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HEART RHYTHM SOCIETY 2014

Big data a big deal, but puzzle is missing the analytics piece

By Mark McCarty, Washington Editor

SAN FRANCISCO — This year's edition of the **Heart Rhythm Society** (HRS; Washington) scientific sessions led with the opening plenary talk full of forward-looking speculations, including from a speaker who painted a picture of the future of medicine in which data would flow unimpeded from the patient to the cloud and back to the patient. Indeed, each of the speakers at the opening plenary spoke of the many ways that big data would one day transform medicine, but what was missing was a discussion of the analytical tools that will be necessary to convert the deluge of data into something more meaningful

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SEMDA 2014

Cardinal's Ashby says healthcare is 'the' fastest growing market

By Omar Ford, Staff Writer

ATLANTA — Lisa Ashby, president of the medical devices and diagnostics segment for **Cardinal Health** (Dublin, Ohio), delivered the keynote address at the **Southeastern Medical Device Association**'s (SEMDA; Norcross, Georgia) 2014 meeting on Wednesday and said there were tremendous pressures occurring within the space.

Ashby, who started her healthcare career in the Southeast, also pointed out to the audience that there is no other market that has moved as quickly or has seen so much change in such a short amount of time.

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DIGESTIVE DISEASE WEEK

Doctors get hands-on training with ESD tech at Olympus booth

By Amanda Pedersen, Senior Staff Writer

CHICAGO — A steady stream of gastroenterologists took turns getting hands-on training this week at **Olympus**' (Center Valley, Pennsylvania) booth at Digestive Disease Week (DDW). Attendees had an opportunity to meet experts in endoscopic submucosal dissection (ESD) and participate in hands-on demonstrations of Olympus' ESD technology. The doctors practiced ESD procedures on a pig intestine with guidance from expert physicians in the field.

This year 14,270 people attended DDW. The meeting was jointly sponsored by the **American Gastroenterological**

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MED-TECH INVESTING CONFERENCE

Conference focuses on the benefits of IT in support of the golden years

By Jonathan Goldstein, Israel Editor

Beautiful Lausanne on Lake Geneva in Switzerland was the site of the small, exclusive MedTech Investing Conference that is already in its 10th year of activity in the area of medical technology investing, managed by Campden Wealth Management (London). The program integrated the local regional sponsors, together with a broader Europe-wide support by a major EU-based program, the Ambient Assisted Living (AAL) Joint Program.

AAL sees chronic disease as one of the key risks of aging, and focuses on generating "Information Technology (IT) for

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DIAGNOSTICS EXTRA

Staff Writer Omar Ford on one of med-tech's key sectors

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BELTWAY BRIEFINGS

CMS panel iffy on benefit-risk for low-dose lung cancer screen

By Mark McCarty, Washington Editor

The U.S. Public Services Task Force proclaimed that low-dose CT (LDCT) screening for lung cancer merits a B recommendation for some patients, but a government advisory panel recently drew a somewhat different conclusion. According to a report on a meeting of a Medicare coverage panel, the voting members expressed a confidence of only 2.2 on a scale of one to five that the evidence is adequate to ensure that the benefits of LDCT screening for lung cancer outweigh the risks. The panel further indicated it was less than confident that the risks associated with CT exposure would be minimized in routine medical practice, leaving the Centers for Medicare & Medicaid Services with something short of a full mandate to move ahead with coverage for the USPSTF recommendations.

The USPSTF recommendation was predictably endorsed by medical specialty societies and by makers of diagnostic imaging equipment, including the **American Cancer Society** (ACS; Atlanta), which came up with its own guidelines in January 2013. The ACS principles include the recommendation that screening of those between the ages of 55 and 74 with a 30 pack-year history of smoking take place at an institution staffed with a multi-disciplinary team to address any positive findings.

The difficulty for CMS is that it is required by the statute to address any USPSTF recommendations earning a grade of B or better, but the participants in the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC), which convened in April to address the recommendation, indicated that the panelists had more than one problem with the evidence accumulated to date. Besides determining that the data did not adequately address the risk/benefit question, the committee also voted that it was convinced that evidence gaps remain where the use of LDCT is concerned, at least outside a clinical trial setting, a conclusion that could leave CMS with a coverage-with-evidence-development proposal as the only viable answer to the USPSTF guideline.

The skepticism over LDCT screening of high-risk populations is not without precedent, as the **American College of Chest Physicians** (ACCP; Northbrook, Illinois) determined in 2007 that the evidence even for high-risk patients did not add up (*Medical Device Daily*, Sept. 13, 2007). The publication of the USPSTF recommendations seemed to bring others off the sidelines, however. A similar body in Canada offered a parallel recommendation late last year (*MDD*, Sept. 11, 2013), seeming to add to the stampede toward screening. The **American Association for Thoracic Surgery** (AATS; Beverly, Massachusetts) offered its endorsement of the USPSTF recommendation, a move backed by the **Medical Imaging & Technology Alliance** (MITA; Arlington, Virginia) as well (*MDD*, Sept. 24, 2013).

FDA: AI REQUESTS FOR 510(K) TRACKING DOWN

Device makers have complained loudly about requests for additional information for their 510(k) applications, a chorus of jeers FDA and Capitol Hill heard loud and clear. The latest FDA report on the agency's performance on device applications shows that reviewers at the Office of Device Evaluation are

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COURT REPORT

St. Jude finds itself under DoJ microscope once again

Staff Report

St. Jude Medical (St. Paul, Minnesota) is under the Department of Justice microscope again for alleged kickbacks given to physicians for implanting its cardiac devices in patients, the company said in a regulatory filing.

It is the third ongoing governmental probe initiated against St. Jude Medical since 2010, according to an expanded quarterly report filed with the SEC. In early 2011, the company agreed to pay $16 million to settle claims related to a similar kickback scheme. That investigation lasted 5 years.

Earlier this year, St. Jude reported a major shakeup in its top ranks that resulted in merging its cardiovascular and implantables divisions into a single, companywide R&D division. Eric Fain was named to lead the combined division, replacing Frank Callaghan, the former head of the Cardiovascular and Ablation Technologies Division. Previously, Fain headed the Implantable Electronic Systems Division.

The reorganization was attributed to St. Jude's efforts to streamline the company back into profit. In 2013, the company's stock rose more than 70%, though net sales for the full year were relatively flat at $5.501 billion compared to the $5.503 recorded in 2012.

In the official Form 10-Q statement, the company admits that: "In April 2014, the company received a CID from the Civil Division of the DOJ stating that it was investigating the Company for potential False Claims Act violations relating to allegations that certain healthcare facilities and a physician group may have submitted false claims to federal health care programs as a result of alleged inducements paid by the company to implant the company's cardiac devices. The company is working with the DOJ in responding to the CID.

The company is cooperating with the three open investigations and is responding to these requests. However, the company cannot predict when these investigations will be resolved, the outcome of these investigations or their impact on the company. The company has not recorded an expense related to any potential damages in connection with these governmental matters because any potential loss is not probable or reasonably estimable. The company cannot reasonably estimate a loss or range of loss, if any, that may result from these matters."

In other legal news:

OPKO Health (Miami) said on May 5, the Eighth Judicial District Court of the State of Nevada in and for the County of Clark granted the company's motion to dismiss the securities class action lawsuit brought against the company on behalf of the shareholders of Prolor Biotech in connection with the acquisition of Prolor by OPKO.

The court dismissed all claims as to all defendants including Prolor and its former officers and directors asserted in the case without prejudice.

OPKO is a biopharmaceutical and diagnostics company by leveraging its discovery, development and commercialization expertise and novel and proprietary technologies. //

Washington

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heeding the call to avoid the urge to require more data, although the percentage of additional information (AI) requests during the first review cycle are still nearly double the level in 2002.

According to FDA's Medical Device User Fee Agreement III (MDUFA III) report for the first quarter of calendar year 2014, reviewers at ODE greeted nearly two thirds (64%) of 510(k) applications with AI requests, a number down significantly from the 77% in 2010. The all-time low since the turn of the century came in 2002, when only 36% of such applications triggered an AI request.

The numbers for second-cycle AI requests are likewise ebbing, falling to 8% for the quarter ending Sept. 30, 2013, a sharp drop from the 35% seen in 2010, and a level matching the 8% in 2002.

The third edition of the device user fee agreement roughly doubles the fees FDA can collect from device and diagnostics makers to a sum just short of $600 million over five years, but the negotiations were from all indications protracted and difficult. At stake for industry was a need to reverse a trend of ever-increasing review times while the agency was faced with critics inside and outside of government alleging the 510(k) path was a "fast track" to approval.

FDA data indicate the backlog of pending 510(k) filings is ebbing, from more than 1,900 in 2010 to nearly 1,350 in the first quarter of this year. The number pending at 90-plus days at that date is at a low for this century at 14, plummeting from the apogee set – yet again – in 2010. Also, the share of 510(k) applications deemed substantially equivalent was 84% in 1Q14, up from 73% in 2010.

The trajectory for PMA filings varies somewhat where major deficiency letters are concerned. FDA's data indicate that 78% of PMAs filed in 2013 were caught by a major deficiency letter, which is down from the 86% in 2010. However, the ratios in 2011 and 2012 were 70% and 71%, respectively, a statistical wobble that runs counter to the track set by total PMA review times over the past half decade. Total days for PMAs averaged 464 in 2009, but only 297 in 2012. The PMA backlog is down to 49 from a high of 92 in both 2009 and 2010. //

FINANCINGS

K2M rings opening bell of Nasdaq with $132M IPO

Staff Report

K2M Group (Leesburg, Virginia) rang the opening bell of the Nasdaq Thursday morning in celebration of its $132 million IPO.

The company sold 8.8 million shares at $15 per share, expecting to net $120 million after costs and discounts. Underwriters have a 30-day option to purchase more than 1.3 additional million shares, the company said.

The company, which launched 10 years ago, said it has already commercialized 57 product lines and sells in 27 countries including the United States. International marketing began in 2008, its regulatory filing noted.

K2M had nearly $157.6 million in 2013 revenue, representing a robust increase over the previous two years. However, it lost $37.9 million in fiscal 2013. According to *The Washington Business Journal*, nearly 30% of its revenue was derived overseas. //

WORLD IN REVIEW

Saudi authorities destroy illegal medical equipment

Staff Report

Saleh Al-Tayyar, deputy president of the Saudi Food and Drug Authority (SFDA) for the medical devices sector, has revealed that the authority destroyed illegal equipment valued to be worth SR260 million found in the Saudi ports.

Al-Tayyar made the statement on the sidelines of a workshop organized by his department on Sunday at the Marriot Hotel in Riyadh.

Around 649 liaison officers in government and private hospitals participated in the workshop, which aimed to discuss means to resolve the issue of expired medical equipment entering the Saudi market.

The official told local media that his department has recently demolished millions of devices and health supplies, including sterilizers, health kits and other products.

"We have also seized expired equipment stored in warehouses under unhealthy conditions and high temperatures," he said .

Al-Tayyar indicated that the department arrested individuals who were found guilty of tampering with the validity dates of some medical products. They were brought to the Bureau of Investigation and Prosecution, he added, and fined SR100,000 each.

The official pointed out that routine inspection tours are performed on manufacturing and import companies to ensure health regulations are maintained. //

Advanced Circulatory's ResQCPR gets favorable recommendation

Staff Report

Advanced Circulatory (Minneapolis), a maker of medical devices providing intrathoracic pressure regulation (IPR) Therapy, will continue to work with the FDA on a pathway to PMA for the company's ResQCPR system, based on recommendations from the FDA Circulatory System Devices Advisory Panel meeting on May 6.

The panel considered approval of the ResQCPR System for use in the performance of CPR to increase the likelihood of survival with favorable neurologic function in adult patients with non-traumatic cardiac arrest. The panel voted unanimously that there is a reasonable assurance that the device is safe, and a majority agreed that the benefits of the ResQCPR System outweigh the risks for the device's proposed indications. While the panel members questioned whether the data provide a reasonable assurance of effectiveness of the system based on the numerous statistical analyses presented by the company and FDA at the meeting, several explained their positive vote on risk-benefit by stating that there was a strong "signal" of effectiveness and indicated that this should be studied in a post-market setting. The panel's discussion also focused on the complexity of performing prehospital cardiac arrest research and the need to find innovative solutions to improve survival of the nation's third leading cause of death, cardiac arrest.

The ResQCPR System is comprised of the ResQPOD Impedance Threshold Device (ITD) 16 and the ResQPUMP Active Compression Decompression CPR (ACD-CPR) device. The company is seeking approval of the product combination for use in the performance of CPR to improve the likelihood of survival with favorable neurological function in adult patients with non-traumatic cardiac arrest based on the results of its pivotal clinical study, the ResQTRIAL. The ResQCPR System is Advanced Circulatory's next IPR Therapy technology, which is intended to regulate negative intrathoracic pressure to enhance blood flow in states of poor perfusion, including cardiac arrest and shock.

PRODUCT BRIEFS

• **Z-Medica** (Wallingford, Connecticut), a maker of hemostatic agents, reported the results from a study conducted by a major medical organization on the effectiveness of tourniquets and hemostatic bandages in civilian emergency medical services (EMS) systems. The study, entitled, *Pre-hospital Use of Hemostatic Bandages and Tourniquets; Translation From Military Experience to Implementation in Civilian Trauma Care*, shows that the use of tourniquets and hemostatic bandages in pre-hospital civilian care, is comparable to combat situations and highly effective in saving lives, with success rates using both methods at 95% or better.

ASIA IN THE SPOTLIGHT

Both young and old patients will propel Thai device market

By Cornelia Zou, Contributing Writer

Changing demographic patterns and increased inter-Asian trade have led to a shift in the dynamic of the market for medical devices in Thailand.

Device importers at this week's Medical Devices and Supplies Fair in Hong Kong, which runs until today, said buyers in Thailand are likely to buy more products targeting the elderly and infant markets over the next few years.

Despite the current political turmoil, Thailand still has a strong rate of economic growth and this growth is, in no small measure, based on increasing expenditure on healthcare both at the government level and among the general consumers – in particular the emerging middle class.

At the top end of Thailand's age spectrum, the elderly are looking for more and newer products to meet their increasing health care needs. At the bottom, a more affluent middle class requires more devices to meet the needs of infants and young children.

"In 2010, we had a large working population but 20 years later, the elderly population will grow," said Wantana Petcharit, import manager at Chumroen Medical Products. "This is a great opportunity to enter this market."

By 2030 the population between the ages of 50 and 74 will increase the most compared with 2010, according to a study by the Institute for Population and Social Research at M**ahidol University** (Bangkok). Some of the more sought-after products for elderly care include monitoring systems, orthopedic equipment and wheelchairs.

Aside from elderly care, there has been a visible uptick in demand for infant care products such as breast-feeding pumps, nipple shields and baby products.

"Baby products are quite popular in Thailand nowadays," said Petcharit. "Parents are willing to pay as much as they can for their babies' health, so this sector should grow in the future."

In another shift, Thai importers of medical devices are increasingly likely to source more of their products from other Asian countries rather than from the well established European or American manufacturers and suppliers.

The U.S., Japan, Germany, the Netherlands and China are currently the top sources of medical devices for the Thai market. But the kingdom is opening up to Asian suppliers, especially new suppliers from China, South Korea and Taiwan, because of the increasing product quality of the products and geographic advantages.

The import of pharmaceuticals and medical devices in Thailand has climbed from nearly 27 billion baht ($0.8 billion) in 2004 to 67 billion baht in 2013, the fastest growing period being between 2011 and 2012. Import growth hiccuped in 2013 when the political crisis affected the pharmaceutical and medical device markets in Thailand.

"The medical device supply market in Thailand is growing constantly," said Petcharit. "The government is encouraging people to care more about their health."

In 2001, with the passing of the Health Promotion Act, the government established the independent state agency Thai Health Promotion Foundation (Thaihealth) to promote the well-being of Thai people. The agency is funded by 2% surcharges on the tobacco and alcohol excise taxes. It supports more than 1,000 projects a year with as much as $100 million spent on promotional activities.

"Another reason for healthcare market growth is education," said Petcharit. "We try to make people read more and learn more about healthcare."

Educational institutions also play an important role in healthcare education in Thailand. They often partner with Thaihealth to exchange ideas and design and implement the promotional campaigns.

"Media is the last component, and a very important one," said Petcharit. "You can see on TV and in newspapers that Thai people have more access to healthcare information now."

In addition to products related to care for the elderly and infants, Petcharit also said that homecare products such as heart rate monitors, glucose meters and blood pressure monitors are also focuses of her visit to the fair, as people in Thailand are becoming more involved in health monitoring at home.

However, international suppliers who want to enter the Thai medical device market must prepare themselves for the lengthy process of document preparation. //

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DEALS

IMS Health acquires Forcea applications

Staff Writer

IMS Health (Danbury, Connecticut) has acquired **Forcea** (Brussels, Belgium), a provider of business intelligence applications and analytics, to advance performance management capabilities for hospitals and life sciences organizations. The companies believe the acquisition brings together IMS Health's comprehensive information and technology services with Forcea's hospital-based technology solutions to drive more effective clinical and cost decisions. Forcea solutions will leverage IMS One, the company's intelligent cloud-based platform that seamlessly provisions industry information and integrates IMS Health, client and third-party data for faster, more insightful decision making. Financial terms of the transaction were not disclosed.

With this acquisition, IMS Health says it further strengthens its leadership in business intelligence capabilities focused on enabling better care coordination and improved operating performance. rable performance gains.

IMS Health is an information and technology services company providing clients in the healthcare industry with comprehensive solutions to measure and improve their performance. By applying sophisticated analytics and proprietary application suites hosted on the IMS One intelligent cloud, the company connects more than 10 petabytes of complex healthcare data on diseases, treatments, costs and outcomes to help its clients run their operations more efficiently. Customers include pharmaceutical, consumer health and medical device manufacturers and distributors, providers, payers, government agencies, policymakers, researchers and the financial community. Additional information is available at www.imshealth.com.

In other dealmaking news, **ICON** (Dublin) has completed the previously announced acquisition of **Aptiv Solutions** (Reston, Virginia).

Aptiv Solutions specializes in the design and execution of adaptive clinical trials for pharmaceutical and biotech customers. The company has experience in the management of medical device trials and its Japanese subsidiary, Niphix, is a full-service, oncology-focused CRO serving both Japanese and international customers.

ICON is a provider of outsourced development services to the pharmaceutical, biotechnology and medical device industries. The company specializes in the strategic development, management and analysis of programs that support clinical development – from compound selection to Phase I-IV clinical studies. //

PEOPLE IN PLACES

• The **Advanced Medical Technology Association** (AdvaMed; Washington) said Nadim Yared, president/CEO of CVRx, has been named chairman of the association's Emerging Growth Company Council Board of Directors for a two-year term. Yared has served on the EGCC board since its inception in 2012 and has been an active member of AdvaMed's board since 2011, representing the voice of smaller manufacturers. Yared succeeds Abiomed chairman, president/CEO Michael Minogue, who served as inaugural chair of the EGCC board. AdvaMed member companies make medical devices, diagnostic products and health information systems.

• **CareFusion** (San Diego) said that Supratim Bose has been elected as the 10th member of its board of directors. Bose is currently executive VP and president, Asia-Pacific, Middle East and Africa for Boston Scientific, a position he has held since January 2013. Carefusion is a medical technology company.

• **Elekta** (Stockholm, Sweden) has named Åsa Hedin as executive VP of corporate strategy. Hedin has led Elekta Neuroscience since 2007. Elekta is a human care company pioneering innovations and clinical solutions for treating cancer and brain disorders.

• Thomas Crane, a member of the Health Law Practice of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, has been elected to the board of the **Massachusetts Medical Device Industry Council** (MassMEDIC; Boston). Crane will serve a three-year term. MassMEDIC is an organization of medical device manufacturers, suppliers and associated non-profit groups in Massachusetts and the surrounding region.

• **Physiotherapy Associates** (Exton, Pennsylvania) has named Hank Balavender as its CEO. Previously, Balavender was an industry advisor for physical therapy practices around the country. Physiotherapy Associates is a provider of outpatient rehabilitation services.

• **Premune** (New York) has named Michio Soga as chief financial officer. Most recently, Soga was a life sciences consultant advising firms on strategic financial management, capital raising and corporate development initiatives. Premune is a research and development stage animal health company focused on new therapeutics for companion animals.

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HRS

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than a ceaseless barrage of bits and bytes.

Leslie Saxon, MD, of the Keck School of Medicine at the **University of Southern California** (Los Angeles), characterized providers as "woefully reluctant to embrace connectivity," but said that at some point in the future, patient data would stream unhindered by the current set of restraints. She remarked "the human-machine interface is dramatically changing" already, claiming, "this relation between human and machine . . . will change our relationships to ourselves and other humans," and will "incorporate things we wouldn't ordinarily think of" as medical care, including music.

Saxon, the director of the USC Center for Body Computing, drew an analogy based on the evolution of recorded music. "We're still in the days where you have to buy the record to listen to the song," she said as an LP record appeared on the three monster displays in the main hall at the **Moscone Center** (San Francisco). Now, however, "I can listen to a variety of things on demand" on many platforms, she observed. The primary impetus behind digital medicine did not come from doctors or device makers, Saxon suggested. "Nobody set the stage for this reality more than Steve Jobs," the deceased co-founder of **Apple** (Cupertino, California), she asserted.

Saxon said continuous diagnostic data is the proper objective of digital medicine, and remarked that those who invest in big data do so "thinking that the monetization is going to come from people's information." She added that venture capital's "digital health investment is expected to exceed $3 billion next year," a sum she said is more than VC will apply to traditional med-tech investments.

The race is on for primacy in big health data, and Saxon asked, "who's going to win? One can't help think about **Google**" (Mountain View, California) she observed, but she posed the question of whether Google is possessed of the right culture to take the lead in this field. However, she said there is little indication that traditional med-tech has the required mindset, either.

Saxon argued that social media have a role to play in all this, adding that privacy "is often used as an excuse" not to go digital. She said that business strategies devised to claim turf in the digital health marketplace will revolve largely around mobile platforms, with the end result being, "from birth, human beings will provide their information to the cloud."

Eric Topol, MD, of the **Scripps Translational Science Institute** (La Jolla, California), tackled the question of personalized medicine, and led his remarks by quoting naturalist Emmet Densmore in saying, "medicine is not a science; it is an empericism based on a network of blunders."

Topol had other pointed remarks for the current state of medical care, but he focused much of his presentation on novel diagnostic technologies as a means by which patients could sidestep the need to check into a hospital. He reminded attendees that modern mobile devices of several sorts can tell the doctor what the diagnosis is, including the so-called ICU on the wrist and a digital "necklace" that serves as a remote monitoring tool for a number of conditions, including stroke. The advantage is in part that such technologies can aide physicians in helping patients to distinguish between events that do and do not require immediate medical attention, "but also that they improve outcomes at reduced cost," Topol said.

Topol made reference to technologies that would enable smartphones to perform assays, and silicon chips that are edible and embeddable, including nanosensors in the bloodstream that could advise the patient of an impending event. He said that with the proper technology, "you have the opportunity to detect sloughing of endothelial cells" from the coronary arteries, an event these nanosensors could relay to the patient or clinician via an alert that could substantially cut down on the number of infarcts.

Topol took a Shakespearean jab at what he described as "the edifice complex," a reference to bricks-and-mortar healthcare. "Why do we need hospitals when we can" treat patients "more safely in the comfort of their own homes?" he queried. He said one of the Mayo Clinics and its nurse practitioners have devised a system allowing patients more routine contact via mobile devices, a development that can dampen demand for precious MD time, which he pointed out is becoming more precious by the day.

"The driverless car, which is an exemplar case of artificial intelligence," Topol said, will not be the last instance of a computer replacing at least some human functions. "We're moving to an era of the doctorless patient," he speculated, adding that he sees a future for medical care that is "incredibly bright." //

BRIEFLY NOTED

DaVita using new testing technology

DaVita Kidney Care (Deland, Florida), a division of DaVita HealthCare Partners and a provider of kidney care services, said that DaVita Labs, the diagnostic laboratory servicing both dialysis organizations and physician practices, has implemented molecular diagnostic testing using technology from Roche Diagnostics.

This molecular diagnostic testing will allow DaVita Labs to be the first dialysis laboratory in the country to test for Hepatitis C (HCV) virus levels in the blood (viral load) using the COBAS Ampliprep/COBAS TaqMan HCV v.2 test from **Roche** (Basel, Switzerland). This DNA-based technology will enable DaVita Kidney Care to help nephrologists manage patients with chronic HCV in conjunction with clinical and laboratory markers of infection. The test can be used to predict the probability of sustained virologic response (SVR) early during a course of antiviral therapy, and to assess a patient's response to antiviral treatment.

SEMDA

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"As we think about what's happening within the healthcare and products industry today, there are a couple of things to me that are clear known qualities," she said. "One is that the system is under a tremendous amount of pressure. [The pressure ranges] all across the system in every piece and part of it. The second is, as we think about speed, nimbleness and agility . . . I've never seen a market and industry move so quickly. Whether that's private life cycle; whether that's change in payments; and how systems are changing in the market place; [the industry] is moving fast and it's also moving globally."

"The third [quality] is scale," Ashby said. "So as you think about it, whether that scale is manifesting itself in health systems out there today consolidating and buying up; whether that's physician employment trends; whether that's community-based hospital trends; whether that's clinic practices; whether it's scaled from a device company standpoint; it's out there and it's happening."

As an example of the expanding scale of the industry, Ashby pointed to **Zimmer** (Warsaw, Indiana) acquiring **Biomet** (also Warsaw) for $13.35 billion (*Medical Device Daily*, April 25, 2014). The transaction is expected to close in the first quarter of 2015 and came as a surprise to some ortho-followers because less than two months ago Biomet filed paperwork with the Securities and Exchange Commission to go public. Analyst reports suggest the deal could have positive implications for all ortho-players as it should help alleviate pricing pressures in the hip and knee markets.

"That's all about scale at the end of the day," she said in reference to the Biomet acquisition. "It's created the second largest orthopedics company in the marketplace. Those things are going to continue to happen. From my perspective, a lot of those opportunities to increase scale are going to happen because of cost."

Ashby then went down a list of the key trends she thought were shaping the industry and the healthcare environment. Aware of that other presenters had presented their own lists throughout the day, she quipped that this was her own unique take on the situation.

"Everyone's had a list today right?" Ashby asked the audience. "Everyone has a list that these are the three trends, four trends, five trends, whatever they are. Here's my list, [of] seven things."

She pointed to seven key factors; a growing population of sick and aging patients; care moving from acute care hospitals to more efficient models; information transparency; waning trust; increased access; consumer knowledge; and involvement and increased focus on coordination of care.

"A lot of these [factors] you've already talked about [in earlier sessions]," she told the audience. "And a lot of them you see, feel and touch every day within all of your risk factor businesses as well."

One of the greatest needs that those in the healthcare need to focus on is segmentation and focusing on the individual customer.

"One thing we can't talk enough about as an industry is segmentation," Ashby said. "As you think about who your customer is and what type of problem you're trying to solve at the end of the day, segmentation is going to be really critical."

Ashby told the audience that ultimately, segmentation along with innovating the business model from a horizontal perspective, will lead to success in the industry.

"It's not about innovating this widget that I brought to the healthcare market today, it's about how am I innovating around how this widget is used, when it is used and how the whole eco-system is responding to that perspective."

Another key component is utilization of products - a topic that strongly resonated with customers.

"Many of us in the device industry haven't liked to use the word utilization, but customers are now recognizing and talking to me virtually every day, that when they think about individual products it's about price type utilization equals cost," she said. "When you think about that the solutions for getting utilization is going to be really important for customers at the end of the day, whether that's evidence-based purchasing; or whether that's sort of protocols that are put in place."

Ashby noted there is a shift in the purchasing power and that's something that the med-tech industry needs to not only be aware of, but to also take advantage of.

"Physicians, as some would say, are losing their influence from a buying standpoint," she said. "Physician preference items aren't at the levels that they were five or 10 years ago. "We continue to see the market move to integrated delivery network-driven decisions vs. individual physician preference." //

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DDW

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Association Institute (AGA; Bethesda, Maryland), the **American Association for the Study of Liver Diseases** (AASLD; Alexandria, Virginia), the **American Society for Gastrointestinal Endoscopy** (ASGE; Downers Grove, Illinois), and the **Society for Surgery of the Alimentary Tract** (SSAT; Beverly, Massachusetts).

Natural orifice transluminal endoscopic surgery (NOTES) with endoscopic submucosal dissection (ESD) has been around for quite some time now, but advancements in the technology has helped the field really take off in the U.S. in recent years. The technique is used to treat early stage cancers in the gastrointestinal tract. Endoscopic mucosal resection (EMR) is another technique for removing cancerous or other abnormal tissues from the digestive tract.

Olympus noted that all of its endoscopic devices are designed to work with Olympus scopes and offer advanced solutions for EMR and ESD.

"Some lesions you simply cannot remove with EMR techniques," Peter Draganov, MD, of the **University of Florida** (Gainesville), told a crowd of about 30 people at Olympus' DDW booth.

Draganov said there are three key benefits to performing ESD. One, he said, is lower recurrence rates. Second, the technique allows unblocked resection regardless of size, according to the company. Finally, ESD preserves organ integrity and patient quality of life, Draganoc said.

"Quality of life is much better if you have the rectum in place," he said.

ESD also allows for accurate histopathologic assessment, Draganov told the physicians. "I don't have to spend long to convince you that this is better than this as for histopathologic assessment," he said.

During the hands-on demonstrations, *Medical Device Daily* watched Naohisa Yahagi of **Keio University School of Medicine** (Tokyo) assist Tarik Akar of Turkey in performing a practice ESD procedure on a pig's intestine. All the doctors and company representatives scrubbed in wearing gloves and disposable yellow lab coats to protect themselves from potential infections. To see a picture of Yahagi assisting Akar during the demo at DDW, visit *MDD*'s twitter account @MedDevicesDaily.

The demonstration physicians received at DDW was introductory level, a company spokesman told *MDD*. If any of those doctors are interested in learning more about using Olympus technology for ESD procedures, they would need to receive further training before heading for the operating room.

Other technologies Olympus spotlighted at DDW included the company's new next-generation EU-ME2 ultrasound processor. According to the company, the EU-ME2 can integrate endoscopic and endobronchial ultrasound (EUS/EBUS) on a single workstation. EUS technology is designed to combine ultrasound with endoscopy to better visualize the tissues of the digestive tract and adjacent anatomical structures inside the human body. With EUS, the transducer is endoscopically inserted into the body via the digestive tract, putting it closer to the area of interest to obtain higher resolution images, the company said.

For EUS, the EU-ME2 is designed to offer image quality comparable to a large radiology processor but in a compact model, according to Olympus. Features of the processor include improved B-mode for more accurate identification of tumors and tissue properties and boundaries; high resolution flow mode to image small vessels around the tip of the endoscope for more precise anatomical identification; Pulse Wave Doppler mode to measure blood flow velocity in a specific location to help identify the target area of interest; Elastography mode to map tissue elasticity, which may help indicate disease and highlight areas to biopsy; and Tissue Harmonic Echo mode for improved resolution, signal-to-noise ratio and reducing imaging artifacts.

Olympus also launched an automated endoscope leak tester, dubbed the ALT-Pro, designed to prevent human error while enhancing efficiency in endoscope reprocessing.

Conventional endoscope leak testing includes pressurizing an endoscope with an air pumping device while submerging the scope in water, angulating the scope's distal tip and manually flexing and manipulating the entire exterior area of the endoscope while observing the water for air bubbles. By finding endoscope leaks sooner, Olympus noted, the potential for endoscope cross-contamination and costly endoscope repairs can be reduced. Olympus said the ALT-Pro's dry leak testing technology is fully computerized, creating a "highly repeatable" leak testing process for all skill levels. //

BRIEFLY NOTED

NanoString to market Prosigna in Canada

NanoString Technologies (Seattle) has received a Class III Medical Device License from Health Canada, clearing the company to market its Prosigna Breast Cancer Prognostic Gene Signature Assay for assessing a woman's 10-year risk of distant recurrence and accurately identifying the intrinsic biologic subtype of the tumor.

Prosigna is an *in vitro* diagnostic breast cancer assay run on the nCounter Dx Analysis System that assesses the gene expression profile of cells found in a woman's breast cancer tissue. This information is then used to identify intrinsic subtype of the tumor and assess the risk of distant recurrence of disease in postmenopausal women with hormone receptor-positive (HR+) early-stage breast cancer. The Prosigna Assay is the first diagnostic test approved by Health Canada for use in local, qualified clinical laboratories, enabling oncologists and pathologists to meet the diagnostic needs of patients with breast cancer without sending tissue samples outside of Canada.

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IT

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Aging Well." AAL invests in European companies/consortia which are 1-3 years from market launch, which adopt a 'disease-maintenance' approach: they address the elderly patient's quality of life, and aim to delay the major upheaval (and the disruption of the social fabric) from these conditions, in spite of the slow progression of disease.

AAL believes that left as is, chronic disease will paralyze the world's health system in coming years. "The demographics are worrying across the whole developed world, through to China, Russia and beyond," Juan Carlos Castrosin, an AAL advisory board member explained to *Medical Device Daily*, "as we consider the major overhaul that the healthcare system will need to perform, not merely to deal with the acute facilities, but additionally with the numbers of patients needing support and attention on a constant basis." The spectrum of diseases may range from Alzheimer's, Parkinson's and stroke patients, to high-risk cardiac or many physically frail patients. The populations must – while waiting for therapies to emerge from the laboratories and clinical settings - address potentially lower-hanging fruit of technology solutions that in the short term might ease the burden of disease.

Two examples of AAL-sponsored projects were presented at the MTI Conference. Both companies are designed to suit a large patient population, with their technology scalable, and hopefully indifferent to the healthcare system incorporated in the designated country.

Vision Localization Systems (VLS, Seville, Spain) has developed the Keruve system which is designed to act as a mobile GPS system, to share with the caregiver the exact location of the early-stage Alzheimer's Disease (AD) patient both in buildings and in open areas. "Getting lost in familiar places is the first step of a terrible chronic disease, but if we can maintain some level of normalcy during that difficult stage, it can be most helpful and re-assuring to both patient and caregiver," explained Abilio Caetano Pereira, CEO of VLS.

Keruve uses a wearable wristwatch and a portable receiver to ensure that the AD patient is monitored, safe, but not over-managed. Pereira explained. "It enables the family not to lock the doors and stop activity/socialization. These limitations certainly exacerbate the social damage of AD to both patient and families, and might accelerate disease progression."

This option of 'delayed reduction in quality of life' perfectly suits the goals of AAL. It also carries with it major commercial potential for a product that currently costs approximately $1000, and may justify far higher cost savings associated with carers and/or lost work hours. In 2011, the company started commercializing efforts in Germany, UK and the U.S., with native sales teams based in Seville. The company has sold more than 3,000 systems merely by selling over the Internet, and plans targeted marketing campaigns across the EU and the U.S. in the coming quarters. They have competitors who have location tracker systems, but the company states that no other player with such equipment has an exclusive eye on the AD population, or has suited the product for both the AD patient and AD caregiver population in terms of interface and usability.

Social care is becoming a delivery point for healthcare. On that premise, another AAL-affiliated company, **Giraff Technologies** (Vasteras, Sweden) presented its hardware solution. The Giraff is a mobile human-size communication avatar, placed in the elderly patient's home, in order to enable interaction and virtual house visits by care personnel. Giraff allows the healthcare/social care provider to 'log-in' and conduct a natural, secure (virtual) visit of the patient, and the home at any time, balancing the need to have a communication and consultation method on one side, with patient independence and quality-of-life on the other. The remote-managed mobile system can use its 'instant presence' as a surrogate helper in many cases, and hence delays the patient's need for full-time on-site presence and/or transition to a care facility.

At a figure of $2000 for the hardware, and approximately $250 for a monthly subscription, this system can reduce the payor's bill of up to €5000 ($7000) per month in a healthcare facility, while maintaining a higher quality of life to both patient and family too. In Scandinavia, for example, the product can be a major cost saver for the healthcare system, which is responsible for patient 'social healthcare environment.' With more than 100 systems installed across the EU, the country's health system is – to date - the payor for this system. "Payment from the healthcare payors would not occur in the U.S. system," Stephen Von Rump, CEO, told the audience, "In the U.S., we believe that we will be saving the family enough money and stress, to easily justify the outlay." The company is now piloting the Giraff+ product, which also enables the upload of patient-monitored data through the Giraff interface to a practitioner, in order to enable increased quality of analysis of complex variables by the physician, where necessary.

AAL and these two companies do not directly delay chronic disease, but delay the devastating effect of the disease. They might be a critical direction to consider across the world of health management in the coming decade. While investing in disease treatments and prevention programs is essential, using IT developments to reduce the need for significant social upheaval is a positive direction that deserves to be effectively addressed. It is therefore good news that just this week, the European Parliament approved the decision to extend the AAL Joint Program to AAL-2, ensuring another €600 million ($840 million) over the next six years for Europeans supporting the opportunity to live more fully while aging. //

AGREEMENTS/CONTRACTS

Palyon Medical to make CORE's delivery pumps

Staff Report

Palyon Medical (Santa Clara, California) and **CORE Manufacturing** (Valencia, California) have entered into a strategic partnership for the manufacturing of Palyon's line of implantable drug delivery pumps.

Palyon, a developmental stage company, has a pump portfolio that includes programmable devices for maximum clinical flexibility and constant flow devices for lower cost steady drug delivery. CORE is an ISO 13485, ISO 9001 and FDA approved manufacturer of implantable devices. CORE Manufacturing will provide manufacturing services, procurement coordination and dual quality control oversight, reducing Palyon's time to market introduction.

Palyon says its implantable infusion pump platform will offer accurate drug delivery rates and incorporate safety features including sensor-based feedback flow control, refill error detection capability, a non-motorized pumping mechanism that is less susceptible to wear and tear, catheter occlusion detection and a highly favorable MRI profile.

Palyon Medical is a privately held medical device company focused on creating treatment systems to alleviate symptoms of chronic pain, spasticity, diseases of the central nervous system and chronic metabolic diseases. CORE Manufacturing makes implantable, minimally invasive, and peripheral medical devices.

In other agreements/contracts news:

• **Flextronics** (San Jose, California), an end-to-end supply chain solutions company, said its Medical Group will provide design and manufacturing services to **Ichor Medical Systems** (San Diego) for the development of its TriGrid DNA Delivery System, an electroporation device used to deliver DNA vaccines and treatments addressing a broad spectrum of disease indications. The TriGrid technology has recently been licensed by Pfizer for the intracellular delivery of their DNA-based cancer vaccines.

Supply chain services for this next generation TriGrid system will be performed at Flextronics facilities in Texas.

Ichor's TriGrid Delivery System is an automated device for electroporation-mediated DNA administration in humans. Electroporation is a potent method for enhancing DNA vaccine delivery with the application of electrical fields at the site of DNA administration, resulting in increased antigen expression and enhanced immune responses to the encoded antigen.

Ichor Medical Systems provides its enabling TriGrid platform as a means for delivery of DNA drugs and vaccines in disease indications such as cancer, malaria, hepatitis B virus infection, human immunodeficiency virus infection, as well as for multiple biodefense agents.

• **Affymetrix** (Santa Clara, California) and **Leica Biosystems** (Nussloch, Germany) reported the launch of Affymetrix' fully automated RNA *in situ* hybridization assays ViewRNA eZ Assays on the Leica BOND RX staining platform. These assays detect coding RNA as well as novel non-coding markers in formalin-fixed paraffin-embedded (FFPE) tissues.

Dedicated for research use only, the assays provide researchers with an automated solution for drug discovery, translational research, and the development of new diagnostic tests for personalized medicine.

The Leica BOND RX system automates the staining process, bringing all the benefits of consistency, reduced labor, and speed. This fully automated assay is hands-free from tissue de-waxing to counter staining, and offers high sensitivity, specificity, and reproducibility with easy standardization across laboratories. ViewRNA eZ Assays represent a major technological advancement offering a robust and reliable platform to easily interrogate the function and disease relevance of any expressed genes.

Leica Biosystems provides anatomical pathology laboratories and researchers a product range for each step in the pathology process, from sample preparation and staining to imaging and reporting.

Affymetrix technologies enable multiplex and simultaneous analysis of biological systems at the cell, protein, and gene level, facilitating the rapid translation of bench-top research into clinical and routine use for human health and wellness.

• **Desert Valley Radiology** (Phoenix), a physician-owned private practice with six locations in the Phoenix area, has partnered with McKesson Business Performance Services (Atlanta) for revenue cycle management and assistance with regulatory compliance, including mandated quality reporting.

McKesson will provide the practice with revenue cycle management services, including coding, billing, claims submission, denial management and financial reporting. McKesson will also help Desert Valley meet the physician reporting requirements of the Centers for Medicare & Medicaid Services' Physician Quality Reporting System, as well as prepare for the ICD-10 coding system transition in October 2015. Desert Valley previously handled coding, billing and compliance through a separately held billing company. //

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DIAGNOSTICS EXTRA

Keeping you up to date on recent developments in diagnostics

By Omar Ford, Staff Writer

CARDIODX REPORTS PUBLICATION OF REGISTRY STUDY RESULTS

CardioDx (Palo Alto, California), a molecular diagnostics company specializing in cardiovascular genomics, reported the publication of the REGISTRY I study, which examined the assessment of non-acute chest pain and related symptoms that may be suggestive of obstructive coronary artery disease (CAD) in the primary care setting with the Corus CAD blood-based gene expression test. The study, published online in the *American Journal of Medical Quality* in May 2014, found a strong association between cardiac referral rates by low (≤ 15) and elevated (> 15) Corus CAD score groups, with only 6% (10/167) of the low Corus CAD score patients vs. 70% (122/175) of the elevated Corus CAD score patients being referred for further cardiac evaluation (P < .0001).

Corus CAD is a blood-based gene expression test that provides a current-state assessment of obstructive CAD in non-diabetic patients presenting with typical or atypical symptoms. With a 96% negative predictive value and 89% sensitivity, Corus CAD can help clinicians accurately rule out obstructive CAD as the source of their patients' symptoms, so that they may investigate other non-cardiac causes.

The REGISTRY I study, which was conducted in collaboration with Humana Comprehensive Health Insights, measured the impact of Corus CAD testing on primary care referral decisions among 342 patients in seven community-based primary care practices based on each patient's individualized gene expression score. About 49% of patients had a low Corus CAD score, allowing their primary care providers to focus on other causes for their symptoms. Each 10-point decrease in a patient's Corus CAD score was associated with a 14-fold decreased odds of referral for further cardiac evaluation or testing (P < .0001). In addition, patients with a low Corus CAD score had a 94% reduced odds of referral relative to patients with an elevated Corus CAD score (P < .0001).

SURGEONS 'LIGHT UP' GI TRACT TO SAFELY REMOVE GALL BLADDER

A green fluorescent dye is helping surgeons at the **University of Illinois Hospital & Health Sciences System** (UI; Chicago) perform robotic gall bladder surgery more safely. UI Health surgeons used near-infrared light to make the indocyanine green dye light up, allowing them to better see the biliary tract. Injury to the bile duct is rare — only 0.3% of the nearly 600,000 cholecystectomies performed in the U.S. annually — but it can cause severe complications to patients. Surgeons are increasingly performing the gall bladder surgery robotically — for better ergonomics, visualization and placement of surgical instruments.

The retrospective study, published online in the journal *Surgical Innovation*, looked at 184 robotic cholecystectomies performed at UI Hospital between July 2011 and February 2013 that used the non-radioactive dye to image the bile duct.

Of the procedures performed, 112 were multiport and 72 were single-incision robotic cholecystectomies.

"We found that indocyanine fluorescence allowed us to visualize at least one biliary structure in 99% of cases," said Pier Cristoforo Giulianotti, chief of general, minimally invasive and robotic surgery and senior author of the study. These structures included the cystic duct (seen in 98% of cases), the common bile duct (96%) and the common hepatic duct (94%).

Visualization helped surgeons to identify variations in anatomy, and in four cases, to detect the presence of gallstones impacted in the cystic duct, Giulianotti said. No major complications, such as biliary injury or allergic reaction to the dye, were reported during the procedures.

GENETIC RISK FACTOR FOR PREMATURE BIRTH FOUND

Researchers at the **University of California**, **San Diego School of Medicine** have discovered a genetic risk factor for premature birth. The risk factor is related to a gene that codes for a protein that the scientists have found helps the body's immune cells recognize and fight Group B *Streptococcus* (GBS) bacteria.

These bacteria are found in the vagina or lower gastrointestinal tract of approximately 15% to 20% of healthy women, but may cause life-threatening infections, such as sepsis or meningitis in newborns, especially those born prematurely. The study is published online in the May 5, 2014 issue of the *Journal of Experimental Medicine*.

"Pregnant women are universally screened for these bacteria during pregnancy and administered antibiotics intravenously during labor if they test positive to protect the infant from infection," said Victor Nizet, MD, professor of pediatrics and pharmacy and co-author. "Our research may explain why some women and their infants are at higher risk of acquiring severe GBS infections than others."

In the study, scientists identified two proteins on fetal membranes of the placenta that are involved in immune function. One of the proteins (known as Siglec-5) binds to the GBS pathogen and suppresses immune response to the microbe, while the other protein (known as Siglec-14) binds to the pathogen, and activates killing of the bacteria. Siglecs are cell surface receptors found typically on immune cells. They recognize (bind) sialic acids — sugar molecules that densely coat our cells.

"We have one protein that tells the body to attack the

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pathogen and another that tells the body not to attack it," said Raza Ali, PhD, a project scientist in the Nizet laboratory and the study's lead author.

Scientists believe that the pair of proteins together helps balance the body's immune response to pathogens, by directing some antimicrobial response without provoking excessive inflammation.

Interestingly, the gene for Siglec-14 is missing in some individuals, and the researchers have found that fetuses that lack the Siglec-14 protein are at higher risk of premature birth, likely due to an imbalanced immune response to the bacterial infection.

MONITORING RNA LEVELS YIELDS DYNAMIC PICTURE OF FETAL DEVELOPMENT, DISEASE

Recent research has shown that tiny fragments of DNA circulating in a person's blood can allow scientists to monitor cancer growth and even get a sneak peek into a developing fetus' gene sequences. But isolating and sequencing these bits of genetic material renders little insight into how that DNA is used to generate the dizzying array of cells, tissues and biological processes that define our bodies and our lives.

Now researchers at **Stanford University** (Stanford, California) have moved beyond relying on the static information delivered by DNA sequences in the blood. Instead, they've generated a much more dynamic picture by monitoring changing levels of another genetic material — RNA — in the blood. It's the biological difference between a still photo and a video when it comes to figuring out what the body is doing, and why.

"We think of this technique as a kind of 'molecular stethoscope," said Stephen Quake, PhD, professor of bioengineering and of applied physics at Stanford. "It's broadly useful for any tissue you care to analyze. There are many potential practical applications for this work. We could potentially use it to look for things going wrong in pregnancy, like pre-eclampsia or signs of preterm birth. And we hope to use it to track general health issues in various organs."

Quake and his colleagues combined the use of high-throughput methods of microarrays and next-generation sequencing to analyze the sequences and relative levels of RNA in the blood of pregnant women, healthy volunteers and Alzheimer's patients. By focusing on RNA messages encoding proteins known to be produced only in certain tissues, they were able to track the development or health of particular organs throughout the body.

Quake is the senior author of a paper describing the research to be published online May 5 in the *Proceedings of the National Academy of Sciences*. Graduate students Winston Koh and Wenying Pan are lead authors of the study.

With a few exceptions, your genome, encoded by your DNA, is shared among every cell in your body. Specific tissues and organs are formed by expressing only certain subsets of genes from the thousands of options in your genome. This gene expression is accomplished in part through molecules called messenger RNAs, which carry instructions encoded in genes to the cell's protein-making factories. The proteins in turn do much of the work of the cell.

Specialized proteins and other regulatory molecules in each cell control which genes are expressed, when they are expressed and how much of each RNA message is made. As a result, the particular sequences of messenger RNA used can vary widely among tissues and various biological and environmental conditions.

It's been known for decades that blood contains miniscule amounts of free-floating DNA and RNA released by dying or damaged cells throughout the body. Often this cell death represents natural cellular turnover; sometimes it's the result of disease processes. But, until recently, analyzing this genetic material has been difficult due to its scarcity.

New sequencing techniques capable of handling very tiny amounts of genetic material are opening broader vistas for researchers everywhere. Most efforts are focused on analyzing the DNA in the blood, either to determine its sequence or to compare the relative amounts of certain chromosomes. These techniques have applications in diagnosing cancers by looking for particular mutations not present in the patient's genome. Quake's lab pioneered an approach that allows clinicians to determine whether a fetus is likely to have conditions such as Down syndrome that are defined by abnormal chromosomal copy numbers. It is estimated that in 2013, more than 500,000 pregnant women used a version of Quake's noninvasive prenatal test to learn more about the health of their fetuses.

In the new study, the researchers used a technique previously developed in Quake's lab to identify which circulating RNA molecules in a pregnant woman were likely to have come from her fetus, and which were from her own organs. They found they were able to trace the development of specific tissues, including the fetal brain and liver, as well as the placenta, during the three trimesters of pregnancy simply by analyzing blood samples from the pregnant women over time.