

Endomag raises \$10M in series C funding round to focus on U.S. Magseed adoption

By Nuala Moran, Staff Writer

LONDON – [Endomag Ltd.](#) has raised \$10 million in a series C round, enabling it to ramp up U.S. adoption of its [Magseed](#) magnetic sensing technology for localizing tumors in advance of breast cancer surgery.

The company also is within sight of FDA approval for its related imaging agent, Sienna, for use in pinpointing sentinel lymph nodes, positioning Endomag to become the first to offer combined tumor localization and sentinel node detection using the same handheld probe.

See Endomag, page 3

VA, IBM Watson Health extend genomics deal for two years, aim to publish in 2018

By Stacy Lawrence, Staff Writer

The U.S. Department of Veterans Affairs (VA) and [IBM Watson Health](#) originally signed a deal two years ago as part of the National Cancer Moonshot initiative. Now, they've opted to re-up on the partnership for another two-year stint, even as

See Watson Health, page 4

Ankle-brachial index fails to wow U.S. task force as screen for PAD

By Mark McCarty, Regulatory Editor

The U.S. Preventive Services Task Force recently concluded that the data do not offer particularly vigorous support for the use of the ankle-brachial index (ABI) as a screening instrument for peripheral artery disease in asymptomatic

See ABI, page 5

Sovereign immunity decision raises questions regarding university-held patents

By Mari Serebrov, Regulatory Editor

A Federal Circuit decision that tribal sovereign immunity cannot be asserted in inter partes reviews (IPRs) could be the slippery slope that eventually makes biopharma and med-tech patents held by state universities fair game for

See IPRs, page 6

Medtronic-sponsored study aims to help develop tool for OIRD prediction

By Liz Hollis, Staff Writer

A major problem for patients in hospitals receiving opioids is respiratory compromise. However, it is difficult for nurses and clinicians to determine who may experience opioid-induced respiratory depression (OIRD) as they recover. A recent study could point to a tool that could help hospitals identify these patients.

[Medtronic plc](#), of Dublin, sponsored the postmarket, international Prediction of Opioid-Induced Respiratory Depression in Patients Monitored by Capnography (PRODIGY) study

See Medtronic, page 7

Robotic disinfection system bound for U.S., not Canada, says Solaris

By David Godkin, Staff Writer

Mississauga, Ontario's [Solaris Disinfection Inc.](#) began developing its [Lytbot](#) core technology five years ago because of deficiencies it saw in other disinfection technologies at U.S. and Canadian hospitals. These include systems that use low

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BioWorld MedTech's Cardiology Extra

Staff Writer Liz Hollis
on one of med-tech's key sectors

Read this week's edition

Financings

Bone Biologics Corp., of Burlington, Mass., reported the completion of a \$5.9 million funding, \$3.9 million in equity and a \$2 million credit facility. For the equity funding, the company issued 330,325 shares of common stock to four unnamed investors and 3.5 million shares of common stock to Hankey Capital. Hankey Capital also provided the credit facility. Proceeds will be used for working capital, protein development, animal testing, and other research and development activities. Bone Biologics is developing Nell-1, a bone graft substitute product on bone regeneration in spinal fusion.

Orthospin Ltd., a Misgav, Israel-based portfolio company of The Trendlines Group Ltd., completed an investment round of \$3 million for its smart, robotic external fixation system for orthopedic treatments. Johnson & Johnson Innovation led the investment round.

Regulatory front

Palmetto GBA of Columbia, S.C., said it will provide “limited coverage” of the Confirmmdx epigenetic assay for prostate cancer by Mdxhealth of Irvine, Calif., to reduce the volume of unnecessary prostate biopsies. The Medicare administrative contractor said the evidence in support of clinical utility is “promising . . . at the current time,” and that clinical studies underway will establish the utility of the test for men whose previous biopsies were negative. Palmetto said that the coverage with evidence development program for the test entails a semi-annual review of the evidence. Mdxhealth SA of Herstal, Belgium, said the latest update to L35632, which goes into force Sept. 3, deleted references to a clinical study and removes patient number limitations.

The **Medicare Payment Advisory Commission** (MedPAC) said in its most recent report to Congress that hospital discharges

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for circulatory systems admissions accounted for 27 percent of all discharges in 2006, a measure that fell to 20 percent by 2016. The report said that 10 major diagnostic categories had accounted for 92 percent of all discharges in both years, and that infectious disease discharges were responsible for 9 percent of all discharges in 2016, up from 4 percent in 2006. The uptick in musculoskeletal system discharges, from 12 percent to 14 percent, was chalked up to major joint replacement surgeries, MedPAC said, adding that all-payer hospital outpatient visits rose nearly 25 percent over the index period, while inpatient admissions dropped 5 percent. The number of Medicare per-beneficiary surgical discharges had fallen by 26 percent between 2006 and 2015, but the rate of discharges had rebounded in 2016 so as to represent only a 23 percent drop from baseline. Length of stay fell by nearly half a day for Medicare beneficiaries (from 4.94 to 4.48 days), but rose from 3.91 to 4.04 for non-Medicare patients.

The **Medical Device Manufacturers Association** (MDMA) said it remains concerned that the Centers for Medicare & Medicaid Services’ (CMS) use of “overly stringent criteria” for participation in the new technology add-on program (NTAP) will blunt device makers’ appetites for taking part in the NTAP program. MDMA’s president and CEO, Mark Leahey, directed his comments to the draft inpatient prospective payment system rule for fiscal 2019, recommending that the criteria for newness in connection with the NTAP program be modified so as to recognize a new mechanism of action that improves outcomes, and that CMS add shorter length of stay to the list of characteristics that would qualify as substantial clinical improvements.

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Endomag

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Since the U.S. launch of Magseed in 2016, there has been significant uptake by leading cancer centers, where it has replaced the use of both wire-guided and radioisotope localization.

“We are at the point where we have convinced a lot of people, but the market is significantly bigger, and we are in an arms race to scale,” said Mathew Stephens, commercial director of Endomag. “We can now hire more global product specialists, set up evaluations and go and do demonstrations,” Stephens told *BioWorld MedTech*.

Implantation of the Magseed device takes place during routine presurgical radiology or ultrasound assessment, at any time up to 30 days before surgery. Once in the operating theatre, the location of the tiny implant – which is less than the size of a grain of rice – is detected using Endomag’s handheld Sentimag probe.

Sentimag works by generating an alternating magnetic field, transiently magnetizing iron oxide particles in Magseed, and enabling its location to be imaged.

By removing the need for wire placement in the breast on the day of surgery, Magseed decouples radiology from surgery, making for simplified scheduling. It also offers the advantage that, unlike wire guidance, the implant is entirely enclosed and once in position cannot be dislodged.

While clinical trials have demonstrated Magseed offers equivalent accuracy to the use of radioactive localization, it has the obvious benefit of being easier to handle. According to Stephens, “Some very, very big centers that do 2,000 [radioactive] seed procedures per year” are looking to convert to Magseed.

The benefits will increase once the Sienna injectable tracer receives approval. “It increases the appeal significantly. There are companies that offer lesion location and others offering lymph node localization. But no one does both in a single box,” Stephens said. “It will be a game changer.”

After injection 20 minutes before surgery, Sienna flows to the lymph nodes draining from the primary tumor site. That makes it possible to find the closest lymph node and remove it for biopsy at the same time as tumor.

If the subsequent analysis indicates the node is cancerous, radiotherapy or chemotherapy can be administered. If not, a patient is spared debilitating, unnecessary and expensive treatment.

Stephens said Cambridge, U.K.-based Endomag is well-placed to apply the new funding. “The nice thing is, hospitals are contacting us. In 15 years in med tech, it’s the first product where I’ve known that to happen,” he said.

The evaluations involve a two week “test drive” where hospitals switch to using only Magseed. “They get a feel of what life is like going wire-free and realize the amount of time it frees up,” Stephens said.

The \$10 million series C brings the amount raised by Endomag since it spun out of University College London in 2007, to \$22

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Mathew Stephens
Commercial director, Endomag Ltd.

million. The round was led by Draper Esprit, the European division of the Silicon Valley VC firm, Draper Venture Network.

“The round was a bit larger than we planned. It was a different environment from in the past, due to the more advanced stage of the company. Now we are not just into revenue, but into profit,” said Stephens.

Endomag also is working with clinicians to apply Magseed to the localization of other tumor types.

That follows an expanded FDA clearance, granted in February, allowing Magseed to be used for longer than 30 days and to be implanted in any soft tissue. (See *BioWorld MedTech*, Feb. 23, 2018.)

Last week, the Magseed/Sentimag combination was used for the first time in surgery to treat sarcoma, in a procedure carried out at MD Anderson Cancer Center. In this case, four Magseeds were used to delineate the perimeter of the tumor.

With advances in lung cancer screening, localization of lung nodules is another area where Magseed could improve treatment. “We have talked to companies with a number of visualization techniques . . . but no way of marking what they see to guide surgeons later on,” Stephens said. Now there is the potential to pair Magseed with minimally invasive endoscopic surgery to ease the removal of lung nodules.

However, the immediate focus will be on growing and consolidating the breast cancer franchise, and introducing Sienna into the mix, once approved.

“We are looking at other applications, working with a number of clinicians. But first we want to go for the expanded indication in breast cancer,” said Stephens. ♦

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Watson Health

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publicly available data on their efforts remain pending.

Watson Health has been under fire, of late, after widespread reporting on layoffs that left some in the media questioning the vigor of the group, but that the company itself has chalked up as synergies in the wake of a string of major acquisitions.

Healthy AI?

In a second-quarter earnings call on July 15, IBM offered some reassurances on Watson Health, but it does not breakout sales for the unit and only characterized it as having “good growth.” Overall, IBM revenue was up 4 percent during the second quarter over the same period last year to \$20 billion.

“In Watson Health, we had good performance in areas like payer and life sciences,” said IBM SVP and CFO Jim Kavanaugh on the call.

In response to an analyst query on the skeptical media reports about Watson Health, he only added, “We got growth in the life sciences segment, imaging, payer and we’re seeing good SaaS (software as a service) signings in our government segments within that business. Yes, we are driving acquisition synergies, and you’re seeing that play out.”

The Watson Health-VA deal is specifically for the use of Watson for Genomics. Under it, a VA physician takes a tumor sample from a cancer patient and sends it to a qualified lab for analysis of genetic mutations. The physician then receives a report based on an artificial intelligence (AI) analysis of medical literature and treatment guidelines that advise on the best specific treatment or clinical trial for that patient.

There are a few limitations to this approach. One is that, unless it’s part of a published study, patient outcomes data from EMR analytics are not included. That’s the sort of AI analytics conducted by competitor Flatiron Health, which was acquired outright recently by partner Roche AG. Ultimately, treating current patients based on documented outcomes for previously treated patients with similar tumor genetic profiles is expected to be the gold-standard in this field.

Last option

Still, systematically interrogating the medical literature and guidelines can be beneficial, particularly for patients who are being treated at facilities that are not cutting edge research hospitals, as is the case for many of the VA cancer patients.

Interestingly, the VA partnership remains confined only to solid tumor patients who have stage IV cancer or later. These patients have often run out of treatment options.

“If you think about stage I, II and III, there is often a strong amount of evidence-based treatments that are available to people that are effective,” Kyu Rhee, chief health officer for IBM Watson Health, told *BioWorld MedTech*. “So, this does primarily support stage IV cancer patients who have typically exhausted other treatment options, where you’re looking for unique studies, unique therapeutic options, that are connected to the unique genetic mutations that are connected to the tumor.”

Rhee said that the VA and Watson Health are working to publish

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So, this does primarily support stage IV cancer patients who have typically exhausted other treatment options, where you’re looking for unique studies, unique therapeutic options, that are connected to the unique genetic mutations that are connected to the tumor.

Kyu Rhee

Chief Health Officer, IBM Watson Health

and present data from their partnership later this year. He noted a study by Guangdong Lung Cancer Institute in China and Watson for Genomics that was presented at the American Society of Clinical Oncology meeting in Chicago in June, which found that the AI system matched the tumor board treatment recommendations for 43 percent of lung cancer cases, but that in the remaining 57 percent of cases Watson found an average of an additional 1.54 relevant mutations that had been missed.

Another study, published in *The Oncologist*, was a retrospective analysis of more than 1,000 patient cancer cases treated at the University of North Carolina’s Lineberger Comprehensive Cancer Center. It found that 99 percent of the time, Watson agreed with the physician’s treatment decisions, but that in more than 300 cases it offered clinical actions that the doctor had not.

The VA partnership offers a quintessential opportunity for Watson Health to prove its case, when it does produce data. It has the largest group of cancer patients of any health care group in the U.S., with 3.5 percent of the nation’s cancer patients.

“Our mission with VA’s precision oncology program is to bring the most advanced treatment opportunities to veterans, in hopes of giving our nation’s heroes better treatments through these breakthroughs,” said Acting VA Secretary Peter O’Rourke. “We look forward to continuing this strategic partnership to assist VA in providing the best care for our veterans.” ♦

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ABI

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patients, but the authors of an editorial noted that many patients with PAD are asymptomatic, a predicament that seems certain to allow the disease to fester until drastic and expensive measures are necessary.

The task force noted that the data for use of the ABI as a screening tool for both peripheral artery and cardiovascular disease was sparse. The authors said they had located two good-quality studies identified to characterize the benefits of daily aspirin use in unselected populations, which failed to demonstrate any benefit. The two studies for exercise therapy likewise came up short of demonstrating any benefit, leaving the underlying recommendations unchanged from 2013, the previous review of the question.

The authors noted that survey data from 1999-2004 suggest that roughly 6 percent of Americans aged 40 and older had an ABI of 0.9 or lower, which is seen as indicative of PAD. However, the authors acknowledged that the true incidence is difficult to establish due to the fact that half these patients are either asymptomatic or present with atypical symptoms. Likewise problematic is the absence of a gold standard test for population screening, and the data, perhaps predictably, offer no evidence of benefit for screening and early detection of PAD with regarding to prevention of disease advancement or prevention of downstream cardiovascular disease.

While the harms associated with false positives include the use of contrast agents with any one of several imaging modalities, study data suggest that 7 percent of those with asymptomatic PAD intermittent claudication, and 1 in 5 of those with claudication will go on to develop critical limb ischemia. The five-year incidence of cardiovascular mortality for those with asymptomatic disease and a low ABI measurement was estimated at 9 percent, nearly double the rate of 5 percent in those with a normal ABI. There was a 13 percent incidence of five-year cardiovascular mortality in symptomatic patients with a low ABI as well.

The paper called for large, population-based, randomized studies of screening, and the authors said that three ongoing studies might provide information but for several confounders, including that screening for abdominal aortic aneurysm is also part of one of the studies in question. One of the ironies of the report is that Future Market Insights Inc. (FMI), has predicted that the market for stents for the peripheral vasculature will nearly double over the next decade. FMI said the global market is expected to grow by an average of 6.6 percent annually between now and 2028, rising to \$5.3 billion, with the North American market expected to account for nearly 49 percent of this volume.

The Society for Vascular Surgery (SVS) said in comments to the draft task force report that the association agreed that the evidence fails to support a recommendation regarding screening in asymptomatic patients. The Feb. 9, 2018, SVS letter said, however, that the interpretation of this test in some patient sub-groups “is not well understood or established.” SVS said the hazards associated with over-diagnosis and over-

testing “include invasive treatments” and the potential adverse events associated with those treatments, such as critical limb ischemia triggered by treatment-related restenosis. The letter said that asymptomatic patients with abnormal ABI readings do not typically require invasive treatment.

However, SVS said that development of an understanding of high-risk patient groups that would be screened for PAD “is likely to be more focused and patient-centered, as well as cost-effective, with appropriate benefit-to-risk ratios.” Among these are those with diabetes or histories of coronary artery disease and related treatment. ♦

Daily M&A

Durham, N.C.-based **Bioventus** entered a definitive agreement to divest its next-generation bone morphogenetic protein (BMP) development program to a new company formed by **Viscogliosi Brothers LLC**, a New York private equity investment firm focused on developing neuromusculoskeletal technologies. Bioventus acquired the exclusive, worldwide license to the BMP portfolio of development programs and associated intellectual property from New York-based **Pfizer Inc.**, in 2013.

Product briefs

Biocept Inc., of San Diego, said it will work with **Moore's Cancer Center** at UC San Diego Health to conduct two clinical studies in patients with a variety of solid tumors. These studies will use Biocept's Target Selector liquid biopsy assays to detect circulating tumor cells (CTCs) and circulating tumor DNA and compare results with findings from CT or PET scans. The first study is designed to determine the feasibility of using liquid biopsy to predict disease recurrence in patients with stage II or III cancer at high risk for recurrence. The second study will evaluate the feasibility of using liquid biopsy to predict response to therapy in patients with metastatic solid tumors. The studies will focus primarily on CTC biomarkers in patients diagnosed with breast, lung and colon cancer.

Medicalgorithmics SA, of Warsaw, Poland, and U.S. subsidiary **Medi-Lynx Cardiac Monitoring LLC**, said the U.S. FDA has granted 510(k) clearance for the PocketECG cardiac rehabilitation system, a smartphone-sized device designed to provide high-quality electrocardiography (ECG) monitoring and automated arrhythmia detection during rehabilitation training. The device is currently approved and marketed in the EU.

Neumodx Molecular Inc., of Ann Arbor, Mich., received FDA 510(k) clearance for its automated Neumodx 288 molecular system and its Neumodx GBS assay, a qualitative in vitro diagnostic test designed to detect Group B *Streptococcus* (GBS) DNA in pregnant women. The Neumodx 288 molecular system can run up to 288 patient samples in a continuous random-access mode. It uses dry format reagents, which require no refrigeration with an on-board stability of greater than 60 days and ambient temperature storage shelf life of greater than one year.

IPRs

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IPR challenges.

In writing the unanimous decision handed down Friday in *Saint Regis Mohawk Tribe v. Mylan Pharmaceuticals Inc.*, Federal Circuit Judge Kimberly Moore concluded, “In this case, we are only deciding whether tribal immunity applies in IPR. While we recognize there are many parallels, we leave for another day the question of whether there is any reason to treat state sovereign immunity differently.”

Much of the analysis and case law the three-judge panel cited in reaching its decision applied to “sovereign immunity” – not just tribal sovereign immunity. For instance, the Federal Circuit leaned on *Federal Maritime Commission (FMC) v. South Carolina State Ports Authority*, a state sovereign immunity case in which the Supreme Court distinguished between adjudicative proceedings brought against a state by a private party and federal agency-initiated enforcement proceedings.

In his concurring opinion, Federal Circuit judge Timothy Dyk wrote, “Under FMC, it is clear that sovereign immunity cannot bar agency denial of an original patent application filed by a sovereign entity or, consequently, agency reconsideration of an original patent grant. Such reconsideration simply does not involve agency adjudication of a private dispute, but rather agency reconsideration of its own prior actions.”

Dyk traced the history and need for post-grant patent reviews, characterizing an IPR as “an agency reconsideration rather than an adjudication of a private dispute.” As such, an IPR doesn’t “implicate sovereign immunity,” Dyk said.

His assessment of what an IPR is echoed Moore’s decision. Citing the Supreme Court’s recent *Oil States* opinion, Moore said the high court “recognized that IPR is ‘simply a reconsideration of’ the PTO’s original grant of a public franchise, which serves to protect ‘the public’s paramount interest in seeing that patent monopolies are kept within their legitimate scope.’”

However, the Patent Trial and Appeal Board (PTAB) has routinely exempted patents owned by state universities from IPR challenges on the basis of sovereign immunity. It is that practice that led to the Saint Regis Mohawk Tribe acquiring patents and then licensing them back to companies as a way to diversify its revenue streams to support tribal programs and community services. (See *BioWorld MedTech*, Sept. 20, 2017.)

One of those licensing deals was with Dublin-based [Allergan plc](#) and involved six patents protecting blockbuster dry eye drug [Restasis](#) (cyclosporine). Several generic drug companies were already challenging the patents through the IPR process when Allergan transferred the patents to the tribe and then licensed them back.

Although the U.S. Court of Appeals for the Federal Circuit skirted the state sovereign immunity question in Friday’s decision, it is a question the court may have to answer soon in the form of *Ericsson Inc. v. University of Minnesota*. In that case, the PTAB ruled that the university had waived sovereign immunity from an IPR challenge when it prosecuted the

patents in court. The analysis the Federal Circuit used in *Saint Regis* could be raised in *Ericsson* to question whether states ever have sovereign immunity from IPRs.

Regardless of *Ericsson*, the Federal Circuit may not have the last word on what boils down to a constitutional issue and the definition of an IPR. Dale White, general counsel for Saint Regis, told *BioWorld MedTech* that the tribe is reviewing the appellate court’s decision with its attorneys and considering further appeals. He said the tribe was “very disappointed” with the decision and “fundamentally disagrees” with the court’s characterization of IPRs. ♦

Product briefs

Owen Mumford Ltd., of Oxford, U.K., acquired exclusive rights to sell and distribute the rapid diagnostic HIV test, Simplitude Pro HIV across Europe. Simplitude Pro HIV is a rapid diagnostic test with a built-in safety lancet, blood collection unit and strip test. The company said it will be available to the European market in early 2019.

Perflow Medical Ltd., of Tel Aviv, Israel, reported the first clinical cases of the Cascade dynamic non-occlusive remodeling net, which occurred earlier this month at Hospital Vall d’Hebron in Barcelona, Spain. The Cascade device provides mechanical support during coil embolization of intracranial aneurysms.

Other news to note

Bridge Medicines, of New York, reported an agreement with **Memorial Sloan Kettering**, also of New York, to develop a platform designed to deliver drugs specifically to the kidney. The first disease target will be acute kidney injury.

San Francisco-based **Idigital** reported in partnership with **Zazmic Inc.** the release of a diagnostic radiology cloud-based digital assistant platform (DAP), which will be fully integrated with Google’s artificial intelligence and machine learning technologies. DAP is designed to remove the current “conveyor belt workflow” found in health care systems. Zazmic is also of San Francisco.

I-Med Pharma Inc., of Montreal, has signed an exclusive agreement with **Medicals International**, of Mansourieh, Lebanon, for distribution rights in the Middle East for its patented I-Pen tear osmolarity system. The system offers eye care professionals a tool for screening dry eye patients.

Horsham, Pa.-based **Strata Skin Sciences Inc.** reported a fully paid exclusive and perpetual license agreement with a strategic entity for a deidentified digital image library of pigmented lesions and their related documentary information. The deal relates to the company’s discontinued Melafind device. Strata retains all intellectual property rights related to the Melafind device and product line, including patents, design files and PMA approval. The strategic entity will be allowed exclusive rights to the deidentified digital images.

Medtronic

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(NCT02811302). Its objective is to develop a predictive model to identify those at risk of experiencing these episodes while monitored by capnography. Specifically, it is examining the value of continuous Microstream capnography and Nellcor oximetry monitoring. Preliminary findings have been published in an article titled “Respiratory depression in low acuity hospital settings—Seeking answers from the PRODIGY trial,” which appeared June 18, 2018, in the *Journal of Critical Care*.

While a number of researchers have tried to confront the OIRD problem, one group has tackled the issue head on for years. “We at the Cleveland Clinic did a series of smaller studies [in which] we identified the scope of the problem,” Ashish Khanna, an anesthesiologist at the Cleveland Clinic, told *BioWorld MedTech*, adding that larger groups, as well as database analyses, have evaluated the issue.

All of the evidence has led to a push by experts for continuous monitoring moving forward. “I share this vision. I do believe in the next five to 10 years, we are looking at an era [in which] every patient should be able to walk into a hospital and get a Fitbit, or an Iwatch, or . . . a smart device,” Khanna said. “That device should be able to monitor that patient all through [his or her] hospital stay, and even a few days [after] going back home.” Having such monitoring could allow for the identification of signals of respiratory depression hours ahead of time, Khanna added, as he likened technology watching patients for signs of the condition to a black box helping identify the reason for a crash.

He noted that once all of the data have been gathered and a predictive score and algorithm identified, he and his colleagues will push for a continuous monitoring solution on the hospital floor that is portable, so that it does not add a burden to patients. He also wants to create a “smart” floor with different levels of monitoring for varying levels of patient risk. An “intelligent” central monitoring system also needs to be in place to filter out the noise and false alarms.

Ultimately, Khanna hopes that device companies will develop intelligent monitors that do not add to the noise on hospital floors.

Years in the making

Looking back, Khanna noted that in the 2013/14 time frame, “we put all our patients who were recovering from surgery on the regular floor on continuous monitoring, but we blinded the bedside nurses and the health care providers to those monitors,” he explained. In addition, the group silenced the alarms and covered the faces of the monitors. Although the monitors were continuously collecting data, everyone was blinded to that. At the same time, nurses were still doing their four-hour vital sign check.

“What we uncovered . . . was that up to 90 percent of patients in that cohort had hypoxemia,” or an abnormal oxygen saturation. “That period of hypoxemia lasted for at least an hour in a 48-hour monitoring period. Now, this is again not to say that

Cleveland Clinic is not doing a good job of monitoring its patients post-operatively when they go to the floor to recover,” Khanna explained. Rather, no one knew how pervasive the problem of hypoxemia was in between spot checks. The group published its findings, and Khanna continued his research into the area, looking at obstructive sleep apnea patients, who, as a group, are more likely to have post-operative complications. In addition, he looked at the nature and kind of pain medication used.

After a series of papers, the group determined that “respiratory depression, as defined by hypoxemia, is common,” said Khanna. However, “we did not find a clear relationship in the most obvious predictors for respiratory depression, as defined by hypoxemia.” Further muddying the waters is that respiratory depression is not just defined by hypoxemia, he added. It also is defined by hypoventilation, or taking shallow breaths, as well as hypercapnia, or excessive carbon dioxide in the bloodstream. “It can also mean an indirect effect on the heart, which would translate either into bradycardia . . . or tachycardia,” he explained.

With all of this in mind, the researchers wanted to look beyond hypoxemia and examine a combination of oxygen saturation, respiratory rate, end tidal carbon dioxide and heart rate. “And that’s where the PRODIGY trial came in,” Khanna said. “The PRODIGY trial uses Medtronic plc’s Capnostream monitor, which had all of the four monitoring parameters.”

As part of the study, researchers used continuous, blinded monitoring, but went beyond post-surgical subjects to examine medical patients, as there is no literature on why they can decompensate cardiovascularly and respiratory-wise. The roughly 1,500 patients were put on 48 hours of continuous, blinded monitoring with Capnostream. “[This] was really an amplification of the initial hypoxemia work we had done at the [Cleveland] Clinic, but this was taking it to another level, because we had four different mechanisms to understand respiratory depression,” he said.

The previous work also was amplified in that patients from the U.S., Europe and Asia were being assessed, giving the researchers an insight into cultural and regional differences in treating respiratory depression. Further, all patients had to be on intravenous or epidural opioids for inclusion in order to allow researchers to assess the role of pain medication on respiratory depression. “We’re fortunate to have 16 of the leading academic medical centers throughout the world that helped us with the trial and helped us enroll a very representative patient population,” Khanna added.

When asked whether he anticipated additional studies in this area, Khanna noted that he expected a number of secondary analyses associated with PRODIGY, including one evaluating costs and benefits for additional smart monitors. “[W]e’re hoping that out of the about 1,500-odd patients, we should be able to get actual cost data on at least 50 percent,” he said. That data could shed light on the expense of additional monitoring and whether that cost is justified. In addition, the researchers are interested in pattern detection to identify those in distress, as well as understanding of a clustering of events. ♦

Solaris

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pressure intensity mercury vapor that generates enough UV radiation to eliminate approximately 50 percent of the pathogens in hospital rooms. That's nowhere good enough, said Solaris COO Adam Steinhoff.

"The advantage here is that by using a pulsed UV disinfection system, you're able to reduce the pathogen load in the room making the environment safer for patients," Steinhoff told *BioWorld MedTech*. "Our clients in the U.S. are very happy. People believe in the technology."

A blast multiplier

Following the manual clean of a hospital room, mercury-based disinfection systems launch a continuous, single wave of ultraviolet radiation at pathogenic DNA on high contact surfaces; by contrast, the Lytbot uses heat generated by UV light to destroy thicker cell wall organisms such as the deadly *C. difficile* spore. Steinhoff likens it to the enormous heat that builds up inside a black car sitting outside in July.

"On a cellular level where water is present, high heat causes the cell to expand and eventually rupture," Steinhoff said. The efficacy of that approach is supported by third party labs using this system, Steinhoff added, and "published studies about mercury UVC systems that show stronger outcomes utilizing our technology."

What Steinhoff's customers also like, he said, are quick three-to five-minute cycle times. That compares with the 20 to 40 minutes mercury needs to disinfect a room, Steinhoff said. "That just isn't practical in a health care setting. The longer you don't have a patient in a room, it's bad for revenues and hospital efficiency."

Steinhoff said many of his competitors fix stationery disinfection systems in the middle of a hospital room so that light "shoots out in all directions indiscriminately." By contrast, the Lytbot uses a rotating robotic head to blast pathogen-killing light in a 360 degree sweep of the room.

"Eighty to ninety percent of the pathogen load is on high touch surfaces between your knee and your shoulder. We're making an extra effort to hit those surfaces with as much energy as possible."

In the hands of health workers, disinfection equipment gets

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The advantage here is that by using a pulsed UV disinfection system, you're able to reduce the pathogen load in the room making the environment safer for patients.

Adam Steinhoff
COO, Solaris Disinfection Inc.

banged about, Steinhoff added. "That's why we make sure these things stand up to the test of time," building the device's outer shell of tough rotomold plastic for consistent wall thickness and strong, thick corners.

Worth the cost?

Approximately 24 Lytbot units are at work disinfecting rooms in U.S. hospitals. Not so in Canada where experts in infection control question the efficacy of pulse UV disinfection in relation to the costs. Allison McGeer, director of infection control at Toronto's Mount Sinai Hospital, said evidence suggests UV light works but that a simpler and more cost effective solution may be to manually clean a room twice rather than purchase costly new equipment.

"Until these technologies become less expensive, I'm probably not going to use them in my hospital," McGeer told *BioWorld MedTech*. "Now, if somebody comes out with better data showing that some of this technology is better than my less expensive and more boring cleaning disinfection, that would change my mind."

For his part, Steinhoff noted the Lytbot is just over half the roughly US\$100,000 it costs to buy other pulsed UV and mercury-based disinfection systems. He also responded to concerns that UV pulse rates above 5 Hz may trigger seizures in the event someone enters the room while the technology is at work. "Our pulse rate is above that. That's why we have motion detectors on the door to ensure that if the door is opened to the room (the Lytbot) shuts down."

Entirely self-financed, Solaris has spent nearly US\$8 million developing the technology. Canada's reluctance to fully embrace pulsed UV disinfection, he said, has forced him and his colleagues to focus their attention on broadening their presence in the U.S. market. ♦

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Cardiology Extra

Keeping you up to date on recent developments in cardiology

By Liz Hollis, Staff Writer

Exercise helps heart even with poor air quality

New research is pointing to the benefits of exercise for the heart, even in areas with moderate-to-high levels of traffic pollution. In fact, regular physical activity can reduce the risk of first and recurrent heart attack, according to the article “Effects of leisure-time and transport-related physical activities on the risk of incident and recurrent myocardial infarction and interaction with traffic-related air pollution: A cohort study.” The research was published July 18, 2018, in the *Journal of the American Heart Association*. Researchers in Denmark, Germany and Spain evaluated outdoor physical activity levels and nitrogen dioxide (NO₂) exposure in 51,868 adults between the ages of 50 and 65. They compared self-reported activities and lifestyle factors against heart attack, finding that over a 17.7-year period, there were 2,936 first heart attacks and 324 recurrent ones. While higher levels of NO₂ exposure were associated with more heart attacks, the risk was lower in those who were physically active. “Our study shows that physical activity even during exposure to air pollution, in cities with levels similar to those in Copenhagen, can reduce the risk of heart attack,” Kubesch said. “Our research supports existing evidence that even moderate levels of regular physical activity, such as active commuting, are sufficiently intense to get these health benefits.”

Company unveils human iPSC-derived atrial cardiomyocytes

Cambridge, U.K.-based Axol Bioscience Ltd. launched human induced pluripotent stem cells (iPS)-derived atrial cardiomyocytes for the discovery and development of treatments and advancing the understanding of cardiovascular disease. Generated from the same donor as Axol’s highly validated human iPSC-derived ventricular cardiomyocytes, this cell line is quick and easy to use, ready in just seven days from thaw, for electrophysiology, cardiac contractility study, screening and the investigation of cardiomyopathies. “We are delighted to announce the launch of Axol’s atrial cardiomyocytes. We are proud to say that they are the first and only iPSC-derived atrial cardiomyocyte product currently available to the research market,” said Yichen Shi, CEO of Axol Bioscience. “These cells will provide researchers with a quick and easy to use platform for studying human atrial muscle cells, creating models of atrial-specific diseases, and later developing assays for identifying disease modifying treatments.”

Investigational medicine for Parkinson’s strengthens heart contractions in animals

A drug candidate being evaluated for treating symptoms of Parkinson’s disease could hold promise for treating heart failure, according to results of early animal studies by Johns Hopkins Medicine researchers. The candidate is a

phosphodiesterase type I (PDE1) inhibitor and apparently shows promising effects in dogs and rabbits. Their findings were described in the journal *Circulation* July 20, 2018, in an article titled “Acute enhancement of cardiac function by phosphodiesterase type 1 inhibition: A translational study in the dog and rabbit.” In the article, Johns Hopkins researchers demonstrated that the new compound works differently than current offerings, suggesting that it may increase heart contraction strength in a safer manner. “Our results are intriguing because so far it’s been largely uncharted territory to come up with a way of increasing contractility that doesn’t ultimately hurt patients,” said David Kass, the Abraham and Virginia Weiss Professor of Cardiology at the Johns Hopkins University School of Medicine and principal investigator of the study. The drug explored in the new study, ITI-214, inhibits the enzyme PDE1. These inhibitors have shrunk abnormally thick heart muscle caused by high blood pressure and dilated blood vessels in mice. Dogs and rabbits have a PDE1 composition more similar to humans, Kass said. Researchers used six dogs surgically outfitted with sensors and heart pacemakers, and tested ITI-214’s effects before and after inducing heart failure. When given at an oral dose of 10 mg for every kg via a peanut butter-covered pill, ITI-214 increased the amount of blood pumped out by the heart each minute by 50 percent in the healthy hearts and by 32 percent in the failing hearts. Heart failure affects about 5.7 million U.S. adults, according to the CDC.

3D model of left ventricle could help develop treatments

Harvard University researchers have developed a 3D model of a human left heart ventricle. It is hoped that this development could be used to study diseases, test drugs and develop patient-specific treatments for heart conditions. The tissue was engineered with a nanofiber scaffold seeded with human heart cells. The scaffold aims to guide the cells and their assembly into ventricle chambers, allowing researchers to study heart function using many of the same tools found in the clinic. “Our group has spent a decade plus working up to the goal of building a whole heart, and this is an important step towards that goal,” said Kit Parker, senior author of the study. “The applications, from regenerative cardiovascular medicine to its use as an in vitro model for drug discovery, are wide and varied.” To recreate that scaffold, the researchers used a nanofiber production platform known as pull spinning, which utilizes a high-speed rotating bristle that dips into a polymer reservoir and pulls a droplet from the solution into a jet. The fiber travels in a spiral trajectory and solidifies before detaching from the bristle and moving toward a collector. Their research is published July 23, 2018, in *Nature Biomedical Engineering* in the article “A tissue-engineered scale model of the heart ventricle.”