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## Volume 20 - Issue 2, 2020 - Spotlight

### Bright Ideas

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HealthManagement.org rounds up exciting developments that have all the marks of healthcare game changers. What do you think?

#### Advancements in Cardiac Imaging

Conventional imaging still remains important for the assessment of cardiac structure and function. However, advanced echocardiography with strain imaging techniques, tissue characterisation with cardiovascular magnetic resonance (CMR), and the assessment of biological processes with nuclear imaging techniques have helped clinicians implement early intervention strategies to either prevent or halt the progression of cardiovascular disease.

Echocardiography is also the imaging technique of choice to assess valvular heart disease. Also, the use of transthoracic focused cardiac ultrasound (FoCUS) has gained popularity in emergency departments and intensive care units. In addition, elevated carotid artery wave intensity, as measured on Duplex Doppler ultrasound, was found to be independently associated with faster cognitive decline in the Whitehall II study. These findings highlight the relevance and importance of ultrasound imaging outside the heart.

In recent years, cardiovascular magnetic resonance has made a significant contribution to the diagnosis and management of cardiomyopathies. Similarly, computed tomography has also now evolved into a one-stop-shop imaging tool providing valuable diagnostic and prognostic information in patients with suspected or known coronary artery disease. Coronary artery calcium (CAC) score on CT was also increasingly used to guide statin therapy.

There is no doubt that invasive and non-invasive cardiovascular imaging is developing at a rapid pace. Today, clinicians have access to different imaging modalities, which are now even more effective with fusion imaging as well as the introduction of AI and machine learning. In particular, machine learning has been rapidly adopted and allows automated analysis of electrocardiograms, echocardiography, nuclear perfusion imaging, and CCTA.

Finally, deep learning has also been applied quite effectively to analyse echocardiographic data, including view identification, image segmentation, quantification of structure and function, and disease detection.

#### PET/MRI Pinpoint Notable Breast Cancer Biomarkers

Researchers have pinpointed breast cancer biomarkers that have the potential to indicate malignancy presence and risk.

A research team from Memorial Sloan Kettering Cancer Center in New York compared healthy contralateral breast tissue of patients with malignant breast tumours and benign breast tumors. They found that PET/MRI imaging could assess multiple biomarker differences that could impact risk-adapted screening and risk-reduction strategies in clinical practice.

Early detection of malignancy is critical in breast cancer for best prognosis and survival. Screening has been successful in decreasing breast cancer patient mortality but is limited for women with dense breast tissue.

The study included 141 patients with imaging abnormalities on mammography or sonography on a tumour. The patients underwent combined PET/MRI of the breast with dynamic contrast-enhanced MRI, diffusion-weighted imaging (DWI) and the radiotracer 18F-FDG.

Several imaging biomarkers were recorded in the tumour-free breast in all patients with differences analysed by two independent readers.

The readers assessed 100 malignant and 41 benign lesions. In the contralateral breast tissue, background parenchymal enhancement and breast parenchymal uptake were decreased and showed significant differences between patients with benign and malignant lesions. The difference in fibroglandular tissue came close but did not reach significance, and the mean apparent diffusion coefficient did not differ between the groups.

As hybrid PET/MRI scanners are increasingly being used in clinical practice, they can simultaneously assess and monitor multiple imaging biomarkers - including breast parenchymal uptake - which could consequently contribute to risk-adapted screening and guide risk-reduction strategies.

#### MRI and Radiomics Predict 10-Year Breast Cancer Recurrence

Breast cancer is complex for clinicians to diagnose owing to how greatly cells within one tumour can vary. This complexity and challenge is highlighted by the fact that a biopsy only targets a sample of cells.

A study from Penn Medicine has addressed this. Using MRI and radiomics, clinicians can find it easier to understand a person's individual breast

cancer through better clarity on the heterogeneity of cancer cells within a tumour.

As part of the study, the research team wanted to see how a combination of imaging and radiomics could be deployed for personalised tumour characterisation.

With MRI, the team extracted 60 radiomic features (biomarkers) from 95 women with primary invasive breast cancer. Ten years later, the researchers followed up. They found that scans could accurately predict cancer recurrence when high tumour heterogeneity had been detected at the time of diagnosis.

They found that women who had more heterogeneous tumours tended to have a greater risk of tumour recurrence.

Clinical trial scans from 2002-2006 were retrospectively analysed and, for each patient, a "signal enhancement ratio" (SER) map was generated. From this map, researchers extracted a range of imaging features to understand their link with conventional biomarkers (gene mutations or hormone receptor status) and patient outcomes.

The algorithm could successfully predict recurrence-free survival after 10 years.

The team said the findings were interesting because, while imaging would not necessarily replace the need for biopsies, radiologic methods could provide a more individual profile for personalised care.

## **New Way of Fighting AMR**

Discovery of a new group of antibiotics promises to facilitate the fight against antimicrobial resistance.

These antibiotics, corbomycin and complestatin, come from the glycopeptides family produced by soil bacteria. Unlike other antibiotics, such as penicillin, which prevent building of the bacteria cell wall, these have a unique approach to killing bacteria by blocking the function of the wall critical for cell to divide. The new antibiotics are also able to block infections caused by the drug resistant *Staphylococcus aureus*, as was demonstrated in mice.

The researchers, led by Beth Culp, a PhD candidate in biochemistry and biomedical sciences at McMaster, studied the genes of those members of the glycopeptides, which lacked known resistance mechanisms. Assuming that these might demonstrate a different way to attack bacteria, the group used cell imaging techniques in collaboration with the Université de Montréal to confirm that these new antibiotics acted on the bacterial wall.

According to Culp, this approach can be applied to other antibiotics, which may lead to discoveries of those with different mechanisms of action.

## **Automation of Blood Sampling**

A new automated blood drawing and testing device, created by a team at Rutgers University – New Brunswick, performed as well or better than people at blood sampling, the first human clinical trial showed. The results were published in the journal *Technology*.

In the trial with 31 participants whose blood was drawn, the robot's results were comparable to or exceeded clinical standards, with an overall success rate of 87%. This was even higher for the 25 people whose veins were easy to access: 97%.

The ultrasound image-guided robot is a fully integrated device, with a module that handles samples and a centrifuge-based blood analyser. It could potentially be used at bedsides and in ambulances, emergency rooms, etc.

Venipuncture is the world's most common clinical procedure, but previous studies showed that in 27% of patients without visible veins, 40% of patients without palpable veins and 60% of emaciated patients, clinicians fail to perform it properly. This may lead to a number of negative outcomes and increase overall risk to patient safety.

According to the researchers, procedures such as IV catheterisation, central venous access or dialysis are the prospective areas of the device application. Further adjustments of the robot will focus on improving success rates in patients whose veins are difficult to access.

## **3D Printed Burn Care**

A novel approach to treating large burn wounds by using a new handheld 3D printer is being developed by a team of researchers at University of Toronto Engineering and Sunnybrook Hospital.

As reported in the journal *Biofabrication*, the device can deposit sheets of skin to cover the wounds, while also facilitating the healing process. The printer covers wounds with a uniform sheet of biomaterial composed of mesenchymal stroma cells (MSCs), which promotes skin regeneration and reduces scarring.

Currently, autologous skin grafting is used to care for burns, ie transplantation of healthy skin onto the wound. But with large, full-body burns this can be problematic as there may not be sufficient healthy skin available.

The team presented the first prototype of the skin printer in 2018, which since then has gone through 10 redesigns. Back then the device could form tissue in situ, depositing and setting in place in two minutes or less, but now the researchers added evidence of its wound-healing capabilities. In the current prototype a single-use microfluidic printhead ensures sterilisation, and a soft wheel that follows the track of the printhead provides better control for wider wounds. In the future, the researchers aim to also reduce the amount of scarring. They hope to see the handheld skin printer in a clinical setting within the next five years.

## Artificial Intelligence-Assisted Care in Medicine: Friend or Foe?

Technical innovation has always been a driver for medical breakthroughs in the field of cardiology. These include the Laennec's stethoscope, the electro- and echocardiogram, percutaneous coronary interventions, transcatheter structural heart interventions, open-heart surgery, ventricular assist, and implantable electronic devices.

However, while we see many examples of such technologies, many have not translated to routine clinical care so far. Artificial Intelligence is one such example. It is important to note that AI is not a specific technology per se and it does not have any artificial features. It is actually machine intelligence (MI) and so far, MI has seen more disappointments than success. The expectations associated with AI/MI seem to over-inflated as far as cardiology is concerned.

There could be multiple reasons for this including a hospital's infrastructure and regulations. Hospitals are still in the process of transitioning to functioning as digitalised units, and data harmonisation is still a challenge for most hospitals. Also, with the introduction of the new EU Medical Device Regulation (MDR) in 2017, which is to become effective in 2020, several software are now considered medical products and have time-consuming and costly requirements for certification.

Machine intelligence is here to stay, but its application still poses a challenge for most hospitals. These can be overcome by using statistical models and by combining knowledge-based approaches with deep learning. MI has the potential to disrupt healthcare systems and clinical care. Computers can process large quantities of data and structured representation of knowledge in just a short time without loss of information. Both digitisation and desire for personalised medicine are likely to establish new clinical domains that will focus on computer-assisted medicine. It's just that both hospital management and clinicians have to keep up with this rapidly developing technology.

## German Doctors to Prescribe Health Apps in 'World First'

The German healthcare system is undergoing several digital upgrades in 2020 in order to improve the service.

One of the key features of the plan is that, for the first time, doctors will be able to prescribe healthcare apps to patients.

Expected to pass into law this year, the policy means that health insurance companies will provide health services digitally on tablets, computers and smartphones. An example of such an app would be one specially designed for diabetes monitoring and care.

German Federal Minister of Health, Jens Spahn described the move as a "world first."

There have been some reservations however. The Green Party has criticised the government for implementing new procedures with apps having proven their benefit.

Addressing this, the Federal Institute for Drugs and Medical Devices is set to examine app quality and safety, after which the developer must prove that the product better score.

Other digital upgrades to the German healthcare service this year include provision of online doctor consultations, digital prescriptions and digital sick notes.

## Promising Technology for Managing Pulmonary Diseases

A new non-invasive technology developed by Monash University (Australia) researchers can be used to diagnose, treat and manage respiratory lung diseases, such as cystic fibrosis, asthma and lung cancer.

Existing technology, eg 3D CT scans, cannot capture the spatial distribution of lung function in a breathing lung, which hampers early diagnosis and monitoring. New four-dimensional X-ray velocity (XV Technology) imaging provides high-definition images at 30 frames per second, allowing to see the movement of air in real-time and assess functional airflow in healthy and diseased lungs in live organisms, as was demonstrated by the research on mice. A comparison of a cystic fibrosis mouse model against a healthy control mouse allowed researchers to pinpoint localised areas of deficiency in a lung.

The study led by Dr Rhiannon Murrie from the Department of Mechanical and Aerospace Engineering at Monash University and published in Scientific Reports in January 2020, shows the potential application of this technology in respiratory disease detection, monitoring and treatment through non-invasive and non-terminal means. Another promising direction is assessment of how effective early interventions may be for respiratory illnesses.

The technology, commercialised by an Australian med-tech company 4Dx Limited, is being tested in human clinical trials in the USA, with Phase I already completed successfully.

## ACC, HeartHero to Advance Out-of-Hospital Cardiac Arrest Treatment

The American College of Cardiology (ACC) has partnered up with HeartHero to form an alliance to combat sudden cardiac death (SCD) and improve survival rates. For many years, the ACC has been on a mission to improve cardiac care. Now it aims to improve survival with the help of HeartHero's portable defibrillator.

SCD is a leading cause of mortality in the USA, claiming about 360,000 lives every year. A large majority of these patients die before they reach a healthcare facility. Also, a significant number of sudden cardiac death episodes occur in the home (65%), followed by a public setting (21%) and nursing homes (11%). About 37% of cardiac arrest is witnessed by a bystander and 12% by an EMS provider. Among the patients managed

by EMS, about 20% have an initial rhythm (ventricular tachycardia or ventricular fibrillation) that is shockable by an external defibrillator. Today, external defibrillators can be found in most public places including airports, hotels, government buildings, airplanes, cinemas, etc.

HeartHero's AED was the recipient of the Innovative Challenge award in New Orleans. It is small, portable, and user-friendly. The miniature size means that individuals at risk for sudden cardiac death can now store the device in their car, carry it home, and even have it in the office, ensuring instant access. The HeartHero AED has a visual indicator that guides the user through the resuscitation process. It also has auditory and visual aids that guide the user through the resuscitation process.

## **World Economic Forum Promotes AI Toolkit**

While about 29 countries have established national AI policies to address potential risks, very few companies have followed suit.

To address this challenge, the World Economic Forum (WEF) has worked with more than 100 companies in six countries and experts in the field of technology to develop the Empowering AI Toolkit.

The kit has been designed with the structure of a board meeting in mind. It aligns 12 learning modules with traditional board committees and working groups. The objective is to support companies in making informed decisions on AI solutions for protection of customers and shareholders.

WEF said that AI was a tool in a corporate board's toolkit and that boards need to know when to deploy it and how it aligns with a company's overall strategy.

The Empowering AI Toolkit was created by the World Economic Forum with Centre for the Fourth Industrial Revolution Network Fellows from Accenture, BBVA, IBM and Suntory Holdings. Among the many others who contributed to its development were AI4All, Australian Institute of Company Directors, Best Practice AI, Latham & Watkins, Saudi Aramco and Splunk.

## **Machine Learning and Early Diagnosis of CVD**

Despite significant advances in the diagnosis and management of cardiac disease, cardiovascular disease continues to have high morbidity and mortality. In some cases, the diagnosis is delayed, while in others, the diagnosis is mistaken for another disorder. Advanced technology and machine learning have opened up new opportunities to evaluate image-based data.

Currently, image analysis is completely reliant on observer visual assessment and using crude quantitative measures to assess cardiac function and structure. Clinicians agree that there is a need for more advanced analytical techniques that can allow for more refined quantification of imaging phenotypes. That is why machine learning is slowly creeping into mainstream medicine, especially cardiology. Machine learning approaches to image-based analysis/diagnosis rely on models/algorithms that learn from past clinical cases through the identification of complex and hidden imaging patterns.

Preliminary data show the superiority of image-based cardiovascular diagnosis with machine learning for cardiac disorders like heart failure and coronary artery disease. The vastly superior diagnostic performance of artificial intelligence-based image analysis may help lower the burden of certain cardiac disorders by facilitating earlier and more accurate diagnostic decision making.

However, we are still in the early stage of machine learning, and researchers have systematically started to add the different case scenarios for each cardiac disorder with all the possible permutations and combinations. The more data is entered into the system, the more likely it is that the performance of the model will improve. Also, machine learning requires accurate output diagnostic labels and a suitable application to predict the right cardiac diagnosis based on the imaging data. But in any case, it is an effective tool and can help improve early diagnosis of cardiovascular disease.

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