

## Baylor Research Shows Ultrasound-Targeted Microbubble Destruction May Offer Treatment for Type I Diabetes

### Overview

- Baylor researchers have identified a new gene therapy technique offering potential treatment for Type I diabetes
- Microscopic bubbles target the pancreas, releasing insulin genes directly into the organ
- Long-term goal is to study regeneration of insulin-producing cells

**A** NEW GENE THERAPY technique using ultrasound-targeted microbubble destruction (UTMD) may offer a potential treatment for Type I diabetes, say researchers at Baylor University Medical Center at Dallas (Baylor Dallas) and Baylor Research Institute (BRI). UTMD therapy would deliver insulin genes to the pancreas by microscopic bubbles. Upon reaching their target, physicians would use ultrasound to burst the bubbles, which releases insulin genes into the pancreas.

Researchers delivered bubbles containing human insulin genes into the pancreas of rats and later found that the rats' blood sugar had been subsequently lowered. Another gene that regulates insulin production, hexokinase I, was successfully delivered using UTMD as well, and resulted in increased blood insulin and decreased blood sugar in the rats.

"Not only was their blood sugar lowered, but there was no evidence of any damage to the pancreas," says Paul Grayburn, M.D., a cardiologist on the medical staff at Baylor Dallas and principal investigator of the study. "Other forms of gene therapy are usually invasive and unlike the UTMD technique, do not target the tissues and organs specifically."

UTMD evolved from microbubble-based contrast echo agents used to improve image quality. Dr. Grayburn formed his hypothesis based on the discovery that microbubbles were destroyed by ultrasound. Additionally, research by Sanjiv Kaul, M.D., showed that microbubble destruction caused small capillary leaks. Dr. Kaul, formerly at the University of Virginia and currently on staff at the Oregon Health & Science University, was the first to develop myocardial contrast echocardiography.

"These discoveries led me to hypothesize that if microbubbles could be loaded with genes, we could use ultrasound to destroy the microbubbles and deliver genes across the capillary endothelium, which prevents intravenous

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# Baylor Offers Innovative Stroke Prevention Treatment Using Self-Expanding Stent

## Overview

- New stent offers preventive measure for patients with ICAD
- Self-expanding design features flexible and traceable delivery system to facilitate access and durability in the neurovascular anatomy

**B**AYLOR UNIVERSITY Medical Center at Dallas (Baylor Dallas), whose stroke program has been designated a Stroke Center of Excellence by the Joint Commission on Accreditation of Healthcare Organizations, was the first hospital in North Texas to use a self-expanding stent to open clogged arteries in the brain for the prevention of stroke. The Wingspan™ Stent System with Gateway™ PTA Balloon Catheter, approved last fall by the Food and Drug Administration under the Humanitarian Device Exemption program, is used to treat patients with intracranial atherosclerotic disease (ICAD). These patients traditionally have been treated with blood thinning drugs, which are not effective in all patients.

“This stent provides a valuable new option for patients with hardening of the arteries in the brain, who are still at risk of stroke despite traditional medical therapy,” says Ike Thacker, M.D., an interventional neuro-radiologist on the medical staff at Baylor Dallas.

Stents have been used a great deal in cardiac blood vessels. The new

Wingspan stent, however, is designed to be effective in the intracranial vessels, which are more fragile and twisted than cardiac vessels. It is the only device available in the United States for the treatment of ICAD.

“We have never had dependable methods for opening up intracranial arteries before,” Dr. Thacker says. “Now we can address the arterial anatomy with good and durable results.

“The clinical trials using the Wingspan stent indicated that the device can give patients long-lasting relief from transient ischemic attack (TIA) symptoms, as well as protection from future strokes,” Dr. Thacker adds.

The procedure to insert the Wingspan stent involves threading a catheter through an artery to the brain from a small incision in the hip. The catheter is inserted through the blockage, and a balloon is inflated to slowly open the clogged artery. The balloon and catheter are removed, and the stent is deployed using a second catheter. The stent has a self-expanding design, which allows it to keep the artery walls open even in curved areas of the vessel.

Patients who are not candidates for the procedure are: those who cannot take antiplatelet and/or anticoagulation

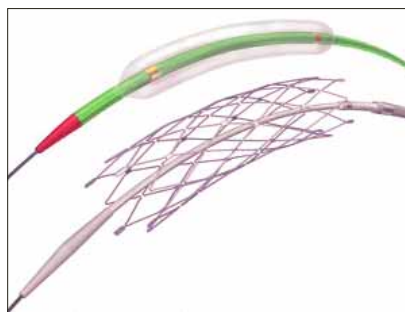
drugs, or those who have a lesion that is highly calcified or could prevent access, balloon angioplasty or appropriate expansion of the stent.

Stroke is the third leading cause of death and the leading cause of serious, long-term disability in the United States, affecting more than 700,000 individuals annually. Ischemic strokes account for about 88 percent of all strokes; ICAD causes ischemic strokes in approximately 60,000 Americans every year. (Source: *American Stroke Association*)

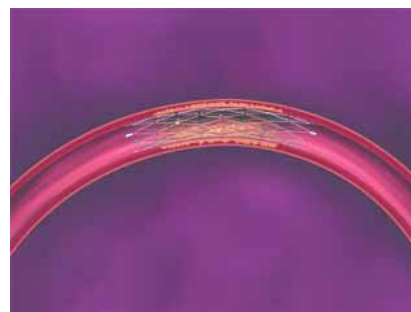
To refer patients for the Wingspan™ stent, contact ConsultLines at **1-800-9BAYLOR**.



**The stent is effective in the intracranial vessels, which are more fragile and twisted than cardiac vessels.**



**The first catheter opens the clogged artery, the second deploys the stent.**



**Self-expanding design keeps the artery walls open even in curved areas.**

# New Drugs for Renal Cell Carcinoma Target Angiogenesis

## Overview

- Clinical trials at the Baylor Sammons Cancer Center helped obtain Food and Drug Administration (FDA) approval of two new drugs targeting angiogenic pathways
- Ongoing trials focus on new drugs and combinations of the recently approved drugs

**R**ENAL CELL CARCINOMA (RCC) is typically resistant to chemotherapeutic agents, but a new generation of drugs targeting angiogenic pathways offers exciting options for patients with advanced metastatic disease.

The drugs—sorafenib (Nexavar®) and sunitinib malate (Sutent®)—received U.S. Food and Drug Administration (FDA) approval in December 2005 and January 2006, respectively. Findings from clinical trials at leading cancer centers, including the Baylor Charles A. Sammons Cancer Center at Dallas, revealed the drugs' significant clinical benefits for patients.

Thomas E. Hutson, D.O., Pharm.D., director of the Genitourinary (GU) Oncology Program at Baylor Sammons Cancer Center, was one of the lead investigators in the trials.

"Systemic chemotherapy for RCC has shown a less than 10 percent response rate in patients, and immunologic therapy with interferon or interleukin-2 offers only a minimal response," Dr. Hutson says. "There was an urgent need to pursue additional options for late-stage treatment for RCC. These targeted

agents are showing response rates of 70 percent to 85 percent of patients experiencing some level of tumor shrinkage."

Nexavar® is a multi-kinase inhibitor that targets angiogenic pathways, helping slow down tumor progression and growth. The drug interferes with the growth of new blood vessels and new cells by targeting the vascular endothelial growth factor (VEGF) and other proteins involved in angiogenesis. In what was the largest and most comprehensive clinical trial for advanced kidney cancer, researchers found Nexavar effective at slowing growth and increasing the length of time the tumor did not grow. Nexavar was initially tested on patients who had undergone treatment with other cancer-fighting drugs. Currently, it is being tested on patients with no prior treatment history.

Sutent® received priority review and was approved in less than six months (January 2006) after clinical trials showed the drug reduced the size of tumors in study participants. The drug is a tyrosine kinase inhibitor of the VEGF and PDGF receptors, depriving the tumor cells of blood and nutrients necessary for growth. Sutent also was approved for treating gastrointestinal stromal tumors.

Both drugs were well tolerated among patients, Dr. Hutson reports. The most common side effects included skin reactions, hand-foot syndrome, hypertension, diarrhea, mouth irritation and altered taste.

"We have taken a lead role in trying to find new agents for treating metastatic renal cell carcinoma," Dr. Hutson says. "We are proud to have been a key partner in the clinical trials that led to the FDA approval of these new drugs.

"We also have additional studies underway that are examining the use of these drugs in combination with other drugs for additional ways to treat RCC," he adds.

Every year in the United States there are approximately 36,000 new cases of RCC and 13,000 deaths. Approximately 50 percent of RCC patients present with or acquire metastatic disease (30 percent at diagnosis). Median survival of patients with metastatic disease is 18 months; 2 percent survive five years (*Motzer et al.*).

The RCC program at the Baylor Sammons Cancer Center is a collaboration between the Center and Texas Oncology, PA, and is designed to provide comprehensive medical services for patients. In addition to patient care and support services, the RCC program also conducts ongoing clinical research, with six to eight trials underway or about to begin.

For more information about the RCC program at Baylor Sammons Cancer Center, or to inquire about clinical trials, please call (214) 820-3535.



**Baylor is ranked in 7 specialties—more than any other hospital in Texas**

*U.S. News & World Report's* "America's Best Hospitals" ranked Baylor University Medical Center at Dallas as one of the top 50 hospitals in more specialties than any other hospital in Texas. The 2006 issue ranks Baylor among the best for digestive disorders, endocrinology, gynecology, heart and heart surgery, kidney disease, neurology and neurosurgery, and orthopaedics.

# ESCAPE Clinical Trial Studies Connection Between Patent Foramen Ovale (PFO) and Migranes

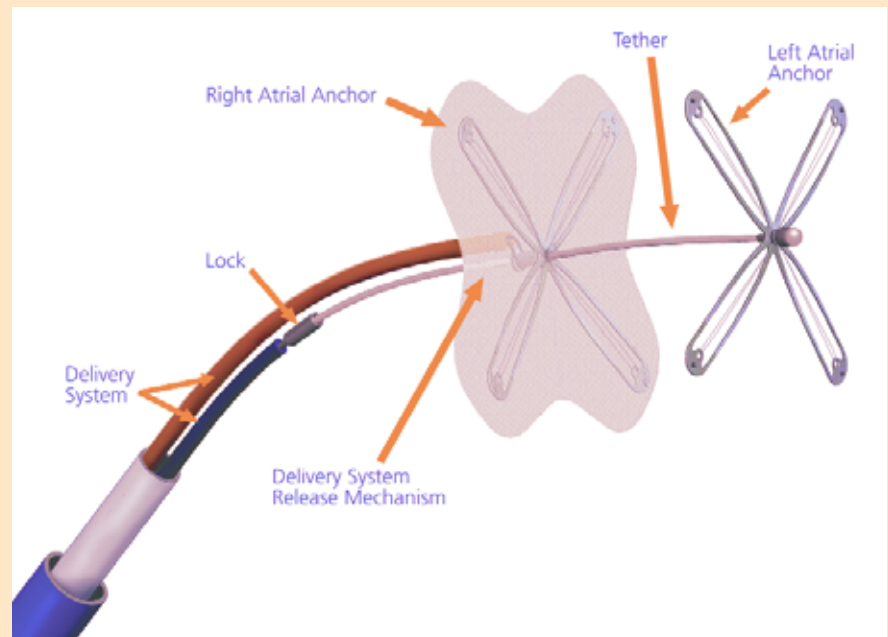
**N**EUROLOGISTS and cardiologists at Baylor University Medical Center at Dallas (Baylor Dallas) are collaborating on a clinical trial to study the link between a heart condition known as patent foramen ovale (PFO) and the incidence of migranes. The Effect of Septal Closure of Atrial PFO on Events of Migraine with Premere™: ESCAPE Clinical Trial, sponsored by St. Jude Medical, is underway at research facilities in 20 states across the country.

Steven Herzog, M.D., a neurologist on the medical staff at Baylor Dallas, is principal investigator. Azam Anwar, M.D., an interventional cardiologist on the medical staff at Baylor Dallas, is the lead cardiologist on the trial.

“PFO is a flap-like opening in the upper chamber of the heart, which is seen in about 25 percent of the population,” Dr. Anwar says. “This opening in the heart is important for survival in babies in the womb, but it usually closes at birth. In some people, it does not close and on rare occasions causes headache, shortness of breath and even stroke.”

PFO allows blood to pass directly from the right to left atrium, bypassing the lungs where it would normally be filtered. Researchers suspect chemicals in the unfiltered blood may trigger migranes in some individuals.

“The assumption is that if someone has a PFO and therefore, a right to left shunt, there are certain humoral substances circulating in the blood that may be triggering factors for migranes,” Dr. Herzog says. “Nitrates or tannins ingested in food, for example, may reach the brain in higher quantities in patients with PFO. That is a presumed mecha-



**The PFO closure procedure is performed using the Premere™ PFO Closure system**

nism and we hope to learn more about this through the ESCAPE study.”

Over the last five years, physicians observed the PFO-migraine connection among patients who underwent PFO closure to prevent recurrent strokes. After surgery, many patients reported a cessation of migranes, especially those with aura.

“We hope to document whether or not closing the PFO actually reduces the severity and frequency of migranes,” Dr. Herzog says. “The real significance will be the outcome of our results, whether they are positive or negative. If the study shows that there is no correlation between PFO and migranes, we want that well documented so there is no indiscriminate use of the procedure, and if the study shows positive correlation, then we will be able to make recommendations based on sound scientific advice.”

*(Continued on page 7)*

## Overview

- Baylor researchers are studying the correlation between patent foramen ovale (PFO) closure and migraine headaches
- 25 percent of the population has PFO, which may allow unfiltered blood with emboli and/or higher levels of chemical triggers to reach the brain
- 28 million Americans suffer from migraine headaches

# Gamma Knife® Offers Additional Tool for Treatment of Tumors and Rare Diseases of the Brain

## Overview

- The Gamma Knife allows intracranial tumors and other localized brain diseases to be treated while sparing surrounding normal brain tissue
- The Gamma Knife may offer patients an option when other methods fail
- The Baylor Radiosurgery Center offers seamless and timely support to physicians and their patients

**A**DVANCES IN TECHNOLOGY continue to position radiosurgery using Gamma Knife® as an accepted, mainstream option for patients with intracranial tumors and other lesions of the brain. Radiosurgery, defined as the use of highly focused beams of radiation to ablate a pathologic target, enables physicians to meet surgical objectives through noninvasive mechanisms—with the primary benefit of sparing surrounding tissue.

Cole Giller, M.D., Ph.D., a neurosurgeon on the medical staff at Baylor University Medical Center at Dallas (Baylor Dallas) and medical director of the Baylor Radiosurgery Center, reports that patients with recurring or difficult intracranial tumors that are less than 3 cm in diameter, and those with certain other localized lesions of the brain are candidates for Gamma Knife. Gamma

Knife is one of the most precise technologies designed to treat small targets.

Patients with metastases from any type of systemic cancer, benign brain tumors, inoperable or deeply seated meningiomas, acoustic neuromas, trigeminal neuralgia, arteriovenous malformation (AVM), or small recurrent primary gliomas may benefit from Gamma Knife.

“One of the most valuable features of the Gamma Knife is that it may be effective even when other measures fail. Many recurrences—after surgery, radiation therapy or chemotherapy—can be successfully treated with the Gamma Knife to give meaningful levels of local control,” Dr. Giller says. “The Gamma Knife is also a good option when the patient has multiple intracranial tumors.”

Karen Fink, M.D. Ph.D., a neuro-oncologist on the medical staff at Baylor Dallas, says the Gamma Knife may offer an alternative treatment for patients with metastases to the brain who want to avoid whole-brain radiotherapy. “Whole-brain radiotherapy is the standard of care, but it can cause long-term side effects,” she says. “As patients with brain metastases are living longer due to improved cancer treatments, it becomes

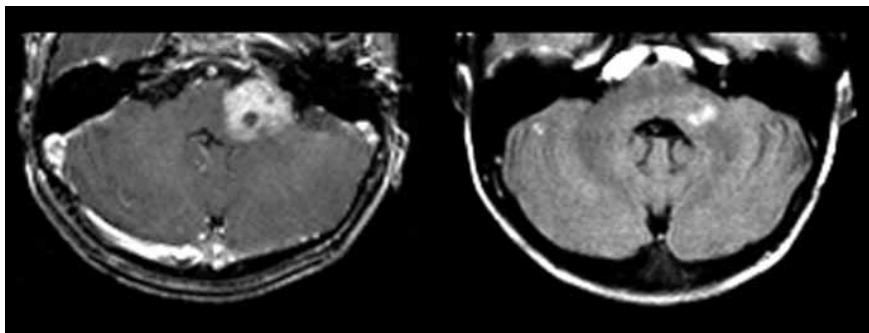
important to avoid the long-term cognitive problems that can occur with whole brain radiation therapy. Gamma Knife can treat patients with more than one metastasis, while avoiding toxicity to the rest of the brain.”

Gamma Knife directs 201 focused beams of radiation at the targeted lesion by means of a large helmet-like collimator. A special stereotactic frame is attached to the patient’s head to provide the required accuracy. Gamma Knife at Baylor Radiosurgery Center features a motorized, automated positioning system that allows shorter treatment times.

While not all brain tumors can be treated with this technology, Gamma Knife expands the options available to physicians and their patients. “The goal is to find the most appropriate treatment for each patient,” Dr. Fink says.

The Baylor Radiosurgery Center at Baylor Dallas houses both Gamma Knife and CyberKnife in one location. Baylor Dallas was the first medical center in Texas and one of the few in the world to combine these technologies within a single dedicated radiosurgical suite. The Center includes an interdisciplinary team of neurosurgeons, radiation oncologists,

*(Continued on page 7)*



**4-year-old boy with brainstem glioma treated with Gamma Knife radiosurgery. Scan at time of treatment on left; MRI scan 4 years later on right**

© 2006 Cole Giller, M.D., Ph.D.

# Baylor Receives \$3 Million Grant for Cancer Vaccines

“This grant is further validation for the advanced, clinically-relevant research being performed at BIIR. These world leaders in immunology research are making a difference in the way we diagnose and treat disease in the areas of cancer, autoimmunity, infectious disease and transplantation. The success of this program will bring new innovative therapies to the community.”

Michael Ramsay, MD  
President of Baylor Research Institute

**T**HE NATIONAL CANCER Institute has awarded Baylor Research Institute a three-year, \$3 million grant to develop vaccines against melanoma, a deadly form of skin cancer. The multi-project grant is led by Jacques Banchereau, Ph.D., director of Baylor Institute for Immunology Research (BIIR). “This grant is an exciting achievement for us,” says Dr. Banchereau. “This will be our seventh clinical trial to test patient-specific melanoma vaccines. It builds off of our first trial, which has been very successful.”

Dr. Banchereau and BIIR scientists Karolina Palucka, MD, PhD, the Michael A. E. Ramsay Chair for Cancer Immunology Research, and Joseph Fay, MD, director of the Division of Immunologic Therapy for Cancer, each will lead a project funded by the grant. The research at BIIR focuses on using dendritic cells, the ‘sentinels of the immune system,’ which are the first line of

defense against immune challenges. However, melanoma and other cancers normally manage to evade the immune system. To overcome this problem, BIIR scientists are specifically activating a patient’s dendritic cells against melanoma. Because the vaccines are the patient’s own cells, there is a reduced risk of side effects. “If everything goes according to plan, the dendritic cells, activated against melanoma, will signal the immune system to attack the cancer and destroy it. We have seen this type of response in our other clinical trials where we have tested these dendritic cell-based cancer vaccines and are very encouraged by it,” explains Dr. Banchereau.

“We have an outstanding research and clinical team, a new leading edge vaccine manufacturing facility and, most importantly, a technique for making melanoma vaccines that are able to mount an immune response against the cancer. It is a very exciting time to be involved in cancer vaccine research at Baylor,” adds Dr. Banchereau. To support the manufacturing of the vaccine, Baylor Health Care System (BHCS) recently completed construction and equipped a \$2.4 million, 2,200-square-foot customized cell-processing and vaccine development facility, located at BIIR on the Baylor Dallas campus. In 2004, BHCS formed its first biotech company ODC Therapy, Inc., to develop, produce and distribute customized cancer vaccines.

BIIR is devoted to translating basic laboratory discoveries made about the immune system into effective treatments for patients. This interdisciplinary program focuses on developing new therapies to treat conditions that involve the immune system, such as cancer, autoimmune diseases, infectious diseases and organ transplants. For more information about the melanoma clinical trial, call **1-800-9BAYLOR**.

## Continuing Medical Education Program

### 10th Annual Tyler Breast Cancer Conference

The conference is designed to provide the physician and allied health professional a comprehensive review of the latest advances in clinical aspects of breast cancer research, prevention, diagnosis and treatment.

February 10, 2007

Harvey Convention Center  
Tyler, Texas

Fee: TBD

Credit: AMA PRA Category 1, ANCC applied for, AAFP applied for, ASRT applied for

Sponsored by A. Webb Roberts Center for Continuing Medical Education, Baylor Health Care System, Dallas, Texas

To register or for more information, contact NaBrina Webb, (214) 820-2317.

(Continued from page 1)

## Ultrasound-Targeted Microbubble Destruction

genes from reaching cells," Dr. Grayburn says.

The research was supported by a grant from the National Institutes of Health and by the Mary Alice M. and Mark Shepherd, Jr. Endowment Fund in Cardiology and Cardiovascular Surgery and Research. The study also was held in conjunction with researchers from Duke University and UT Southwestern Medical Center. Results of the research were published in the May 2006 issue of the *Proceedings of the National Academy of Sciences*.

The UTMD technique is one of the most important steps in the development of a successful treatment of diabetes without the need for daily insulin injections, Dr. Grayburn says.

"Now that we have successfully delivered insulin genes to the pancreas of rats, our ultimate goal is to research the regeneration of insulin-producing

cells in patients with diabetes," he adds. "Our next steps are to try numerous genes and combinations of genes implicated in islet growth to see if we can grow new islets in patients with diabetes."

In addition to Type I diabetes treatment, the UTMD technique for gene delivery may offer multiple benefits in the future.

"There are many possible applications of UTMD, including gene or drug delivery to almost any tissue or organ, including cancers," Dr. Grayburn says. "It is still experimental and we have a long way to go, but we are encouraged by the results of this study and specifically, the impact it may have on the management of Type I diabetes."

To refer a patient to the ultrasound-targeted microbubble destruction (UTMD) study, call **1-800-9BAYLOR**.

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## Gamma Knife® Offers Additional Tool

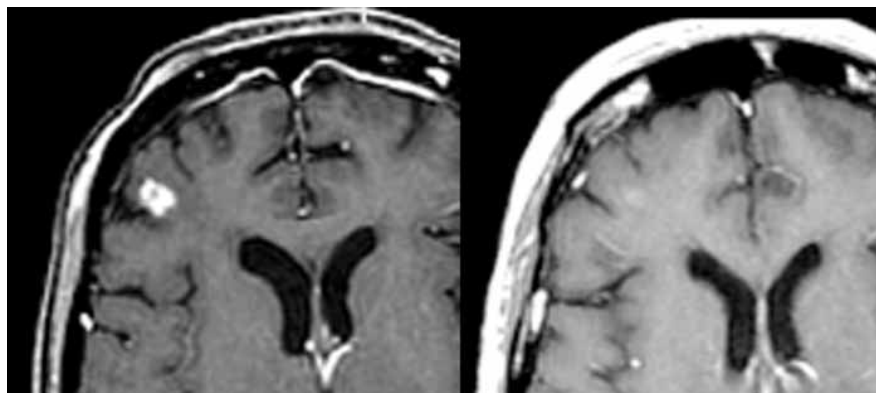
physicists, radiation therapists, and nurses, with an emphasis on a seamless and rapid evaluation and treatment.

"With brain tumors, the clock is ticking," Dr. Giller says. "The Baylor Radiosurgery Center is a resource to physicians and their patients, providing

them a valuable tool in their treatment plan."

To learn more about Gamma Knife radiosurgery and the Baylor Radiosurgery Center, call **(214) 820-HOPE** (4673). To refer a patient for neuro-oncology services at Baylor University Medical Center, call **1-800-9BAYLOR**.

Gamma Knife and Leksell Gamma Knife are U.S. federally registered trademarks of Elekta Instruments, S.A., Geneva, Switzerland.



**Gamma Knife treatment of metastatic lung cancer. Scan at left on 03/30/05, scan at right on 06/03/05.**

(Continued from page 4)

## ESCAPE Clinical Trial

Patients who may be candidates for the study are those who are 18–55 years of age and generally experience 4–12 migraines a month, with little relief from medications. After initial qualification, patients will maintain a headache diary for 28 days. If patients still qualify, they will undergo testing by echocardiogram and transcranial doppler to determine if a PFO exists.



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### Premier™ PFO Closure System

The PFO closure procedure is performed using the Premere™ PFO Closure system, manufactured by St. Jude Medical, and is inserted through a catheter in the groin. The device includes flexible, low-profile anchors that conform to the septal wall. Independent anchors facilitate positioning and implantation. An adjustable tether connecting the left and right anchors is designed to adapt to varying septal anomalies. (Source: *St. Jude Medical*) The procedure takes about one hour to perform and patients go home the same day.

"The bottom line is that this may not be a cure for migraine, but PFO closure may be one way to reduce the frequency and severity of migraines," Dr. Herzog says. "If that is the case, this study will help uncover one more piece of the puzzle for migraine relief."

To refer a patient for the clinical study, call **1-800-9BAYLOR**.

# Referring a Patient to Baylor University Medical Center at Dallas

With one phone call, a referring physician can request a referral to a specialist, an appointment for a patient, a consult, or an inpatient transfer. Call **1-800-9BAYLOR** and a dedicated ConsultLines representative will try to assist you and your requests. You or your office staff can use the ConsultLines to reach specific Baylor departments for information as well. You also can request a copy of the newest Physicians and Services Directory for Baylor University Medical Center at Dallas.

**DIRECT/INPATIENT,  
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NEONATAL TRANSFERS:**

**Call 1-800-9BAYLOR**

Baylor University Medical Center at Dallas (Baylor Dallas) has dedicated a

nurse to try to coordinate the transfer of inpatients for physicians in the region to Baylor Dallas. This includes those transfers without an accepting physician. Inpatient transfers should be current acute inpatients who may require a continuation of acute care, specialized care or a higher level of care not available at your local hospital. The nurse will attempt to find an accepting physician, reserve a bed, and work with Baylor's Access Service to verify insurance coverage.

All the referring physician or his representative needs to do then is to call 1-800-9BAYLOR to contact the nurse coordinator and give the clinical and financial data required to facilitate the transfer process. Baylor Access Service will need a face sheet faxed to them at **(214) 820-2411**.

To be removed from the mailing list, call 1-800-9BAYLOR.

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