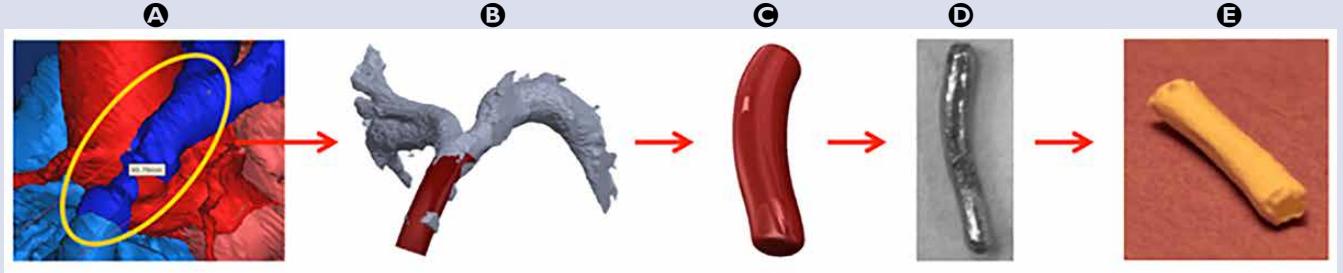


Driving Innovation in Cardiac Tissue Engineering

One of the major challenges in cardiovascular surgical care for children is the need to accommodate a growing heart and blood vessels. A pulmonary graft implanted in a toddler has maybe a five- to 10-year lifetime before it might need to be replaced; that means a second—and eventually, a third—surgery and recovery period. But what if these grafts could be made to grow as the child grows?

Thanks to advances in tissue engineering technology, this dream is starting to become a reality. Johns Hopkins pediatric cardiac surgeon and biomedical engineer **Narutoshi Hibino** is one of the leaders in this field and has developed advanced approaches to engineer more lifelike cardiovascular grafts. Using 3-D printing, Hibino and his colleagues can create an exact replica of a patient's heart based on preoperative imaging, and then print and implant a new cardiovascular structure that is designed to precisely fit the patient's unique anatomy.¹



Although the technique is not yet applicable to the aortic root, it is being used for other cardiovascular components and could be expanded to include this structure in the coming years. Hibino and his colleagues are also harnessing advances in stem cell technology, which they hope will enable ways of seeding these 3-D printed structures with stem cells—thereby programming them to grow as the patient grows, reducing the need for future surgeries.



Narutoshi Hibino
nhibino1@jhmi.edu

Flow chart depicting the proposed process for manufacturing patient-specific tissue-engineered vascular grafts.
A Segmenting 3-D image of the vasculature.
B Creating a patient-specific graft design from the preoperative CT image using the computer-aided design system.
C Finalized mandrel.
D 3-D printed mandrel from stainless steel.
E Patient-specific nanofiber graft.²

References

- Hibino N. Three dimensional printing: applications in surgery for congenital heart disease. *World J Pediatr Congenit Heart Disease* 2016;7(3):351-2.
- Fukunishi T et al. Preclinical study of patient-specific cell-free nanofiber tissue-engineered vascular grafts using 3-dimensional printing in a sheep model. *J Thorac Cardiovasc Surg* Published online Nov. 14, 2016

**Physician Referrals
for Pediatric Heart Patients**

For **physician-to-physician referrals** 24 hours a day,
7 days a week, call 410-955-9444 or 1-800-765-5447

New Treatments for Connective Tissue Disorders

Removing all tissue at risk of aortic catastrophe while preserving the native aortic valve in the growing child

Connective tissue disorders can compromise tissues throughout the body, but their most alarming effects are on the cardiovascular system. Conditions such as Marfan syndrome, Loeys-Dietz syndrome and Ehlers-Danlos syndrome often impair the function of the heart and major blood vessels. Children with these disorders can develop dilation of the aorta, particularly the aortic root and arch, which can lead to life-threatening aneurysms and dissections, and chronic valvular problems.

Johns Hopkins has a long, distinguished history of advancing the diagnosis and treatment of connective tissue disorders. For more than three decades, **Harry “Hal” Dietz**, director of the William S. Smilow Center for Marfan Syndrome, has studied the molecular basis of connective tissue diseases, revealing deep insights that spur novel treatments. Although connective tissue disorders are relatively rare—for example, Marfan syndrome affects roughly one in 10,000 children—Johns Hopkins physicians currently treat more than 1,000 families affected by these conditions, one of the largest clinical practices worldwide to specialize in diseases of connective tissue.

Correcting Pediatric Cardiovascular Defects

This legacy of excellence also extends to the surgical suite, where cardiologists and cardiac surgeons at Johns Hopkins have pioneered new ways to correct pediatric cardiovascular defects. **Luca Vricella** has pushed the frontiers of cardiac surgery for children with connective tissue disorders and other congenital heart conditions. Vricella, who directs pediatric cardiac surgery at the Johns Hopkins Children's Center, has worked with colleagues to establish a technique first applied in adults, known as aortic valve-sparing root replacement, as a viable approach in pediatric populations.^{1,2}

Preserving patients' own aortic valves offers distinct advantages, particularly in children with connective tissue disorders who often require aortic root surgery at a relatively early age. For example, if the aortic valve is replaced rather than

Aortic valve-sparing root replacement is a viable approach in pediatric populations.

preserved, these patients would require lifelong anti-coagulation with inherent risks, including thrombosis and hemorrhage. Through these advances and others, including advanced tissue-engineering approaches (see sidebar), Johns Hopkins has emerged as a global

leader in the understanding and treatment of aortic disorders in children, with the goal of removing all tissue at risk of aortic catastrophe while preserving the native aortic valve in the growing child.



Valve-sparing aortic root replacement in a 6-year-old child with Loeys-Dietz syndrome with aortic root aneurysm and bicuspid valve. The aortic valve is re-implanted and preserved within a prosthesis, retaining its functionality while the tissue at risk of rupture or dissection is replaced with the prosthesis.

A Cross-Disciplinary Clinic Approach

Johns Hopkins physicians' deep expertise in the cardiovascular aspects of connective tissue disease is complemented by equally deep experience in other clinical domains. World-renowned physicians from diverse specialties come together in a unique, cross-disciplinary clinic, which provides comprehensive, coordinated care for children and families grappling with these conditions. This clinic offers expert care in multiple areas, including cardiology, orthopaedics and ophthalmology. Indeed, patients with connective tissue disease often exhibit multisystem symptoms, so they require a clinical team that is focused on the heart and has wide-ranging, head-to-toe capabilities.

Moreover, connective tissue disorders require lifelong care from physicians with advanced training and experience not only in pediatric specialties, but also in managing these congenital conditions in adults. Johns Hopkins physicians have advanced training in an important and emerging area of medicine—caring for adults with congenital heart disease—and can provide the best possible care for patients of all ages.

References

- 1 Vricella LA, Cameron DE. Valve-sparing aortic root replacement in pediatric patients: lessons learned over two decades. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann* 2016 (in press).
- 2 Vricella LA et al. Early experience with valve-sparing aortic root replacement in children. *Ann Thorac Surg* 2005 80(5):1622-7.



Luca Vricella
lvricella@jhmi.edu