Progress Report: 10 New Technologies that Could Change Healthcare

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Introduction

The following bulletins are updates to original articles written over the last 16 months by MD Buyline Clinical Analyst, James X. Laskaris. All of the original articles are archived in Fact Files, located on the member menu under Process Intelligence, at mdbuyline.com. The bulletins are sequenced according to estimated market availability.

Available Now

Update on Artificial Discs: Originally Published 11/2003

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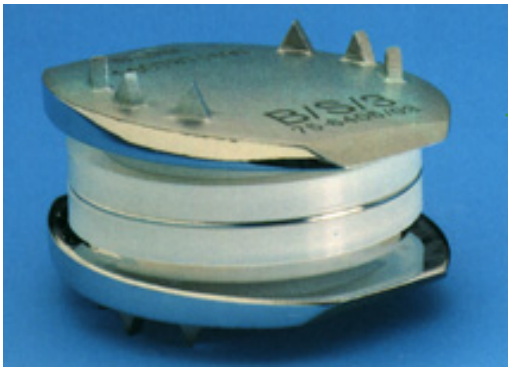
On October 26, 2004, the FDA approved the CHARITE Artificial Disc manufactured by DePuy Spine, Inc., a Johnson & Johnson company. The disc consists of a plastic core sandwiched by two artificial plates and is intended to replace spinal fusion surgery. It is approved for use in patients who have degenerative disc disease at one level of the lumbar spine (L4-S1) and who have had no relief from low back pain after at least six months of non-surgical treatment. The FDA is requiring DePuy Spine to conduct a post-approval study to assess the product's long-term safety and effectiveness, including the impact on other discs and on the bony structures of the spine.



Currently, there are 15 spine centers throughout the U.S. that offer disc replacement with the CHARITE. Many more centers are expected to open within the next several months as physicians receive mandatory training. Patient wait time for the implantation procedure is already several weeks to months.

CMS ruled in August 2004 that the $10,600 disc replacement implant is only eligible for reimbursement under code 80.51, which is the code for excision of the intervertebral disc material. At best, that code would allow for reimbursement at less than half the expected cost of a disc replacement implant. According to the CHARITE clinical trial data, two-year disc outcomes were shown to be functionally equivalent to an existing procedure that is half the cost.

Ongoing FDA approved clinical trials include Medtronic Sofamor Danek's MAVERICK Artificial Lumbar Disc, the BRYAN Artificial Cervical Disc (metal on plastic) and the PRESTIGE Artificial Cervical Disc (metal on metal). SpineCore, now owned by Stryker Spine, is testing the FlexiCore Intervertebral Disc and the CerviCore Disc

Replacement. Synthes Spine Solutions is testing the ProDisc-C for anterior cervical use and the ProDisc for lumbosacral utility. Market launch dates are projected for 2007 to 2008.

Additional technologies are in various stages of investigation. Minimally Invasive Surgery (MIS) utilizes microsurgical visualization and other optics technologies. Such methods provide more precise incisions, less muscle trauma and scarring, and ultimately less post-op pain with faster recovery. Prosthetic Disc Nucleus (PDN) replaces the existing nucleus of the degenerated disc by deflating the inner nucleus portion of the disc and re-inflating it with a synthetic polymer substance. The benefits are similar to that of the MIS with an added advantage of reversibility should the prosthetic not provide the anticipated relief.

Physician Interviews

Domagoj Coric, M.D., Carolina Neurosurgery & Spine Associates, Charlotte, NC

"In the foreseeable future I think the artificial disc procedure is going to be a quantum leap forward. The biggest advantage of the artificial cervical disc is that patients like it because it maintains motion. The device is like an artificial shock absorber. It therefore maintains motion and integrity at levels above and below and thus may decrease the risk of adjacent level problems.

"There are very few risks that are particular to the device. The issue is not really risk but reality; that is, do they maintain the motion, they do they need to be replaced, they do they have wear. We are not totally blind to these things since the surgery has been performed in Europe for several years.

"Cost is just coming to bear now and the cost is going to be an issue. The surgeons actually get paid less to do these but manufacturing and cost of the implant will be more, not to mention the hospital cost. However, all of this may be offset because of the lower surgeon fees and hopefully the patient's quicker recovery.

"The biggest thing about this technology is that it's patient-driven –- the patients are enamored with the concept of the artificial disc. They just come into the office saying 'artificial disc, artificial disc.'"

Robert J. Hacker, M.D., Oregon Neurosurgery Specialists, Eugene, OR

"The risks of the procedure at this time, I think, have to do with the fact that we don't know the long-term outcome of using this technology in the cervical spine. There simply hasn't been any similar device used in a human situation so that we can gauge what the results might be or what the potential side effects of a device like this might be. Specifically, we don't know from a biomechanical standpoint what might change at adjacent disc levels or how this might impact the spine overall. Our assumption is that it is a better solution than cervical fusion, which is one of the most common treatment approaches for degenerative cervical disc disease. But we don't know that; it is a hypothesis at this point.

"The biomechanical testing that has been done shows that the devices meet and exceed the life expectancy of comparable devices used for the hips and knees. But I don't think anyone knows. This is part of the problem with this technology -- it just has many unknowns as to long-term side effects and changes.

"Patients are receptive particularly because of this caveat in the cervical spine: if you have an artificial cervical disc and somehow either failure or recurrence of problems necessitates that the device be removed, that surgical approach is relatively straightforward. Hence, if somebody has an artificial disc in the neck and something goes bad, the repair/revision is fairly simple. Contrast this to the lumbar spine, where almost every surgeon I know regards a revision procedure for the lumbar artificial disc as a real challenge -- something that is high risk, potentially dangerous, and very difficult surgery. In that regard, the long-term results or longevity of the device are not as disconcerting to not know versus the same situation in the lumbar spine.

"Personally, I think all the artificial disc devices may hopefully -- and this may be a wild dream -- be obsolete someday, if some of the new gene therapies come along and allow us to simply reconstitute or re-grow the disc, re-grow the annulus and we find ourselves not replacing discs with artificial devices but replacing them with new discs."

Available Q1 2005

Update on Iris Recognition: Originally Published 4/2004

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Tarvinder Sembhi, Director of Product Marketing for Iridian Technologies, commented, "The feedback regarding our early healthcare deployments has been very positive. In this market, the practitioners really appreciate the fact that IR is non contact. They can still authenticate even if they are wearing latex gloves or surgical masks because their iris is always visible."

Reports indicate that iris recognition technology has seen only incremental growth in healthcare over the last six months or so. Sembhi could not provide specific numbers but commented that the primary growth Iridian has seen in this area has been in the deployment of additional pilot projects versus full enterprise deployment.

Iridian recently announced an exciting new mobile, handheld wireless device that should have a positive impact on healthcare facilities using iris recognition solutions. "We are very close to completing the development of an iris recognition camera that will fit into the SD (secure device) slot of a PDA for use in mobile and remote authentication," Sembhi told us. Rather than come to a dedicated workstation, nurses and doctors will be able to access patient information and perform transactions while seeing patients.

The device will also open an iris recognition-based patient tracking mechanism for use when a patient is on a gurney or isn't able to sit or stand in front of an IR camera. In those situations, the nurse or administrator can use the PDA to do the patient tracking. "We believe these remote imager capabilities will help us even further penetrate the healthcare market space," Sembhi said. This solution is planned for beta testing early Q1 2005 and is targeted for general availability in late Q1 2005.

The most significant cost associated with an IR solution is the camera. "Five to six years ago some IR cameras were in excess of $1,000," noted Doggett. "Now those cameras are in the low $200 range." That price range has remained fairly stable over the last six months.

According to Sembhi, "The industry is making a very strong effort to put standards in place for iris recognition and other biometric technology. Many groups are working on standards development and two of these are International Organization for Standardization (www.iso.org) and BioAPI Consortium (www.bioapi.org), which focuses on biometric-related interfaces. Iridian recognizes the importance of establishing standards and has been very actively involved in the standards process."

Iris recognition is a highly accurate, non-intrusive biometric technology used to authenticate the identity of an individual. Unlike a password, PIN or token device, biometric characteristics are unique to the individual, cannot be forgotten, lost, or stolen, and can be effectively used to prevent fraud. This type of authentication technology offers security for facilities, networks, information, and transactions. Iris recognition is accepted as a superior solution compared to other biometrics like fingerprinting, voice and facial recognition, and retinal scans.

One of the most important uses of iris recognition in healthcare is compliance with HIPAA. Most covered entities must be in compliance with the final HIPAA Security Rule by April 21, 2005. Iris recognition technology is part of the solution for some healthcare facilities in their efforts to ensure the confidentiality and integrity of health information as prescribed by HIPAA.

"The rapid acceleration in deployment of strong authentication or advanced security systems in the healthcare market is being driven predominantly by HIPAA," noted Thomas Doggett, Director of Marketing for SAFLINK. "Although HIPAA has been around awhile, hospitals have some pretty complex systems and it takes them some time to change those systems. We are really starting to see plans that have been underway for some time materializing into actual deployment of new solutions."
We have seen no significant change in the key IR players in the last six to eight months. Following is a summary of the primary vendors and their roles:

- Iridian Technologies – primary software developer (www.iridiantech.com)
- SAFLINK Corporation – turnkey login/authentication solutions (www.saflink.com)
- Politec, Inc. – integrator, systems solution partner (www.politec.com)
- Panasonic Corporation – hardware/cameras (www.panasonic.com)
- Oki Electric Industry Co., Ltd. – hardware/cameras (www.oki.com)

"Interest in iris recognition has increased since last year in all markets and we are seeing continued interest in the technology. Lack of awareness has been as much of a hurdle as any technical issues but we are starting to see traction in the healthcare space," said Sembhi. Going forward, I believe you will see a growing trend of IR moving from the government space into commercial and consumer type applications including areas such as financial services and healthcare."

Physician Interviews

Lynn Sims, MIS Director, North Florida Medical Center, Gainesville, FL

"Under the HIPAA security phase we must be able to verify to HIPAA that the user logging in is really that person and not someone to whom the user has loaned their ID or password. Before we implemented iris scan, we could not verify that at our facility."

"When we started looking into biometrics, we tested finger scan and iris recognition. Because there is no physical contact with iris scan, providers can leave exam gloves on when logging in and the build up of oils, creams, etc. is not an issue. The login time for iris scan is also faster than finger scan. Users just look into the camera and in three seconds or so they are logged in and happy. This technology has been very well received by our users."

North Florida also found iris scan has a lower level of rejections and failures than finger scan and has continued to track these daily. Sims reported, "Some days the rate is as high as 8% to 9% but it's around 5% on average." He cited lighting issues as the key reason for the false accepts and rejects. "People will take a camera off the top of the monitor and place it on the desk where it is looking up into fluorescent lights or change something else that affects the lighting," he explained.

Sims cited the camera's low maintenance requirements as another key positive. "We have encountered no hardware issues whatsoever. When we tested the finger scan, we constantly had to clean the sensors. With the iris scan cameras, we just have to wipe the lens off occasionally to remove dust. Once installed and configured the system has run flawlessly."

Update on Revolutionary Technology for Cervical Cancer: Originally Published 10/2003

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SpectRx, a company based in Norcross, GA, has developed a handheld spectrophotometer Cervical Neoplasia Detection System (CNDS) to identify and diagnose the cervix of abnormal cells. The system utilizes a computer with software developed for cancer diagnosis and a spectrophotometer with a calibration device and infection barrier.

The CNDS unit is not yet FDA approved; approval is expected in Q1 2005. The last of the clinical trials are currently being completed. Because the unit is pending FDA approval there is no CPT or APC code established. An important issue in terms of reimbursement for CNDS is the fact that there is no lab result involved. This means all of the reimbursement goes to the physicians. While it is difficult to predict all of the financial ramifications of CNDS, if an estimate of $96 for non-invasive cervical cancer diagnosis is applied then the revenue generated based on 1000 procedures would be $183,000 versus $33,000 for current method of diagnosis – biopsies -- over a five year period.

Multimodal Hyperspectral Imaging (MHI), which uses reflectance and fluorescence to access tissue, is incorporated in the CNDS device. MHI uses various wavelengths of light to illuminate the cervix while the software algorithm analyzes the absorption and reflectance rate which differentiates between abnormal and normal cell growth. The cost of the system is approximately $12,000. The test takes around five minutes with immediate results. Clinical trial results indicate a sensitivity of 97% with CNDS and a 72% with a Pap smear; thus, 28% of Pap smear screens resulted in a missed diagnosis while only 3% of diagnoses were missed using CNDS.

Physician Interviews

Core Director of NIH Program Grant, Assessment of Emerging Optical Technologies for Cervical Neoplasia, BC Cancer Research Center, British Columbia, Canada

"Optical methods of diagnosis are essentially the oldest known to man. Every time a mother looks at her child and says, 'You have a fever,' because their face is flushed, she is doing an optical diagnosis. Changes in appearance and comparing them to the normal patterns of tissues are the oldest techniques. In the last 15 to 20 years we have come to understand why they are such useful techniques. When light interacts with tissue, it interacts at the molecular level. Light interacts with the electrons of molecules. Depending on the structure of those molecules and how they are conformed and their environment, that determines how light is absorbed and remitted. It also determines how fluorescence happens and how light is scattered in tissue. We are looking at the absorption of wavelengths of light, how light scatters and propagates through tissue, and the fluorescence properties of light.

"Since we know that the fundamental basis for a disease, the changes that happen to tissue, all happen at the molecular level, we understand why being able to use an energy form that interacts at the molecular level gives us such a wealth of useful information about tissue. When the molecular structure of tissue changes, the way light interacts with those tissue changes and if we can interpret the way that light interacts with sufficient sophistication, we can make a diagnosis.

"The Pap smear has been around 50 years. It works at a particular level of sensitivity and specificity. It is useful because cervical cancer is a slowly progressing disease. It gives you time to go back and check. But the Pap smear is notoriously inaccurate. The average sensitivity/specificity rate across the U.S. is roughly 60/60. If you get an 80%, it means you have a one in five chance of missing disease when it is present and a one in five chance of saying it is present when it isn't. Saying it is present when it isn't increases cost for the system because women are scheduled for colposcopies and biopsies. The one in five you miss means that woman has disease that goes

undetected. Hopefully by the second or third Pap smear we hope to catch the disease. The Pap smear is only effective where you have decent quality standards; I believe 60% is the lower limit of sensitivity/specificity at which this thing works effectively. Thankfully, our rates are higher than 60% due to higher standards.

"Our vision for optical diagnosis is to replace the Pap smear. I don't see the smear fading away in our world for another 10 years. What we can do now with our studies is to achieve a good sensitivity/specificity with spectroscopy-based systems. You have to improve the sensitivity so you can detect a change. You have to improve the specificity to have a good diagnostic test. If you have a test with high specificity but have no adequate to apply the test, it is of no use. Many companies are focusing on developing systems to improve the sensitivity/specificity of colposcopy. I question the actual financial rewards from that. I also question the level of adoption you will see of those techniques. Most of the companies are focused on developing an integrated spectral imaging system but these are costly, somewhat bulky and to a fair degree quite invasive -– some more than others. Also, they don't fit into what I call the conventional workflow. I don't see them going anywhere big.

"One of the most sensitive methods for picking up cervical cancer is colposcopy. It tends to catch abnormalities really well. But you need someone who can see those changes. A useful technique is a method of imaging that enhances the sensitivity of detection of abnormality. A GP, nurse, or nurse practitioner should be able to see these with good sensitivity. But you should also have another way to screen. We are working on an optical wand that touches the area of abnormality and it does a reading with high specificity –- a point spectroscopy technique. A multi spectral system is basically doing spectroscopy all through an image, gathering a bunch of images. The problem is that the algorithm becomes much more complex and proving those algorithms becomes more difficult. Based on the current technology out there, the simplest thing is to produce a low cost imaging device that lets you look at the field of view, locate the abnormality and a low cost point measurement device that can make that diagnosis. We know spectroscopy can do this because we are achieving this right now. You can build a handheld imaging system for about $1,000 and a low cost spectrometer for less than $2,000. Now, these tools become available with specificity levels of 75% to 80%, which is comparable to what we can produce in the lab. If you can do 80%, you are better than the Pap smear. A small handheld device can be taken into the developing world and save thousands of lives. Pap smears are very expensive to operate and require too many cross-checks to be set up in the developing world.

"In our world, there is a big incentive for a GP to put a small handheld device, priced around $3,000 to 4,000, in his or her office. When a doctor does a Pap smear, the lab makes the money. The GP gets very little for doing the test. With the device, the GP can make an immediate diagnosis and charge for it. Plus, the service to the patient is better.

"We are getting some good results with a cheap $500 security camera with a few filters in front of it. But we are also working with some high-end cameras ($12,000 to 20,000 range) with more resolution and sensitivity than anyone would want. This will help us determine how good the resolution has to be and how sensitive the imaging device has to be to be effective. This will tell us how inexpensive a camera has to be to be effective. My gut feeling is that the technology will go to the lower cost side."

Manocher Lashgari, M.D., OB/GYN, Saint Frances Care, Hartford, CT

Dr. Lashgari, who has completed one of the phases of the CNDS clinical trial, said he is currently waiting for direction to proceed from SpectRx. Dr. Lashgari told us that he is very excited about the potential for CNDS.

Available Q4 2005

Update on SmartPill Technology: Originally Published 9/2003

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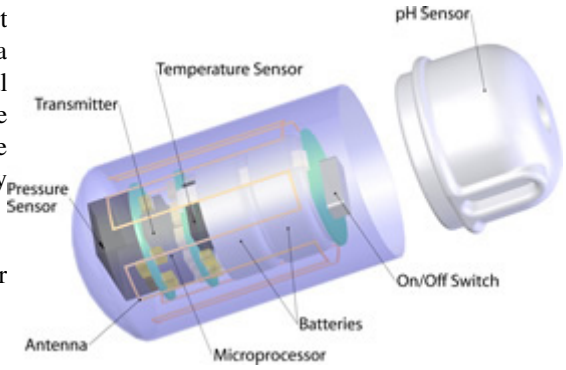
MD Buyline reported on SmartPill technology in 2003. The past year has been a busy one for SmartPill Diagnostics, the company which developed the concept and technology, as well as for those sites approved to test the technology.

The SmartPill Capsule is a patented, computer monitored, inert capsule that contains electronics and is ingested orally. It is a unique, non-invasive measuring device that captures biomedical parameters as it moves through a patient's GI tract. The SmartPill Capsule wirelessly transmits its data to a small mobile receiver/controller worn by the patient. The data captured by the SmartPill Capsule include:



- gastrointestinal peristaltic pressure (the muscular contractions that propel matter within the intestinal tract)
- temperature
- pH levels
- transit time (spontaneous movement of mass through the intestine)

Interpretation of the biomedical data is achieved through proprietary software that gives the gastroenterologist a 3D representation of the SmartPill Capsule's movement through the GI tract correlated with the measured values.

The second generation SmartPill Capsule system will enable real-time, site-specific tracking of the SmartPill Capsule's position within the GI tract. The system's tracking software will discriminate multiple capsules and track them simultaneously in a patient, as they transit the bowel, by repeatedly mapping or monitoring the entire GI tract. In addition, the SmartPill Capsule system will provide the gastroenterologist with a real-time diagram of the patient's alimentary tract.

The SmartPill has successfully completed Proof-of-Principle trials and is expected to receive FDA 510(K) approval in Q305 and become available for physician use in Q4, 2005.

Timeline

- **March 2004** – Announced that Massachusetts General Hospital's IRB approved the SmartPill Capsule for Phase I "Proof-of-Principle" Clinical Trials (read press release), wins Life Sciences Achievement award (read press clipping).
- **June 2004** – Successfully completed Phase I "Proof-of-Principle" Clinical Trials at Massachusetts General Hospital (17 patients, Boston, MA), and VA Hospital (14 patients, Buffalo, NY), demonstrating the SmartPill's ability to measure gastric emptying and characterize and reproduce pH and peristaltic pressure profiles within the GI tract.
- **July 2004** - Announced that the American Motility Society accepted an abstract on the results of Phase I clinical trials for oral presentation at the 13th Biennial American Motility Society Meeting at the Mayo Clinic in September, 2004 (read press release).

Physician Interviews

Robert J. Genco, D.D.S., Ph.D., SUNY Distinguished Professor, The State University of New York at Buffalo, Vice Provost and head of the SUNY Buffalo Office of Science, Technology Transfer and Economic Outreach

"SUNY Buffalo recognized the tremendous potential of SmartPill technology, and licensed patent rights to the inventor's company. Today, we are pleased to see that a strong management team has come together to move this innovative technology to market. We are looking forward to developing further collaborations between the university and SmartPill Diagnostics to support the growth of this new Western New York biotech company."

Robert C. Logel, Founder and Managing Director of Spaulding Ventures (www.spauldingventures.com, the principal investor in SmartPill Corporation)

"We are pleased with the terms of the asset purchase and very supportive of the idea of SmartPill and APPRO combining their relative strengths to form a new, vertically integrated development company. We have great faith in SmartPill Diagnostics' business plan, technology and management team. The fact that both companies are rooted in Western NY not only strengthens this region's biotech industry but gives me even more reason to expect other biotech investment opportunities to emerge from this community in the near future."

Available in 2006

Update on the SARA System: Originally Published 2/2004

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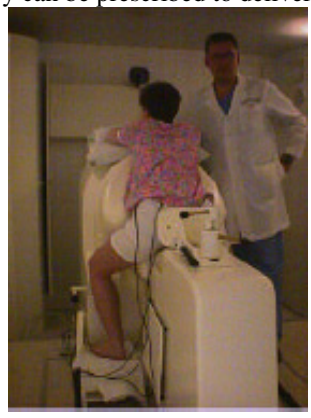
The SARA system is non-invasive technology designed to analyze the brain and cardiologic activity of a fetus. Designed to measure the natural magnetic field that is produced from neurological activity in the fetus, the system uses a measuring device called SQUID (superconduction quantum inference device) to measure the magnetic signal changes of the fetal brain (fMEG) and heart (fMCG). The procedure takes approximately 15 minutes and is performed on an outpatient basis. The results of the fMEG and fMCG studies allow the physician to determine if the fetus has brain damage or a life threatening arrhythmia. If brain damage is detected the physician has the option to deliver the baby early in order to minimize the extent of brain damage. If an arrhythmia is detected and accurately identified then proper drug therapy can be prescribed to deliver the baby as close to term as possible.



Magnetoencephalography (MEG) has been available since 1996. Currently, there are approximately 110 of these systems from various vendors being used for research and clinical applications worldwide. Due to the position of

the fetus and the interference from the maternal electromagnetic signals, current MEG technology has not been applicable for fetal brain or ECG studies.

Since the original article on this topic, fetal applications for this technology have still not been FDA approved. fMCG technology is expected to be available by 2006 in the U.S.; fMEG should be available soon after. Actual reimbursements for fMCG and fMEG applications have not been established but anticipate a similar reimbursement as that for adult MEG procedures, which are now being reimbursed under "new technology codes." New technology codes are used until CMS has enough time to establish the actual cost of performing the study; historically, this has been two to three years.

One added advantage of this technology is CMS has aggressively reimbursed MEG studies for adults. With this in mind, the breakeven point for this technology is 1,039 studies. Based on 400 studies per year, the breakeven point is 2.5 years. CMS has historically reimbursed promising new technologies aggressively. This is designed to encourage hospitals to adopt new, costly technologies that have the potential to improve patient outcomes.

As of January 1, 2004, CMS raised the MEG reimbursement rate from $2,250 to $5,250, an increase of 133%, by assigning it a "New Technology Code": APC 1528. A new technology code is typically used long enough for CMS to establish the actual costs of the technology; as noted above, it takes up to three years for CMS to acquire the actual cost data in order to refine the reimbursement. By this time, SARA would have paid for itself.

Physician Interviews

Ronald Kawai, Ph.D., Associate Professor of Department of Medical Physics, University of Wisconsin, Madison, WI

"I'm not aware of any significant development of the SARA System since the beginning of the year. At our lab, I have a different system that I use for doing the studies. It is not the same as the SARA System. It is really more of a conventional system that is designed to do adult studies. It can be used for fetal studies but it is not designed for that. However, for our fetal heart studies, it works quite well and it has shown a lot of promise. We can easily detect the signal with fMCG and convert it to a meaningful waveform. It is more difficult for brain studies because the signals are so much smaller so it will take a few years to fully understand the numbers behind the calculations."

Nina Gotteiner, M.D., Pediatric Cardiologist, Associate Professor of Pediatrics Feinberg School of Medicine, Northwestern University, Chicago, IL

"I am not aware of any changes to fetal MCG in the past six months. It is still a very helpful technology in that it can help determine what type of arrhythmia the fetus is having and thus help us decide on a treatment. It then can show what effect the treatment has on the fetus, whether it is helping or hurting. We are also interested in looking at heart block; we look at fetuses with very fast rhythms and we also look at very slow rhythms. We are trying to learn about the mechanisms of these two phenomena. There are things that are only possible with fMCG, like when dealing with a long QT interval (ventricular rhythm problems). This symptom has a very specific treatment path but there is no way to identify this problem without fMCG. The other thing that can only be diagnosed with fMCG is pre-excitation, or a very fast heart rhythm.

"The data indicates that 1% to 2% of pregnancies in the U.S. have some sort of arrhythmia, which is overall not a large number. This number in reality is probably higher because not everyone goes to the doctor. The big reason for identifying a fetal arrhythmia is the baby has a greater chance of doing poorly if it is not treated. If we can identify a fetal arrhythmia it is very treatable and we can positively affect the outcome."

Gregory L. Barkley, M.D., Neurologist, Clinical Director, Oakland University/Henry Ford Hospital, Detroit, MI

"Although I am not aware of any updates to this technology I have reviewed some of the research articles and have seen the equipment in use. There is still a lot of work to be done but there are some practical reasons to identify abnormalities while the baby is in the womb. Some say an fMEG study has the ability to show brain damage before delivery. This could be used as a defense for the obstetrician, who is so often held liable for brain damage after birth."

Optical Imaging Shines New Light on Breast Cancer: Originally Published 8/2003

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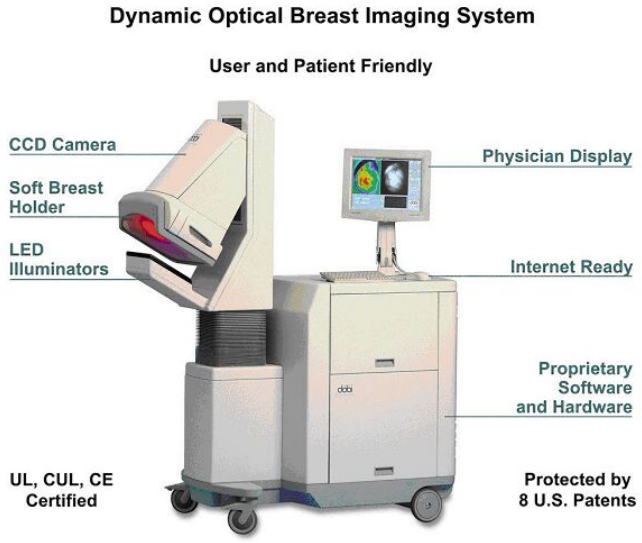
Optical imaging is an emerging technology in breast cancer detection that will allow improved detection without radiation or patient discomfort. DOBI Medical International is developing the dynamic optical breast imaging (DOBI) ComfortScan™ system. This technology utilizes near infrared light to identify increased vascularity (angiogenesis) after slight compression. The near infrared light is then passed through the breast and approximately two images per second are recorded with the camera system. After the scan, the system displays the breast image which highlights light absorption in angiogenic areas that can be caused by increased volumes of blood and blood being deoxygenated by the presence of the malignant tumor (cancerous tumors tend to consume oxygen up to four times faster than normal tissue).

In November 2004, DOBI Medical International, Inc. announced that it has initiated the clinical trial, which will be the subject of the fifth and final module of its Pre-Market Approval (PMA) application with the U.S. FDA. Patient enrollment has begun at several leading U.S. medical sites, including Hackensack University Medical Center, Hackensack, NJ; Sally Jobe Breast Centers, Greenwood Village, CO; and Comprehensive Breast Center of Coral Springs, Coral Springs, FL. Additional sites are expected to begin enrolling patients in early 2005. This final module is a clinical study to generate patient data relative to the performance of the ComfortScan system in a clinical setting. The clinical testing is expected to continue for another 18 months, after which FDA approval is anticipated.



Physician Interviews

Phillip Thomas, Co-Founder/Chief Executive Officer, DOBI Medical International, Mahwah, NJ

At RSNA 2004, Thomas said that DOBI Medical has been working on this project for six years and has raised approximately $25,000,000. They went public a year ago (ticker symbol: dbmi.ob). They have tested over 1,500 women in the U.S. and in Europe and are now also doing testing in South America.

Thomas stated, "We are on track in seeking FDA approval and have completed four of five data submission modules to the FDA. We are also now testing in three sites in the U.S. and another four or five will be added over the next 30 to 60 days. All data gathering is expected to be finished by the third quarter of 2005 with the final submission to the FDA following successful completion of the clinical trial."

Thomas said that he sees this technology as being especially helpful for women under 50 who have the most missed malignancies and false positives on mammograms because of the denseness of their breast tissue. He says they are getting some good results in this area. He also sees the technology as an ideal way to improve breast cancer diagnosis in rural underserved areas because it has low costs and could be easily portable if put on a mobile platform. Another area in which he sees increased usefulness is providing additional physiological diagnostic information when used as an adjunct to mammography for patients who have strong family histories of breast cancer or who test positive for the BRCA 1 or 2 genes.

Thomas added that currently they are focusing on breast cancer but this technology may be applicable to other types of cancer, such as skin cancer. According to industry experts, angiogenesis has been identified in virtually all cancer patients as well as over 70 other diseases in the body. "If you go to www.angio.org, the website for the angiogenesis foundation, you will find enormous amounts of information about the identification of angiogenesis in obesity, Alzheimer's, rheumatoid arthritis, and over 70 other diseases. It is somewhat of the hot new topic that our blood supply is evolving and expanding in response to what is going on in the body such as its response to perceived wounds and other damage, or in response to tumors. It is an exciting area that will have many implications besides just breast cancer."

Thomas concluded, "We want women to know that there is new technology being developed that can make a difference, based on the very latest understanding of how cancer develops. I have known a number of women who have had to deal with breast cancer and one of the biggest things they need is hope. It may not affect them today but they don't want their daughter or granddaughter to go through the same thing they have been through. I believe this new technology will be making a difference in the lives of many women and that is our focus. You will see more mammography, more ultrasound, more CT, more MRI but this is truly new technology that has never been seen before."

Thomas Stavros, M.D., Radiologist, Sally Jobe Breast Center, Denver, CO

"We have been participating in the clinical trial for about a month. We're actually accruing patients, those who are going to undergo biopsy, who are in the probably benign or suspicious Category III or IV. We're not doing any patient where we are more than 90% sure that it is cancer. Everyone is going to have histological proof of what the diagnosis is the same day. There is a long list of inclusion and exclusion criteria but probably about half our patients qualify."

When asked if the size of the breast affects image quality, Stavros stated, "The machine is so sensitive to light that it has to be in an inside room where you completely seal out ambient light, so if the breast is too thin or too small you might get too much through or if the breast is too large or too dense or too thick you might not get enough light through, so there are problems with some people. Interestingly enough, tattoos and skin moles can also absorb light and create some problems."

"This study is designed to evaluate the future of optical breast imaging. Theoretically, the study looks at things that we haven't been looking at. It is designed to look at tumor neovascularity and tumor vessels are not normal. They don't have normal muscular walls so they are very easy to compress. The woman puts her breast inside this rubber membrane and with a very light amount of pressure. The pressure is increased slightly and that increase is enough to collapse the tumor vessels so the blood doesn't drain out. Because the metabolic rate of the tumor cells is higher than metabolic rate of normal cells in most instances, the tumor cells take more oxygen from hemoglobin that accumulates while the draining veins are compressed. The theory is that since the tumor vessels are easier to compress the blood in them will be more deoxygenated than in surrounding tissues. And they are using light transmitted through the breast at the proper wavelength to be absorbed by deoxygenated hemoglobin. The compression lasts a matter of seconds and the machine generates a curve in the light transmission which is displayed as a color image."

"This technique is not comparable to mammography, ultrasound or MRI in terms of spatial resolution but in terms of color resolution and absorption resolution, it is very sensitive. Exam times are quick, virtually painless and no radiation, so it would probably be the safest thing you could use."

Update on Hattler Catheter: Originally Published 3/2004

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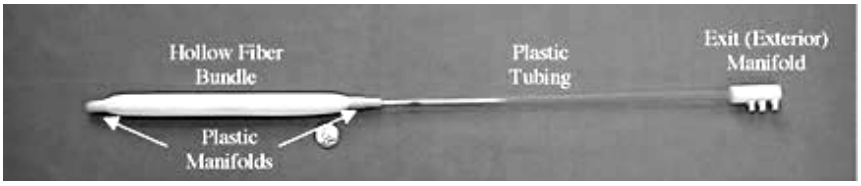
The Hattler Catheter is a unique alternative to mechanical ventilation. It is designed to assist the lungs at a fraction of the cost and at a minimal risk to the patient. It does this by providing oxygen directly to the bloodstream. The initial target market for the device will be chronic obstructive pulmonary disease (COPD). Phase 1 Clinical Trials in Europe and Mexico will begin soon, according to its designer.

The Hattler Catheter can supply 20% to 30% of an adult's oxygen requirements and it can remove 40% to 60% of the CO2. The catheter can also improve a patient's quality of life. The patient does not need either a tracheotomy or intubation and without a tube blocking the airway there is no need for sedation. The patient can be awake and communicate, eat, and drink, contributing to a more rapid recovery.

The Hattler Catheter looks like a long intra-aortic balloon catheter surrounded by fibers. It is inserted in either the common femoral vein or the internal jugular vein. This gives the physician the option of either using the neck or the groin. At the start of the procedure, a guide wire is first inserted into the vein. Then the catheter is guided into place as it is threaded over the wire. The procedure lasts 15 to 20 minutes and can be performed by a pulmonologist or a critical care physician. The catheter occupies the area of the vena cava and the right atrium once it is in place.

The catheter is smaller than the size of the vessel so it does not obstruct blood flow though the vein. The balloon that is located in the center of the fibers allows it to exchange a significant amount of oxygen. It moves at 300 beats per minute and creates convective currents at the tip of the fibers. This helps break up the liquid membrane boundary layer and significantly enhances the gas exchange.



If clinical trials can prove the effectiveness of the Hattler catheter, hospitals should see a significant reduction in the length of stay of COPD patients with lower costs and improved outcomes. A COPD patient on a mechanical ventilator can expect to spend on average 11.3 days in a critical care setting. One day in a critical care area can cost a hospital from $1,200 to $5,000. By eliminating the need to wean a patient off of a ventilator, a critically ill COPD patient's stay in this area may be reduced to six days, saving five days in a critical care setting. These five days alone can generate $6,000 to $25,000 in savings. At this time, there have been no changes that would impact the financial calculators or other financial data that were reported in March 2004.

Physician Interviews

Brack Hattler, M.D., Executive Director of the Artificial Lung Laboratory, University of Pittsburgh, Pittsburgh, PA

Dr. Hattler, the physician primarily involved with the design and development of the device, revealed steady progress has been made in the catheter and plans for initiating clinical trials. "Everything is in place for us to begin Phase 1 clinical trials at The University of Cambridge in England as well as two additional sites that will begin in Mexico. The trials in Mexico will be in Mexico City, population 20 million plus, and Monterrey, population four million plus. The Mexico locations are of particular interest due to the high altitude (about 7,000 feet). Since the success of the Hattler catheter is critical to gas exchange, if we can prove the catheter is safe and viable in Mexico City at an altitude of 7,000 feet, we can be sure it will work anywhere. Clinical trials are slated to start in January 2005 and the projected dates of availability, Q1 2006 for Europe and Q4 2006 for the U.S., still appear to be reasonable."

"The past year has been spent improving on the design. The catheter is fully percutaneous, allowing access via introduction by a catheter sheath inserted into a vein. The size has also diminished to a 29 FR catheter size, making insertion easier and quicker. This is the size often used in ECMO applications, which are well known and utilized throughout the world."

"Additional improvements have been made to reduce the risk of clotting while the catheter is in use. It now has a nice heparin bonded coating that has allowed a significant reduction of IV heparin needed. The ACT is running about 150 to 180."

The device has been used on a limited number of human subjects. These patients were end-stage pulmonary disease patients whose family members graciously agreed to allow the Hattler catheter to be used for a limited period of time. "The information gathered from those limited instances solidified our belief that we were ready to proceed to the Phase 1 clinical trials. This will provide safety data based on a formal human study. The pivotal trial of the device will begin later in 2005."
Investment in the technology continues to be steady. "We are still jointly working with the government on a study to evaluate the use in combat conditions. Treatment in an intensive care setting with and without the use of the catheter is ongoing to assess if utilizing the catheter makes a difference in the patient's outcome. Congress has appropriated funding this year to continue investing in the technology. The venture capital community has also shown interest in the technology. Although not related to what I am interested in (clinical success) it is certainly a necessary business factor that is critical to making this a viable clinical technology in the future."

In Early Clinical Trials or Technology Still Evolving

OptoSonics' Thermoacoustic Computed Tomography: Originally Published 5/2004

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OptoSonics' Thermoacoustic Computed Tomography (TCT), utilized for breast imaging continues to be in the research phase for demonstrating cancer tumors at 0.5 mm. Imaging tumors at 0.5 mm, TCT may be able to identify breast cancer in the earliest possible stages. Magnetic resonance (MR) presently has the highest resolution for breast cancer detection (between 1 mm and 3mm). OptoSonics is a private research company that continues to focus on bringing TCT into clinical applications for breast screening applications. The company is led by Robert A. Kruger, Ph.D., the president and co-founder of OptoSonics, who has been working with the system since the early 1990s; TCT has been evolving since that time.

TCT is based on the acoustic effect of tissue when exposed to electromagnetic energy. It relies on very simple technology: cancerous tissue has a higher water concentration than a non-cancerous cell. Due to this water content dissimilarity, the cancerous cell absorbs energy at a rate two to five times that of a non-cancerous cell. The cancerous cell gives off sound waves of a different frequency than a normal cell of the same tissue, which allows TCT to present an image that can distinguish between a cancerous and non-cancerous cell. Other clinical advantages include:

- It is a non-invasive procedure;
- The breast does not need to be compressed as in conventional imaging;
- It does not require contrast media for imaging;
- It does not use ionizing radiation.

The technology has the potential to image multiple forms of disease functions down to the micro-vascular level. One of the primary target areas is the screening and diagnosis of breast cancer. Larger systems are being researched for other life-threatening diseases, such as cancer in other areas of the body, Alzheimer's, and cardiovascular diseases.

Physician Interviews

Robert Kruger, Ph.D., President, OptoSonics, Inc., Oriental, NCI

Regarding developments in thermoacoustic computed tomography, we are working in a few new directions:

OptoScope
"We are developing a generic TCT detector system that will improve upon our previous detector system by allowing us to incorporate the detector into standard X-ray mammography imaging geometry. The detector, which we call the OptoScope, can be used for anatomy other than the breast. It can be used with visible, near infrared, radio waves, and microwaves. We hope to have a working prototype by Q2 2005. Initial clinical trials are planned for Q3 2005."

Photoacoustic spectroscopy
"In an attempt to better classify breast tissue samples taken during biopsy and during intraoperative procedures, we are applying our technology to measure tissue absorption at multiple wavelengths and to identify absorption patterns that characterize benign and malignant breast cancer. These techniques will allow us to introduce technology that will take over some of the clinical roles currently assigned to histopathology. In so doing, we hope to develop clinical tools that will improve the time response between breast tissue excision and definitive diagnosis. Initial clinical trials are planned for Q2 2005."

Her-2 Imaging
"We will be awarded a $2 million research grant from the National Institutes of Health, beginning March 2005, to develop methodologies for detecting the presence of over-expressed HER-2 genes in certain types of breast cancer *in vivo*. This work will be carried out in collaboration with researchers at Indiana University Medical Center and

Genentech, who will supply Herceptin, which is a humanized antibody that has a high affinity for binding to the HER-2 cell surface receptor. We hope to label Herceptin with dye that absorbs in the near infrared and which will generate thermoacoustic signals when irradiated with a laser. We will detect these with our OptoScope and identify them using photoacoustic, spectroscopic methodologies."

Keith Stantz, Ph.D., Facility Physicist, University of Indiana, Indianapolis, IN

"I have worked with TCT developed by Dr. Kruger. In the last six months, there have been no major breakthroughs with TCT but there has been incremental progress. We haven't had any major studies that would really exemplify how well the system can be used. Those are coming up but it will probably take another six to nine months before we can really define if the system can really perform in a clinical setting.

"Dr. Kruger, who essentially built the prototype TCT here at Indiana, is also looking at breast imaging for breast biopsies via TCT. I also believe he is working on RF frequency to try to improve the technology for breast cancer screening. At present, OptoSonics is working on developing a scanner to study biopsies in very similar ways of spectroscopic imaging. There are certain absorption patterns in cancerous tissue compared to normal host tissue that should allow Dr. Kruger to provide a more definitive understanding of what is in the biopsy sample. This is in general a broad stroke of where TCT will be applied."

Cytoscan Replaced by Newer Technology - MicroScan: Originally Published 6/2004

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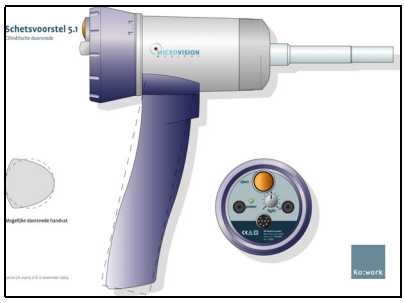
A few months ago, Cytoscan and its intellectual property was sold to Intelligent Medical Devices in Cambridge, MA (www.intelligentMD.com). The company is now working on a non-invasive hemoglobin test. The Cytoscan was a great imaging device but the inability of the company to supplement the product with software to make correlations with clinical outcomes left the great images virtually 'out in the cold.' Most researchers agreed the product had potential but it was never really determined how to use the images provided by the Cytoscan.

The Cytoscan used Orthogonal Polarization Spectral imaging technology (OPS). OPS technology has now taken a back seat to a new technology called Side Stream Darkfiled imaging (SDF). SDF appears to be a big improvement over OPS. The MicroScan is the new device that utilizes SDF. It is produced by MicroVision Medical (www.microvisonmedical.com). The MicroScan is designed to provide real-time intravital video images of the microcirculation with improved image quality and utility.

The MicroScan is a stand-alone device that is powered by a rechargeable battery pack. The battery illuminates low-powered, high-intensity, bright LEDs. The LEDs provide direct illumination on the tissue with the observations made adjacent to the light. The incident and reflected light does not travel down the same pathway giving the user more light on the specific tissue and improved image quality. Analysis software that works with the instrument to make quantitative measurements of changes in the human circulatory system will be available in Q1 2005.



The MicroScan by MicroVision Medical

MicroVison Medical expects to begin shipping research-only models starting January 1, 2005. A special trade-in offer is available for all Cytoscan customers through April 1, 2005. Microvision Medical will focus on the critical care market. There are some new and innovative approaches using the technology to monitor therapy during septic shock, similar to the Cytoscan.

Physician Interviews

Bruce M. Klitzman, Ph.D., Director of Research, Kenan Plastic Surgery Research Laboratories
Duke University Medical Center, Durham, NC

"As an imaging device the Cytoscan was outstanding. That was the sad part: they had very good technology in respect to image acquisition but the question has always been on the back end. What do you do with that?

"It still has great potential. But there are still a lot of problems associated with it, not the least of which is what the physician or the researcher does with the images that the device acquires. It is very good at grabbing images or giving you video microscopy but the question is, what you do with that? That is where the whole thing hinges on developing some objective criteria on which you can evaluate the image. That has been the difficulty historically. In other words, are there things that can be easily quantified and, if so, do those numbers correlate with a clinical outcome, is it good at diagnostics? Those questions have not been answered.

"They tried to come up with some software that would quantify, for example, segment length and the number of microvessel segments in an image but that is not simple. I know that they have spent a lot of money and a lot of effort trying to do that but I don't think that they have achieved that. Right now I think if it was sold in a much cheaper version simply as an image acquisition device, a handheld microscope without any claims as to what one can do with that information, it would be much more desirable. That was their problem and that is why they were bought out few times. That is why they are struggling. The question is, is this something that has clinical use today and the answer to that is still 'no.'

"We used their software early on; we were involved in beta group testing, we gave them advice, and so forth. One of things that we told them was to not make it a clinical instrument yet. If you put it in the hands of researchers and let them do the evaluation and determination as to what possibly is quantifiable then you can find out if it will correlate with anything clinical. They went ahead and thought they could make a lot more money if they could make clinical claims immediately and they put it out there with that intent and it crashed and burned."

Dr. Geoffrey C. Gurtner, M.D., Director of Microsurgery, New York University School of Medicine
NYU Medical Center, New York, NY

"For my purposes, the Cytoscan works pretty well since I am interested primarily in the images. I know the company has a software package that indicates blood cell velocity through a capillary. The software could be pretty useful in a lot of areas but I mostly use it in the operating room to watch blood cell movement through the skin. I don't necessarily need the software.

"I have found this is the best device to answer the question of whether the tissue flap will heal by itself or if it should be redone. I find it useful in preventing minor complications and important when doing breast reconstructive work. I know that the company has had problems but it still works well for what I am trying to do. Naturally, we are open to new technologies on the market."

Update on Breathmeter Biomarker Science: Originally Published 7/2004

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The July 2004 article featured the Breathmeter from Ekips Technologies, Inc. This breath analysis instrument uses laser spectroscopy to measure biomarkers linked to diseases such as asthma. In October 2004, Ekips Technologies, Inc. announced it has been awarded a $750,000 Phase II NIH grant from the National Heart, Lung and Blood Institute. This grant will support clinical studies and product development toward obtaining FDA approval for the Breathmeter.

A mid-infrared laser chip used in the Breathmeter measures the level of nitric oxide and carbon dioxide in exhaled breath. With airway inflammation, the level of nitric oxide in the lungs increases. Increased levels are present in

diseases such asthma, which is a chronic inflammation of the airways. Although it will not replace standard pulmonary function testing, the Breathmeter would serve as a screening tool for asthma with future applications for diseases such as lung cancer. The Breathmeter would also aid in monitoring response to anti-inflammatory therapy for the asthmatic patient.

Physician Interviews

Andrew Naugher, Ekips Technologies, Inc.

"The machines will be installed in Q2 2005 as part of the NIH Phase II trials. I'm not sure of the completion timeline. We are scheduled to have machines tested by clinics in Tulsa and Oklahoma City as part of this grant. At that time we will be able to provide firsthand perspectives from healthcare providers who will be using the Breathmeter with patients."

In September 2004, Aerocrine introduced the NIOX Mino, a handheld analyzer for nitric oxide measurement. The NIOX Mino would provide single-breath measurements with a small, low cost unit. This product is currently in clinical trials. Naugher explained how the Breathmeter differs from the NIOX: "The Breathmeter has proprietary

laser technology that doesn't require a mix of gases, measures in real time, can recalibrate itself in seconds, and can be 'tuned' to measure more than one breath marker per machine. The NIOX is based on chemiluminescence, which requires a combination of gases to measure the samples, takes longer to measure, does not recalibrate automatically, and measures only one breath marker."

Dee Copeland, Oklahoma Chapter of the American Lung Association

The American Lung Association of Oklahoma is partnered with Ekips Technologies. They will be involved in the next phase of clinical trials for the Breathmeter set to begin in 2005. Copeland noted that not enough time has passed to update the MD Buyline report from July. She said they will have additional data available next year.

Questions?

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