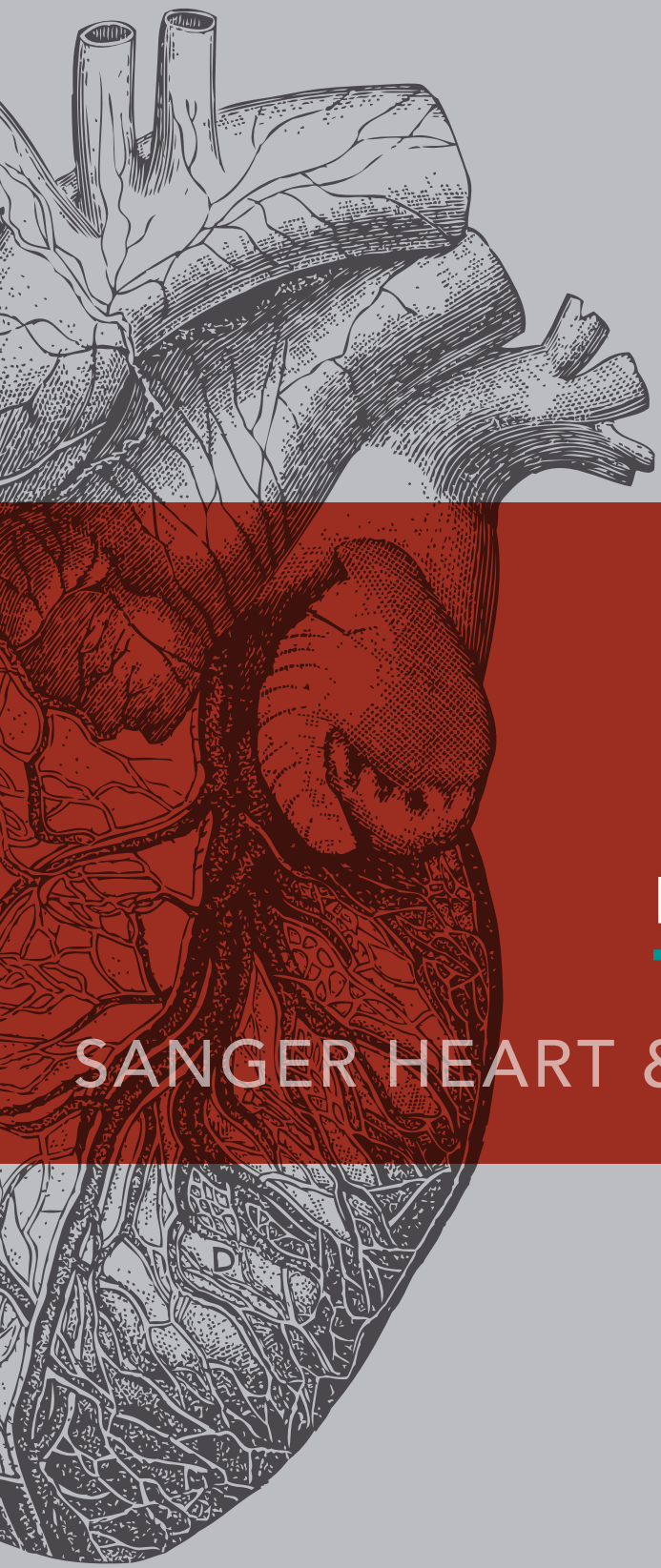
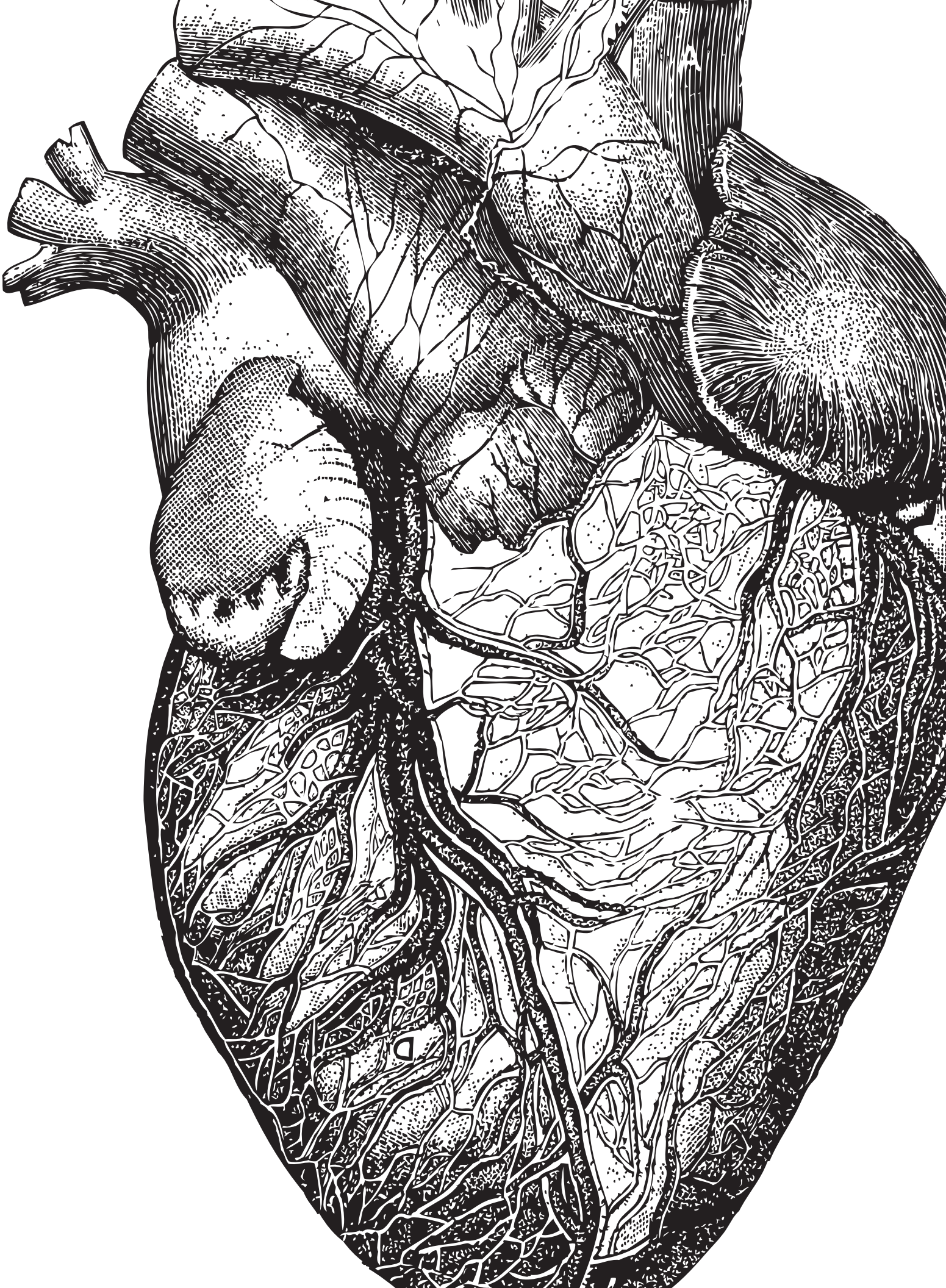


STRUCTURAL HEART DISEASE PROGRAM GUIDE

SANGER HEART & VASCULAR INSTITUTE

Carolinas HealthCare System
Sanger Heart & Vascular Institute



Structural Heart Disease Program Guide

Sanger Heart & Vascular Institute

about us

Sanger Heart & Vascular Institute

In the 1950s, Paul Sanger and Francis Robicsek began Sanger Heart & Vascular Institute as a cardiothoracic and vascular surgery group. Since inception, we have fostered open-door, cross-team collaboration and taken an evidence-based approach to providing highly specialized care. Built on a strong history of innovation, Sanger continues to evolve by applying the latest science and technology to patient care and recruiting nationally and internationally recognized experts. Part of Carolinas HealthCare System, Sanger encompasses more than 100 physicians and 20 care locations.

Structural Heart Disease Program Milestones

2005
Became one of the first 10 centers to offer transcatheter mitral valve repair

2011
Transcatheter aortic valve replacement (TAVR) program started

2012
FDA approval of TAVR

2013
Expanded and enhanced program for transcatheter mitral valve repair
FDA approval of transcatheter mitral valve repair

2014
Performed 100th TAVR

2015
Launched program for transcatheter closure of the left atrial appendage
Performed 200th TAVR

2016
Performed 300th TAVR
First patient treated in PARTNER III clinical trial

What Sets Us Apart

Collaborative Approach

Sanger Heart and Vascular Institute's **Center for Advanced Heart Valve Therapies** is built on collaboration. Cardiac surgeons, interventional cardiologists, advanced imaging specialists, radiologists, specialized advanced care providers and program coordinators work closely with each patient's referring physician to collectively determine the optimal course of care.

Full Spectrum of Care

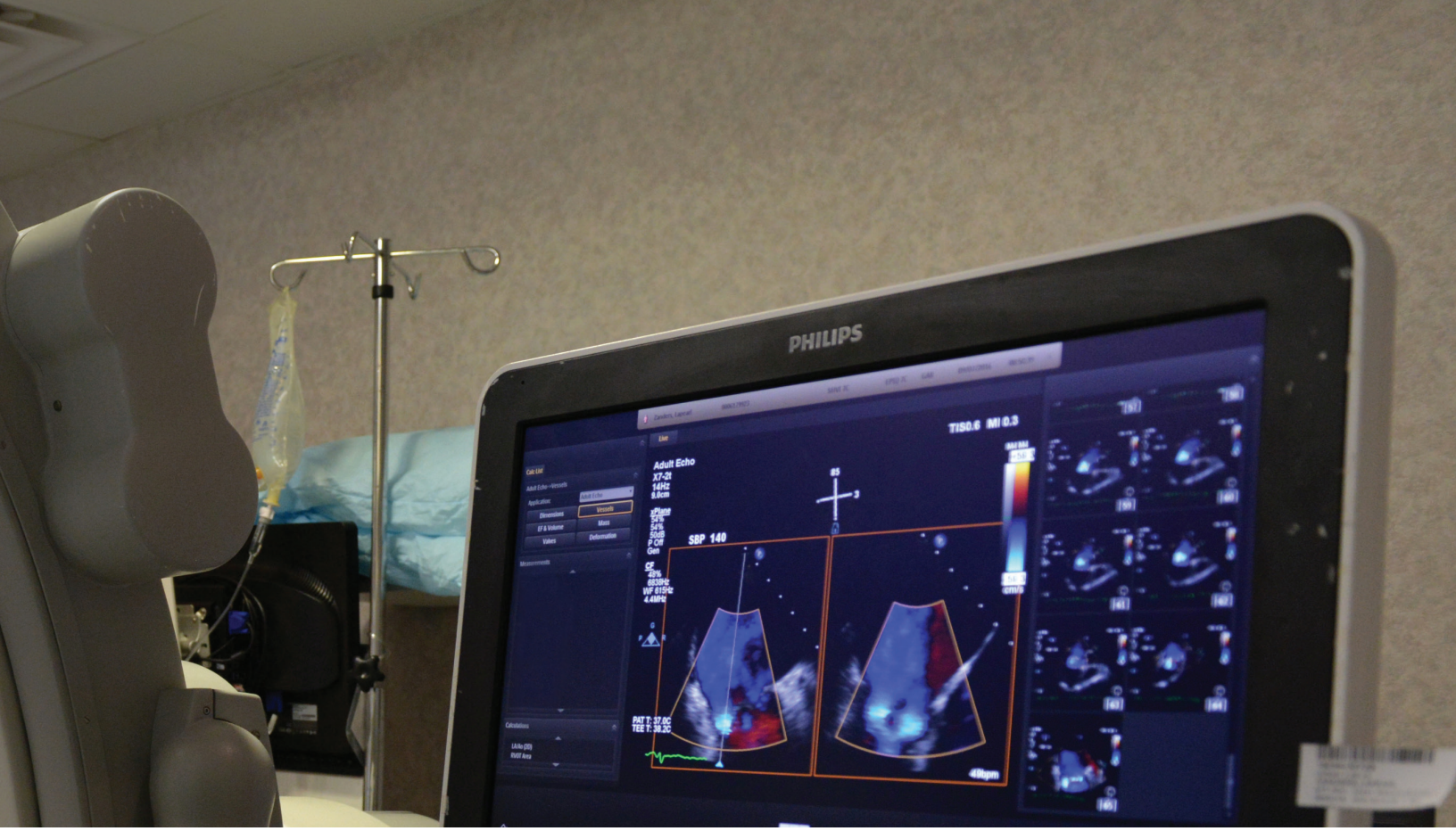
From state-of-the-art diagnostic imaging to the most advanced surgical procedures, Sanger's multidisciplinary team delivers the full spectrum of treatment.

Leading-Edge Technologies and Clinical Trials

Our center stands at the forefront of structural heart disease treatment and research. We were one of the first hospitals globally to perform transcatheter mitral valve repair through EVEREST and one of a select few centers nationally participating in PARTNER III, the first randomized trial of transcatheter aortic valve replacement (TAVR) in low-risk surgical patients. This gives patients additional therapies not available at other centers.

Superior Outcomes

Not only are we one of the highest-volume centers in the nation, but we consistently perform in the top quartile, and often decile, in published outcomes for the TVT registry.



Charlotte Location Means Convenient Access to Care

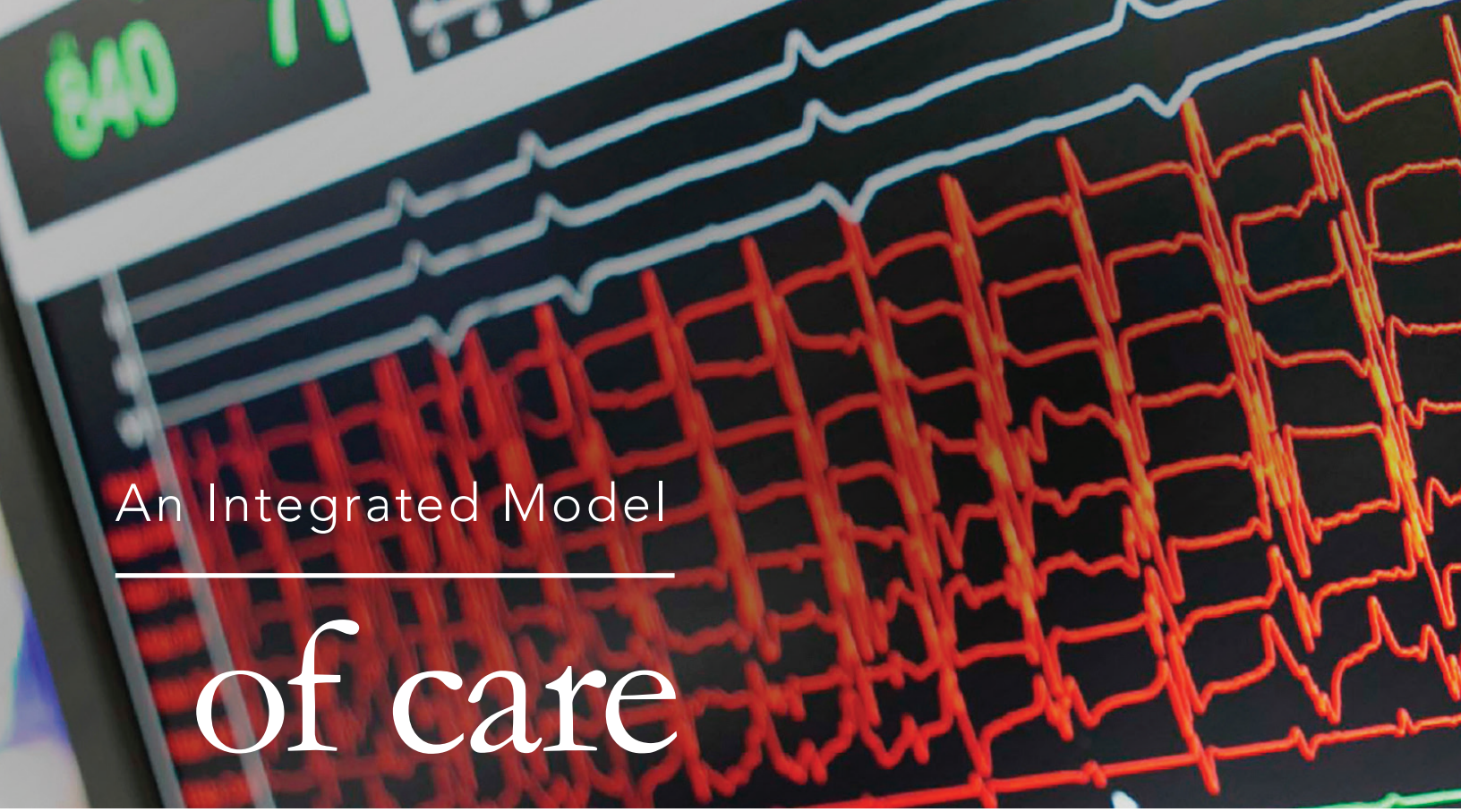
- Top 30 Most Popular Domestic Cities for American Travelers[1]
- Top 10 Speediest Major Airport[2]
- No. 2 Best Airport[3]

- Greenville, SC: 1.5 hours
- Raleigh, NC: 2 hours
- Charleston, SC: 3 hours
- Wilmington, NC: 3.5 hours

1 March 2014 Hotels.com, of 50 US cities
2 June 2013 *USA Today*, of commercial airports
3 April 2012 *Travel + Leisure*, of 22 major airports

Global Patient Services

If your patient has to travel, our Global Patient Services program is here to help. We will coordinate everything – from medical appointments to travel and hotel arrangements. For additional information, call 888-327-3915.



An Integrated Model of care

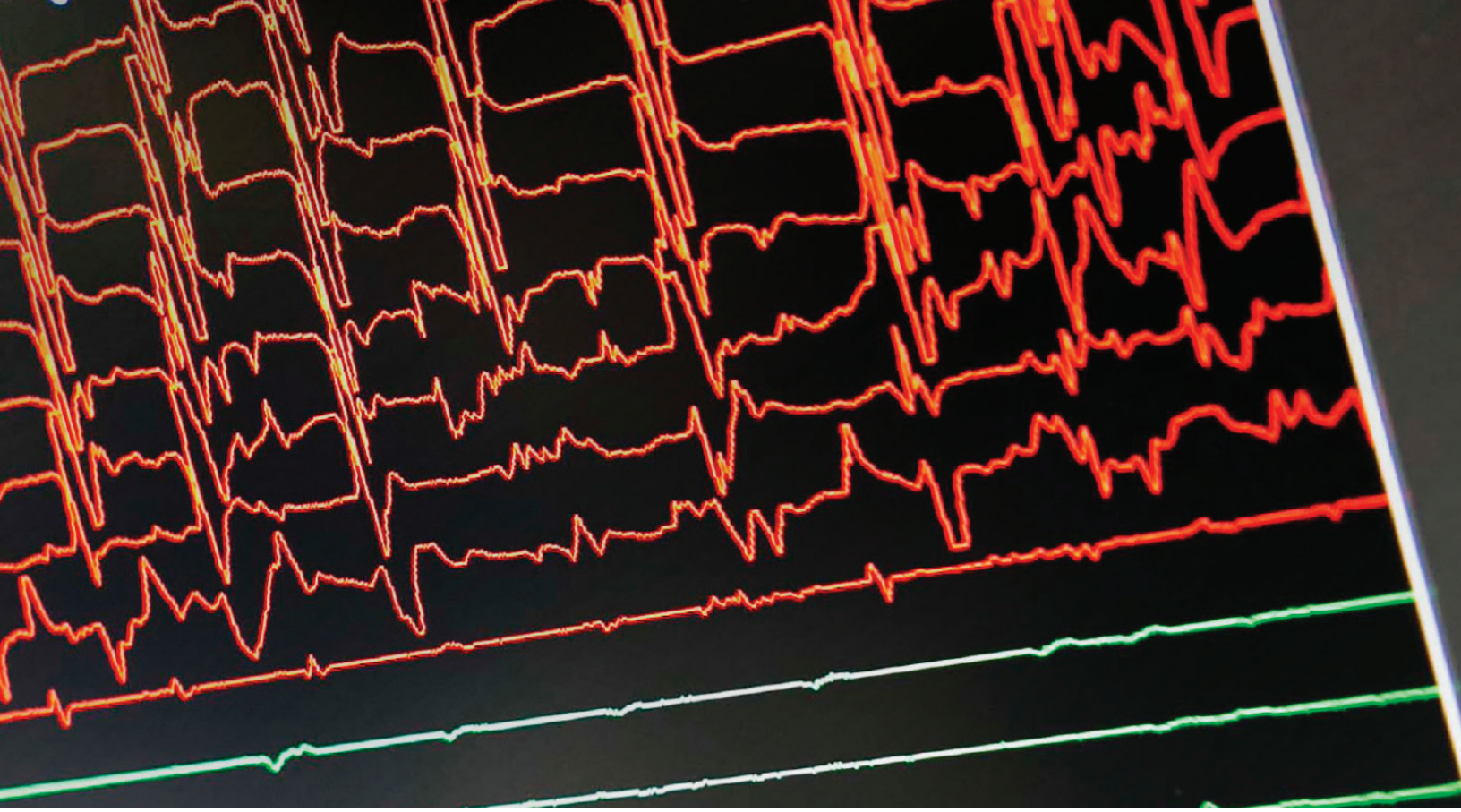
The Sanger Model of Care

The integrated model of care at the Center for Advanced Heart Valve Therapies begins with the referring provider, who remains a critical team member throughout the patient's evaluation, treatment and follow-up.

After referral, the patient undergoes an extensive clinical evaluation, including consultation with the appropriate physicians. As part of the evaluation, we perform diagnostic testing, which may include transthoracic echocardiograms and cardiac catheterizations. Our team also uses advanced imaging, such as 3D transesophageal echocardiography (TEE), 2D transthoracic echocardiography (TTE), cardiac MRI, cardiac CT and coronary CT.

Our team regularly evaluates patients with a variety of structural heart conditions, including:

- Aortic regurgitation
- Aortic stenosis
- Atrial fibrillation (for consideration of transcatheter left atrial appendage closure device)
- Atrial septal defect
- Bioprosthetic aortic valve failure (AI or AS)
- Mitral stenosis
- Mitral valve prolapse
- Mitral valve regurgitation
- Patent foramen ovale
- Prosthetic paravalvular leak



After the patient's evaluation, our team reviews the patient's medical history and test results, discusses our recommendations with the patient and referring physician, and moves forward with treatment. This process ensures all of our patients receive the best, most individualized treatment for their needs.

Procedures commonly performed include:

- Balloon mitral valvuloplasty
- Minimally invasive surgical aortic valve repair and replacement
- Minimally invasive surgical mitral valve repair
- Open mitral commissurotomy
- Transcatheter closure of atrial septal defect
- Transcatheter closure of left atrial appendage
- Transcatheter closure of patent foramen ovale
- Transcatheter repair of prosthetic paravalvular leaks
- Surgical aortic valve replacement
- Surgical mitral valve repair
- Surgical mitral valve replacement
- Transcatheter aortic valve replacement (TAVR)
- Transcatheter aortic valve replacement for failed bioprosthetic valves
- Transcatheter mitral valve repair

The team ensures a smooth transition from pre-procedure hospital care to outpatient maintenance and follow-up. Through each step of the process, program coordinators guide the patient, helping to make appointments, manage record collection, coordinate post-operative care and facilitate the patient's return to their referring physician. Patients also undergo scheduled follow-ups at Sanger to ensure optimal progress and a smooth transition back to their primary cardiologist.

Specialized Care for Aortic Valve Disease

The Center for Advanced Heart Valve Therapies provides open surgical, minimally invasive as well as transcatheter procedures to treat aortic valve disease. Depending on the patient's condition, comorbid disease and valve anatomy, treatments may include medical management, valve repair or valve replacement.

Aortic valve procedures we commonly perform include:

- Minimally invasive aortic valve repair and replacement
- Surgical aortic valve repair or replacement
- Transcatheter aortic valve replacement (TAVR)
- Transcatheter aortic valve replacement for failed bioprosthetic valves
- Valve-in-valve procedures

We consider a number of factors – including a past history of heart surgery, age, and comorbid conditions – when we determine our treatment recommendation, whether it be for an open surgical, minimally invasive, or transcatheter procedure. The Center for Advanced Heart Valve Therapies has demonstrated excellent outcomes in all three types of procedures, with a focus on individualized treatment plans.

Transcatheter Aortic Valve Replacement (TAVR)

As one of the first regional providers of transcatheter aortic valve replacement (TAVR) outside of clinical trials, Sanger is leading the way in the development and application of this technology. TAVR is a less invasive procedure to replace the aortic valve for those at moderate to high risk for conventional open heart surgery.

During the TAVR procedure, a specially constructed tissue heart valve is delivered to the diseased aortic valve via a catheter and deployed with the guidance of fluoroscopy and echocardiography. The procedure is performed in a hybrid cath lab/OR by a team of interventional cardiologists, cardiac surgeons and advanced imaging experts with valve disease expertise.

We perform this catheter-based procedure via a range of access options, including transfemoral, subclavian, transapical and direct aortic approaches, with the most common being transfemoral. In fact, greater than 95 percent of procedures are now performed transfemorally – the least invasive approach to TAVR – which reduces the risk for complications and decreases length of stay.

Our team has performed the TAVR procedure since FDA approval in 2012 with consistently excellent outcomes and is committed to advancing technology and innovation within the field. Sanger is also participating in the clinical trial, PARTNER III, which evaluates TAVR in the low surgical risk population.

The FDA has approved the commercial use of TAVR in patients with symptomatic, severe aortic valve stenosis who are deemed to have a moderate to high risk for conventional aortic valve replacement. Potential TAVR candidates include those with comorbidities suggestive of an elevated surgical risk, as well as individuals with:

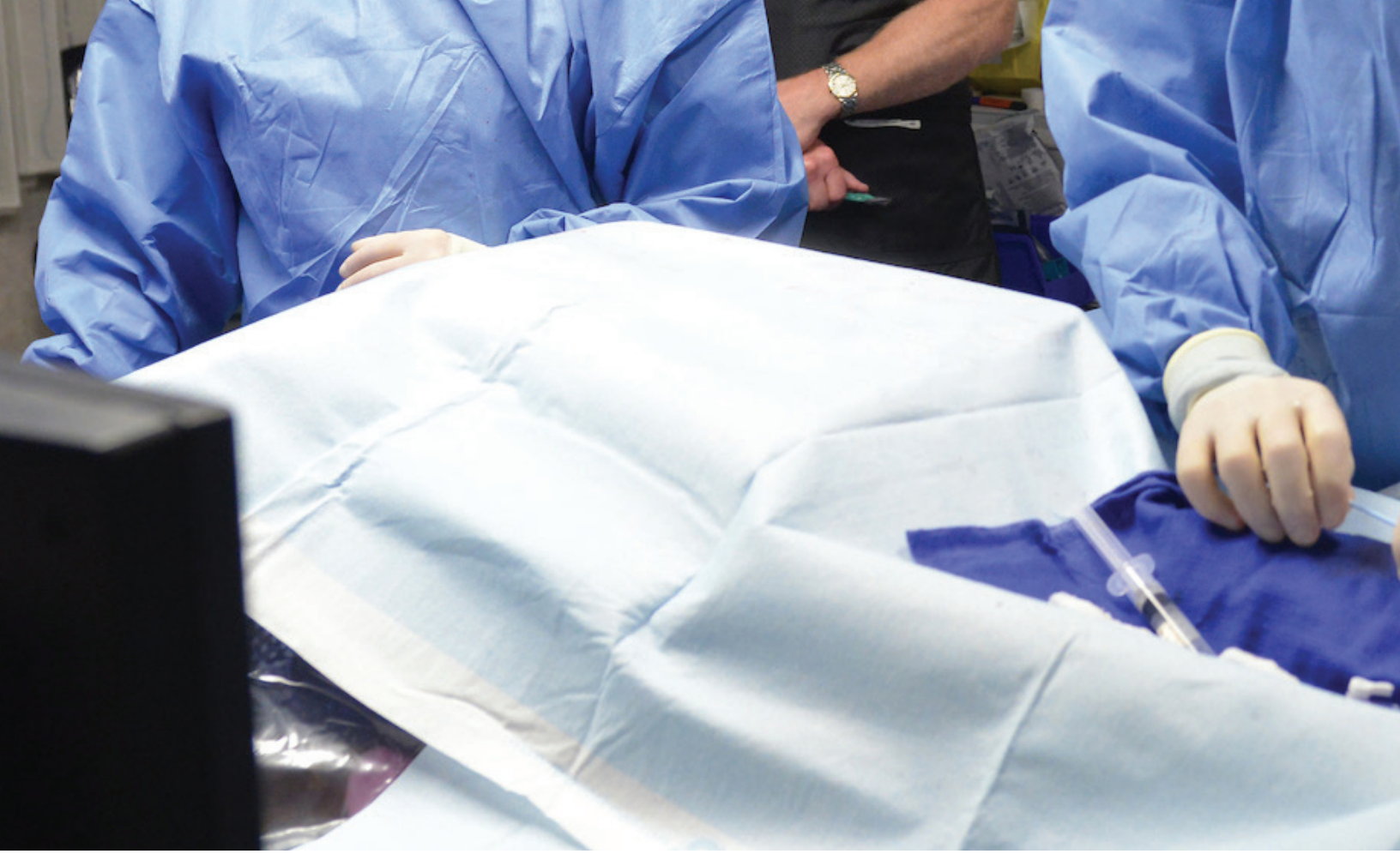
- Advanced age
- A prior history of open heart surgery or cerebrovascular accident
- Multiple comorbidities (but greater than one-year life expectancy)
- Renal insufficiency
- Chronic obstructive pulmonary disease
- Calcified aorta

Patients referred to Sanger for a potential TAVR undergo a thorough evaluation, including specialist consultations and TAVR-specific testing (cardiac catheterization, TTE, CTA, pulmonary function tests, carotid duplex imaging and arterial blood gas tests). If components of this evaluation are available locally, Sanger will coordinate appropriately.

Following this comprehensive evaluation, the full TAVR team – interventional cardiologists, cardiothoracic surgeons, imaging cardiologists, advanced clinical practitioners and nurses – convenes to determine the best treatment plan. Should TAVR be pursued, faster recovery times and shorter hospitalizations should be expected, as conscious sedation is used for most patients. An average hospital stay is two to four days, and patients are followed closely by the TAVR team and supporting staff. Patients return to the Center for Advanced Heart Valve Therapies for post-discharge follow-up one week, and as soon as one day, after the procedure to ensure stable clinical course, as well as 30 days and one year post-procedurally (per national registry requirements).

Valve-in-Valve Procedures

Patients who have developed severe regurgitation or stenosis of a previously placed bioprosthetic aortic valve and have a high or prohibitive risk for repeat surgery, may be excellent candidates for TAVR. Following Sanger's commitment to providing patients with the most up-to-date technology, the team has been performing valve-in-valve procedures since FDA approval in 2015.



Leading the Field in Mitral Valve Disease Treatment

Our team frequently treats various forms of mitral valve disease through open surgical, minimally invasive and transcatheter procedures. Depending on the patient's condition, comorbid disease and valve anatomy, the team customizes care and may recommend medical management, valve repair or valve replacement.

Mitral valve procedures we commonly perform include:

- Balloon mitral valvuloplasty
- Minimally invasive surgical mitral valve repair or replacement
- Transcatheter mitral valve repair
- Surgical mitral valve commissurotomy
- Surgical mitral valve repair or replacement

The Center for Advanced Heart Valve Therapies offers the entire spectrum of therapeutic interventions for mitral valve disease. For appropriate patients, minimally invasive surgical mitral valve repair or replacement is an excellent option for treating mitral valve disease. In cases where replacement is necessary, the team considers multiple factors such as age, comorbid conditions, lifestyle and ability for ongoing medication use.

Transcatheter Mitral Valve Repair

Our center has been performing transcatheter mitral valve repair since its investigational beginnings a decade ago, and we remain one the nation's top-volume centers since its FDA approval in 2013. In that time, we have excelled in providing a safe, effective transcatheter option for extreme- and high-risk patients with severe,

symptomatic degenerative mitral regurgitation. Sanger is also participating in the clinical trial, COAPT, which evaluates optimal medical management versus transcatheter mitral valve repair in patients with functional mitral regurgitation (MR).

Patients experiencing symptomatic MR can be referred to our center, where our specialists will determine the mechanism of MR and the appropriate management. As part of the evaluation, patients most often undergo a TTE, TEE and cardiac catheterization, in addition to a multidisciplinary assessment by an expert interventional cardiologist and cardiothoracic surgeon. When indicated, the team collaborates with Sanger's electrophysiology experts and heart failure team. If the etiology of the MR is functional, enrollment in COAPT will be considered.

For patients undergoing transcatheter mitral valve repair, the hospital stay is approximately two days. During the procedure, a steerable guide catheter is inserted through the femoral vein and delivers a clip delivery catheter to the anterior and posterior mitral leaflets through a transseptal approach, providing mechanical edge-to-edge coaptation. Patients undergo follow-up at our center one week post-procedure to ensure stable clinical course, as well as 30 days and one year post-procedurally (per national registry requirements).

Appropriate candidates for transcatheter mitral valve repair are patients who are severely symptomatic with three or more years of MR and are of extreme or high surgical risk. Other factors include those who are of advanced age, have a history of open heart surgery, a prior history of cerebrovascular accident, multiple comorbidities (but greater than one year life expectancy), renal insufficiency, or chronic obstructive pulmonary disease.

Balloon Mitral Valvuloplasty

Our team specializes in conducting balloon mitral valvuloplasty. Used for those with moderate or severe symptomatic mitral stenosis, often of rheumatic origin, the procedure inflates a balloon across the stenotic mitral valve to split the fused commisures and increase the valve area. For many patients, it replaces open mitral commisurotomy and has been associated with low restenosis rates.

Patients evaluated through our center are assessed to determine their candidacy for mitral valvuloplasty based on leaflet anatomy, commisure characteristics and subvalvular apparatus degeneration. Our extensive experience and specialized focus have made Sanger a regional referral center for this procedure.

When valve anatomy is unsuitable for mitral valvuloplasty or patients are already undergoing surgery for concomitant coronary artery disease, we can perform open mitral commissurotomy.

Other Specialized Transcatheter Interventions

The breadth and depth of the Center for Advanced Heart Valve Therapies includes transcatheter offerings for other forms of structural heart disease, including atrial septal defects (ASDs), patent foramen ovales (PFOs) and prosthetic paravalvular leaks.

ASD

Often asymptomatic until adulthood, atrial septal defect is one of the most common congenital lesions. In the setting of right ventricular enlargement, with or without symptoms, closure is usually indicated. Transcatheter closure of ASD has become the treatment of choice with excellent results. A high sealing rate, fewer procedural risks, shorter procedure time and faster recovery all make transcatheter closure a preferable option if anatomically appropriate.

PFO

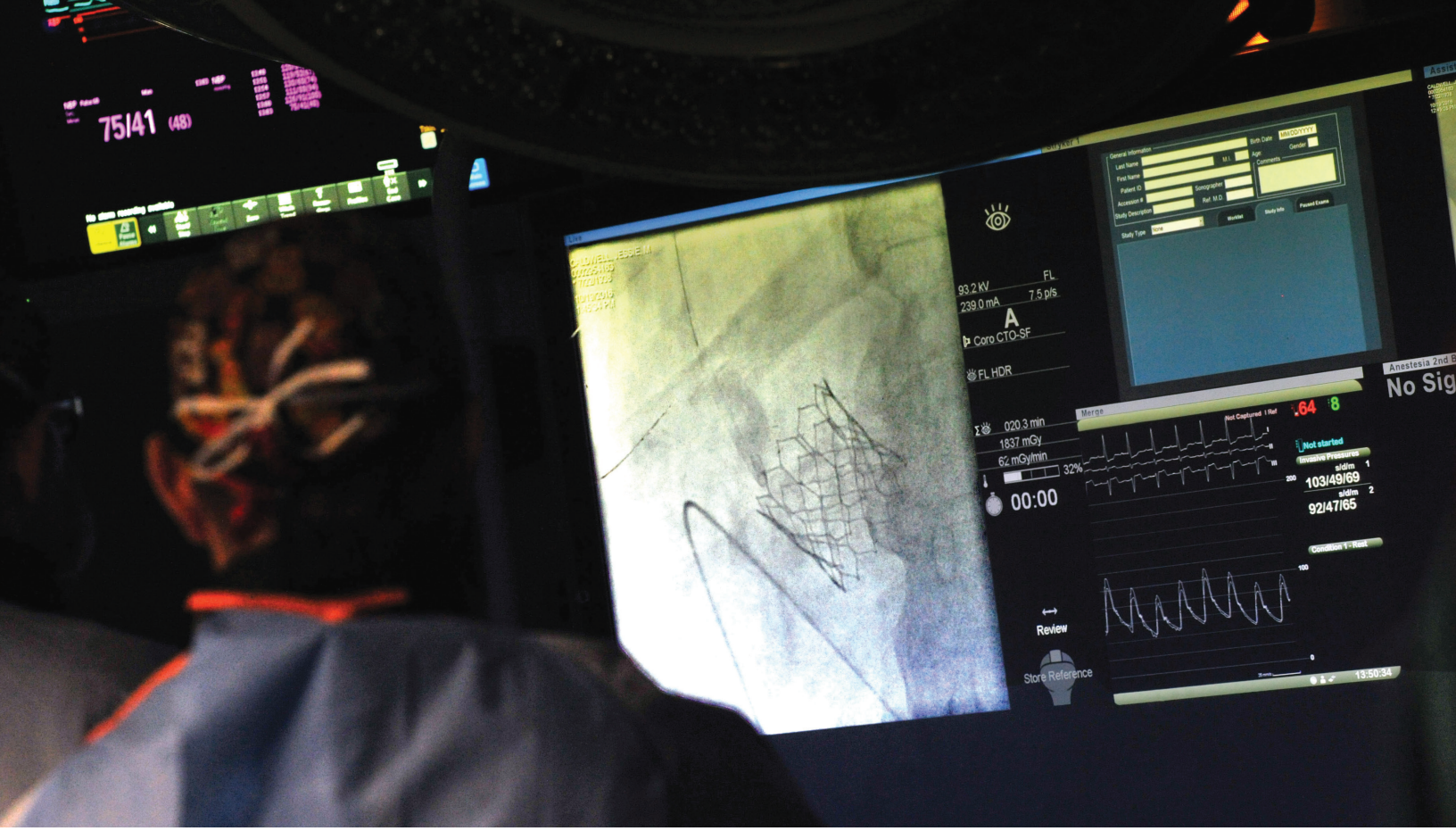
PFO closure may be clinically indicated for patients with prior history of stroke or symptoms consistent with orthodeoxia platypnea syndrome.

After 25 years of investigation, the FDA has approved a specialized device to reduce the risk of recurrent stroke in patients with initial stroke presumed to be due to PFO. Based on long-term data collected from the RESPECT trial, PFO closure reduced the annual risk of recurrent stroke from ~1 to ~0.5 percent. Recently published long-term data shows that this benefit continues to accrue out to 10 years, resulting in a substantial absolute reduction in stroke risk over time. As indications for PFO closure evolve, our team will continue to work hand-in-hand with cardiologists and neurologists to provide up-to-date recommendations and treatment options. For the vast majority of patients, PFO closure can be performed percutaneously.

We also have robust experience in treating patients with orthodeoxia platypnea syndrome, a consideration in patients who have hypoxia out of proportion to their comorbid medical issues. In close collaboration with pulmonologists, this diagnosis is confirmed and transcatheter closure of PFO can be accomplished with remarkable improvement in symptoms thereafter.

Prosthetic Paravalvular Leaks

Between 5 and 17 percent of the more than 60,000 prosthetic valves implanted each year in the United States will develop some degree of paravalvular regurgitation. Because a second surgery is generally associated with significant morbidity and mortality, the Center for Advanced Heart Valve Therapies has focused on offering a transcatheter treatment option. Sanger is a regional referral center for transcatheter repair of prosthetic



paravalvular leaks, seeing a high volume of these patients annually. Depending on valve anatomy, we use different techniques, approaches and devices.

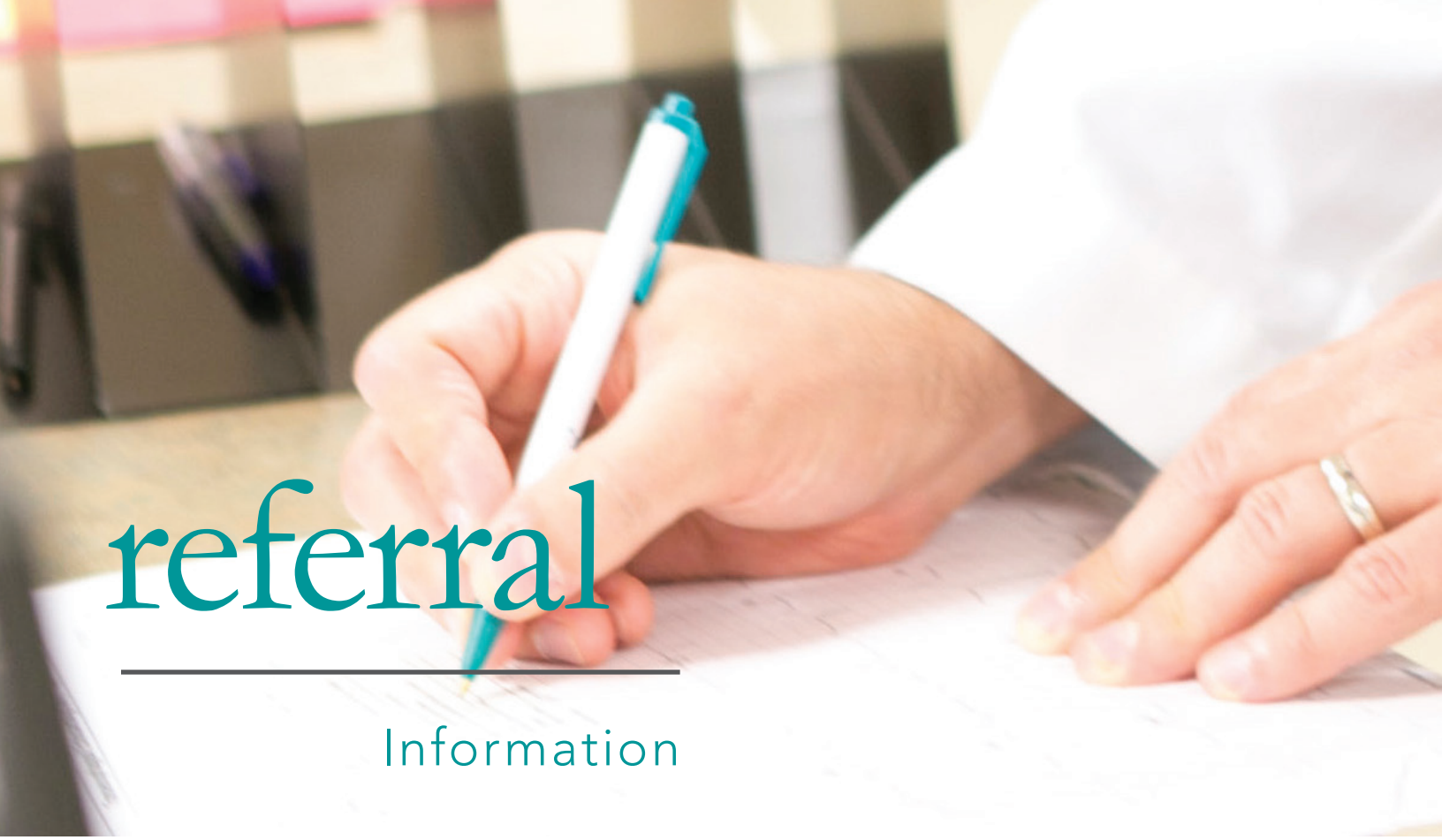
Specialized Interventions for Atrial Fibrillation

Sanger also boasts a comprehensive program for those with atrial fibrillation (AFib). Sanger's cardiologists and electrophysiologists not only drive excellent treatment of disease symptoms, but also provide options for targeting stroke risk reduction.

In 2015, the FDA approved use of a trademarked implantable closure device designed to reduce the risk of stroke associated with non-valvular AFib. Although the device is now more widely available, Sanger has been successfully implanting it since participating in the PREVAIL trial, which began in 2010.

The device is implanted using a standard transseptal technique in an approximately one-hour-long procedure that necessitates a 24-hour hospital stay. It is made of a self-expanding, nickel titanium frame and is placed using a transseptal access sheath and delivery catheter. We conduct a pre-procedural transesophageal echocardiography TEE or CT scan to measure the left atrial appendage (LAA) and determine device size and then again, along with fluoroscopy, to confirm release criteria after placement.

Appropriate patients for this procedure include those who are at an increased risk for stroke based on their CHA2DS2-VASc scores and can tolerate short-term anticoagulation therapy but have an appropriate reason to seek a mechanical, non-pharmacological method of stroke prevention. These patients may include those with a history of major bleeding while on anticoagulation therapy, those who have had labile INRs on Warfarin therapy, and those who may be at high risk of major bleeding secondary to trauma.



referral

Information

Referral Information

To refer patients to Sanger Heart & Vascular Institute's Center for Advanced Heart Valve Therapies, physicians may call 704-373-0212 or fax 704-446-2489. Referrers may also email the program at SHVIStructuralHeart@CarolinasHealthCare.org.

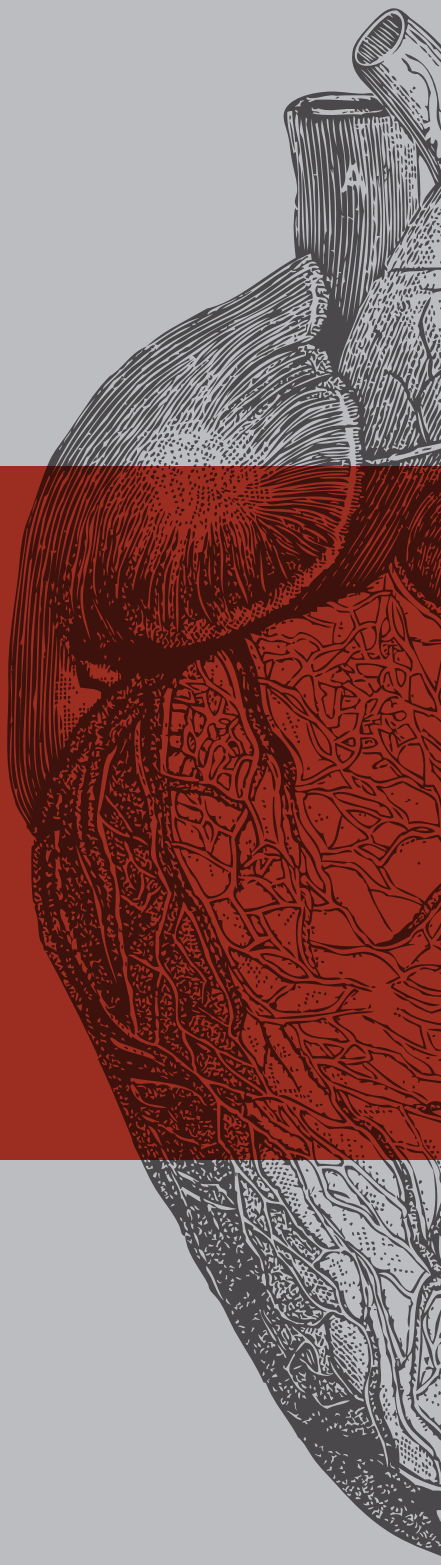
For questions or more information about the program, call 704-617-8154.

Carolinas HealthCare System

Sanger Heart & Vascular Institute

supplemental

Program Information



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