

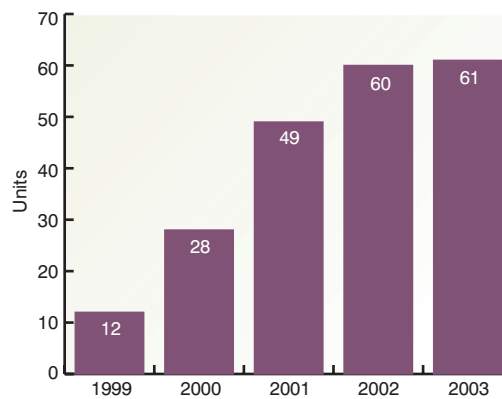
## Telesurgery to Impact Medical Care

Computer- and robotic-assisted surgery and medical care introduced within the last decade will have a tremendous impact on the way health care will be delivered in the future. Already, surgical and medical care are provided using computer-enhanced information, networking, and robotic intervention.

Over a 30-year period, the worldwide industrial robotics business went from single-digit annual growth for the first 10 years to more than 50% for the next 20 years. Now that the industry has matured, growth is back

(Telesurgery, see page 5)

Worldwide Installations for da Vinci Systems



Source: MedMarket Diligence

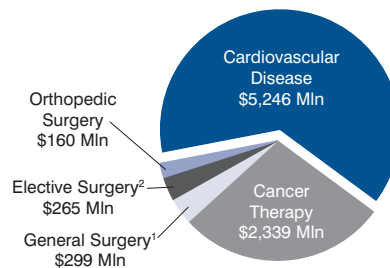
## Ablation of Cancerous Tissue Poised for Growth

Usage of energy-based therapies has a promising future in the treatment of various types of cancer. Development of many technologies in this arena is still in early stages, yet they offer a bright future for patients with cancer, promising minimally invasive or noninvasive procedures with fewer complications and quicker recovery than that seen with current invasive procedures.

Energy-based removal of cancerous tissue is big business, expected to grow at roughly

(Ablation of Cancerous Tissue, see page 11)

U.S. Energy-based Therapies Market by Clinical Application, 2003



<sup>1</sup>Includes systems for fecal incontinence, gastroesophageal reflux disease, gynecological disorders, urological disorders, and tonsillectomies.

<sup>2</sup>Includes cosmetic and ophthalmic technologies.

Source: MedMarket Diligence Report #S110, "Trends and Opportunities in the U.S. Markets for Ablation Technologies and Other Energy-based Therapies (March 2004)

### The Push for Transparency

Public pressure is causing industry and the FDA to alter practices and open regulatory processes for public inspection. **See page 4.**

### NCI Launches Nanotech Development Program

A five-year plan takes effect, sponsoring development of nanotechnology for cancer diagnosis and therapy.

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### Applying Heat to Drug Implants Shows Promise

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### Vista Medical Focuses on Obesity

Vista Medical has shifted away from imaging to focus on surgery for obesity.

**See page 18.**

### FDA Rejects Vagus Nerve Stimulator

The FDA will not approve Cyberonics' Vagus Nerve Stimulator.

**See page 19.**

### Myopia IOLs Nearing Market Entry

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### Biotechnology Update: Aneurysms Affected by Asthma Inflammatory Pathway

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## Letter From the Publisher

Patient enrollment has begun for Abbott Laboratories' ZoMaxx drug-coated stents, the newest likely competitor to target the \$5 billion worldwide market that was started by J&J's Cypher, then divvied up with Boston Scientific's Taxus stents last year. But before Abbott reaches the market, Guidant's and Medtronic's products could gain approval as early as 2006.

The drug-coated coronary stent market has been a volatile, huge one and therefore very interesting to watch. Both J&J and Boston Scientific have demonstrated the size of the stakes, with every misstep resulting in large financial impact.

But on the horizon, the question arises, are there other technologies that will rival drug-coated

stents? A wide range of reperfusion techniques continue to be developed, and statin therapies may ultimately pull the rug out from under the coronary artery disease management market.

But even if heart disease is here to stay, don't count out coronary artery bypass, since off-pump technologies, anastomosis devices and other minimally invasive approaches are starting to make great headway in eliminating trauma as the single largest impediment to bypass.

It's intense competition and the only definitive winner is the patient.

Patrick J. Driscoll  
Publisher

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## The Push for Transparency

Clinical trials determine safety, efficacy and—in case it's not obvious—market potential. As trial data now moves from being a moldable tool serving the interest of establishing the largest or most attractive market to an objective, almost harsh, statement of the true limitations of a pending product, it is altering the practices in industry and the FDA.

Although any changes, even small ones, that are to occur under the auspices of the federal government will rarely happen quickly, public pressure is mounting to increase the transparency of the regulatory process.

The interest in the clinical trial process becoming more transparent has arisen from reports of increased risk of suicidal tendencies in adolescents taking antidepressant drugs, as was the subject of congressional hearings in September. While noteworthy for its public airing, this is simply a recent event added to the momentum for change that is already taking place. Other indicators include:

◆ **Trial Results.** The Pharmaceutical Research and Manufacturers of America have set up a voluntary program to present clinical trial results through a new web site, [ClinicalStudyResults.org](http://ClinicalStudyResults.org).

◆ **Legislation.** Senators Henry Waxman and Edward Kennedy are working on legislation that would reform the process of reporting clinical trial data.

◆ **Study Designs.** The American Medical Association has proposed the establishment of a registry administered by the U.S. Department of Health and Human Services and including detailed data on study designs, populations and, importantly, links to published journal studies on trial results when trials are terminated early.

◆ **Company Reporting.** GlaxoSmithKline, Lilly and Forest plan to or already have established publicly accessible databases.

◆ **Peer Review.** A coalition of peer-reviewed journal editors, the International Committee of Medical Journal Editors, has adopted a policy of refusing to publish study findings for any drug

for which all studies involving it are not listed in a free, publicly accessible database.

While it is empirical that manufacturers would be targeted first in pursuing clinical trial reform, the heat for clinical trial misrepresentation addressed in the September congressional testimony was less on the manufacturers and more on the FDA who, it was argued, was guilty of “stonewalling, slow-rolling and plain incompe-

*Public pressure is mounting to increase the transparency of the regulatory process*

tency.” Indeed, Bristol-Myers Squibb and Wyeth (manufacturers of Serzone and Effexor, respectively) indicated that the FDA had in fact declined to allow label changes indicating that these drugs had not been proven to perform appreciably better than placebos.

By all accounts, the FDA is conflicted—saddled with a lot of baggage in seeking to fulfill its mandate while satisfying the stakeholders in the process. The medical products industry has historically had greater influence over the FDA than does the consumer, but this recent evidence is indicating that the shift, already in process, has gained a sort of critical mass.

But let's recognize that where incentives exist, there will be temptation, and on face value there are millions of dollars in incentives and limitless opportunities for industry. Put another way, if a prosecutor can prove motive and opportunity, the case is fairly well made for guilt. From a practical standpoint, the industry has much more to gain than to lose (e.g., Pfizer's \$430 million neurontin debacle) by aggressively responding to the perception that data is misrepresented, such as by establishing programs like those noted above that project an objective, transparent (if not open) view of trial data on products.

This trend toward increased transparency in clinical trials is nothing new and can, in fact, be



reasonably argued to be the latest example in the evolution of health care. (It can also be tied to the drive for corporate transparency à la Enron, Tyco, Global Crossing, MCI, etc.)

Healthcare delivery has been shifting steadily away from its history of a black box that was largely controlled by medical product manufacturers and physicians who held all the information *and* all the power, and toward an era in which increasingly little if any part of health care delivery is not abundantly known in advance—and then directed by—consumers. Examples of past shifts toward transparency include: (1) the removal of the pedestal that held physicians' decision to be beyond critique by third party payers, (2) the dissolution of the artificial walls between multiple therapeutic alternatives when they have little or no difference in clinical benefit, (3) the awakening of

the consumer, i.e., the patient, to the reality that health care costs cannot be allowed to spiral upward indefinitely, and (4) by extension, the increased awareness of the patient to the alternative health care options available and relative risks/benefits/costs of each.

The health care industry has already demonstrated its huge inertia and corresponding resistance to change, but these current forces are significant and likely to increase over time and the incentives that will move the industry are equally real and appreciated for their significance. 🌱🌱

*Note: In the October issue of MedMarkets, we will begin an online quarterly column addressing the driving forces and events in the regulatory world with the assistance of contributing articles by Reglera (<http://www.reglera.com>).*

## Telesurgery

*Continued from page 1.*

down to single-digits, yet the growth in medical robots is expected to be significant. According to a report by the United Nations Economic Commission for Europe (UNECE) and the International Federation of Robotics (IFR), there will be some 875,000 robots in use in 2005, of which 333,000 will be in Japan, 303,000 in the European Union and 135,000 in North America. In comparison, there are less than 2,000 med-

*There are less than 2,000 medical robots in use today...the expected annual growth rate is 25%*

ical robots in use today and, at the expected annual growth rate of 25%, this will increase to 2,500 in 2005, still a small percentage of the worldwide robotics market.

Today the standard surgical robot—the da Vinci system by **Intuitive Surgical**—has barely pene-

trated the market, posting annual sales of \$100 million. For example, the robotic-assisted procedure performed most frequently, laparoscopic radical prostatectomy (LRP), accounts for little more than 1% of all radical prostatectomies, generating annual revenues of about \$60 million. Analysts forecast that the worldwide market for all procedures will grow at an annual rate of 25% until 2009. Beyond 2009, it is estimated that the market will grow by 30%–45% annually until 2025, due to two main reasons: (1) systems will improve in ease of use and features; and (2) new players will enter the market as the opportunity grows and as medical robotics generally becomes more established in health care.

Initially, surgical robotic products required both the patient and surgeon to be in the same operating room. Two competitive products, however, appeared several years ago that had the potential to further revolutionize the delivery of health care. The ZEUS system by **Computer Motion** and the da Vinci system by Intuitive

Surgical were two products that could, in concept, allow the surgeon and the patient to be in two different geographical locations. In this way, the concept of surgery accomplished via telecommunication—telesurgery—could be realized. (In June 2003, however, Computer Motion was acquired by Intuitive Surgical, after which the ZEUS system was discontinued.)

While the concept of telesurgery was being refined, Computer Motion was also developing AESOP, a robotic platform for minimally invasive surgery designed to hold the laparoscope required in such procedures. This introduced a new paradigm in robotics—that of robotically enhanced operations where the robot would neither be autonomous nor mimic movements of the operator, but rather be an extension of the human operator. As surgeons and patients grew more comfortable with the concept of robots in the operating room, more capable next-generation technologies were introduced when new players such as **Armstrong Healthcare** and Intuitive Surgical entered the market for computer-assisted surgery. These were the foundations of robotics in medicine,

standing in contrast to automotive and electronics industries where robotic technologies had already matured and become irreplaceable.

In 1992, **Integrated Surgical Systems** introduced RoboDoc for orthopedic surgery, specifically total hip arthroplasty. This robotic system, which allowed orthopedic surgeons to pre-plan their operations while performing more accurate surgery, received the Prestigious Computerworld Smithsonian award. While this robot gained acceptance for use in Europe, it still has not received FDA clearance for marketing in the U.S. (see chart, “Medical Robot Manufacturers and U.S. Regulatory Status”).

**The Power of Telecommunication**

With a price tag of more than \$1 million, today’s state-of-the-art da Vinci robotic system has only proven its return on investment when used in LRP because it allows surgeons to perform the procedure less invasively within a time limit that is comparable to standard open procedures. Therefore, patients get the best of both worlds—positive outcomes with a small incision and quick recovery. Nonetheless, institutions

**Medical Robot Manufacturers and U.S. Regulatory Status**

Developer	Device	Procedure	Regulatory Status
Armstrong Healthcare	Endoassist	Laparoscopic, thoracoscopic surgery	FDA approved for abdominal and thoracic
	PathFinder	Frameless stereotactic neurosurgery	Submitted 510(k)
Computer Motion	AESOP	Laparoscopic, thoracoscopic, and cardiac surgery	FDA approved for laparoscopic in 1993; Thoracic and cardiac in 1997; Remote controlled in 2001 (named SOCRATES)
	SOCRATES (robotic telemedicine device, controlling AESOP)	Laparoscopic, thoracoscopic, and cardiac surgery	FDA approved October 2001
	ZEUS V2P	Assist using blunt instruments in laparoscopic and thoracoscopic surgery	FDA approved October 2001
	ZEUS MicroWrist	General surgery (laparoscopic cholecystectomy, Nissen)	FDA approved October 2001
Integrated Surgical Systems	RoboDoc	Hip and knee implant surgery	FDA approval expected 2005
Intuitive Surgical	da Vinci	General surgery assist	FDA approved October 1997
	da Vinci	General surgery (laparoscopic cholecystectomy, Nissen)	FDA approved July 2000
	da Vinci	General noncardiac thoracoscopic surgery	FDA approved March 2001
	da Vinci	Radical prostatectomy	FDA approved March 2001
	da Vinci	Assist in coronary artery bypass surgery <sup>1</sup>	FDA approved July 2004
	da Vinci	Coronary artery bypass surgery	FDA approval expected 2005
Mazor Surgical Technologies	Spine Assist	Orthopedic and neurosurgery	FDA approved March 2004

<sup>1</sup>Where there is direct access to the chest using standard open chest techniques (sternotomy or thoracotomy)

Source: MedMarket Diligence, LLC

paying upwards of \$1 million for a robotic system that can be used to perform laparoscopic cholecystectomy, Nissen fundoplication, etc., find it difficult to realize their return on investment—one reason why this market is not growing as rapidly as it might (see chart on page 1, “Worldwide Installations for da Vinci Systems”).

At the same time, the telesurgery platform used in Canada, developed by **Interface Surgical Technologies** and based on a much less capable ZEUS V2P platform—which has a standard endoscopic interface with 2-D visualization while the da Vinci has full articulation and true-to-life 3-D visualization—is an invaluable tool that allows expert surgical care to be provided to rural areas without the need to travel.

With telesurgery, the expert surgeon does not travel to where the patient is located and therefore does not lose up to three days, thereby allowing him to use his time more efficiently and reduce the cost of the procedure. In addition, patients and their families do not travel to the expert surgeon and patients can heal at home. Finally, the inexperienced rural surgeon will learn from the expert surgeon and improve with each procedure as he will perform the more complicated procedures in his local operating room, procedures that in other circumstances would go to the experts. This latter point helps with attracting young, less-experienced surgeons to these rural areas and with their continued training/education and retention in these areas.

### Clinical Studies Prove the Worth of Telesurgery

On September 7, 2001, a modified ZEUS system was used to prove the technical feasibility of telesurgery. Dr. Jacques Marescaux in New York performed a laparoscopic cholecystectomy while his patient was 4,000 miles away in Strasbourg, France. The operation took less than an hour to complete and was hailed as the medical breakthrough of the year. Though technically feasible, however, this was not an indication of how surgical care would be delivered for two main reasons: (1) the private ATM telecommunication link used was too expensive for everyday use; and (2) it makes sense to have a qualified surgeon next to the patient where possible.

However, the next phase was both clinically and financially much more realistic. On February 28, 2003, Dr. Anvari of Hamilton, Ontario,

Canada participated in two back-to-back laparoscopic Nissen procedures, assisting and guiding the local surgeon, Dr. McKinley, who was 250 miles away in North Bay, Ontario. Dr. Anvari had performed more than 1,500 such procedures and Dr. McKinley, though a skilled laparoscopic surgeon, had performed less than 100. During the operations, Dr. Anvari routinely pointed out proper angles of approach, needle placement while suturing, hidden clues and other intricacies that only can be seen by the eyes of an expert. It was at this point that it

*Beyond 2009, it is estimated  
that the market will grow by  
30%–45% annually until 2025*

became obvious that telesurgery is an extremely valuable tool, not in the distant future but today. Furthermore, though Dr. McKinley performed most of the procedure, the procedure time was comparable to an expert surgeon’s time (the first case took less than an hour and the second case took about 90 minutes to complete). Dr. McKinley learned from Dr. Anvari’s experience hands-on, and, most importantly, the patient received the best quality of care without leaving her hometown. In addition, the financial feasibility was enhanced because an affordable and readily available public MPLS telecommunication network was used.

Between February 2003 and December 2003, Dr. Anvari and Dr. McKinley performed more than

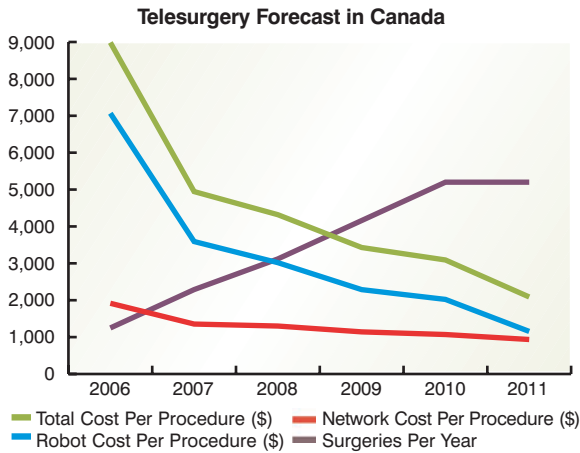
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Source: MedMarket Diligence, LLC

20 such procedures, from Nissen fundoplications to hernia repairs and bowel resections. These demonstrations showed that providing state-of-the-art expert care could be economically feasible in the underserved rural areas. However, the study was halted because the Canadian government wanted more results to properly fund this project and Intuitive Surgical (owner of the ZEUS telesurgery system after acquiring Computer Motion) pulled the system from these two sites.

### Clinical Indications for Telesurgery

The telesurgery robot is a delivery tool that extends the reach of the expert surgeon to deliver surgical care and educate less-experienced surgeons. Therefore, in theory, the telesurgery robot can remotely perform any procedure that can be performed by a physician using a robot in the same operating room. So far, the system has been used for laparoscopic cholecystectomy, Nissen fundoplication, hernia repair, and bowel resection. When the local surgeon also uses a surgical robotic system, the advantages of telesurgery will increase because the expert surgeon can assist and also teach the local surgeon by literally controlling the local surgeon's robotic instruments.

In this case, the local surgeon would have his robotic surgical console (like a ZEUS or da Vinci unit) where he sits, with five robots at the table—one for a scope, and four for instruments that are shared by the local and remote surgeon. Then at any time during the operation, the expert can take over the local surgeon's robot, control it and also move the local surgeon's hands as in a driver's education scenario where the teacher adjusts the movement of his wheel

and the pupil's wheel moves in the same fashion, yet moving the pupil's hands.

Telesurgery is a field still in its infancy. Through Computer Motion's support and the tremendous success of the Canadian study, provincial and federal support was garnered for continuation to further the study. However, Intuitive Surgical's acquisition of Computer Motion and the company's subsequent lack of support for telesurgery will undoubtedly hinder this growth. Canada and Australia are prime candidates for adoption and growth beginning in 2006 (see chart, "Telesurgery Forecast in Canada"). The U.S. will be a follower, as is seen in the adoption of other medical technologies, due to two main reasons: (1) a slow and costly regulatory approval process in the U.S., and (2) lack of a U.S. federal healthcare program with a single payer.

As for standard robotic surgery (not telesurgery), the market is growing worldwide at an average rate of 25% annually, due in large part to the approval of new procedures such as single- and multi-vessel, closed-chest CABG on a stopped heart, and single and then multi-vessel closed-chest CABG on a beating heart.

*Canada and Australia are prime candidates for adoption and growth beginning in 2006*

In addition, given better acceptance in the general marketplace among surgeons, hospitals, and patients, this growth rate will likely increase. It must be noted that the growth of robotic surgery will directly support and help the growth of telesurgery because surgical robotics are, of course, an integral part of telesurgery.

### Challenges of Today

While telesurgery has the potential to be immensely popular in the U.S., it is impractical for any of today's medical robotics companies to pursue a telerobotic approval in the U.S. due to a combination of factors. First, with a more conservative stance than its Canadian and European counterparts, the FDA has a Class III classification for telesurgery robots, although this may change much like with the ZEUS and

*(Telesurgery, see page 20)*



# Aneurysms Affected by Asthma Inflammatory Pathway

While studying the development of aneurysms in mice, researchers from the University of Pennsylvania School of Medicine found that the same inflammation reaction that was taking place on arterial walls also occurs in the lungs' bronchial tubes. This discovery has possible implications for finding new ways of treating aortic aneurysms, say the scientists involved.

If compounds used to treat asthmatics are found effective in patients with aortic aneurysms, some patients being treated with devices could be converted to pharmaceutical therapy. Also, scientists are hoping to find a way to treat these patients before their health becomes critical. About 15% of patients with ruptured aneurysms die before reaching the hospital. Despite the best in medical care, another 20%–40% will not survive after reaching the hospital. Ruptured aortic aneurysms account for more than 15,000 deaths annually, making it the thirteenth leading cause of death in the U.S.

## Increased Aneurysm Risk Shown

Reported by Colin D. Funk, PhD, former Professor of Pharmacology and Medicine, and Lei Zhao, MD, PhD, Research Association, both of Penn's Center for Experimental Therapeutics, the findings are being published in *Nature Medicine* (September 2004). Researchers used an atherosclerotic animal model to show that susceptibility for developing aneurysms increases significantly when a particular inflammation pathway—one commonly seen in asthma—is activated.

The researchers were initially studying the connections between arteriosclerosis and leukotrienes when they made the surprise finding. Leukotrienes, which constrict airways in asthmatics and contribute to inflammation in the lungs, are also associated with cardiovascular disease. They are secreted by inflammatory cells that gather at injured blood vessels. The 5-lipoxygenase enzyme required to synthesize leukotrienes has been associated with hyperlipidemia and risk for heart disease, heart attack and stroke. The team observed that in mice the enzyme contributed to the formation of aortic

aneurysms. Mice with the active 5-lipoxygenase gene had an increase in aneurysms; those without the gene were protected. Researchers concluded that the 5-lipoxygenase enzyme generated leukotrienes, which supply amplifying signals to initiate inflammation and arterial wall remodeling.

## Therapy Options

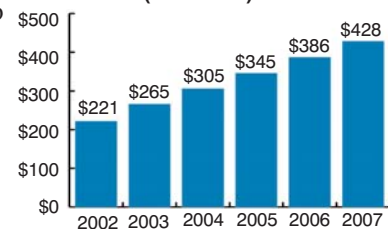
Presently, treatment of abdominal aortic aneurysms (AAAs) is limited to surgical repair involving an endograft. Surgeons also may use conventional neurosurgical clips to seal off the vessel, or simply cut out the bulging section of the arterial wall and sew a synthetic graft in its place. About 15,000 endografts have been performed since 1999. Endografts are successful in many cases, but there is still a risk of future

aneurysm. In addition, some endografts do not completely stop the leakage of arterial blood into the aneurysm sac.

Subsequent pharmaceutical therapy may include antihypertensives, beta blockers, calcium channel blockers, and cholesterol reducing agents may be prescribed, although none of these can prevent the formation of aneurysms. Anti-inflammatory drugs currently used to treat asthmatics may be of use in treating patients who are susceptible to developing aortic aneurysms by blocking their progression and preventing rupture. However, further studies will have to be done before 5-lipoxygenase blockers can be applied to humans. Since surgery to the aorta is risky, with heart attack, stroke or death possible, an anti-inflammatory drug having less risk would be a highly attractive treatment for aneurysms.

The market for endovascular prosthesis used to treat AAAs is growing and expected to reach \$428 million by 2007 (see chart, "U.S. Market for AAA Endografts").

U.S. Market for AAA Endografts (USD Mlns)



Source: MedMarket Diligence, LLC



## Early Stage Companies

### Automated Coronary Anastomosis

Cardica has announced results on the multi-center trial of its C-Port distal anastomosis system for use in coronary artery bypass. The results of the trial, comparing the performance of C-Port against traditional, suture-based anastomosis, were presented at the 3<sup>rd</sup> European Association for Cardio-thoracic Surgery/European Society of Thoracic Surgeons Joint Meeting in Leipzig, Germany, and showed patency at six months post-bypass to be 96.9%. This compares to 84.9% from historic published data. The trial of over 100 patients is being conducted at Braunschweig Hospital (Germany), Cardiocentro Ticino (Switzerland), University Hospital Eppendorf (Germany), and Herzzentrum Leipzig and Dresden (Germany). The C-Port, which is not yet approved in the U.S. but received CE Mark for Europe in April, creates an end-to-side anastomosis using eight stainless steel staples into the overlap of graft/target vessels.

### Impedance Cardiography

CardioDynamics announced the results from the PREDICT trial of its BioX impedance cardiography (ICG) in 212 patients at 21 U.S. heart failure centers. In the study, a strong correlation was found between the patients' BioZ ICG scores and the occurrence of a major heart failure outcome. Impedance and ECG in tandem enable monitoring of stroke volume, cardiac

output and a number of other critical parameters. In the PREDICT trial, patients with a high-risk ICG score were 8.4 times more likely to experience an ER visit, hospitalization or death.

### Sleep Apnea Device Cleared

Restore Medical has received 510(k) clearance to market its Pillar palatal implant system for the treatment of sleep apnea, a condition affecting roughly 12 million Americans, according to the company. During the Pillar procedure, which is performed as an outpatient procedure under local anesthesia, three woven polyester supports are inserted into the soft palate. The procedure in essence causes the soft palate to act more like a hard one to reduce the palate's vibration during sleep. The procedure is considered completely reversible.

### Adult Stem Cell Company Gets Phase I NIH Grant

Regenerex, LLC, has received a \$150,000 NIH Phase I Small Business Technology Transfer grant, along with the University of Louisville. Regenerex is focused on processing bone marrow to optimize use of adult stem cells, the ultimate objective being to reduce or eliminate the need for immunosuppressive drugs in organ transplantation. In 2003, Regenerex received FDA approval to begin a trial in 15 heart transplant patients, 30 kidney transplant patients and 60 sickle-cell anemia patients receiving

## Recent Medtech Start-ups

Company	Principal(s)	Location	Technology/Application	Founded
Applied Spine Technologies, Inc.	Jeff White	New Haven, CT	Flexible spine fusion	2004
ArmaGen Technologies	William Partridge, MD	Santa Monica, CA	Antisense treatment of brain cancer, and other CNS drugs	2003
Orthocon, LLC	Alan Horwitz	Westlake Village, CA	Therapeutic bone devices employing absorbable biomaterials and drug-device hybrids	2004
Orthopeutics, LP	Thomas Hedman, PhD	Santa Clarita, CA	Nonsurgical treatment of degenerative disc disease and scoliosis	2004
Sentrx Surgical	Dr. Glenn Prestwich	Salt Lake City, UT	Synthetic extracellular matrix for treatment of adhesions, other applications	2004
SpineForm, LLC	Joe Reynolds	Cincinnati, OH	Spine staple	2004
Theken Disc, LLC	Randall Theken	Akron, OH	Artificial elastomer spinal disc	2003
X-spine Systems	Janet Webb	Centerville, OH	Spine fixation (with motion preservation), disc augmentation	2003

Source: MedMarket Diligence, LLC



## Early Stage Company Financings

Company	Amount/Round	Investors	Technology
Affinergy	\$2M/Series A	MCNC Research and Development Institute, Trinity Healthcare, Charleston Angel Partners, Wilmington Investor Network	Biomaterials coatings
BioSurface Engineering Technologies, Inc.	\$5.1M/Series B	EDF Ventures, Memphis Biomed Ventures, New Markets Growth Fund, The Vertical Group, Maryland Venture, Boston Scientific	Heparin, growth factor and other coatings for devices
Ceregene	\$32M/Series B	Alta Partners, MPM Capital, Hamilton-Apex Technology Ventures, California Technology Ventures	Gene therapy of neurodegenerative disorders
SurgRx	\$12M/Series D	Alta Partners, Prospect Venture Partners, California Technology Ventures	Surgical sealing instruments
Suros Surgical Systems	\$12M/Undisclosed	Morgan Stanley Capital Partners, Piper Jaffray Ventures, River Cities Capital Funds	MR-guided breast biopsy

Source: MedMarket Diligence, LLC

## Ablation of Cancerous Tissue

*Continued from page 1.*

30% annually between 2003 and 2008. Within the market for ablation technologies, devices to treat cancer comprise the second biggest market segment behind cardiovascular applications (see chart on page 1, "U.S. Energy-based Therapies Market by Clinical Application").

Ablation of cancerous tissue can be performed with cryosurgery, fluidjet or hydrotherapy, laser, microwave, radiofrequency, thermal and ultrasound technologies. Often these forms of ablation are used in combination with other therapies such as chemotherapy or targeted therapeutics. The types of cancers most frequently targeted are prostate, liver kidney and breast.

### Cryotherapy

Cryoablation has been shown in various studies to be effective in ablating cancers of the prostate, liver, kidney and breast. This is because cryosurgery is generally less invasive than other forms of surgery and offers patients a quick recovery.

**Endocare** markets its Cryocare TCAP (Targeted Cryoablation of the Prostate) system, a targeted cryosurgery system that is FDA-cleared for treating prostate cancer. Cryocare is a less invasive alternative to procedures such as radical prosta-

tectomy or, alternately, those involving external beam radiation or brachytherapy. Cryocare's advantages include a decreased risk of subsequent incontinence (5% versus 10%–30%). But more importantly, the recovery period is two to three days versus several weeks for radical prostatectomy or external beam radiation and the efficacy rate has been shown to be 97% versus 78% for radical prostatectomy or brachytherapy and 56% for external beam radiation.

*Energy-based removal of cancerous tissue is expected to grow at roughly 30% annually between 2003 and 2008*

Another participant in the cryoablation marketplace is **Oncura**, a company that was created in July 2003 from a merger between Galil Medical's urology business and Amersham's brachytherapy business. While Oncura offers brachytherapy for low- and intermediate-risk patients, it also offers cryotherapy for patients who have failed with radiation therapy or are otherwise at a higher risk level. The company's SeedNet cryotherapy targets prostate and renal tumors. The SeedNet system is easy to learn as it uses a process similar to brachytherapy and familiar to

many urologists, except instead of delivering radioactive “seeds” to the target area, argon gas is used to create tiny ice balls that effectively kill targeted tissue and tumor cells. The procedure is usually completed in less than two hours and requires only an overnight stay in the hospital.

**Sanarus Medical** is an up-and-coming company developing an office-based cryoablation system for breast fibroadenomas. The Visica system targets biopsy-proven fibroadenomas with an ultrasonic guidance system that uses argon gas as a cooling agent and helium as a warming agent. (Biopsies can be obtained with Sanarus’ Cassi and Centrica systems. The former is to be released this year; the latter is already FDA-approved and commercially available.) The Visica system comprises a lightweight console, and single-use disposable devices and TempProbes to effectively ablate targeted tissue via a 3-mm incision without requiring sutures or general anesthesia.

### Hydrotherapy

Although **HydroCision** was the first company to use hydrotherapy (dubbed fluidjet therapy) in medical applications, it currently markets related technology for orthopedic applications via its SpineJet device. The company’s hydrotherapy VersaJet technology for wound debridement was sold to **Smith & Nephew** in January 2004.

**ERBE USA** has taken similar technology and applied it to eradication of brain and liver cancer cells. Its Helix Hydro-Jet system is used laparoscopically for radical prostatectomy and partial nephrectomy; other applications are also being developed. The device delivers an extremely thin, rotating jet of liquid to precisely treat specific targets while preserving nerves, vessels and ducts, making it ideal for liver surgery. The company also markets its Erbokryo CA cryosurgery system, which creates intracellular formation of ice crystals to destroy targeted cells.

### Microwave Therapy

**Celsion** is a leader in the development of ablative microwave therapy systems for oncology applications, having obtained exclusive rights to the Adaptive Phased Array (APA) system developed by the Massachusetts Institute of Technology. The minimally invasive system focuses microwaves to eradicate breast tumor

cells while protecting the skin and surrounding tissue.

Celsion also is conducting clinical trials on its ThermoDox drug, which is based on delivering doxorubicin particles encapsulated in a heat-activated liposome (licensed from Duke University). Delivery of the ThermoDox drug is combined with its Prolieve thermodilation microwave system to target prostate cancer cells. (Prolieve is currently approved to treat benign prostatic hyperplasia or BPH.) Another study is planned that will combine ThermoDox with radiofrequency ablation. In addition, Celsion is working with its academic partners to develop heat-activated gene-based therapies for treating various types of cancer.

Another developer in the early stages of product development is **Vivant Medical**, which obtained \$6.5 million in January 2004 to fund development of a microwave ablation technology. Founded by Thomas Fogarty, MD, the company is working on the VivaWave ablation system, which targets larger areas of tissue with its VivaRing and VivaTip microwave probes. VivaWave has received FDA 510(k) clearance for soft tissue ablation.

*Ablation devices to treat cancer  
comprise the second biggest market  
segment behind cardiovascular*

### Radiofrequency Ablation

The primary participants in the market for systems based on radiofrequency ablation (RFA) are **Boston Scientific**, **RITA Medical Systems** and **Valleylab**.

With a unique umbrella-shaped needle electrode, Boston Scientific’s RF 3000 system quickly ablates larger areas of tissue containing liver cancer cells. The system uses a generator with an impedance-based feedback system to monitor the extent of tissue desiccation and permit continued delivery of RF energy until ablation is completed.

RITA Medical Systems is the leader in tumor ablation. Its radiofrequency system targets several types of cancer, including those in the kid-

ney and liver. Effective July 2004, RITA merged with Horizon Medical Products in a \$100 million deal that gave RITA Medical Systems an extensive line of vascular access ports used with its RFA system.

Ongoing clinical studies being conducted by RITA Medical include a study presented in May 2004 by Jeffray Cadeddu, MD, at the American Urological Association's annual meeting. The results showed a 98% success rate in 33 patients with small renal tumors, who were treated laparoscopically with the company's RFA system. Another study, this one presented by Riccardo Lensioni, MD, in June 2004 at the annual meeting of the American Society of Clinical Oncology, showed a 92% survival rate in 14 patients with Stage I non-small cell lung cancers who were treated with the RFA system.

This month (September 2004), CIGNA HealthCare (the largest private health insurance payer in the U.S.) established national coverage for the treatment of liver cancer with RFA, joining United Health Care, HealthNet, Kaiser, Humana, PacifiCare and 38 Blue Cross Blue

Shield plans in 44 states in providing such coverage. The CIGNA policy specifies surgical, laparoscopic or percutaneous RFA treatment of unresectable liver lesions and unresectable colorectal liver metastases less than 5 cm in size.

Valleylab's RFA Cool-tip system, acquired from Radionics in 2002, can be used for various types of cancer. The system uses a patented electrode, which internally circulates water to cool adjacent tissue, thus maximizing energy disposition while reducing tissue charring.

## Thermal Ablation

ATI Medical's ThermoTherapy system includes its IsoRod, ThermoRod and ComboRod implants to treat localized solid, cancerous tumors in minimally invasive procedures. The implants are being applied primarily to prostate cancer. The ThermoRod implants are not radioactive and heat targeted tissue to thermal ablation temperatures. IsoRod is being developed to deliver a standard radiation dose, after which, should recurrence occur, the IsoRod can be used in an ablation procedure. The ComboRod takes advantage of the increased effectiveness of radi-

**Developers of Energy-based Cancer Therapies**

Company	Device Name	Type of Technology	Primary Indication(s)
Acoustic MedSystems	ACOUSTx	Ultrasonic ablation	Prostate cancer
ATI Medical	ThermoTherapy	Thermal ablation	Prostate cancer
Boston Scientific	RF 3000	Radiofrequency ablation	Liver cancer
Celsion	Adaptive Phased Array (APA)	Microwave therapy	Breast cancer
	ThermoDox	Encapsulated doxorubicin combined with microwave thermotherapy	Prostate cancer
	ThermoDox	Encapsulated doxorubicin combined with radiofrequency ablation	Liver cancer
	Heat-activated Gene Cancer Treatment	Gene therapy	Various cancers
EDAP	Ablatherm	High Intensity Focused Ultrasound (HIFU) ablation	Prostate cancer
Endocare	Cryocare TCAP	Targeted cryosurgery	Prostate cancer
ERBE	Helix Hydro-Jet	Fluidjet	Brain, liver, prostate cancer
Focus Surgery	Sonoblate 500	High Intensity Focused Ultrasound (HIFU) ablation	Prostate, kidney cancer
Oncura <sup>1</sup>	SeedNet	Cryotherapy	Prostate, liver, kidney cancer
RITA Medical Systems <sup>2</sup>	RITA System	Radiofrequency	Kidney, liver cancer, other
Sanarus Medical	Visica	Office-based cryoablation	Breast fibroadenomas
Valleylab <sup>3</sup>	Cool-tip	Radiofrequency	Various cancers
Vivant Medical	VivaWave	Microwave	Liver, lung, kidney and other tumors

<sup>1</sup>Oncura created in a merger between Galil Medical's urology business and Amersham's brachytherapy business in July 2003.

<sup>2</sup>RITA Medical Systems and Horizon Medical Products merged in May 2004.

<sup>3</sup>Radionics sold all its radiofrequency products to Valleylab in 2002.

Note: Several technologies can also be used for noncancerous indications or are being developed for additional cancer types.

Source: MedMarket Diligence, LLC


ation when delivered simultaneously with heat using hyperthermia technology.

### Ultrasonic Ablation

**Acoustic MedSystems** uses its ultrasonic ACOUSTx device to target prostate cancer. The system comprises small ultrasound transducers located at the tip of a disposable applicator needle or catheter. After being inserted to the treatment site, high-power ultrasonic energy is emitted, producing temperatures in the range of 50–100 degrees Celsius that rapidly coagulate and thermally destroy the targeted tissue cells. The outpatient procedure can be performed with local anesthesia and minimal side effects.

The Ablatherm system by **EDAP** utilizes high intensity focused ultrasound (HIFU) to ablate targeted tissue. Often used in BPH, the noninvasive technology also effectively treats prostate cancer via application of a heated high-intensity convergent ultrasound beam produced by high power transducers. U.S. clinical trials are being conducted on patients with localized cancer at stages T1 or T2 who are not candidates for prostatectomy or those who have local recurrence after external radiotherapy salvage treatment.

**Focus Surgery** also has a HIFU system, the Sonoblate 500, which targets prostate and kidney cancer as well as other soft tissue. With this noninvasive system, imaging and ablation is accomplished via a single probe in a procedure known as “acoustic ablation.” In this type of procedure, intersecting precision-focused ultrasound waves raise the temperature of targeted tissue to more than 80 degrees Celsius within two or three seconds. This destroys the cancerous cells while leaving surrounding healthy cells and organs untouched.

In May 2004, study results were presented privately to physicians at the American Urological Association annual meeting, highlighting preliminary results from a Phase I U.S. clinical trial. Physicians who have been using HIFU energy reported that so far, early results have been “impressive” with no evidence of recurrence as determined by PSA of less than one. In addition, no incontinence or erectile dysfunction has resulted and no morbidity or other complications have been seen. Similar results have been reported in various medical journals published in Europe and Asia, where HIFU has been available since 1992. 




## Drivers

### NCI Launches Nanotech Development Program

A new five-year plan to develop nanotechnology products for cancer therapy was introduced by the U.S. National Cancer Institute (NCI) in mid-September 2004.

The \$144.3 million initiative will be carried out by the newly established NCI Alliance for Nanotechnology in Cancer. The NCI Alliance is designed to bring together researchers, clinicians, public organizations and private companies in an effort to discover new ways to create nanotechnology products for the prevention, diagnosis, and treatment of cancer.

At least five centers of excellence will be created with \$90 million set aside by the alliance. Another \$16 million is earmarked for training and \$38 million for research grants. Over the next five years, research will be supported in: molecular imaging and early detection; *in vivo* imaging; reporters of efficacy (e.g., real-time assessment of treatment); multifunctional therapeutics; prevention and control; and research enablers (i.e., opening new pathways for research). *For additional information about the NCI Alliance for Nanotechnology in Cancer:* <http://nano.cancer.gov>. 



# Leading Clinical Edge

## Biotechnology

### Applying Heat to Drug Implants Shows Promise

Scientists at Georgia Institute of Technology have developed microthin implantable films that are capable of releasing a drug for a period of more than one month. In their study, they loaded insulin in layers of microgel films and then exposed it to a heat source, which caused the insulin to disperse. The films currently release the medication at 31 degrees Celsius, 6 degrees below human body temperature, but the researchers are working on extending the release point to a temperature slightly above that of the human body. The hope is that these implanted films could be placed on chips with resistive heaters and could then be programmed to release drugs according to a time schedule or other trigger. *Christine Nolan, et al., Biomacromolecules, 5(5): 1940–1946 (September 13, 2004).* <http://pubs.acs.org/biomac>

## Endocrinology

### New Imaging Device Detects Early Signs of Type 1 Diabetes

New imaging technology enables researchers to detect the earliest stages of the inflammatory process leading to Type 1 diabetes in mice, report scientists at the Joslin Diabetes Center and Massachusetts General Hospital. The imaging device uses long-circulating magnetofluorescent nanoparticles (CMFN), which contain magnetic nanocrystals of iron oxide that can be easily detected by MRI. The CMFN is injected into the body and travels through the blood vessels of the pancreas. If these vessels have started to become permeable due to islet inflammation, more CMFN leaks out and collects around the surrounding tissue, as seen on the MRI. The process allows researchers to observe this early inflammatory process over a period of time and also indicates the effects of experimental or therapeutic interventions aimed at halting its progression. The technique already has been used safely and effectively in human clinical trials to detect the spread of prostate cancer to the

lymph nodes. *Maria Denis, et al., Proceedings of the National Academy of Sciences, 101(34): 12634–12639 (August 24, 2004).* <http://www.pnas.org>

## Imaging

### Novel MAS Technology Proves Effective

Slow-magic-angle spinning magnetic resonance spectroscopy, also known as slow MAS, has shown promise as a tool to diagnose diseases and assess the body's response to drugs, according to researchers at the Department of Energy's Pacific Northwest National Laboratory. Unlike conventional nuclear magnetic resonance, slow MAS has the ability to reveal previously unseen biochemical compounds appearing in living tissue by slowly spinning the subject at a specific angle to the magnetic field. Before conducting human studies, the researchers will perform safety trials in animals to determine magnetic field and speed limits. Pacific Northwest National Laboratory plans to make the technology available for licensing. *Presented on September 8, 2004, by Robert Wind at the Applications of Magnetic Resonance in Food Science Conference in Copenhagen, Denmark.* <http://www.models.kvl.dk/NMRinFood>

## Nanotechnology

### New Class of Molecules Could Result in "Nano-device" Advances

A team of scientists at Cornell University has designed a new class of macromolecules that could lead to advances in ultra-miniaturization of electronic devices, as well as improvements in solar-cell and fuel-cell technology. The molecules self-assemble into structures with dimensions of about 10 nanometers, an unusual process that imitates nature's system of organizing living tissue. Using these molecules, the researchers claim it is possible to design nanoscale structures that otherwise would be impossible to manufacture, which could lead to the construction of devices with dimensions measured in nanometers. One of the notable



characteristics of these molecules is that they change their structure several times as the temperature rises. Even small changes in temperatures can suddenly change the molecules' electrical conductivity. *B.K. Cho, et al., Science, 305(5690): 1598-1601.*

<http://www.sciencemag.org>

### RNA: A Vital Ingredient of Nanotech Device Construction

Ribonucleic acid (RNA) could be used to build the scaffolding to hold the components of nanotech devices, report Purdue University researchers. In their study, the scientists were able to make RNA molecules self-assemble into 3-D shapes, resembling spirals, triangles, rods and hairpins. These shapes help form the building blocks in constructing complex microscopic machines. The researchers have already built arrays that are several micrometers in diameter and their goal is to build microscopic devices with sizes measured in nanometers. *Dan Shu, et al., Nano Letters, 4(9): 1717-1723 (August 2004).*

<http://pubs.acs.org/NanoLett>

## Oncology

### Rhodium-based Agents Used With Light Fight Cancer

Purdue University researchers have developed rhodium-based compounds that when exposed to light can destroy cancer cells and a virus closely related to West Nile and yellow fever viruses. Unlike chemotherapy agents that are generally harmful to the body, the rhodium-based compounds become lethal to DNA only when activated by a light beam set at a certain

frequency. Chemotherapy uses platinum-based compounds to poison cancer cells; however, these chemicals also destroy many other healthy cells during this process. Called DPPZPHEN, the rhodium-based compound also may serve as an antiviral or blood sterilizing agent because it is lethal to any nucleic acid it encounters, including the RNA found in viruses. *Elton Menon, et al., Inorganic Chemistry, 43(17): 5373-5381 (August 23, 2004).*

<http://pubs.acs.org/journals/inocaj>

### Study Reveals Earliest Stages of Prostate Cancer

Researchers from Fred Hutchinson Cancer Research Center have discovered what may be the earliest stage in the development of prostate cancer. Their study found that when mice are engineered to lose a single copy of the gene Rb in their prostate, they develop a precancerous condition comparable to the earliest stages of human prostate cancer. This implies that the loss of Rb in prostate cells could be the precursor to prostate cancer. Rb is known to be defective in a variety of cancer types, including up to 60% of human prostate cancers. This discovery could result in the development of new tests that predict whether the cancer will become aggressive. *Lisette Maddison, et al., Cancer Research, 64(17): 6018-6025 (September 1, 2004).*

<http://cancerres.aacrjournals.org>

## Ophthalmology

### Diagnostic Device for Eye Disease Shows Promise

The diagnosis and evaluation of glaucoma, diabetic retinopathy and age-related macular degeneration may some day be easier due to a new technique that uses spectral imaging, a noninvasive and safe means of taking pictures of the retina. Scientists at Heriot Watt University in Edinburgh adapted a standard ophthalmoscope by adding a liquid crystal filter, which allowed them to take images of the retina at a series of specific wavelengths. Wavelengths between 580nm and 600nm indicate the oxygenation state of the eye's blood vessels, which reveals unhealthy areas.

*Presented by Andrew Harvey on September 8, 2004, at the Institute of Physics' Photon 04 conference in Glasgow.*

<http://www.photon04.org> 

### Now Published!

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# Developments

## Cardiology & Cardiovascular Surgery

### FDA OKs Expanded Indication for Heart Failure Therapy

The FDA has approved an expanded indication for **Guidant's** cardiac resynchronization therapy defibrillators (CRT-D), which means thousands more heart failure patients will be eligible for this therapy. The Guidant CRT-Ds are now indicated for patients with moderate-to-severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction (an ejection fraction less than or equal to 35%) and QRS duration of greater than or equal to 120 milliseconds. In the past, patients were required to be indicated for both an implantable cardioverter defibrillator and resynchronization therapy in order to receive a cardiac resynchronization therapy defibrillator. Now heart failure patients no longer need to have an implantable defibrillator indication to receive a Guidant CRT-D.

The expanded indication is based on results from Guidant's Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Trial, which was published in the May 20, 2004, issue of the *New England Journal of Medicine*. The trial involved 1,520 heart failure patients from 128 clinical trials in the U.S.

### Human Implant of Self-Expanding Stented Aortic Heart Valve

**CoreValve** announced that its proprietary self-expanding stented aortic heart valve has been implanted successfully in a human for the first time, using the company's percutaneous ReValving system. ReValving involves the percutaneous implant of a new heart valve over a defective valve instead of surgically removing it. This ReValving system allows patients to have a less invasive form of cardiac surgery than open-heart surgery. The procedure was performed in the cardiac catheterization laboratory of a hospital in Asia and the patient was a 62-year-old man with aortic calcified stenosis.

### Cleveland Clinic Researchers Develop Heart Pumps

A team of biomedical experts at the **Cleveland Clinic** is developing a right-ventricular assist device (RVAD), which would work in combination with the clinic's successful CorAide left ventricular assist device (LVAD). A \$7 million grant from the National Institutes of Health has been awarded to the clinic to develop the RVAD, which will benefit heart failure patients who need a more comprehensive implantable device than now exists. The use of LVADs has assisted the growing population of patients with end-stage congestive heart failure, yet up to 40% of these patients have significant right ventricular failure that limits the benefits of the LVAD therapy. Under terms of the grant, Cleveland Clinic biomedical engineers will develop, design and clinically evaluate an implantable RVAD that can be used as a component of an implantable biventricular assist device for patients with severe biventricular failure.

### Medtronic Receives FDA Approval for Defibrillator

**Medtronic** received FDA approval for the Intrinsic dual-chamber implantable cardioverter-defibrillator, the first implantable cardioverter defibrillator (ICD) with a new pacing system designed to promote natural heart activity and reduce unnecessary pacing in the lower right chamber of the heart. This is made possible with a proprietary feature that enables the Intrinsic ICD to automatically adapt the way it paces, allowing the heart to function normally as often as possible. Research has shown that disrupting normal electrical conduction with unnecessary ventricular pacing can possibly lead to heart failure and atrial fibrillation.

## Gastroenterology

### FDA Reviews Boston Scientific Device After Patient's Death

The FDA is currently investigating the death of an elderly woman last month after she was treated with a **Boston Scientific** Enteryx device for acid reflux disease. The investigation will also focus on the injuries of six other patients



who were treated with the device. The FDA is considering whether physician technique or the device itself caused the woman's death, which occurred when her aorta ruptured. The Enteryx device is used by injecting a plastic substance into the esophagus, which strengthens the area of the esophagus close to or at the lower esophageal sphincter. This development comes at a challenging time for Boston Scientific as the company continues to deal with the recent recall of its Taxus coronary stent. Boston Scientific received FDA approval for the Enteryx device in 2003 and has since received patient and physician feedback. In a 12-month study of 85 patients who received the Enteryx, 67% were able to discontinue all their proton pump inhibitor (PPI) medications.

### Device Studied for Treatment of Crohn's Disease

Otsuka America Pharmaceutical has begun a pivotal study of its Adacolumn apheresis system for the treatment of Crohn's Disease. The study will enroll 230 patients in 40 clinical sites in the U.S. and Canada. These studies will be conducted while a pivotal study for ulcerative colitis will be conducted using the same device. The device operates as an adsorptive apheresis, hema-perfusion process by which certain cellular or fluid elements of a patient's own blood are removed. The device returns the remaining blood to the patient.

### Implantable Weight Loss Device for Bariatric Patients

Transneuronix has begun clinical trials for its battery-powered, implantable weight-loss device for obese patients. A handful of medical facilities across the country are testing the device, which consists of a battery-powered pulse generator and a 15-inch lead wire with two elec-

trodes. Designed like a pacemaker, the device sends out impulses that are generally not detectable to patients but cause an uncomfortable feeling of fullness after they begin eating. An earlier study showed that of 30 obese patients who received the device, 80% lost some weight during the first nine months after surgery, and 60% lost more than 10% of their body weight. Transneuronix hopes this last round of clinical trials will lead to FDA approval of the device.

### Vista Medical Focuses on Obesity

Vista Medical Technologies has made a major shift in business strategy by focusing on the growing obesity surgery market rather than medical imaging, its original core business. Last April, Vista sold off its medical imaging business to Viking Systems and has since created a wholly owned subsidiary, VOW Solutions, which provides assistance to physicians and hospitals caring for bariatric patients. Vista Medical, however, still receives royalties from Viking's sales and, in addition, owns part of Viking Systems.

## Imaging

### New X-ray Imaging Film Cuts Radiation Dose by Half

Eastman Kodak has developed a new medical imaging X-ray film that will require half the radiation dosage currently used in radiographic machines. This is the first time in 20 years that a new radiographic film will be able to offer high-resolution imaging from a significantly reduced radiation dose. Another benefit of the film is that it will feature an increased "speed" that will reduce the need for retakes due to patient movement during exposures, which contributes to reduced radiation for patients. The new film is currently being tested at medical centers in the U.S. and several European countries.

## Neurology

### FDA Approves Concentric's Device to Clear Blood Clots

The FDA has granted clearance to Concentric Medical to market the Merci Retriever, the first medical device approved by the FDA to remove blood clots in patients with ischemic stroke. Of

### Clinical Management of Obesity: Products, Technologies & Markets in the U.S. and Europe

This detailed assessment includes current and projected incidence and prevalence of patient populations, surgical and nonsurgical management approaches, and clinical trends. Product assessments include those for bariatric surgery, drug therapy, gastric stimulation, brain stimulation, combination therapies and genetic therapy. Current and forecast markets in the U.S. and Europe are included.

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the 700,000 annual strokes in the U.S., about 83% are ischemic. The device was approved after an extensive review of data from a clinical study at 25 medical centers in the U.S. The Merci Retriever is inserted in a small puncture in the groin and is then introduced into an artery leading to the brain. Upon reaching the targeted area, the device is able to remove the clot and restore blood flow.

### FDA Rejects Vagus Nerve Stimulator

The FDA has refused to approve **Cyberonics'** Vagus Nerve Stimulator, a pacemaker-like device designed to treat depression. The decision, which surprised many market analysts, rejected the advice of the FDA's own designated experts who had recommended the approval. The FDA criticized the design of the clinical trial and also pointed out that during the study the device resulted in worsening depression in some patients. Clinical trials are usually conducted on a randomized basis in which patients have no knowledge of whether they have received the experimental treatment, but this was not the case with the Cyberonics study. Cyberonics has begun an appeal process to the FDA to determine if the concerns raised by the FDA could be addressed by additional existing study data. If informal and formal appeals are denied, the company will conduct a new randomized controlled study.

## Ophthalmology

### New Type of Cataract Surgery a Major Breakthrough

Indian Army surgeons are now performing a less invasive form of cataract surgery that allows patients to return to normal life within two to three days. Called "phaconit" cataract surgery, the technique is based on traditional phacoemulsification surgery and uses an ultrasound probe and ultra-thin artificial lens. To date, 30 patients have received this treatment and the results have been encouraging. In phaconit surgery, unlike traditional cataract surgery, surgeons remove the cataract through a one-millimeter micro incision by passing a needle-like ultrasound probe in the eye. Then a thin, flexible intraocular lens is implanted into the eye. The ultra-small incision contributes to speedier patient recoveries.

### Myopia IOLs Nearing Market Entry

**Advanced Medical Optics (AMO)** and **Ophtec** have received approval from the FDA for the Verisyse/Artisan phakic intraocular lens for use in patients with myopia. Having been used successfully in Europe for nearly two decades, the lens can reduce or eliminate in adults (age 21 or older) myopia ranging from -5.0 to -20.0 diopters. The Artisan lens is manufactured in Florida by Ophtec USA; AMO will distribute the lens under the Verisyse brand name and will provide surgeon training and certification. Plans are in place to begin releasing the product in the U.S. by October.

A study published in the September 2004 issue of *Ophthalmology* shows that **STAAR Surgical's** implantable contact lenses are a safe and effective way to correct moderate-to-high myopia. In the study, the STAAR lens was implanted in 526 eyes of nearly 300 people with myopia ranging from -3.0 to -20.0 diopters. The implant was inserted through a small incision and placed in front of the eye's natural lens. After three years, about 60% of the patients had 20/20 or better visual acuity and nearly 95% had 20/40 or better. No patients reported increased problems such as double vision, glare halos or difficulty driving at night, which are potential side effects of Lasik surgery. STAAR Surgical is still awaiting FDA approval.

#### •••• **A Market to Watch:**

*The first lens of its kind to receive FDA approval, Ophtec's Verisyse/Artisan was introduced by Ophtec in Europe more than 17 years ago and since then has been implanted safely in more than 150,000 eyes worldwide. With some ophthalmologists claiming that myopia IOLs provide vision that is 50% clearer than that produced by Lasik, these lenses are expected to storm the market much in the same way Lasik did 10 years ago, equating to a market comparable in size to that experienced by Lasik. The Ophtec lens costs roughly \$3,000-\$4,000 per eye, compared to an average \$1,785 per eye for Lasik surgery. An estimated 53% of Americans currently use contact lenses or eyeglasses.*

## Orthopedics

### Angiotech Completes Acquisition of NeuColl


**Angiotech Pharmaceuticals** has completed its acquisition of private orthobiologics company



NeuColl in a \$13 million all-cash transaction. The company plans to develop Neucoll as an emerging orthopedic biomaterials franchise. Angiotech Pharmaceuticals had previously obtained an equity interest in NeuColl through its acquisition of Cohesion Technologies in early January. The company's initial product platform is a synthetic bone graft substitute comprised of collagen, which can be used for total joint replacement, spinal fusion procedures, fracture repair, as an autograft extender and as a filler for bone harvest defects.

### ArthroCare to Acquire Opus

ArthroCare, a medical device company that develops minimally invasive surgical products, has reached an agreement to acquire Opus Medical, a manufacturer of soft tissue orthopedic repair systems. Opus Medical's primary

product is the AutoCuff anchoring system, which is designed to enable surgeons to easily perform total arthroscopic rotator cuff surgery in tandem with arthroscopic tissue modification or ablation devices, such as the ArthroWands used in ArthroCare's Coblation (cool ablation) procedures. Based on the agreement, ArthroCare will acquire all of the capital stock of Opus Medical for \$30 million in cash and \$60 million of ArthroCare stock. The agreement also requires an additional delayed payment of \$40 million and a contingent payment based on Opus' 2005 net sales, payable in cash or stock at ArthroCare's election in the first quarter of 2006. 

**Additional items available online. See page 2.**

### Telesurgery, *Continued from page 8.*

da Vinci devices, which were originally classified by the FDA as Class III but later changed to Class II. In addition, the lack of both universal healthcare within the U.S. and interstate licensure to practice medicine form barriers to U.S. market growth. Existing liability laws and reimbursement structures also frustrate the growth of telesurgery.

The prototype ZEUS telesurgery system was used in Canada primarily because it was able to more readily receive regulatory clearance for the study there. In addition, because it is a large country with a sparse population, Canada is best suited for a trial of telesurgical systems. Also Canada has a federal healthcare program with a mandate that all citizens have access to the same quality of healthcare. Canadian provincial and federal governments spend hundreds of millions of dollars each year transporting patients to expert medical centers. Each patient requiring transportation uses chartered flights that cost about CAD \$10,000 to CAD \$15,000 per flight and, depending on the procedure, the government also pays for the travel costs incurred by the patient's family.

### Solutions of Tomorrow

The future of robotic surgery will include a series of advanced technologies that will combine to improve the quality of surgical care

including: pre-op imaging (i.e., CT scan), surgical simulation for training, real-time intra-op image guidance (e.g., 3-D ultrasound), and force reflection and feedback.

Beyond 2020, a patient with a clogged left anterior descending (LAD) artery needing bypass surgery will be scanned two days prior to the minimally invasive procedure. The next day the surgeon will practice the operation using the scan data, using simulation technology on the robot to determine port placement, angles of approach, and to learn patient-specific pathology. On the day of the operation, using pre-op data and real-time imaging, the LAD is identified using image superimposition (as is used in sports broadcasting today) with the blockage highlighted. This is important as it is difficult to identify the bypass location on a heart during minimally invasive surgery due to a limited and magnified view of the heart. Furthermore, the robot will prevent the surgeon from approaching the wrong coronary arteries or surrounding structures of the heart by limiting the workspace.

Given the improvements in patient outcomes and surgeon efficiency provided by robotics, there can be no doubt that robotic surgery and telesurgery have a significant role to play in future medical care. 