

Start-Up News

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Summary: Noteworthy news from medtech start-ups. This month we profile Nanospectra Biosciences and its near-infrared tumor ablation technology; Vertos Medical, which is developing "ultra" minimally invasive technology for treating spinal stenosis; and Freedom Meditech's noninvasive ophthalmic glucose monitoring technology.

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by Bob Kronemyer

Nanospectra Biosciences: Near-Infrared Tumor Ablation

Most ablative techniques for therapeutic treatment that use light-based therapy or other energy sources rely upon the absorption of that energy by the tissue; in other words, tissue is thermally destroyed wherever the energy source is directed. But the founders of **Nanospectra Biosciences Inc.** believe they have a better idea. The Houston, Texas-based company's *AuroLase* therapy uses an exogenous source: a tiny particle designed to absorb near-infrared light (roughly 800 nanometers [nm]). "Instead of the body absorbing that energy and converting it to heat, the particle does the same," says company president and CEO J. Donald Payne. "We believe this provides a greater specificity and more precise treatment."

Nanospectra Biosciences has initially targeted the oncology market to treat solid tumors. The company is conducting a 15-patient, human clinical pilot trial at three sites in Texas for the treatment of recurrent head and neck cancer, but believes the technology is also applicable to brain, lung, and prostate cancer. Currently, there are over one million solid-tumor diagnoses each year in the US alone, representing over a billion-dollar market. The firm does not expect its first Food & Drug Administration (FDA) approval until 2011. "We think we're eligible for a 510(k), but the FDA has not given us a definitive answer," Payne says. The company also expects to file for European CE mark approval in 2011.

Nanospectra Biosciences was founded in 2001 by Naomi Halas, PhD, and Jennifer West, PhD, both from **Rice University** in Houston, along with Dan Watkins, a local investor with a PhD in materials science. Halas, who is a physics professor, developed the particle used by *AuroLase*, then partnered with West, who is a bioengineering professor, to develop a series of life-science applications in oncology. The start-up holds a total of 11 patents in its portfolio (10 licensed from Rice University; one issued to the company).

The technology takes advantage of recent advances in particle science. Most visible light (ultraviolet, blue, green, red, etc.) is absorbed by the body. However, there are areas in the near-infrared spectrum "that achieve the maximum penetration of light through tissue (also known as the water window)," Payne says. "A fairly recent invention is the ability to make small particles that will absorb within that wavelength window. Therefore, you can now create a series of *in vivo* applications."

Nanospectra Biosciences' nanoparticle is tunable, so it can absorb different wavelengths within the near-infrared spectrum. "In essence, we elevate the temperature in the tumor so all the cells in that tumor will eventually die," Payne says. *AuroLase* aims to treat at a temperature of at least 50 degrees C for greater than 90 seconds, resulting in cell death in the tumor.

The particles, which are 150 nm in diameter (about twice the diameter of a virus), are called *AuroShells* ("auro" is the Greek word for gold, whereas shell refers to the structure of the particle). The *AuroShells* are packaged in a bag for infusion into the bloodstream. As they circulate, a certain percentage of the particles (generally 3% to 5%) will accumulate in a solid tumor and the rest are cleared by the reticuloendothelial system (RES).

"The rapid growth of the blood supply to the tumor results in a leaky vasculature with fenestrations or holes in the blood supplying the tumor," Payne explains. In fact, there is a well-established theory known as the enhanced permeability and retention effect, whereby "particles or molecules within a certain size range will exit the bloodstream and enter a tumor and stay there because of the enhanced permeability of the tumor."

Twenty-four hours after particle infusion, a percutaneous laser fiber is inserted into the tumor in at least one location. The site is then illuminated by near-infrared light. The power level of light is too low to thermally damage normal tissue. "But the particles are designed to absorb that wavelength," Payne notes. The gold

metal shell of the particle used with *AuroLase* surrounds a silicon dioxide (glass) core. "That structure allows the particle to absorb the light, and the metal shell converts the absorbed light to heat with a very high efficiency, the same way that the hood of a car in the summer sun converts absorbed light to heat," Payne says.

The single-session therapy involves one or multiple fibers, depending on the size of the tumor, and each illumination site takes generally three minutes to treat. "Large tumors can take up to one hour to treat, with up to 20 illuminations," Payne says. "However, we don't feel the surgeon or interventional radiologist will have much of a learning curve. You simply map the tumor, decide where you are going to insert the fiber, insert the fiber, and turn on the laser."

Payne also points out that many ablative techniques can only burn round or oval areas. "But not all tumors are round or oval," he states. "Our particles should be able to self-select for the outline of an individual tumor, while sparing surrounding areas. With our technology, the ablation occurs only where the particles are located, not where the source of energy emits." In addition to supplying the particle, the company will likely provide the light source as well.

Competing tumor ablation technologies from **Covidien Ltd.** (radiofrequency), **AngioDynamics Inc.** (laser and radiofrequency), and **Galil Medical Ltd.** (cryotherapy) are not as precise, according to Payne, because they are not particle-directed as to the boundary of the tumor and thus can cause damage to adjacent structures or tissue. "Hence, we believe our outcomes will be better," he says.

To date, Nanospectra Biosciences has raised \$6.5 million, primarily through high net-worth individuals, and \$1.25 million from the State of Texas through its Emerging Technology Fund. A Series B funding round in the range of \$7 million is planned to fund a pilot study on a second indication (prostate cancer) as well as a pivotal trial for head and neck cancer.

Vertos Medical: Expanding the Treatment Options for Spinal Stenosis

Patients suffering from lower back and leg pain from lumbar spinal stenosis (LSS) who have failed standard medical therapies may be able to avoid the more drastic measure of full-blown surgery, thanks to a new "ultra" minimally invasive image-guided procedure from **Vertos Medical Inc.** that debulks the ligamentum flavum (the elastic ligament comprising the back wall of the spinal canal). An overly enlarged ligamentum flavum is the primary cause of LSS, a degenerative, age-related narrowing of the lower spinal canal that places pressure on the nerves. Besides causing considerable pain, LSS often severely limits mobility.

Vertos Medical's *mild* (minimally invasive lumbar decompression) procedure, accomplished using an accompanying tool kit of instrumentation, enables a virtually percutaneous approach to access the lumbar spine. Fluoroscopic guidance with an epidurogram guides the therapeutic intervention into the epidural canal. "You hear the words less invasive and minimally invasive bantered about," says president and CEO James Corbett. "But our procedure is ultra minimally invasive. Nothing else comes close when treating the spine. The physician is able to remove the bone or tissue causing the pressure on the nerves through a skin puncture the diameter of a pencil."

The company received 510(k) market clearance for the *mild* Tool Kit in early 2008 and European CE mark approval in the first quarter of 2009. Corbett, who joined the company in November 2008, previously was chairman, president, and CEO of ev3 Inc., where he led the development of the peripheral and neurovascular device business from 2001 to 2008. During that time, Corbett also served as chairman and CEO of MicroTherapeutics Inc., now a wholly owned subsidiary of ev3. His background also includes eight years as president of Boston Scientific Corp.'s Boston Scientific International BV.

"Each year, at least one million people in the US are diagnosed with LSS and have some form of intervention," Corbett says. Of that number, about 25% undergo surgery and the remaining 75% rely on

conservative therapies (eg, pain intervention via epidural injections). "We believe our *mild* Tool Kit (priced at \$4,300) represents a potential market in excess of \$2 billion," Corbett notes. The company's analysis of the Centers for Medicare and Medicaid Services' database suggests some 700,000 Medicare-eligible patients undergo some form of LSS treatment each year.

Vertos Medical was founded in 2005 by two Denver-based interventional neuroradiologists: Donald Schomer, MD, and David Solsberg, MD. "These doctors had a lot of cancer patients who could not undergo the rigors of major surgery, like a laminotomy (open surgery to decompress pressure on the lumbar spine)," Corbett explains. "They wanted to find a way to treat patients much less invasively, while relieving their pain and improving their mobility."

During a *mild* procedure, surgeons use between five and eight devices from the tool kit, depending on the needs of an individual case. The larger devices consist of three versions of a bone sculptor for removing bone and a tissue sculptor for trimming the ligament. The kit also includes a two-piece trocarlike device to create a treatment canal and a control device to help control the depth of insertion. All individual components of the one-use disposable kit are made of stainless steel and molded plastic.

The normal diameter of the ligamentum flavum is 2 mm; however, degenerative pressure from aging causes this ligament to buckle and become thicker, up to 10 mm diameter, which causes muscles and nerves to experience pain. This thicker ligament can be detected by an epidurogram.

After detection, the trocar-like device is slid directly toward the area of the stenosis and under the lamina to access the ligamentum flavum. Once the device is placed against the lamina (a thin layer of bone), the inner part of the device opens up the canal into the spine. The bone sculpting device then cuts and removes one to three sections of bone to open up a space on the edge of the lamina, for a clear opening to the ligamentum flavum.

The tissue sculptor, which is uniquely designed with a backward spoon-shaped tip, then allows the surgeon to shave the ligament as opposed to cutting it with a laminotomy. "At all times, you're keeping the ligament between your cutting tool and the epidural space, so it is a very safe procedure," Corbett says. After the tissue sculptor captures the trimmed tissue and the device is removed, a second epidurogram is performed. "With a successful decompression, you will see a thicker and straighter epidurogram, where the stenosis was previously," Corbett says. Empty space is left where bone has been removed. At that point, another level of the lumbar spine or the bilateral segment of the already treated area might be treated.

The final stage of the procedure is removing the trocar-like device and closing the entry site with a *Steri-Strip*. The *mild* procedure takes less than one hour to perform and is typically conducted under local/monitored anesthesia care. Some patients have been treated in an outpatient setting, which is a growing trend, but the length of stay for an inpatient procedure averages less than 1.5 days.

The company is currently recruiting 75 patients for its first human clinical trial. "We expect that 50% of study patients will at least be able to delay surgery," according to Corbett, who believes "*mild* can be considered sometime after an epidural steroid injection has failed, but well before contemplating a traditional laminotomy." And although you increasingly hear the expression minim laminotomy for patients who are at the surgical stage, it is dramatically more invasive than *mild*, he points out.

Sales of *mild* began May 2008 with an internal sales force (presently about 10 employees) and the procedure is reimbursed under laminotomy codes. But the company may eventually pursue its own code. Vertos Medical is headquartered in Aliso Viejo, CA, and has three issued and 37 pending patents. It does not share revenues/royalties with any other entity.

To date, the company has raised \$17 million through its C round of funding, nearly all of it from traditional medical venture capital firms. [W#200830380] The company plans to raise one more round of financing, but

declines to say when or what amount.

The company is also working on a next-generation *mild* procedure and tool kit, which is expected to launch next year. This new technology will broaden the portions of the spine that can be treated with the same access, and is designed primarily to address foraminal stenosis, a related lumbar spinal stenosis condition that affects nearly as many individuals.

Freedom Meditech: Noninvasive Ophthalmic Glucose Monitoring

A compact handheld ophthalmic device currently in early clinical development may eventually prove a welcome alternative to the pain and inconvenience of traditional finger-stick methods for monitoring blood glucose in patients with diabetes. The noninvasive glucose monitoring device being developed by **Freedom Meditech Inc.** of Cleveland, OH and San Diego, CA, uses a beam of red light to detect the concentration of glucose in the eye and is expected to be sold directly to consumers and through traditional diabetes product distribution channels. The company is also in the final stages of development with an in-office diabetes screening system that employs similar technology to identify individuals who may have undiagnosed diabetes or prediabetes.

"Glucose monitoring development in the optical field has always been a challenge because platforms pursued have traditionally generated a large amount of noise relative to the signal generated from glucose," says Craig Misrach, president and CEO of Freedom Meditech. Such noise prevents accuracy and repeatability and can potentially impact specificity as well, he says. However, *in vivo* data collected so far on Freedom Meditech's system suggest that it may overcome this problem and enable the commercialization of an accurate, convenient, and pain-free noninvasive glucose measurement device.

Every year, nearly 800,000 people are diagnosed with diabetes in the US alone, according to the **Centers for Disease Control & Prevention**. The glucose monitoring market "is well established. It's over a \$10 billion global market," Misrach says. The company pegs the potential of its in-office screening system at over \$1 billion worldwide.

Misrach declines to comment on the timeline for its regulatory pathway, but says the company intends to obtain CE mark approval in Europe and requisite international regulatory approvals in other selected countries around the world before pursuing FDA approval (likely via a PMA).

Prior to founding Freedom Meditech in December 2006, Misrach was president and COO at EyeChem, a diabetes medical-device company focused on the commercialization of an eye-related glucose measurement and monitoring system, from 2004 to 2006. "Diabetes is a global epidemic," he states. "Pricking your finger is clearly an archaic method of glucose measurement in comparison to the evolution of bioengineering technologies and medical device product development over the past 10 to 15 years."

Freedom Meditech owns exclusive commercialization rights to five patents in the US and numerous others internationally for its technologies, some of which it obtained in 2007 through a royalty bearing, worldwide license from the **University of Toledo**. [W#200720106] Ongoing research and development and preclinical testing are based in Ohio, and the company has entered into a number of strategic partnerships in the state, including agreements with **Battelle Memorial Institute** in Columbus, the **Cleveland Clinic** and the University of Toledo.

Freedom Meditech's technologies focus on the eye an optical window into the body which strongly differentiates its technology from the vast majority of historical noninvasive glucose measurement and diabetes screening pursuits that have focused on detection through the skin. One method historically pursued to detect the concentration of glucose in the blood has been the use of light reflectance or scatter via the skin. "If you can quantify the amount of light reflectance or scatter attributable to glucose, you can try to develop algorithms that can estimate the amount of concentration," Misrach explains.

Other researchers have heavily pursued the use of a specific wavelength of light on the skin, such as mid- or near-infrared light. "We are looking at other attributes of glucose with a much differentiated and novel technical approach that enable us to calculate concentration," Misrach says.

Simplicity is at the heart of the device design. It is anticipated that once the monocular-shaped device is positioned at the person's brow, the person will press a button and a glucose measurement will be taken and then digitally displayed on the device. "We are developing further software for data management, which will likely allow the user to easily manage respective glucose data, make appropriate treatment decisions, and transmit such data to the pertinent clinician," Misrach conveys. Moreover, the company expects that data from the device can be stored and used either by a computer via USB-compatible hardware or through wireless functionality.

"We are also engineering a variety of safety parameters within the device itself that are anticipated to alleviate some standard and understandable concerns of the FDA most notably inaccurate measurements attributable to user error or improper alignment," Misrach says.

The company expects to price its consumer monitoring device competitively in relation to the average annual costs of finger-prick supplies (\$1,200 to \$1,500 yearly). A consumable calibration test cartridge (approximately 100 tests per cartridge) is incorporated to enable the device. "Currently, the recommendation for intensive and appropriate glucose management is to test on average four times a day," Misrach says. "Unfortunately, statistics indicate that over 97% of people with diabetes are not testing as frequently as suggested, and on average, people test less than twice a day. Our technology stands to make it easier and more cost-effective to manage the disease."

Freedom Meditech's in-office diabetes screening system uses similar technology to identify potential undiagnosed diabetes in individuals and to provide screening for prediabetes in patients deemed to be at risk by clinicians. The technology lets the clinician know if the patient either has diabetes or has a greater than average chance of developing it. The screen can provide five to eight years of advance warning for those who appear to be on the path to diabetes in market channels where blood testing currently does not occur. The company plans to lease the desktop, light-based screening system for a few hundred dollars a month to select health care providers.

Without revealing launch dates for either product, Misrach says the in-office screening device is "much closer to market than the home-use device. We already have several thousand persons worth of human data." Human clinical trials for its daily monitoring technology are expected to start later this year. The company also plans to debut the screening device internationally before rolling it out in the US.

In September 2008, Freedom Meditech raised an undisclosed amount in a Series A round in which JumpStart contributed \$380,000. [W#200830508] This month, it closed the second tranche of its A round. Return investor JumpStart was joined by individual investors including Catherine Stiefel, a long-time director of Stiefel Laboratories.

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