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DEATHS LINKED TO DEVICE

Spectranetics eyes quick response to warning letter over validation issues, recordkeeping

By Liz Hollis, Staff Writer

In the wake of an FDA warning letter that highlighted complaints of sparks and visible light during the operation of a laser system and an unspecified number of deaths reported with its devices, Colorado Springs, Colo.-based Spectranetics Corp. said it intends to respond "timely and fully" to the agency by Friday.

"We believe that the response will primarily involve updates in processes and documentation and will have no material impact on our business," a Spectranetics spokesperson told *Medical Device Daily*.

In a note, Stifel analysts wrote that company "has already begun to address several of the outstanding, initial 483 inspection-related citations," citing conversations with

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ASCO 2016

Study validates BCI prognostic model for some breast cancer patients

By Amanda Pedersen, Senior Staff Writer

CHICAGO – Because of the higher risk of recurrence in lymph node-positive breast cancer, oncologists often recommend more aggressive therapeutic regimens for these patients, such as extending anti-estrogen therapy for five additional years after they complete the first five years. Validated tools to help guide this treatment decision have been lacking,

See BCI, page 4

REGULATORY

Ontario HTA recommends kyphoplasty be covered for group of cancer patients

By Mark McCarty, Regulatory Editor

Health technology assessments continue to pile on from an ever-widening range of sources, and Canada's Health Quality Ontario (HQO) has published a recommendation that kyphoplasty and vertebroplasty be covered for some cancer patients with vertebral compression fractures.

See Cancer, page 5

STATE-OWNED COMPANIES EVEN BEING SOLD

China's med-tech industry seeing further consolidation in bid to spur sector growth

By Haky Moon, Staff Writer

HONG KONG – Med-tech companies in China have recently been on an M&A spree, with both businesses and government playing an active role in the sector.

In an effort to shore up growth in a slowing medical device industry, domestic companies are pushing for M&As to create growth. At the same time, Chinese authorities are supporting moves by larger companies to acquire smaller ones in an attempt to find a leading household name for its fragmented industry, which is also becoming more highly regulated.

"Indigenous companies are increasingly buying up other companies to expand into new fast growing product areas to offset a slowdown in their core businesses," said

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IN THIS ISSUE

FINANCINGS

Airxpanders Inc., of Palo Alto, Calif., received commitments from investors to subscribe for 26,315,790 CHESS Depositary Interests (CDIs) (representing 8,771,930 shares of Class A Common Stock) at a 76 cents per CDI to raise a $20 million placement. The placement was significantly oversubscribed, with strong demand from existing and new institutional funds, both domestically and overseas.

Nanthealth Inc., of Culver City, Calif., closed its initial public offering of 6.5 million shares of its common stock at a price to the public of $14 per share (which reflects a 1-for-5.5 reverse stock split of Nanthealth's common stock effected in connection with the conversion of the company from a limited liability company to a corporation). In addition, Nanthealth has granted the underwriters a 30-day option to purchase up to an additional 975,000 shares of its common stock.

Nevro Corp., of Redwood City, Calif., reported the pricing of its public offering of $150 million aggregate principal amount of 1.75 percent convertible senior notes due 2021. In addition, Nevro granted the underwriters a 30-day option to purchase up to an additional $22.5 million aggregate principal amount of such notes to cover any over-allotments. J.P. Morgan and Morgan Stanley are acting as joint book-running managers for the offering. Leerink Partners and JMP Securities are acting as co-managers. Nevro intends to use about $21 million of the net proceeds to repay in full an existing term loan agreement, including the associated closing and repayment fees, with Capital Royalty Partners and certain of its affiliates. Nevro plans to use any remaining proceeds for general corporate purposes, which may include continuing commercialization of its Senza spinal cord stimulation system, funding research and development and increasing working capital.

Omicia Inc., of Oakland, Calif., completed a $23 million series B financing round. Several new investors participated in the round, including UPMC Enterprises, Roche Venture Fund, LDV Partners, Ping An Ventures, and a large genomics investor, as well as existing investors Artis Ventures, Acadia Woods Partners and Buchanan Investments. Omicia's latest financing will be used to fuel acceleration in product development and an expansion in sales, sales support, marketing and operations.

APPOINTMENTS AND ADVANCEMENTS

DNA Diagnostics Center, of Fairfield, Ohio, reported that Robert Bosley is the new executive vice president and chief financial officer. He replaces John Srsen, who is retiring. Prior to joining DDC, Robert was a senior vice president of finance for Serta Simmons Bedding and was responsible for managing the budgeting, forecasting and long range planning processes, providing insightful business analyses and leading transformation initiatives for the company. Srsen is retiring after more than seven years as CFO of the DNA testing firm.

Ann Arbor, Mich.-based **Hygieia**, a digital insulin enhancement company reported that John Brooks III has joined the company's board. Brooks currently serves as president and chief executive officer of Arete Worldwide, LLC, a consulting firm that provides services to a global network of partners and academic experts working together to drive disruptive solutions that address the obesity, pre-diabetes, and diabetes pandemics. He also is a managing director at Healthcare Capital, LLC.

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Spectranetics

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management. Further, the company should be able to resolve the issues "in a matter of weeks to months, rather than years." The note added that none of the issues have an impact on the company's Vascular Intervention business, specifically Stellarex and Angioscore.

The heavily redacted warning letter followed an inspection that took place between Nov. 30, 2015 and Jan. 21, 2016 at the company's Colorado Springs, Colo. facility. The company sought to address the agency's concerns in a Feb. 10 response to a Form 483, and added some clarifying remarks in a March 31 follow up.

The process that particularly caught the FDA's attention is used to manufacture part of the outer jackets subassembly of the Glidelight and SLS Laser Sheath finished devices (sizes 12F, 14F, and 16F). These devices are used in conjunction with the Excimer Laser System for pacemaker and defibrillator lead removal.

"This laser system includes a Class IV laser and part of the function of the outer jackets is to house and contain the laser," the letter stated. "Complaints have been reported for failures such as cracks, splits, damage to the outer jacket and/or sparks and visible laser light through the outer jacket."

The letter added that a company representative and an agency inspector discussed its "30-DAY NOTICE ELCA Coronary Atherectomy Catheters and SLS Spectranetics Laser Sheaths (PMA P910001 and PMA P960042) Alternative Extrusion Equipment." According to that notice, extruded parts will undergo certain verification because validation was not feasible. The inspector took issue with the company's explanation that extruded parts are examined using a redacted process.

The FDA found Spectranetics' Feb. 10 response to the problem inadequate, adding that it does not provide specifics on how the process will be validated.

The letter also stated that the company failed to review and update risk management documents as new information become available. A redacted number of deaths have been reported during procedures involving the Glidelight Laser Sheath/SLS devices since August 2014. The FDA takes issue with the highest applicable risk severity rating listed in the risk analysis, particularly given the number of deaths and complaints.

After reviewing the company's responses, the FDA deemed them inadequate. For example, the company did not discuss the investigation or other steps eyed to ensure the risks are mitigated.

The FDA also pointed out that the company's surgical laser systems are electronic products and thus subject to compliance with Subchapter C of the Act, Electronic Product Radiation Control, the requirements at 21 CFR 1000-1005, and the performance standards at 21 CFR 1010, 1040.10, and 1040.11. However, the company did not comply with regulations covering product safety, reports, and recordkeeping.

The letter hits the company's quality control testing program, saying it is inadequate to prevent unnecessary access to radiation.

The FDA has deemed the Feb. 10 response to this finding inadequate, because it was based on the interpretation that a laser component registration was required. "Such registration does not address the adequacy of your firm's finished product quality control testing program upon which the product certification should be based," according to the letter.

In addition, the company failed to submit the required Accidental Radiation Occurrence reports, including instances in which the outer jacket of the fiber catheter sheath was damaged causing visible light, sparks, and minor burns. However, the company subsequently submitted the AROs in question to CDRH.

There are bright spots in the warning letter, particularly when it comes to Spectranetics documenting its CAPA procedures. It highlights one document that the inspector found did not include requirements for verifying or validating the effectiveness of a corrective or preventive action. The document also didn't ensure "that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems." As a result, a number of CAPA records are deficient.

Spectranetics has laid out a CAPA procedural update to the FDA that appears adequate to the agency and will be assessed at its next inspection.

In addition, the company's implementation of procedure updates for quality reaudits appeared to pass FDA muster. The company had not completed a scheduled postmarket surveillance for cause audit in 2013, explaining that a March 2013 FDA inspection focused on complaint handling. The agency will assess the company's procedural updates during its next inspection. //

BCI

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but new data presented this week at the American Society of Clinical Oncology's (ASCO) annual meeting has the potential to make a difference for this patient population.

According to a study that evaluated a new Breast Cancer Index (BCI) prognostic model specifically developed for estrogen receptor-positive breast cancer patients with one to three positive lymph nodes, the test can now predict the risk of distant recurrence from diagnosis through 15 years for early-stage patients in this category. The prognostic component of BCI was previously only validated for node-negative patients. The study found that 20 percent of these patients had a recurrence risk of less than 1.5 percent, out to 15 years.

"Before this data was released, basically all the patients with [estrogen receptor-positive breast cancer and one to three positive lymph nodes] had to be considered high risk for recurrence," Nicolas Berthel, president and CEO of Biotheranostics Inc., told *Medical Device Daily* at ASCO. "It was a crude measure, but we didn't know how to quantify that."

The San Diego-based company developed BCI as a molecular, gene expression-based test to help identify patients best suited for extended endocrine treatment. The test is designed to predict a patient's prognostic risk of recurrence and the likelihood that they will benefit from extended endocrine therapy (treatment in years five through 10). The company said the test helps oncologists and patients consider the trade-off between wanting to prevent recurrence of the disease and the side effects associated with extended endocrine therapy.

But a third of patients with estrogen receptor-positive breast cancer are lymph node-positive, Berthel said, so prior to this new BCI prognostic model, "a third of patients were not getting the full benefit of the options the test can offer."

In other words, he said, a third of patients had to be treated as if they had a high risk of recurrence. "Now we can better stratify and, as a result, offer more individualized care for patients."

Previously, in a study of 209 estrogen receptor-positive patients with between one and three positive lymph nodes from the landmark TransATAC trial, the BCI algorithm was optimized by incorporating tumor size and grade to develop a new BCI prognostic model specifically for patients with lymph node-positive breast cancer, Biotheranostics said.

The company said the objective of its latest study, which was blinded, was to independently validate the new BCI algorithm and prognostic model in a large cohort of 402 hormone receptor-positive patients with one to three positive nodes. The data allows the company to further support doctors on the prognostic side of breast cancer, Berthel said.

In another ASCO presentation in this category, Hongchao Pan, of the Nuffield Department of Population Health at the U.K's Oxford University, shared the results of a study that also looked at the benefits and effects of extending endocrine therapy for five more years (years five through 14). Pan noted that knowledge of the effects of prognostic factors on absolute risks of distant recurrence and death in years five through 14 if endocrine therapy stops at year five could help decide whether to extend the treatment past five years for lower risk patients.

Pan's study is based on data from 46,138 individual patients with estrogen receptor-positive breast cancer and looked at factors such as nodal status, tumor diameter and grade. He concluded that even after five years of endocrine therapy, estrogen receptor-positive recurrence risk continued steadily over years five through 14. Although the risk was less for patients with favorable triple-negative status and grade, even those with low-grade T1N0 disease had an appreciable risk of distant recurrence, Pan said. //

OTHER NEWS TO NOTE

Avita Medical Ltd., of Cambridge, U.K., has furthered its expansion into the Asian market with the appointment of a specialized wound care distributor for its products in Malaysia. The company said it had concluded a deal with Mintcare, which specializes in the distribution of wound care products throughout the Asia-Pacific region. Avita Medical said Mintcare would first focus on Malaysia in its marketing of Avita's regenerative medical devices for burns, wounds and skin conditions.

Beckman Coulter Inc., of Brea, Calif., and **Ortho Clinical Diagnostics Inc.**, of Raritan, N.J., entered into a strategic relationship regarding sales of Ortho's Vitros 3600 Immunodiagnostic System and infectious disease menu in the U.S. Under this strategic relationship, Beckman Coulter will place Ortho's Vitros 3600 System running HIV and hepatitis assays in labs that currently run Beckman's power processor sample handling systems, and in certain other very high-volume laboratories.

Davita Kidney Care, a division of **Davita Healthcare Partners Inc.**, of Denver, entered into a joint venture acquisition with **Inspira Health Network,** of Woodbury, N.J.. The proposed joint venture would transfer majority ownership of three Inspira dialysis centers located in Vineland, Millville and Bridgeton to Davita and create opportunities to grow dialysis services throughout the communities which Inspira currently serves. Financial details were not disclosed.

Intertek Inc., of Chicago, said it was offering new services to help manufacturers of medical electrical equipment verify that products are environmentally conscious. The services are an expansion of Intertek's existing IEC 60601-1 services and consist of an engineering review of product design and development processes in line with the IEC 60601-1-9 standard on environmentally conscious design.

Cancer

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The HQO recommendation, which presumably addresses coverage only in the province and no other Canadian jurisdictions, recommended that Cancer Care Ontario work with clinicians to devise a scheme for determining which cancer patients should be eligible for either service. The document noted that the agency had commissioned the Ottawa Hospital Research Institute to evaluate the economics of these procedures compared to non-surgical management of fractures, which determined that the per-case cost of kyphoplasty was slightly more than $7,200, while vertebroplasty rings in at a bit less than $3,900.

The economic assessment further determined that the incremental cost effectiveness ratio of kyphoplasty was in excess of $33,400, while that of vertebroplasty was nearly $17,900. The assessment included a clinically significant reduction in pain and an associated decrease in the use of opioid analgesics as well as an improved quality of life. These improvements were seen in several patient populations, including those diagnosed with multiple myeloma and with "mixed primary spinal metastatic tumors."

The report stated that while coverage of these two vertebral augmentation procedures is likely to boost spending, the resulting increase in spending is likely to exert a small effect on the province's budget. However, the authors alluded to a limited number of specialists available to perform the procedures, recommending that referral pathways be bolstered so as to ensure referral.

CANCER DIAGNOSES IN ONTARIO ASSOCIATED WITH AGE

Cancer Care Ontario recently published a few figures regarding the prevalence and incidence of cancer in the nation's most populous province, which is inhabited by nearly 14 million Canadians. The agency stated in a June 8 press release that more than 85,000 Ontarians will be diagnosed this year, triple the number in 1981 when the population was more than half the present population, roughly 8.6 million.

Thanks in part to increased life spans, CCO predicted that about half of the province's residents will develop one form of cancer or another during their lives, while this class of diseases is expected to claim the lives of 25 percent of the population. As of Jan. 1, 2013, roughly 2.7 percent of Ontarians (or 363,000) were living with a cancer.

Five-year survival for all cancers in Ontario is estimated to be 63 percent, with some of the usual suspects for lowest survival dotting the list of the deadliest, including liver and pancreatic cancers. However, these two were among several cancers that demonstrated the largest increases in survival over the past few years, as reported by the Ontario Cancer Registry. The report, part of a series of biennial reports, is intended to foster a policy discussion about treatment and prevention.

DOT'S APNEA DOCKET DRAWS NEARLY 450 COMMENTS

Two agencies of the Department of Transportation opened a docket in March seeking information on the impact of obstructive sleep apnea (OSA) on those whose employments make them safety-sensitive personnel, a docket that drew 445 responses by the June 8 closing date. Many of the comments were from those thus employed, shining a bright light on a need for treatment.

The advanced notice of proposed rulemaking by the Federal Motor Carrier Safety Administration and the Federal Railroad Administration included a request for information on the prevalence of moderate to severe OSA, but also made note of an interest in the "potential costs and benefits from regulatory action" that would be designed to address any associated safety issues.

However, the two agencies are also examining the question of whether a screening procedure would be feasible for transportation workers whose jobs are safety-sensitive. Among the issues associated with the screening proposition is a need to determine the qualifications for a health care professional charged with conducting such screening procedures.

The issue is not precisely a novel one, as a January 2008 report by Manila Consulting Group makes clear, but truckers are apparently not universally impressed with a requirement imposed in 2014 by the FMCSA that truckers be required to undergo sleep apnea testing if they show up for their annual physical exams with a neck measurement of anywhere from 16 to 18 inches. Many of those tested had to pay for the test out of pocket, and the usual problems with continuous positive airway pressure (CPAP) mask fit and the associated discomfort has many truckers up in arms over the requirement.

The agencies held three listening sessions in May, and the docket is littered with comments dissenting with the text of the NPRM on several points. One medical professional suggested that a more appropriate time and place of testing is during transit rather than during sleep, while a tested individual described his CPAP machine as "a dream machine CPAP torture device."

HOUSE PASSES SITE-NEUTRAL LEGISLATION

Site neutrality for reimbursement of a number of procedures has fed a substantial amount of conflict between providers and the CMS in the past few years, but the U.S. House of Representatives has passed legislation that would flatten out reimbursement rates across all sites. However, the Congressional Budget Office has indicated that the legislation triggers pay-go rules, making this an issue for budget-conscious members of Congress.

The Helping Hospitals Improve Patient Care Act of 2016 (H.R. 5273) debuted in the House Energy and Commerce Committee May 18, and breezed through a voice vote on the House floor on June 7. The bill would require the CMS to develop a series of

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Karen Simpkins, medical devices market analyst at market intelligence firm BMI Research.

BMI anticipates more Chinese M&A deals and diversification into new product areas in the face of increasingly intense medical device market competition. According to the firm's latest report "Industry Trend Analysis – Industry will see Further Consolidation", growth in China's med-tech industry is getting stronger, relative to many other Asia Pacific countries, but the latest financial results from China's leading listed medical device makers have grown weaker.

Revenues of these listed companies grew by an average of 19.2 percent in 2015 versus 20.7 percent in 2014. Also, a rise in costs reduced their average gross profit margin to 41.8 percent, down from 43 percent in 2014 and 47.4 percent in 2010.

One of the main reasons the industry is seeing a slowdown is in the constant fine-tuning of China's regulatory framework.

"Companies would like to achieve rapid growth from M&A, so you will find a lot of M&A deals happening in the next few years. This is because regulations of the medical device industry are becoming more difficult. The regulatory updates make it difficult for companies to seek organic, robust growth," said David Li, health care research analyst and vice president at BOCOM International Securities Limited.

These frequent and ongoing improvements of the regulatory framework may be weighing on the industry now but is sought to facilitate market access in the long run. BMI notes that the industry will benefit from government support for innovation under the 13th Five-Year Plan (2016-2020) including accelerating the research and development of high-end medical devices.

Thus the further sophistication of regulations by no means indicates that China is stalling the growth of its med-tech market. Authorities are supportive, however, the support is selective and focused on the fittest companies.

"The authorities in China would like to form a leading company in the whole nation in order to achieve the competitive scale advantage. There are leading companies in each city, but on a national level, there is none. Smaller companies invest less in R&D," said Li.

The government is trying to foster its own leading domestic players – such as the U..S has in Johnson & Johnson or Medtronic plc. – in its much-fragmented medical device market.

"They [smaller companies] are not technologically advanced, so from the authority's point of view, these companies are better off being eliminated," said Li. "On the other hand, authorities want big companies who spend more on R&D to survive and continue to invest more."

"It's been a trend for a couple of years, at least in terms of upgrading China's health care industry. Small players must be eliminated by being merged with larger companies that have more market share."

Also, acquisitions aren't just limited to larger companies taking over smaller ones, rather, they are happening at every level. For example, Shanghai Kinetic Medical Co. Ltd. recently swallowed up all the shares of subsidiary Jiangsu Ideal Medical Science & Technology and Beijing Essen Technology Co. Ltd. to further expand its portfolio. Ideal specializes in orthopedic implants and surgical instruments while Essen manufactures coronary stent systems.

Another unique example is Jiangsu Yuyue Medical Equipment and Supply Co. Ltd.'s acquisition of China Resources Wandong Medical Equipment Co. Ltd. together with Shanghai Medical Instruments Co. Ltd. for $274 million last June. This is the first time a private med-tech company acquired a state-owned one in China. It also ties in with the current government policy to reform large state-owned enterprises.

"M&A in some subsectors of the med-tech industry will create synergy together. For instance, once the upstream players are merged with the middle stream player, you can expect something bigger and stronger," said Li. //

Cancer

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HCPCS codes designed to match outpatient inpatient payment rates for the service in question. Also included in the bill is language that would terminate a moratorium on increases in the number of beds allowed for long-term care hospitals.

The CBO estimated that the legislation would likely boost direct spending to the tune of $50 million between 2017 and 2021, although direct spending would fall by $14 million over the full 10 years. Pay-go rules would require that Congress amend overall spending to cover the discrepancies or carry those amounts forward to be added into the calculation for the following fiscal year.

The website at congress.gov lists a number of related bills, two of which are in play in the Senate. However, S. 202 appears to be targeted toward the long-term care hospital bed count moratorium, while S. 607 would functionally replicate the House bill's five-year extension of a program that would pay rural hospitals on the basis of incurred costs rather than under Medicare prospective payment systems.

Rep. Kevin Brady (R-Texas), chairman of the House Ways and Means Committee, jointly penned a statement with a House subcommittee chairman lauding passage of the bill. Brady and Rep. Pat Tiberi (R-Ohio), chairman of the Ways and Means' subcommittee on health, said in the June 7 statement that H.R. 5273 "strikes the right balance of preserving site-neutral payment policy and providing essential relief for hospitals that were caught up in this policy change from last year's budget deal." //

PRODUCT BRIEFS

C2 Therapeutics Inc., of Redwood City, Calif., initiated its Coldplay III trial with treatment of the first patient at University Hospitals in Ohio. The patient was treated with the C2 Cryoballoon Focal Ablation System by John Dumot, director of the Digestive Health Institute at University Hospitals. The trial is designed to evaluate the efficacy and safety of the system in patients with Barrett's esophagus. The prospective, multi-center, non-randomized, single arm study will enroll 60 patients with multifocal Barrett's esophagus less than 6 cm in full circumferential size and no previous treatment. The primary outcomes measure is eradication of any grade Barrett's esophagus at 12 months post-treatment. This will be evaluated by using the Seattle protocol surveillance strategy that involves targeted biopsies of mucosal abnormalities, plus four-quadrant biopsies obtained at every 1 cm. The presence of Barrett's esophagus and degree of disease will be confirmed by histopathologic analysis.

Enzo Biochem Inc., of New York, said the New York State Department of Health has granted conditional approval for use of Enzo Clinical Labs' Ampiprobe Candidiasis assay. This is the company's second test for the women's health market and the third to be approved using one of the firm's technology platforms.

DAILY M&A

Eizo Corp. reported an agreement with **Panasonic Healthcare Co., Ltd.** Japan to acquire Panasonic's endoscopy monitor business. Eizo, of Hakusan, Japan, said it is a visual technology company seeking to expand its business in specialty markets, including health care. The Tokyo-based Panasonic Healthcare has developed its endoscopy monitor business since August 2010. Financial terms of the deal were not disclosed.

St. Louis-based **Medibeacon Inc**. completed its acquisition of M**annheim Pharma & Diagnostics**, a German life science company

Medina International Holdings Inc., of Duluth, Ga., said it has acquired Arvada, Colo.-based **Medical Innovation Holdings Inc.** and changed its name to Medical Innovation Holdings Inc. The company said it is establishing a state-by-state, multi-disciplinary medical specialist provider/practice network of specialists who serve rural patient populations using telemedicine technology. The company's telemedicine platform is intended to bring together different modalities of telemedicine (electronic medical records, video conferencing, etc.) to create a virtual multi-specialty practice. Terms of the acquisition were not disclosed.

OTHER NEWS TO NOTE

Solvebio, of New York, a contextual knowledge hub, said the National Institutes of Health has funded further development of the Variant Explorer, a genetic variation analysis and visualization system. Solvebio received a Phase I Small Business Innovation Research Grant from the National Institute of General Medical Sciences for the research and development grant, R43GM117644, titled "The Variant Explorer: a cloud-based data integration and visualization system for improving clinical interpretation of sequenced genetic variants".

APPOINTMENTS & ADVANCEMENTS

Personal Genome Diagnostics Inc., of Baltimore, said that Abigail McElhinny has joined the company as senior vice president of research & development, operations. McElhinny joins from the Roche Group, where she most recently was vice resident of assay and reagent development for Ventana Medical Systems, Inc.

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ORTHOPEDICS EXTRA

Keeping you up to date on recent developments in orthopedics

By Holland Johnson, Executive Editor

Rare case of bone cancer identified via brachyury immunostain

Scientists reported the first case of immunohistochemical marker confirming diagnosis of extra-axial dedifferentiated chordoma. An exceptionally rare and aggressive malignant bone tumor was positively confirmed via the expressions of a DNA protein transcription factor, according to a recent study by American researchers. "We herein report an exceptional case of extra-axial dedifferentiated chordoma confirmed by the expression of brachyury, the first case report of this kind," reported surgical pathologist Evita Bonita Henderson-Jackson and her research colleagues from Moffitt Cancer Center in Tampa, Fla., in a case report offering literature review and pathologists' perspective, published by the open-access peer-reviewed journal *Advances in Modern Oncology Research*. Chordoma, or bone tumor of the skull and spine, is a very uncommon type of cancer with low prognosis (55 percent for a five-year survival), and accounts for about 3 percent of all bone tumors. Every year in the United States, according to the Chordoma Foundation, only one new case per million people is diagnosed. In the entire population of 321 million people in the U.S., there are only about 2,400 chordoma patients. The tumor primarily occurs within the axial skeleton, along a human body's spinal axis from the skull to the tailbone. When identified outside of the axial skeleton, these subsets are known as extra-axial chordomas. Chordoma has no known environmental, dietary or lifestyle risk factors, and is believed to emerge from the remnants of embryonic notochord. Notochord cells normally persist after birth, lodged inside the spine and skull, until becoming malignant to form chordoma. Dedifferentiated chordoma, meanwhile, is a fatal variant of conventional chordoma that is even rarer, occurring in only 2 percent to 8 percent of all chordomas. It is typically identified following radiation therapy of primary tumors or as recurrences, and with its additional high-grade sarcomatous elements, dedifferentiated chordoma is known to be very aggressive. It is difficult to identify chordoma – let alone dedifferentiated chordoma – at extra-axial sites, according to the researchers. The ability to accurately identify the extra-axial skeletal and soft tissue chordomas is of paramount importance, according to the researchers, as the treatment and prognosis of this neoplasm is vastly different than that of other neoplasms, which it could be misdiagnosed as. In addition to displaying features of conventional chordoma, dedifferentiated chordoma harbors sarcomatous areas similarly ravaged by other tumors. "The sarcomatous areas commonly appear as high-grade undifferentiated spindle cell sarcoma; however, other histomorphologies have also been reported, such as fibrosarcoma, osteosarcoma, or rhabdomyosarcoma," the study reported. Clinicians examining a neoplasm would still need to review clinical and radiological findings to determine elements of a metastatic carcinoma, according to the study; however, "[i]f history does not indicate metastasis and tumor of unknown origin is raised, a panel of immunostains including brachyury would be of value," it proposed. Brachyury, a member of the T-box protein family bounded to specific DNA sequences, is a transcription factor which initiates and regulates the rate of transcription of genetic information, and it is highly expressed in nearly every chordoma tumor. "[B]rachyury was identified as a sensitive and specific marker for chordoma with the ability to discern between extra-axial chordoma and other chordoma-like lesions such as parachordoma/myoepithelioma," the research team said. For their study, the researchers examined the case of a 68-year-old female suffering from pain and swelling with purple discoloration on her right foot, who was originally diagnosed with plantar fasciitis at a different facility but a post-surgery MRI later reported the presence of a multilobulated and erosive mass. Noted the study, "A core needle biopsy of the right plantar foot mass was performed at an external hospital…and the pathology results showed the possibility of dedifferentiated chondrosarcoma." However, the case referred for consultation at yet another facility, which instead diagnosed the lesion as an epithelioid malignant neoplasm, favoring carcinoma over epithelioid sarcoma, according to the study. When the patient sought a secondary suggestion from Moffitt Cancer Center, her core biopsy was reviewed, and "the histological sections revealed poorly differentiated malignant neoplasm," reported the authors, while noting that carcinoma, melanoma, and sarcoma were all fair diagnoses at that point. Upon immunohistochemical staining, however, the "immunostain panel does not support epithelioid sarcoma, melanoma, angiosarcoma, malignant peripheral nerve sheath tumor, renal cell carcinoma, or leiomyosarcoma," said the researchers. Additionally, closer examination of the core biopsy revealed "small groups of cells that had clear and vacuolated cytoplasm with myxoid matrix" suggestive of a chordoma, according to the study. A brachyury immunostain was performed for confirmation, and it showed uniform and diffuse nuclear positivity.

Vertera Spine reports first implantations of Peek Cohere device

Atlanta-based **Vertera Spine Inc.** reported the first wave of implantations with the Cohere cervical interbody fusion system. Cohere is Vertera's first device featuring the

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ORTHOPEDICS EXTRA

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company's patented porous Peek (polyetherether ketone) Scoria biomaterial technology. While porous metal or metal-coated implants have found their way into spinal fusion applications, the company said that Cohere is the first device in clinical use to be manufactured entirely out of Peek and contain porosity. Cohere is intended for use in anterior cervical fusion procedures to treat complex, single or multi-level spinal pathologies, While competitive Peek fusion devices are treated with metal coatings that can delaminate during and after surgery, porous Peek Scoria is grown directly from the solid Peek implant through a patented processing method, exhibiting twice the shear strength of vertebral trabecular bone. "Using the COHERE implant was a seamless transition from the allograft cage I previously used. I have been impressed with its easy insertion as well as the durability of the porous PEEK during implantation," said Richard Fessler MD, a professor at Rush University in Chicago where the device is already being used. Cohere is available in multiple footprints and heights with a 7 degree lordotic angle. Vertera Spine is planning a full market release of Cohere in the coming months.

Mx Ortho receives clearance on Dynamx screw

Mx Orthopedics, Corp., of Lexington, Mass., reported the recent FDA clearance of the Dynamx nitinol compression screw. The Dynamx screw utilizes the superelastic properties of nitinol to provide higher levels of compression than contemporary bone screws. During manufacturing, the Dynamx is stretched and held in an elongated position with an internal pin. Following implantation, the internal pin is removed and the screw attempts to shorten and return to its original unstretched length, thereby providing desirable compression. The company's line of nitinol fracture fixation implants include superelastic compression screws, staples, plates, and intramedullary implants.