MAYO CLINIC

CLINICAL UPDATE

CURRENT TRENDS IN THE PRACTICE OF MEDICINE

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Inside This Issue

Advances in Ventricular Assist Devices for Bridge Treatments of Congestive Heart Failure

The Challenge

Congestive heart failure (CHF) affects nearly 5 million people in the United States, with an estimated 550,000 new cases diagnosed annually. It is the most common diagnosis in hospitalized patients aged 65 years or older, and hospitalizations continue to increase, rising from 402,000 in 1979 to 1.1 million in 2004, according to the US Centers for Disease Control and Prevention. Although CHF is a serious problem, it can frequently be managed to improve patient quality and length of life through a therapy continuum ranging from medications to placement of ventricular assist devices (VADs) to heart transplant.

The use of VADs as bridge-to-transplant therapy has increased because of several factors. These include recognition that patients with highly advanced CHF who are at risk for worsening cachexia or death on the transplant waiting list can gain strength and become better transplant candidates via VAD implant. In addition, the recent US Food and Drug Administration (FDA) approval of the HeartMate II axial flow pump provides a robust, much smaller pump than previously available outside investigational trials.

Too often, patients with medically refractory CHF are not evaluated at advanced CHF centers early enough to optimize their disease management. This delay may compromise their ability to be suitable candidates for VAD implants. The primary care professional's challenge

Points to Remember

- **VADs are indicated for CHF patients who need bridge support while awaiting transplant. Use of VADs for chronic circulatory support in nontransplant candidates is under active study.**
- **A newer generation of VADs, being evaluated for safety and efficacy at advanced cardiac centers, offers smaller size, increased ease of transplant, and improved durability.**
- **Early referral of CHF patients to an advanced CHF specialty center is critically important, especially patients who have been hospitalized more than once in the preceding year. Late referral reduces the probability of a good outcome with VADs.**

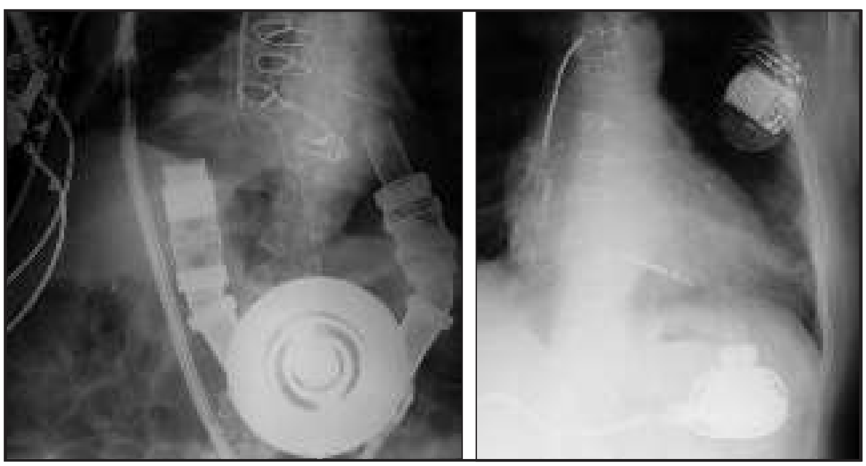


Figure. These radiographic views of VADs implanted in bridge-to-transplant patients show the size difference between the older model of VAD (left) and the newer, smaller, more durable VAD models (right), under investigation at advanced cardiac care centers such as Mayo Clinic.

To refer a patient to Mayo Clinic, please call: Rochester, Minnesota, 800-533-1564; Scottsdale/Phoenix, Arizona, 866-629-6362; Jacksonville, Florida, 800-634-1417.

Indications for Ventricular Assist Devices

Cardiac ventricular assist devices (VADs) are mechanical pumps connected to the heart to support patients with severe, medically refractory CHF. Devices may support the left ventricle alone; both the right and left ventricles ("bi-VADs"); or the right ventricle alone. VADs are used to address 3 categories of medical conditions:

1. **Bridge to transplant** for patients awaiting cardiac transplant, who need support for the failing heart during the waiting period.
2. **Bridge to recovery** for patients with reversible forms of cardiac failure. A VAD can be implanted with the hope that its support will allow the heart to recover, and the device can then be removed.
3. **Destination therapy** for patients for whom cardiac transplant is not an option because of comorbid conditions. Patients who are likely to die of their heart condition within 2 years are potential candidates for destination therapy. The VAD can be implanted to support circulation as a means of improving quality of life and extending life.

with CHF patients is therefore 2-fold:

1. To make patients with refractory CHF aware of the options available, particularly the multiple indications for VADs (see sidebar). An assist device may improve quality and length of life in patients who are not suitable candidates for heart transplant, or it may maintain circulation while the patient waits for a donor organ.
2. To provide these patients, in a timely manner, with a comprehensive evaluation at an advanced CHF center with experience in deploying the full medical-surgical continuum of cardiac care. For example, Mayo Clinic performs this service through its multidisciplinary Heart Failure Clinic. The Heart Failure Clinic brings together cardiologists who are experts in CHF assessment and management, surgeons with expertise in conventional cardiac surgery, assist device implantation, and heart transplant, specially trained cardiac rehabilitation nurses, nurse practitioners, pulmonologists, interventionists, physical therapists, and occupational therapists. With this combined expertise, the Mayo Clinic team optimizes and individualizes patient care through a variety of strategies.

VAD Advances

The original VAD pusher-plate model approved by the FDA for bridge-to-transplant use has design disadvantages that have inspired recent technological improvements to VADs. Mayo Clinic specialists are playing a key role in evaluating new devices and assessing outcomes to assure they are safe and effective.

Among the disadvantages of the older pusher-plate model are its larger size, more challenging implant procedure, and lack of durability. By comparison, newer models are smaller and more durable because they have fewer moving parts (Figure, see page 1).

Although only one of the newer-generation devices (Heartmate II) is FDA approved, and only as a bridge to transplant, this and other investigational devices are being studied, for either bridge-to-transplant or chronic use, at advanced CHF centers, including all 3 Mayo Clinic campuses. In general, preliminary outcome data favor the newer models, especially in terms of durability. The newer models have the potential to last several years compared with approximately 18 months for the older model, an improvement that especially suits extended support of patients who are not candidates for transplants.

Concerns Regarding New VADs

The design of the new VADs introduces new safety concerns, however. Two main issues are now under scrutiny:

1. The primary concerns are VAD-associated clotting and risk of embolic stroke and the need for warfarin anticoagulation with its attendant risk of bleeding. Mayo Clinic experience with the newer VADs indicates varied risk of VAD thrombosis among the devices, resulting in preferential use of those devices that have performed best in the view of Mayo Clinic experts.
2. A second concern is VAD-associated hemolysis, which appears to be related to several factors, including potential for turbulent flow through the VAD. Certain pumps seem more likely to result in this problem than others, which has affected device selection recommendations at Mayo Clinic.

Progress, Not Perfection

The new VADs are not yet perfected, but they offer potential advantages over first-generation pumps. Continued refinements are expected to resolve the current set of problems. While the technology evolves, all can agree that absent perfection, there is real progress compared with the state of the art 25 years ago when bridge-to-transplant interventions were achieved by the mechanical heart. Mayo experts continue to investigate a number of the newer pumps, some of which seem promising.

When to Refer a Patient to the Heart Failure Clinic

Heart failure patients whose condition continues to decline while they are receiving optimal medical therapy should be referred to a comprehensive heart failure clinic as early as possible. The goal of early referral is to provide the best treatment before multiple organ failure (impaired heart, kidney, and liver function) limits the therapeutic options available to the patient.

Clinicians seeing a heart failure patient who has been hospitalized more than once in the preceding year should refer that patient to an advanced CHF specialty center because data show that type of patient is at high risk of dying within 2 years.

Mayo Clinic Transplant Program Helps Shape National Collaboration

The Challenge

From 1995 to 2007, organ donations of all kinds increased 62.5% and transplants of all kinds increased 46% (Table). Despite these successes, the supply of donor organs is greatly exceeded by the demand for them—98,825 patients are currently candidates for some type of transplant and on a waiting list.

In 2006-2007, the US Health Resources and Services Administration (HRSA) undertook a systematic evaluation of best practices in transplant programs to identify elements of success. Mayo Clinic's transplant program was among the 15 high-performing transplant programs that HRSA studied.

Leaders in Liver Transplant

The Mayo Clinic transplant model helped HRSA identify 6 elements of a best-practices transplant program (see sidebar on page 4). The Mayo Clinic liver transplant model was especially helpful because of many factors, including outcomes. For example, Mayo Clinic in Jacksonville, Florida, is the only liver transplant program in the United States currently to exceed the expected patient survival rates at all time points: 1 month, 1 year, and 3 years.

Mayo Clinic's liver transplant program is highly specialized, particularly in the following areas:

- Transplants to treat cholangiocarcinoma
- Maintaining a large and successful living donor program
- Innovation in procuring donor organs after cardiac death

Points to Remember

- **To improve organ transplantation, the US government in 2006-2007 evaluated 15 leading transplant centers and included elements from Mayo Clinic's model in its recommendations.**
- **Six key elements characterize the Mayo Clinic transplant model: 1) institutional vision and commitment, 2) a dedicated transplant team, 3) willingness and skill to treat complex patients, 4) patient- and family-centered care, 5) financial competency, and 6) protocol-driven results.**
- **Mayo has developed liver transplant protocols for procuring donor livers after cardiac death so the procedure is standardized to reduce ischemic time and preserve organ function.**

Cardiac Death Donation

Mayo has developed liver transplant protocols for procuring donor livers after cardiac death that standardizes the procedure and reduces ischemic times to preserve organ function. Mayo Clinic in Jacksonville has performed more than 100 transplants from cardiac death liver donors.

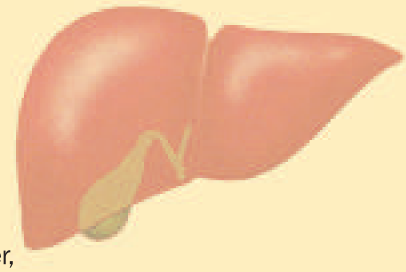
The cardiac death patient is a relatively new organ donor population. The typical donor has been a young adult with brain death from injury. With cardiac death donation, this demographic is changing. The potential donor population is

Table. Increases in Organ Donation and Transplant, All Kinds, 1995-2007

1995 Organ Donation, All Kinds	2007 Organ Donation, All Kinds	% Change in Donors	1995 Transplants, All Kinds	1995 Organ Donation, All Kinds	% Change in Transplants
8,857	14,399	62.57%	19,395	28,355	46.19%

Data source: Organ Procurement and Transplantation Network expanding to include both older and severely brain-injured donors. A patient's living will directive and family members may indicate that withdrawing support for a nonresponsive patient is reasonable, even if the patient does not meet all rigorous criteria for brain death, perhaps because evidence of minimal brain activity remains. If death ensues due to heart stoppage when support is withdrawn, the liver may be procured.

Six Elements of a Successful Transplant Program



According to the US Department of Health and Human Services' Health Resources and Services Administration, 6 elements contribute to exemplary patient outcomes and graft survival in successful transplant programs:

1. **Institutional vision and commitment.** The HRSA analysis cites this factor as "fundamental" to the success of a transplant center, noting: "Hospitals cannot dabble in organ transplantation. They must commit to it fully and provide the resources and support necessary."
2. **Dedicated transplant team.** Attracting and retaining dynamic, dedicated, skilled transplant specialists who consistently function as a transplant team is another key to success. A collegial, nonhierarchical team approaches produces the best care.
3. **Aggressive clinical style.** An aggressive clinical approach to caring for patients before, during, and after transplant is central to making best use of organs that are chronically in short supply.
4. **Patient- and family-centered care.** Leaders organize health care around the needs of patients and families, instead of around the needs of the institution. This leads to practices such as streamlining processes to reduce paperwork burdens on patients; increasing education opportunities for patients and families about lifelong care of the transplant; and creating comfortable spaces in the hospital that do not isolate the patient from his or her family.
5. **Financial intelligence.** Financial strength is a critical success factor. It involves keeping rigorously detailed accounting of program finances, sound financial management, and excellent payer relations.
6. **Protocol-driven results.** The leading transplant centers consistently conduct improvement-oriented performance reviews based on protocols, data-driven quality control methods, innovation, and research.

Innovations in Urologic Robotic Surgery: Beyond Prostatectomy to Partial Nephrectomy

State of the Art

Advanced robotic technologies were first used in urologic surgical procedures in 2000 as alternatives to minimally invasive laparoscopic techniques and conventional open surgery. Since then, the advantages of robotic surgery have rapidly fueled its use (Figure 1).

At Mayo Clinic, prostatectomy remains the most frequently performed urologic robotic procedure. For example, physicians at a single Mayo Clinic campus, in Rochester, Minnesota, have 4 robotic devices in clinical use. Mayo Clinic in Jacksonville, Florida, also has a robotic device, and Mayo Clinic in Scottsdale/Phoenix, Arizona, will soon have 2 devices.

The current focus is on refining the robotic

Points to Remember

- **Advanced robotic technologies were first used in urologic surgical procedures in 2000. In 2007, some 63% of prostatectomies were performed robotically.**
- **A new application for robotic surgery is partial nephrectomy for the removal of renal tumors.**
- **Robotic surgery offers technical advantages, especially the ease of suturing in the challenging angles of the kidneys.**

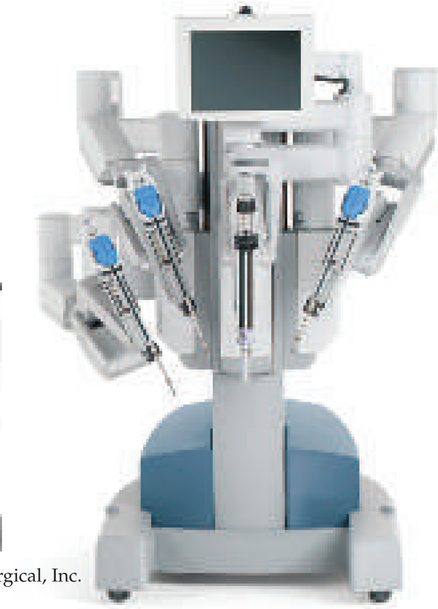


Figure 1. To operate through a robotic system, the surgeon manipulates controls from inside a workstation console a few feet from the operating table. Binoculars equipped with a high-resolution 3-D imaging system enable the surgeon to guide the robotic endoscopic instruments at the operating table with hand and finger movements that are precisely relayed to the instruments.

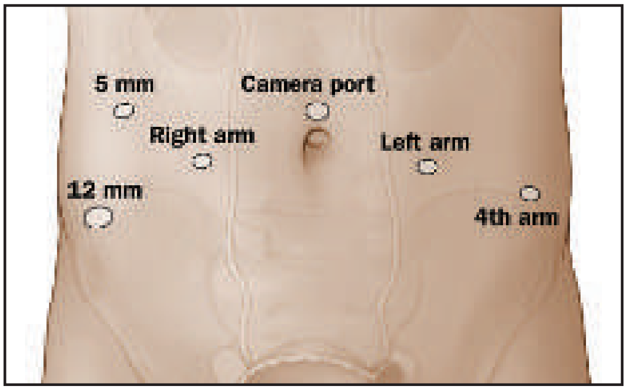


Figure 2. A major advantage of robotic surgery is its minimally invasive nature, requiring only 5 or 6 small incisions to create ports for cameras and the arms of robotic instruments.

partial nephrectomy to treat renal tumors. This procedure has been used experimentally at advanced robotic centers to remove small renal tumors, including complex tumors such as hilar, endophytic, and multiple tumors.

About Robotics

During robotic procedures, the surgeon manipulates controls operating instruments from inside a workstation console several feet from the operating table. While looking through binoculars equipped with a high-resolution 3-D stereoscopic imaging system, the surgeon guides the robotic endoscopic instruments docked at the operating table (Figure 2 above and Figures 3 and 4 on page 8). The controls relay the exact movements of the surgeon's hand and fingers to the instruments and filter out any hand tremor. This sensitivity enhances a surgeon's ability to navigate challenging anatomy, to deftly perform microdissection, and to precisely place sutures. Robotics yields technical advantages, such as ease of suturing in the challenging angles of the kidneys—an efficiency that is needed to minimize warm ischemia time and preserve organ function. Combined, these attributes translate into more effective and faster surgical procedures when performed by high-volume, experienced practitioners.

Partial Nephrectomy

Demand for robotic partial nephrectomy is driven by both the successes and limitations of its minimally invasive precursor, laparoscopy. Laparoscopy's successes include clinical effectiveness in terms of oncologic outcomes and renal function. Limitations include difficulty achieving swift intracorporeal suturing, needed to reconstruct the organ after tumor dissection when blood flow is disrupted. Swift suturing is key to minimize warm ischemia times, which will preserve organ function. Robotic partial nephrectomy overcomes the limits of laparoscopy while maintaining its minimally invasive strengths. Early results with the roboticpartial nephrectomy suggest it is a safe and feasible approach for select patients.

Robotics Advantages

Reduced blood loss is among the most notable advantages of robotic urologic surgery. Nationwide, data show that from 5% to 15% of patients require transfusions when undergoing traditional

Continued on page 8

Expanding Applications of Deep Brain Stimulation: Cluster Headache, Tourette Syndrome, Chronic Pain

Deep Brain Stimulation Surgery

The goal of deep brain stimulation (DBS) is to restore function by stimulating brain tissue at specific sites deep in the brain. DBS was developed in the 1980s in Europe. Neurosurgeons from Mayo Clinic in Jacksonville, Florida, traveled to Europe for training in 1997 and were among the first to perform DBS surgery in the United States. DBS was principally used to treat movement disorders associated with essential tremor and Parkinson disease.

In DBS surgery, electrodes are implanted in a specific area of the patient's brain to target nerve cells that demonstrate irregular behavior. Pulses of electricity are delivered through the stimulation electrode and regulated by programming a pulse generator implanted near the patient's clavicle (Figure 1). The electrical pulses reorganize neural circuits and neuronal activity to normalize brain function. DBS is both reversible—turning off the generator ends the therapy—and highly individualized through adjustments to the pulse generator.

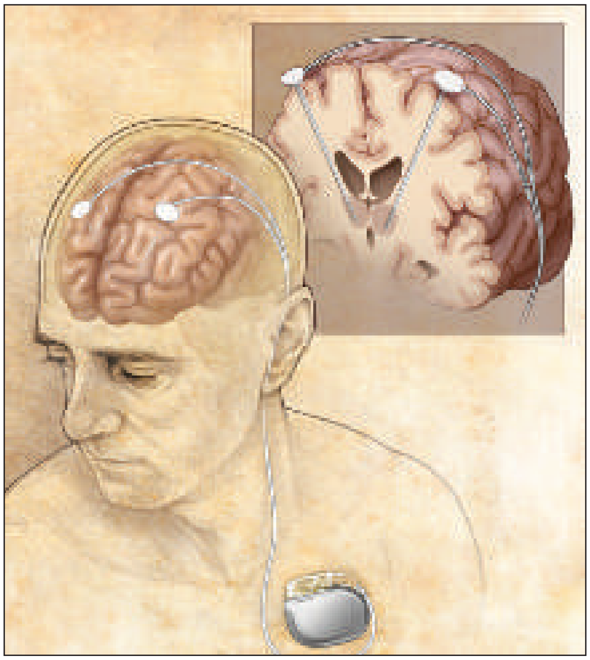


Figure 1. In DBS, the surgeon precisely implants an electrode into a targeted group of nerve cells in an area of the brain that has been identified on an MRI study and electrophysiology recordings. The electrode is secured to the skull, then connected via a thin subcutaneous wire to a pulse generator implanted under the clavicle.

Points to Remember

- **Deep brain stimulation (DBS) is an evolving type of neurosurgery first used to treat movement disorders. It is emerging now as an effective therapy for nonmotor disorders.**
- **Expanding applications for DBS at Mayo Clinic include cluster headache, dystonia, chronic pain, and Tourette syndrome.**
- **DBS is generally reserved for patients in whom pharmacologic and other treatments are no longer effective or who have disabling adverse effects from medical treatments. Careful evaluation and review of potential candidates for DBS surgery by neurologists, neurosurgeons, psychiatrists, and other professionals is necessary to determine the patients for whom surgery is appropriate.**

DBS at Mayo Clinic

Laboratory investigations have produced new insights into the role of electricity in reorganizing neural circuits and brain function. Combined with frank clinical need and excellent results in treating motor syndromes, the new research findings drive the trend of applying DBS therapy to include nonmotor syndromes and conditions.

Mayo Clinic has expanded its DBS program to include new treatment approaches and innovative research to refine and improve DBS surgery. Mayo Clinic neurosurgeons using DBS surgery have treated segmental or focal dystonias such as writer's cramp and spasmodic torticollis. DBS has also been successful in some patients with Tourette syndrome, although this application is under study. Tourette symptoms fluctuate over time, so long-term follow-up, currently under way in an international study, is critical.

Some success has also been seen in patients with cluster headaches and for another rare headache syndrome. Other conditions under consideration for DBS treatment at Mayo Clinic include epilepsy, depression, and obsessive-compulsive disorder.

DBS is generally reserved for patients in whom pharmacologic and other treatments are

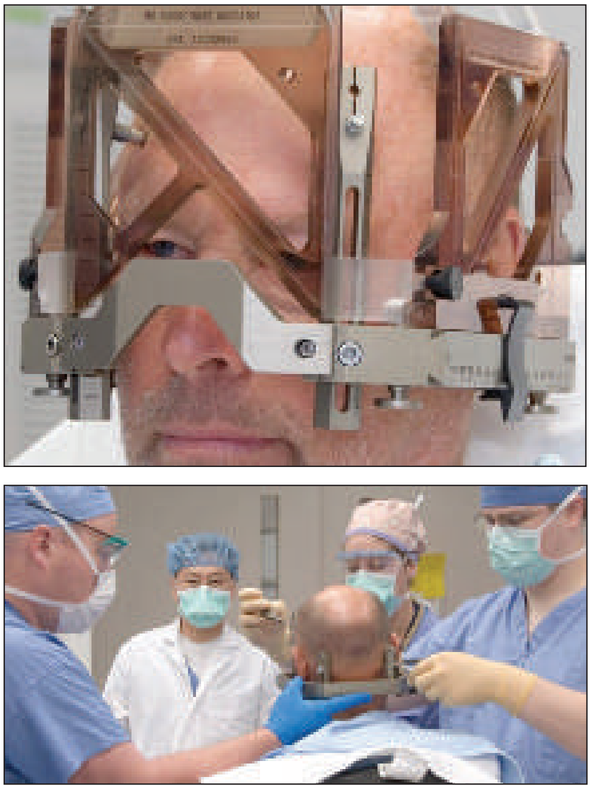


Figure 2. To locate the brain structure target, the patient is fitted with a stereotactic head frame, and an MRI image is merged with a brain atlas.

no longer effective or who have disabling adverse effects. Not all patients with a given disorder are candidates. Interdisciplinary teams meet regularly at each Mayo Clinic site. These teams evaluate patients, formulate treatment recommendations, and provide multiple perspectives on current practice and future clinical and research directions for DBS.

Mayo Clinic is also active in research concerning the mechanisms of DBS. This is creating a better understanding of the procedure and its benefits.

What to Look for in a DBS Program

A successful DBS program needs 3 key components: 1) careful patient selection, 2) precise targeting of the neural structures during the surgical procedures, and 3) intense, highly individualized postoperative care and follow-up to make sure the pulse generator is programmed optimally.

Careful Patient Selection

The first step is comprehensive clinical evaluation by a neurologist on the DBS team that is tailored to the disorder. This evaluation typically includes tests of memory, cognitive function, and speech and language and possibly a psychiatric evaluation for depression or other disorders. Evaluations are also done by a neurosurgeon and possibly a pain specialist.

Surgical Procedure

The brain structures targeted during DBS surgery vary according to the condition being treated. To locate a target a stereotactic head frame is applied to the patient (Figure 2), an MRI is obtained, and that image is merged with a brain atlas. These images, along with electrophysiologic recordings (Figure 3), allow the surgical team to precisely locate the anatomic target. The surgeon aims a microelectrode inserted through a small hole in the patient's skull. The brain-mapping software developed at Mayo Clinic has helped Mayo DBS teams achieve an exceptionally accurate targeting history.

DBS surgery is generally done with the patient awake to evaluate patient responses to intraoperative stimulation. The surgery may include implantation of electrodes and a pulse generator.

Individualized Aftercare

Follow-up requires continued evaluation by an experienced team to adjust medications and make any stimulator programming adjustments, especially during the first 6 months after surgery.

Figure 3. Surgeons review electrophysiologic recordings during the DBS procedure.

Innovations in Urologic Robotic Surgery: Beyond Prostatectomy to Partial Nephrectomy

Continued from page 5

open surgeries for prostatectomy. By comparison, less than 1% of patients undergoing robotic prostatectomy in experienced hands require transfusion. Reduced blood loss promotes faster recovery.

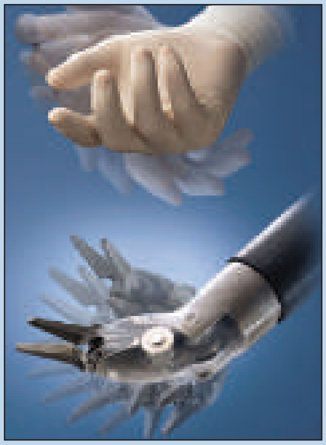


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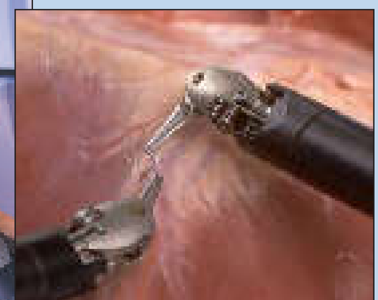
Figure 3. Robotic technology offers greater precision and agility of the endoscopic surgical instruments, including intuitive movements and 7° of freedom.

Figure 4. Magnification of 10 times or higher combined with 3-D vision produces a more detailed view of the surgical field, thus increasing surgical precision.



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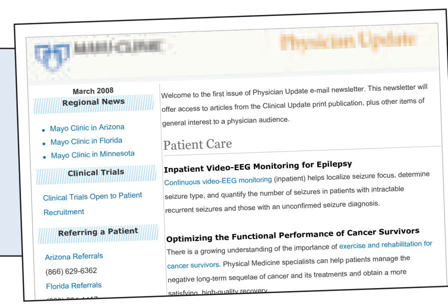

Physician Update

March 2008

Regional News

- Mayo Clinic in Arizona
- Mayo Clinic in Florida
- Mayo Clinic in Minnesota

Clinical Trials

Clinical Trials Open to Patient Recruitment

Referring a Patient

Arizona Referrals

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Florida Referrals

Welcome to the first issue of Physician Update e-mail newsletter. This newsletter will offer access to articles from the Clinical Update print publication, plus other items of general interest to a physician audience.

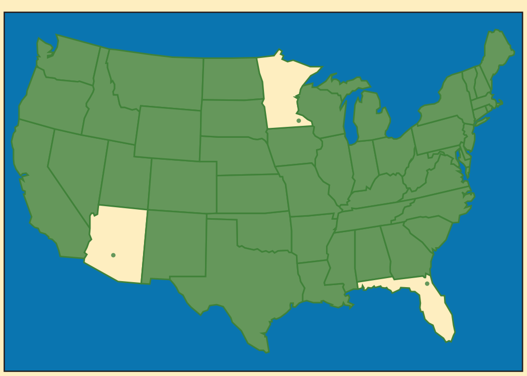
Patient Care

Inpatient Video-EEG Monitoring for Epilepsy

Continuous video-EEG monitoring (inpatient) helps localize seizure focus, determine seizure type, and quantify the number of seizures in patients with intractable recurrent seizures and those with an unconfirmed seizure diagnosis.

Optimizing the Functional Performance of Cancer Survivors

There is a growing understanding of the importance of exercise and rehabilitation for cancer survivors. Physical Medicine specialists can help patients manage the negative long-term sequelae of cancer and its treatments and obtain a more satisfying, high-quality recovery.



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