

Your Partner in Good Health



Seton
Family of Hospitals

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Progress in the Management of Atrial Fibrillation

Technological advances and increased experience now make catheter ablation a mainstream procedure

Atrial fibrillation is the most common cardiac arrhythmia that requires medical attention. In many patients, it dramatically reduces the quality of life and remains a leading cause of embolic events, including cerebrovascular accidents. For years, medications for rate control and antiarrhythmic agents to promote sinus rhythm have been available; however, it has not been until recently that the results of large clinical studies have become

available to dictate evidence-based management options.

It is now well-recognized that in patients with atrial fibrillation and another risk factor for having a stroke (HTN, diabetes, smoking, structural heart disease, history of any prior embolic event or advanced age), the use of warfarin increases survival – mainly by decreasing the incidence of fatal and disabling stroke. In the last five years, randomized clinical trials have also demonstrated that in elderly patients who are asymptomatic

or with minimal symptoms, five-year outcomes are similar with a strategy that includes pursuing sinus rhythm with antiarrhythmic agents and cardioversions, or with a strategy of simply controlling rate and chronic anticoagulation with warfarin.

The main reason for the failure to improve outcomes with antiarrhythmic medications is the fact that, even when using amiodarone (the most effective antiarrhythmic available), the success rate in maintaining sinus rhythm with medications remains below 60 percent after one year of follow up. Furthermore, antiarrhythmic medications have significant side effects that may include life-threatening conditions. Despite the limitations in the ability to obtain persistent sinus rhythm with medications, the same clinical trials have shown that when sinus rhythm is obtained, quality of life does improve significantly and the restoration of persistent sinus rhythm is a strong predictor of improved survival.

For all the above reasons, strategies to obtain sinus rhythm by non-pharmacological means have been pursued. Permanent pacemakers, although helpful in decreasing symptoms in selected patient populations, have been consistently disappointing in decreasing the rate of recurrence of the arrhythmia. On the other hand, the placement of therapeutic electrical scars in areas of atrial myocardium that are responsible for the initiation and maintenance of atrial fibrillation has evolved from a research concept to a clinical reality. In the late 1980s, this treatment was accomplished during open heart surgery, while on cardio-pulmonary bypass, by very small group of specialized cardiovascular surgeons (“Cox maze surgery”).

In the last 10 years, knowledge about the arrhythmia has increased exponentially with the publication in the peer-reviewed literature of outcomes in more than 20,000 atrial fibrillation ablation procedures. The therapeutic techniques have been refined to the point that success rates in obtaining persistent sinus rhythm are now equal to or greater than 80 percent in the majority of patients using minimally invasive catheter-based techniques in the cardiac electrophysiology laboratory. In experienced hands, the risk of complications has also improved dramatically, and is now similar or lower than commonly performed cardiovascular procedures, including percutaneous coronary interventions for management of coronary artery disease.

Patients with symptomatic atrial fibrillation undergo an evaluation to rule out the presence of any treatable condition that may cause atrial fibrillation, including electrolyte abnormalities, ischemia, thyroid disorder

and others. A cardiovascular team, including a cardiologist as well as a cardiac electrophysiologist, are then involved to help make a decision whether a simple strategy of rate control plus chronic anticoagulation with warfarin is sufficient or whether pursuing sinus rhythm is desirable. If sinus rhythm is recommended, an antiarrhythmic agent is then selected, based mostly on the side-effect profile given each patient’s specific comorbidities. For those patients who remain symptomatic or cannot tolerate antiarrhythmic therapy, the option of a catheter ablation is considered, balancing the severity of symptoms, probability of success, the risks of the procedure and the patient’s personal preference. Given the

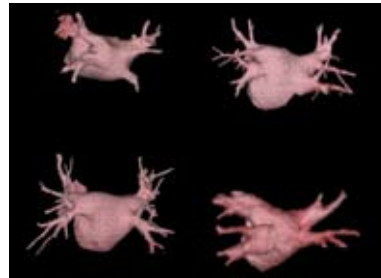


Figure 1

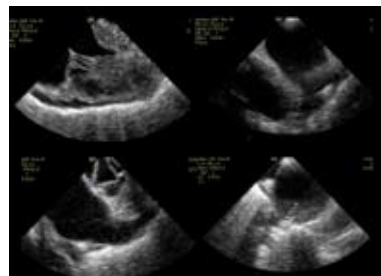


Figure 2

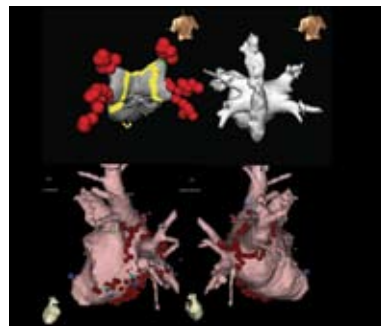


Figure 3

recent improvements in the efficacy and safety of catheter ablation procedures, an increasing number of patients are choosing to undergo ablation therapy.

Patients who have chosen to pursue catheter ablation undergo pre-procedure CT angiography (or cardiac MRI) to evaluate the atria with the intention of tailoring the details of the ablation strategy to each patient’s anatomy. Attention is given to the location, configuration and size of the pulmonary veins, left atrial appendage, coronary sinus and the esophagus. Figure 1 shows a posterior view of the left atrium in four different patients, demonstrating some of the variation that exists between patients. Given the differences in inter-individual left atrial anatomy, the availability of pre-procedure CT angiography significantly improves the electrophysiologist’s ability to adequately navigate within the complex three-dimensional space of the left atrium.

Patients receive pre-procedure antithrombotic therapy as indicated clinically; however, on the day of the procedure, an intracardiac thrombus is a possibility, especially within the left atrial appendage. Although these clots are usually small and commonly non-mobile, their presence contraindicates manipulation of catheters in the left atrium. For this reason, most patients undergo a transesophageal echocardiogram (TEE) on the day of the procedure. After the TEE, a small temperature probe is placed within the esophagus (to record esophageal temperatures at the level of the posterior left atrium) and access sheaths are placed in both femoral veins. A small 4 Fr sheath is also commonly placed in either femoral artery.

During the procedure, catheters are advanced from the femoral access sheaths into the heart under fluoroscopic guidance. Mapping and pacing electrodes are placed in the right atrium, coronary sinus and, transeptally, into the left atrium. The ablation catheter can be manipulated as needed between both atria. An intracardiac echocardiography probe is also commonly placed in the right atrium. Intracardiac echocardiography images are not good enough to rule out the presence of pre-procedure intracardiac thrombus, but they provide adequate visualization of all the relevant cardiac structures and the mapping and ablation catheters within the atria. Figure 2 shows intracardiac echo visualization of the pericardial space, the left pulmonary veins, the left atrial appendage and the right inferior pulmonary vein. Real-time, continuous echo imaging is useful to orient the operator during the creation of a virtual, three-dimensional image of the left atrium with the use of computerized 3-D mapping systems (discussed below). In addition, intracardiac echo facilitates the detection of findings that precede the onset of possible complications.

Examples of 3-D maps created in two different patients with non-fluoroscopic, computerized imaging systems are shown in Figure 3. The availability of this new technology is specially useful in patients with non-paroxysmal atrial fibrillation and in patients with enlarged left atria, which typically require more extensive ablation and therefore demand a more precise mechanism for tracking each ablation lesion. The pre-procedure 3-D CT scan image of the left atrium is now routinely displayed and incorporated into

the computerized image created during the procedure, further decreasing the time required to recognize each patient's anatomy. The synergy obtained by integrating the pre-procedure CT image, continuous intracardiac echocardiography of all relevant structures, computerized 3-D systems and esophageal temperature monitoring increase the efficacy of the procedure, decrease the duration and the radiation used during the procedure and potentially decrease the rate of complications, specially life-threatening events as procedure-related stroke, pericardial tamponade, pulmonary vein stenosis and left-atrial esophageal fistula formation. Extensive atrial fibrillation ablation training and experience is still required from the operator because catheter manipulation within the left atrium is a complex and very unique skill.

A more recent technological advance is the use of magnetic-based, robotic, remote manipulation of the ablation catheter. Seton Medical Center Austin is the first hospital in Austin with this technology. In this system, the ablation catheter consists of a soft and very flexible body attached to an ablation electrode with small permanent magnets embedded near the tip. Two large magnets are placed to each side of the patient's body and a computerized system coordinates the movement of these magnets. Changing the magnetic field steers the ablation tip into any desired position within the heart. This system allows the ablation electrode to be placed in locations where the uneven topography of the left atrium makes stable contact with a conventional, manually controlled and relatively stiff catheter extremely difficult. Although atrial

fibrillation ablation will remain a complex procedure limited to high-volume centers, the addition of robotic magnetic guidance into the armamentarium of tools available to the electrophysiologist will further increase the availability of this procedure for the benefit of larger number of patients.

Javier E. Sanchez, MD, is part of Texas Cardiac Arrhythmia, a division of Texas Cardiovascular. For more information or to arrange for a patient evaluation, please contact Texas Cardiovascular at (512) 458-1366; Seton Medical Park Tower; 1301 West 38th St., Suite 705; Austin, Texas 78705. Dr. Sanchez can also be reached at jsanchez@txcardio.com.

Seton Medical Center Austin is the first hospital in Austin to offer Stereotaxis technology for Atrial Fibrillation.

Five million people worldwide suffer from atrial fibrillation, by far the most commonly occurring cardiac arrhythmia. Previously, in order to map and ablate arrhythmias, the physician had to manually advance and rotate a stiff catheter in an effort to reach specific points within the heart. With Sterotaxis, the computer control and automation allows the physician to more precisely steer soft, magnetically enabled catheters.

What Are the Benefits of Stereotaxis Technology?

- Safer procedures reduce the risk of vessel or other tissue perforation.
- Physicians can now treat more complex arrhythmias.
- More precise and efficient device navigation can reduce radiation levels to the patient.

For more information about Stereotaxis technology at SMC Austin, contact Barbara Borman, RN, MSN, Operations Director, Cardiology, at bborman@seton.org.

Breakthroughs in the Treatment of CML in Adolescents and Children

Chronic myelocytic leukemia (CML) occurs in approximately 8 percent to 9 percent of all leukemia diagnosed in adolescents and children.

is slow and painless, and CML is diagnosed when white blood cell (WBC) counts are in the hundreds of thousands and the spleen is massive in size.

In addition to karyotyping, FISH (Fluorescent, in situ, hybridization) is an even more sophisticated test to evaluate for the bcr-abl abnormality. With follow-up bone marrow aspirations, it is possible

Age-adjusted incidence rates per million for specific leukemia by age groups, all races, both sexes, SEER, 1990-95

Age (in years) at diagnosis	<5	5-9	10-14	15-19	<15*
Total leukemia	72.4 (100%)	38.0 (100%)	25.9 (100%)	26.0 (100%)	43.8 (100%)
ALL	58.1 (80%)	30.6 (81%)	17.4 (67%)	13.0 (50%)	34.0 (78%)
AML (Ib)	10.3 (14%)	5.0 (13%)	6.2 (24%)	9.3 (36%)	7.0 (16%)
CML (Ic)	1.1 (2%)	0.7 (2%)	1.1 (4%)	2.2 (9%)	1.0 (1%)
Other specified leukemias (Id)	0.3 (-)	0.3 (1%)	0.1 (-)	0.1 (-)	0.2 (3%)
Unspecified leukemias (Ie)	2.2 (3%)	1.0 (3%)	0.6 (2%)	1.1 (4%)	1.2 (3%)

*Rates are adjusted to the 1970 U.S. standard population. Numbers in parentheses represent the percentage of the total cases for the specific age group.

Chronic myelocytic leukemia (CML) is a myeloproliferative disorder that occurs in the myeloid cells of the bone marrow where myeloid cells originate. It begins with a change in a cell's genetic makeup with the appearance of the Philadelphia chromosome, which is the hallmark of CML. It is the result of a fusion of a portion of chromosome 9 (abl gene) being attached to chromosome 22 at the breakpoint cluster region (Bcr). The result is that the combination is the bcr-abl gene on the 22q- chromosome (Philadelphia chromosome), which then drives the proliferation of the myeloid cells, while decreasing apoptosis (cell death) – thus leading to extremely high neutrophils in the peripheral blood and invasion of the spleen. This progression

to determine the presence of minimal residual disease.

Eighty-five percent of the time, CML is diagnosed in the chronic proliferative phase where there is ongoing differentiation of the myeloid series from early myelocytes to mature neutrophils: with fewer than 5 percent myeloblasts present. Other times (15 percent of patients), there are increased myeloblasts in the peripheral blood when the disease is in the accelerated phase (myeloblasts >5 percent but < 25 percent or in the blast crisis phase (>25 percent myeloblasts).

Presenting symptoms of CML are primarily non-specific such as malaise, anorexia, weight loss, low-grade fever and, occasionally, night sweats. Hematological problems such as

nose bleeds and bruising may occur. Young adolescent girls may have a change in their menstrual pattern. Physical examination may show only pallor and splenomegaly. Many times, the spleen size is massive, across the mid line of the abdomen down to the pelvis.

Treatment Options

Prior to 2001, CML patients were treated with combinations of hydroxyurea, interferon, cytosine arabinoside, plus other chemotherapy agents. The chemotherapy treatment lasted anywhere from a few hours to as long as a few days. Patients experienced many unpleasant side effects such as nausea, vomiting and hair loss.

However, for the past five years, CML patients at Children's Hospital of Austin's Cancer and Blood Disorders Center have been treated with a less-invasive, faster and safer option that allows "kids to be kids."

"In 2001, Gleevec (imatinib) by Novartis, was approved for the treatment of CML," said Dr. James Sharp, medical director of Children's Cancer and Blood Disorders Center. "Gleevec, an oral agent, is a tyrosine kinase inhibitor with minimal side effects. Our patients simply take a pill twice a day, in the comfort of their own home, and no longer have to make trips to the hospital for chemotherapy and experience unpleasant side effects." Dr. Sharp added, "It's less stressful for both the patient and entire family. And, the remission rates have been comparable to the historical treatment of more aggressive chemotherapy."

Established in 1992, The Children's Hospital of Austin

Cancer and Blood Disorders Center specializes in the care of leukemias, brain tumors and other pediatric cancers, Sickle Cell Disease, Hemophilia and other childhood blood disorders. The health care team is comprised of five physicians with more than 100 years of combined experience. The team of physicians and experienced professionals focus on addressing the emotions and concerns of the children and their families, while providing individualized, effective and progressive medical treatment.

In June of 2007, the center will expand and relocate to the new Dell Children's Medical Center of Central Texas, providing patients with an ambulatory cancer center and, in 2010, bone marrow transplant capabilities.

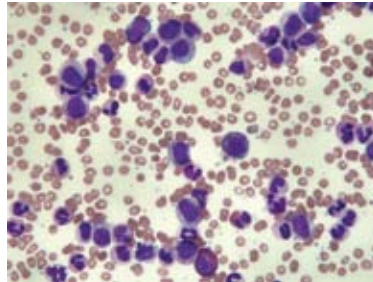
"Our center provides the children of Central Texas with the crucial advantage of rapid diagnosis with access to the most modern treatments – close to home," said Dr. Sharp.

Patient Summaries

Patient One: A 17-year-old male presented with a history of malaise, loss of appetite and fatigue. He had no previous history of significant problems. Immunizations were current, and he had no known allergies. Family history was negative for blood disorders or platelets. He was admitted to the hospital after a CBC showed 305,000 WBC with all stages of maturation of the myeloid series. Myeloblasts were less than 5 percent. Hemoglobin was 8.7 gm percent and the platelet count 950,000 cmm.

The smear of the bone marrow showed essentially the same findings as the blood smear. Cytogenetic studies showed the Philadelphia chromosome, 46

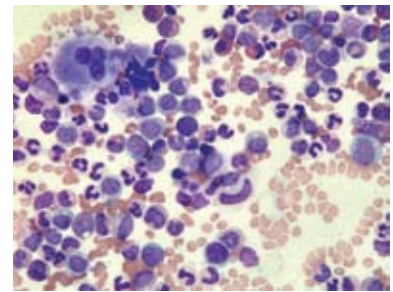
xy t(9;22) (q34;q11.2). Once the diagnosis was confirmed, he was then started on hydroxyurea. The goal was to decrease the WBC to 100,000, or less, then begin Gleevec. Once the Gleevec was begun, the WBC decreased to ~15,000 cmm. He continues on Gleevec. A bone marrow aspiration is scheduled for the near future to ascertain status of the Ph chromosome.



Peripheral Blood Smear with Increased Myeloid Cells

Patient Two: A 16-year-old female was diagnosed in 2003 and presented with symptoms of fatigue and malaise. The primary abnormality on physical examination was pallor and the finding of a massive spleen with the tip of the being palpated near the pelvis and across the mid line. White blood cells were 399,000, with the differential showing mostly myeloid cells from the earliest precursor to the mature neutrophils. Hemoglobin was 9.7 gm percent and the platelet count was 616,000 cmm. Cytogenetics confirmed the diagnosis with 20 cells all showing the Philadelphia chromosome - 46 xx t(9;22) (q34;q11.2). She was begun on imatinib and currently remains in remission.

Patient Three: A 17-year-old male presented to the emergency room with priapism. His WBC at the time was 725,000 cmm, Hgb 9 gm percent and platelets of 177,000 cmm. His priapism resolved with several



Bone Marrow with Marked Increase in Myeloid Cells

procedures performed by the urologist on call. He received an exchange transfusion to reduce the number of WBC because the increased number of WBC had increased the viscosity of his blood with the subsequent priapism. The bone marrow cytogenetics showed 46 xy t(9;22) (q34;q11.2). He was begun on Gleevec once the WBC was less than 100,000 cmm. His remission continues at 3.5 years of treatment.

The Children's Hospital Blood and Cancer Center participates in pediatric cancer treatment regimens designed by the Children's Oncology Group, an international research organization sponsored by the National Cancer Institute. Dr. Sharon Lockhart has served as the center's clinical research director since 1996. In 2002, the center opened a Gleevec study to determine the safety and effectiveness of Gleevec on children diagnosed with CML.

Currently, many clinical studies are in process to determine not only the response rates, but also the long-term survival effects of treatment with imatinib. Occasionally, the leukemia cells may become resistant to imatinib; fortunately, newer tyrosine kinase inhibitors are available that address this issue, and newer ones are being discovered.

At this time, it is unknown whether other chemotherapy agents might be used in combination with the imatinib. Future clinical studies will answer this question.

For more information about Children's Hospital of Austin's Cancer and Blood Disorders Center, please go online to www.childrenshospital.com or call (512) 324-8480.

CONTINUING MEDICAL EDUCATION

The following activities are offered throughout the Seton Family of Hospitals.

***Brackenridge Adult Cancer Management Conference**

Brackenridge Hospital
9th Floor Conference Room
4th Wednesday, 7 - 8 a.m.

***Brain & Spine Clinical Grand Rounds**

Brackenridge Hospital
3rd Floor Boardroom
4th Friday, 7 - 8 a.m.

***Breast Pre-treatment Planning Conference**

Brackenridge Hospital
9th Floor Conference Room
1st Monday, 12:15 - 1:15 p.m.

***Chest Conference**

Seton Medical Center
Front half of McFadden Auditorium
1st Wednesday, noon - 1 p.m.

Internal Medicine Grand Rounds

Brackenridge Hospital
The Annex Classroom
1st and 3rd Thursday, 12:30 - 1:30 p.m.

Neonatal Grand Rounds

Location alternates between Brackenridge/Children's Hospital of Austin and Seton Medical Center
3rd Tuesday every other month
beginning in January
Noon - 2 p.m.

OB/GYN Grand Rounds

Seton Medical Center
Network Boardroom
3rd Monday every other month
beginning in February
12:15 - 1 p.m.

***Pediatric Cancer Management Conference**

Children's Hospital of Austin
Lower Level ABC Conference Room
3rd Tuesday, 12:15 - 1:15 p.m.

***Pediatric Cardiac Conference**

Brackenridge Hospital
Emergency Department Conference Room
Every Friday, 7 - 8 a.m.

Pediatric Grand Rounds

Children's Hospital of Austin
Lower Level ABC Conference Room
2nd and 3rd Thursday, 12:15 - 1:15 p.m.



Seton Medical Center Grand Rounds

Seton Medical Center
Front half of McFadden Auditorium
Every Thursday, except 2nd Thursday
7 - 8 a.m.

***Seton Medical Center Adult Cancer Management Conference**

Seton Medical Center
Front half of McFadden Auditorium
2nd Thursday, 7 - 8 a.m.

***GYN Cancer Management Conference**

Seton Medical Center
Front half of McFadden Auditorium
Quarterly (Jan, Apr, July, Oct), 1st Wednesday, 7 - 8 a.m.

***Seton Northwest Adult Cancer Management Conference**

Seton Northwest
Private Dining Room 2
3rd Thursday, 12:15 - 1:15 p.m.

***Stroke Case Conference**

Location varies: Brackenridge Hospital - 2 North Conference Room, or Seton Medical Center - Support Services Conference Room
3rd Thursday every other month beginning in February
Noon - 1 p.m.

***Transplant Board Meetings**

Seton Medical Center Boardroom
2 Wednesdays/month, date varies
7 - 8 a.m.

***Trauma Rounds**

Brackenridge Hospital
9th Floor Conference Room
Every Thursday, except 3rd Thursday
6:45 - 7:45 a.m.

** Open to all Seton medical staff members, but closed to non-Seton medical staff and all others.*

Q&As:

Are the programs listed above open to all physicians?

Activities are open to all Seton medical staff. An activity with an asterisk is closed to non-Seton medical staff and all others.

How do I obtain my CME report?

Contact Medical Staff Services at **(512) 324-1000, ext. 14621**.

Is there a fee for CME reports?

There is no fee for members of Seton's Medical Staff. For all others, there is a \$25 fee.

Is there a registration fee for the programs listed above?

The activities listed above do not have a fee. The majority of special conferences charge a fee. These conferences can be located on **DoctorLink at www.doctors.seton.org**.

Could I submit topics for an activity or present an activity myself?

Yes. If you are interested in a specific topic, would like to present at one of the activities or for more information regarding application process, please contact the CME office at **(512) 324-3023**.

Get CME Credits for Your Activity

Does Seton participate in Joint Sponsorships?

Yes. Please call **(512) 324-3023** for more information about applying for a Joint Sponsorship activity.

For more information regarding application process, please contact the CME office at (512) 324-3023 or visit DoctorLink at www.doctors.seton.org.

Current listings for each open activity can be found on **DoctorLink at www.doctors.seton.org**, or in the Seton Family of Hospitals *Medical Staff Newsletter*. For more information, please contact **Casey Harrison at (512) 324-3023**.