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July - Aug 2022

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- Liver disease and diabetes
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Nephrolithiasis

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Prognosis

Translational medicine

In this issue we look at some new research published in the fields of paediatrics, MRI and nephrology. An article in the focus on nephrology looks at a good example of scientific research being translated into a beneficial commercial product – in this case for patients with kidney stones. Researchers at the Fraunhofer Institute for Manufacturing Technology and Advanced Materials developed a product made from biocompatible liquid materials that can be endoscopically inserted into the kidney following laser lithotripsy. Here the liquids combine to form a hydrogel that encases the stone fragments. The gel is sufficiently elastic to be gripped with a grasping tool. In this way the tiny stone fragments can be extracted. The two researchers have formed a spin-off company and plan to market the product later this year.

In the focus on paediatrics, we publish a brief review of some research by Aaron Milstone, M.D., who is a professor of paediatrics at the Johns Hopkins University School of Medicine. He looks at how hospitals can reduce antibiotic overuse by avoiding unnecessary blood draws in critically ill children. This is an important contribution in the context of growing antibiotic-resistance and the drive to reduce antibiotic use to combat this.

Saudi Arabia recently announced some major restructuring in the way they deliver public healthcare. The Saudi cabinet has established a Health Holding Company. The move will see the Ministry of Health focussing on regulating and supervising all public and private health institutions, while the Health Holding Company, via its local health cluster subsidiaries, will provide integrated healthcare services for the people of the Kingdom. You can read more about this in the Middle East Monitor.

Also in the news is a report from cyber security company Sophos. They say their research shows that there has been a steep increase in the number of ransomware attacks on healthcare organisations from 2020 to 2021. Healthcare organisations are the most likely to pay the ransom, however only 2% of those that paid the ransom in 2021 got all their data back. Patient data is a valuable commodity in the wrong hands. It is essential that is well protected.

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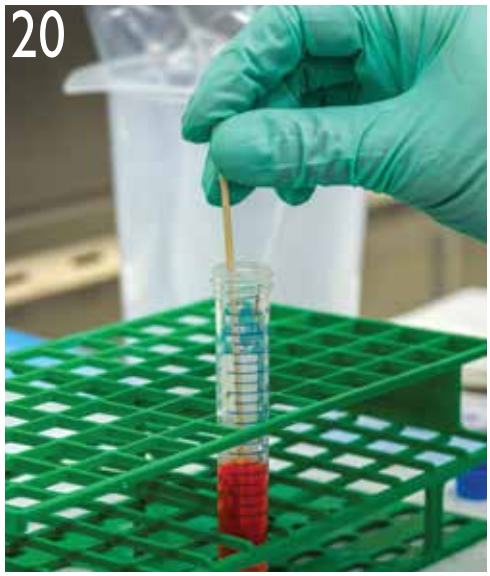

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middle east monitor

Update from around the region

Healthpoint brings new tech to UAE to conduct robotic-assisted knee replacement surgery

Healthpoint has conducted a robotic-assisted knee replacement surgery using the 'Mako' robotic arm by Stryker, a new technology introduced to the UAE by Healthpoint.

The new technology provides greater accuracy, better outcomes, faster recovery, and less pain for patients in comparison to hip and knee joint replacements done with traditional techniques.

Omar Al Naqbi, Executive Director, Healthpoint said: "We are dedicated to delivering the best possible clinical outcomes for our patients, and the introduction of robotic arthroplasty surgery at Healthpoint through this exclusive technology affirms our position as the number one provider of orthopaedic surgeries in the region.

"By introducing this cutting-edge technology, we provide comprehensive care to those who previously had to travel overseas for treatment, further strengthening our position as the leading provider for orthopaedic care in the region."

UK-based Dr Jonathan Conroy, who specializes in robotic-assisted hip and knee surgery, has extensive experience, and offers procedures such as arthroscopic hip surgery and standard joint replacements.

Dr Conroy said: "This type of robotic surgery is offered widely abroad and is now available to patients here in the UAE. In tandem with the surgeon, the system is able to perform extremely accurate incisions on the bone, which results in a quicker recovery and more positive long-term results. We have seen patients receiving the robotic surgery who are able to go home the very same day. From my experience, I've witnessed patients coming off their crutches within two-to-four weeks. We also noticed less swelling and pain."

The orthopaedic robotic arm-assisted surgery helps surgeons plan for the operation. Following a CT scan, a digital 3D model is created that can be viewed from all angles. This allows the surgeon to envisage how the hip or knee joint will move functionally. The joint replacement can be assessed before any surgery is carried out, so that the medical team can model what surgery to do – almost serving as a mock practice. The benefit is ultimately for the patient, whose new joint will work better, with greater accuracy in the size and placement of the implant, as well as the improved angles of cutting into bone that ultimately reduces pain and improves function.

Dr Conroy added: "The surgeries are carried out by an expert surgeon, assisted by robotic technology. Across the world, surgeons are now adopting robotics to further improve clinical outcomes. The robot is there to assist the surgeon, so ultimately, the surgeon is in control, and the robot is only there to perfect the procedure. In my own practice, I have conducted over 750 surgeries with the assistance of a robot."

At Healthpoint, Dr Conroy will be using the robotic technology to carry out hip, total and partial knee replacement surgeries. A fully qualified European trainer in the technology, he will also be training fellow surgeons in the use of a robotic-assisted arm, having previously passed on his knowledge and expertise to surgeons in China, Japan, Europe, and America. MEH

Saudi Arabia moves all healthcare services into National Health Holding Company and launches National Health Insurance Center

The cabinet of Saudi Arabia on May 31 established a Health Holding Company and approved the charter of the National Health Insurance Center. The decision was made in an effort to improve the overall performance of the Saudi healthcare system. The move will see the Ministry of Health focussing on regulating and supervising all public and private health institutions, while the Health Holding Company, via its local health cluster subsidiaries, will provide integrated healthcare services to beneficiaries across the Kingdom.

The National Health Insurance Centre will purchase health services provided by the Health Holding Company or any of its subsidiaries. The Cabinet decision also includes transferring all direct healthcare-related funds allocated in the national budget from the Ministry of Health to the Insurance Centre.

This is being done in accordance with the road map set by the supervisory committee for privatization of the health sector. The Privatization Program was launched in 2018. It seeks to identify government assets and services that can be privatized in a number of sectors, develop the privatization system and its

Eng. Fahad Al-Jalajel, Minister of Health, Saudi Arabia

mechanisms, define public and private sector partnership frameworks to enhance the quality and efficiency of public services, and support contributions to economic development. The aim of the initiative is to improve the quality of services provided and contribute to the reduction of costs, as well as encouraging economic diversity and development, and boosting competitiveness to face regional and international competition.

The Health Holding Company will establish health clusters in the form of independent companies known as Health Cluster Companies to provide services. While the Ministry of Health, as a regulatory and supervisory body, prepares healthcare coverage regulations, which will consider the needs of beneficiaries, protect them from health risks, and ensure the overall quality and fair distribution of services.

Eng. Fahad Al-Jalajel, Minister of Health, Saudi Arabia, explained that the decision embodies the leadership's interest in improving healthcare services provided to all citizens and residents, in pursuit of the Kingdom's Vision 2030 goals.

Eng. Al-Jalajel added that this decision lays the legal foundations for implementing the transformation strategy in the Ministry, which will take place in successive stages over the coming years. The local Health Cluster Companies will implement a set of programmes aimed at enhancing community health through the prevention and early detection of diseases by means of developing primary healthcare services.

The new company will also provide specialized services such as: caring for patients with cancer and kidney failure, developing critical care services; ensuring the efficient handling of heart attacks, strokes, and injuries, and expanding digital health programs and virtual medical care services. MEH

Cleveland Clinic Abu Dhabi surgical team complete UAE's first successful valve-in-valve transcatheter mitral valve replacement

Physicians at Cleveland Clinic Abu Dhabi have successfully performed a valve-in-valve transcatheter mitral valve replacement (VIV-TMVR) in a clinical first for the United Arab Emirates.

The 77-year-old patient, Sfeir Iskandar, who had a history of prior coronary artery bypass graft surgery (CABG) and mitral valve replacement, was referred to the specialists at Cleveland Clinic Abu Dhabi with recurrent heart failure. He was found to have severe mitral valve regurgitation and failure of his mitral valve. His complex case was further exacerbated by multiple medical problems, having previously suffered a stroke, and been diagnosed with kidney disease, while also being significantly frail.

Multiple hospitals had told him that any repeat surgical intervention carried too high a risk.

Dr Ahmad Edris, Interventional Cardiologist at Cleveland Clinic Abu Dhabi's Heart, Vascular and Thoracic Institute, explained: "We are at a stage in our structural heart programme that we can treat very complex valvular heart disease cases using minimally invasive techniques with excellent outcomes."

Dr Edris is the co-director of the structural heart programme with Dr Mahmoud Traina. Both work collaboratively with the cardiac surgery team to make the best treatment decision for each patient.

The treatment involved using a transcatheter heart valve, typically used in the aortic valve position for transcatheter aortic valve replacement (TAVR). The valve was delivered across the interatrial septum from the right to left-side of the heart after making a puncture in the septum and delivered to the mitral position. The procedure was performed in collaboration with the structural heart team physicians at Cleveland Clinic Foundation, in the United States, via web conference.

Dr Edris said: "The success of this procedure is all in the planning, with meticulous attention to detail. It still amazes me that we can perform valve replacement like this with no more than a small puncture through the skin and vein, allowing the patient rapid recovery and discharge from the hospital in two days." Dr Ahmed Bafadel helped with cardiac CT planning and procedural imaging.

Dr Edris said: "I don't know whether patients or families truly understand the importance of seeking cardiac evaluation and treatment early in their heart condition. We often see patients at the end-stage of their disease process when it carries the highest risk of death if left untreated."

Sfeir said: "I knew that I needed help but everywhere I went I kept hitting a dead end and nobody was either willing or able to treat me. That was why I was so relieved when I was referred to Cleveland Clinic Abu Dhabi. Dr Edris and his team were excellent. They really put my mind at ease and I was back in my own home within two days."

Cleveland Clinic Abu Dhabi currently performs more than two-thirds of all structural heart disease cases in the UAE with outcomes that are on par with the best programmes in the world.

"We are lucky to have an amazing and collaborative cardiac surgery, cardiac imaging, anaesthesia and nursing team," noted Dr Edris. "We could not achieve the same level of success without the structural heart team we have here at Cleveland Clinic Abu Dhabi." MEH

New NYU Abu Dhabi research could make cancer treatments more efficient

The research team at the Cell Death Signaling Laboratory at NYU Abu Dhabi

A team led by Professor of Biology, Senior Vice Provost of Research at NYU Abu Dhabi, and UAE national Sehamuddin Galadari, has discovered a novel structural modification in AMP-activated protein kinase (AMPK) during anticancer therapy that could pave the way for the development of more effective cancer treatments.

AMPK normally works as the cellular energy sensor that is activated when there is a shortage of energy in the body. Once activated, AMPK kickstarts events in the cell that restore the energy balance. The major component of AMPK exists as two isoforms – AMPK- 1 and AMPK- 2.

In a paper titled 'Caspase cleavage and nuclear retention of the energy sensor AMPK- 1 during apoptosis' in Cell Reports, <*https://doi.org/10.1016/j.celrep.2022.110761*> the research team identified that the caspase-3 enzyme specifically cleaves AMPK- 1 (but not - 2) during anticancer treatment. The scientists also identified the precise location of the truncation and found that, as a result, cleaved AMPK- 1 gets trapped in the cell nucleus.

The findings are of significant clinical and biological importance because they will help researchers design and develop a drug that specifically targets cleaved AMPK- 1 within the nucleus, which could increase the effectiveness of existing chemotherapy or radiotherapy.

Commenting on the findings, Galadari said: "Despite the advances in biomedical research and clinical applications, cancer remains a leading cause of death worldwide. Most anticancer drugs act by inducing death in cancer cells. However, resistance to therapy continues to be the principal limiting factor in achieving cures against cancer. In our work based on cell culture models, we noticed that the cleaved AMPK- 1 retained in the nucleus confers protection from cell death induced by anticancer drugs, causing resistance to chemotherapy."

The study was done in collaboration with Professor Grahame Hardie from the School of Life Sciences, University of Dundee. Hardie, a pioneer in AMPK research, discovered and defined AMPK in the 1980s and characterized several of its functions.

NYUAD researcher and senior author of the paper Faisal Thayyullathil commented: "Interestingly, the gene encoding AMPK- 1 is frequently amplified in human cancers. Our results suggest that genomic instability in such tumours might precipitate caspase cleavage and nuclear retention of the amplified AMPK- 1, thus protecting the tumour cells against cell death." MEH

King's College Hospital Dubai lab receives accreditation from the College of American Pathologists

The Accreditation Committee of the College of American Pathologists (CAP) has awarded accreditation to King's College Hospital London in Dubai based on results of a recent on-site inspection as part of the CAP's Accreditation Program.

Dr Aaron Han, MD, PhD, FCAP, Consultant and Lab Clinical Director at King's, was advised of this international recognition and congratulated for the excellence of the services being provided. King's Dubai is one of more than 8,000 CAP-accredited facilities worldwide.

"CAP represents the global gold standard for lab quality and continuous improvement. Kudos to the lab team, who worked diligently to achieve this milestone. We are proud of this achievement and will continue to strive to be better for our patients who entrust their lab studies to us," said Dr Han.

Prof. Mohammed Mohammed Redha Souilamas, Chief Medical Officer and Consultant Thoracic Surgery & Consultant Gastrointestinal Surgery at King's College Hospital, Dubai said: "We are delighted to receive the CAP accreditation, the gold standard of lab accreditation for our state-of-the-art lab at Kings College Hospital, Dubai. It is testimony to the commitment and hard work put in by our lab team to deliver the highest quality of care to our patients."

Shirley Luciap, Laboratory and Quality Manager at King's Dubai added: "CAP requires having quality measures in place for all phases of lab testing, proper validation and external quality assurance of all test parameters. The inspection process takes a full day and all the lab sections are thoroughly inspected."

The U.S. Federal Government recognizes the CAP Laboratory Accreditation Program, which begun in the early 1960s, as being equal-to or more-stringent than the government's own inspection programme.

During the CAP accreditation process inspectors examine the laboratory's records and quality control of procedures for the preceding two years. CAP inspectors also examine laboratory staff qualifications, equipment, facilities, safety programme and record, and overall management. MEH

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worldwide monitor

Update from around the globe

Health-climate alliance launched to help countries turn commitments into action

The World Health Organization and the United Kingdom government have launched a new health and climate change platform to support countries' efforts to implement commitments they made at last year's UN Climate Change Conference (COP26) to achieve resilient and low carbon, sustainable health systems.

The Alliance for Transformative Action on Climate Change and Health (ATACH), will act as a platform to bring together government institutions that have signed on to the COP26 Health Programme and relevant partner organizations to coordinate efforts, exchange knowledge and best practices, build networks and access to technical and financial support, link up existing initiatives, tackle common challenges, and monitor global progress.

Currently, 60 countries have formally committed, at Minister of Health level, to at least one of the initiatives on climate resilient and low carbon sustainable health systems promoted under the COP26 Health Programme.

"This new alliance is intended to sustain the momentum and advance action on climate change and health at country level, to help countries bridge the gap between commitments and implementation as a first priority," said Dr Maria Neira, WHO Director, Department of Environment, Climate Change and Health. "Resilient healthcare systems are absolutely crucial to successful adaptation to climate change in any scenario, while also playing an essential role in low-carbon sustainable development and greening supply chains. The health sector is ready to lead by example"

The main objectives of the alliance is to drive and sustain progress and ambition on resilient and low carbon health systems (and their supply chains).

It aims to encourage more countries to make commitments and increase ambition; elevate the agenda in both health and climate spaces, promoting innovation and solutions to overcome global constraints to achieving the goals of the COP26 Health Programme; and support the development and strengthening of the current and emerging evidence and knowledge base, health arguments for climate change action to inform advocacy, planning and implementation.

Action-oriented working groups will be set up to explore and seek solutions to strategic priorities, based on insights and demand from members. The first four working groups are likely to focus on:

- Financing for commitments on climate resilient and sustainable low carbon health systems;
- Climate resilient health systems;
- Low-carbon sustainable health systems;
- Greening supply chains and procurement.

A steering group, made up of representatives from each of the working groups and the co-conveners, will support WHO in defining the strategic direction of the alliance, build synergies across the working groups while promoting a dynamic response to emerging priorities, opportunities and challenges.

WHO will act as secretariat to the alliance. MEH

Global contrast media shortage: Strategies for conservation

In April 2022, a shutdown of Shanghai due to China's "zero COVID" policy caused a global shortage of iodinated contrast media produced by GE Healthcare. Many health

systems, roughly half the market share in the United States, use GE Healthcare as their preferred vendor for contrast media, and GE Healthcare has most of its contrast media manufacturing centred in Shanghai.

Contrast media is used to improve diagnostic imaging, and the shortage has affected millions of examinations. More than 50 million diagnostic imaging examinations using contrast media are conducted annually, including nearly all angiography and approximately half of all CT scans. Contrast media is necessary for some types of exams, such as evaluation of the heart arteries and CT for acute bleeding, and improves diagnostic accuracy for others, like CT for cancer or infection.

GE Healthcare has been increasing production at its Shanghai facility, has increased production at its facility in Ireland and has been airlifting contrast media to the United States. It's estimated that production should be normalized by the end of June 2022. However, China is still pursuing a zero-COVID policy, so the future remains unpredictable, says Matthew Davenport, M.D., a radiologist at University of Michigan Health and vice chair of the commission on quality and safety for the American College of Radiology.

"During this acute shortage, health systems have been forced to compare their stock-on-hand with the anticipated return-to-normal date to determine how aggressively to conserve contrast material," Davenport said. "The goal has been to avoid running out, which would prevent imaging of patients for whom contrast media was necessary, and to conserve contrast media in a way that is safest for patients."

In a recent letter published in *JAMA* <*https://doi.org/10.1001/jama.2022.987*>, Davenport and a team of researchers modelled several ways to conserve contrast media. They found that a combination of methods could reduce contrast media use for CT scans by approximately 80% if a moderate reduction in diagnostic accuracy could be tolerated:

Weight-based dosing and changing CT settings

In the analysis, researchers examined what would happen if a system switched from fixed doses of contrast media to selecting the dose of contrast media based on the weight of each individual patient.

The team found that for a model of 1 million CT scans, moving to weight-based dosing could reduce contrast media use by 12%.

The second method they examined was changing the settings on the CT scanner, allowing the machine to better detect smaller amounts of contrast media. This adjustment, Davenport notes, works best for smaller patients.

"This strategy does not work well for larger patients due to increased image noise," he said. "But in smaller patients, those who weigh under 80 kilograms, the contrast media dose can be reduced by up to 40%."

Unenhanced CT: CT without contrast material

If you are performing a coronary angiogram to examine the arteries of the heart, or a CT scan to look for a possibly fatal aortic dissection, contrast media is required. Imaging of the blood vessels with CT scan or fluoroscopy tends to necessitate use of contrast media. Davenport likens this to using a flashlight in a dark room. Without the flashlight, nothing can be seen.

Some imaging can be done with "unenhanced CT," without using contrast media. However, in many cases, this results in a loss of diagnostic accuracy. A correct diagnosis can often be made, but in some patients, it may be wrong or incomplete. Davenport compares this to the lights on an ambulance.

"You can probably still see the ambulance without the lights but having the lights on the ambulance makes it much more likely you will see it," he said. "The lights and sirens on an ambulance make it easier to perceive. It's similar with contrast media."

Eliminating contrast media by using unenhanced CT conserves far and away the most contrast media (78%), but only if a moderate reduction in diagnostic accuracy can be tolerated.

Systemic changes needed

Most hospitals affected by the contrast media shortage have already made local decisions about how to preserve contrast media and reduce use. However, Davenport says, the shortage raises serious questions about supply chain risk. It will be important to minimize the chance of this happening in the future, Davenport says. MEH

£30 million translational partnership to accelerate development of new treatments for dementia

LifeArc and the UK Dementia Research Institute (UK DRI) have launched a new partnership to accelerate development of new diagnostic tests, treatments, and devices from scientific research discoveries to benefit people with dementia, which around 900,000 people in the UK are living with.

At the heart of the five-year partnership is a £30 million (US$36 million) commitment by medical research charity LifeArc to the UK DRI to support dementia research at six UK host universities where the Institute is based.

Through fundamental discovery science, UK DRI researchers are revealing the mechanisms underpinning neurodegenerative diseases that cause dementia. The funding will be used to translate these scientific discoveries into new diagnostic tests, treatments and devices. These conditions include Alzheimer's disease, motor neurone disease, fronto-temporal dementia and Parkinson's disease. While research has revealed much more about these diseases, there are still no effective ways to prevent them or stop them progressing.

Dr Dave Powell, LifeArc's Chief Scientific Officer said: "Great strides have been made in dementia research in recent years but there is much more that needs to be done. We now have huge opportunity to translate this knowledge into new ways to help patients. This partnership will speed up the development of life changing

treatments and inspire us all to be bold and do more to help people affected by this condition.

"We're delighted to be partnering with UK DRI. Our visions are strongly aligned, and by working together in this partnership, we hope to develop solutions for people affected by dementia much faster. The expertise we both bring means we truly complement each other on the path from discovery science to patients. We hope working together will mean we are more likely to encourage others to take on promising treatments further down the discovery pipeline."

The partnership will provide UK DRI scientists with access to LifeArc's therapeutic and diagnostic platforms to enable them to test potential new diagnostic tests and treatments more easily. Both organisations will collaborate to make decisions on projects which should receive the translational funding. LifeArc will continue to provide technology transfer expertise.

Big increase in ransomware attacks on healthcare organisations

Sophos, a global leader in cybersecurity, has published a new sectoral survey report, "The State of Ransomware in Healthcare 2022." The findings reveal that ransomware attacks on health organizations almost doubled from 34% in 2020 to 66% in 2021.

The survey polled 5,600 IT professionals, including 381 healthcare respondents, in mid-sized organizations (100-5,000 employees) across 31 countries.

• The silver lining, however, is that healthcare organizations are getting better at dealing with the aftermath of ransomware attacks, according to the survey data. The report shows that 99% of those healthcare organizations hit by ransomware got at least some their data back after cybercriminals encrypted it during the attacks. However, those healthcare organizations that paid the ransom got back only 65% of their data in 2021, down from 69% in 2020; furthermore, only 2% of those that paid the ransom in 2021 got all their data back, down from 8% in 2020

John Shier, senior security expert at Sophos

Additional findings from the ransomware report for the healthcare sector include:

• Healthcare is most likely to pay the ransom, ranking first with 61% of organizations paying the ransom to get encrypted data back, compared with the global average of 46%; this is almost double than 34% who paid the ransom in 2020

• However, healthcare pays the least ransom amount: US$197,000 was the ransom amount paid by healthcare in 2021 compared with the global average of $812,000.

• Healthcare organizations had the second-highest average ransomware recovery costs with $1.85 million, taking one week on average to recover from an attack.

Ransomware-as-a-service

The report also revealed that the growing rate of ransomware attacks in healthcare reflects the success of the ransomware-as-a-service model, which significantly extends the reach of ransomware by reducing the skill level required to deploy an attack. Most healthcare organizations are choosing to reduce the financial risk associated with such attacks by taking cyber insurance.

However, there is relatively low cyber insurance coverage in healthcare with the report finding that only 78% of healthcare organizations have cyber insurance coverage compared with the global average of 83%.

Although more healthcare organizations are now opting for cyber insurance, the vast majority of them (93%) with insurance coverage report finding it more difficult to get policy coverage in the last year. With ransomware being the single largest driver of insurance claims, 51% reported the level of cybersecurity needed to qualify is now higher, putting a strain on healthcare organizations with lower budgets and less technical resources.

"Ransomware in the healthcare space is more nuanced than other industries in terms of both protection and recovery," explained John Shier, senior security expert at Sophos. "The data that healthcare organizations harness is extremely sensitive and valuable, which makes it very attractive to attackers. In addition, the need for efficient and widespread access to this type of data – so that healthcare professionals can provide proper care – means that typical two-factor authentication and zero trust defense tactics aren't always feasible. This leaves healthcare organizations particularly vulnerable, and when hit, they may opt to pay a ransom to keep pertinent, often lifesaving, patient data accessible. Due to these unique factors, healthcare organizations need to expand their anti-ransomware defenses by combining security technology with human-led threat hunting to defend against today's advanced cyberattackers."

Best practice

In the light of the survey findings, Sophos experts recommend the following best practices for all organizations across all sectors:

• Install and maintain high-quality defenses across all points in the organization's environment. Review security controls regularly and make sure they continue to meet the organization's needs

• Harden the IT environment by searching for and closing key security gaps: unpatched devices, unprotected machines and open Remote Desktop Protocol ports. Extended Detection and Response (XDR)

solutions are ideal for helping to close these gaps

- Make backups, and practice restoring from them so that the organization can get back up and running as soon as possible, with minimum disruption
- Proactively hunt for threats to identify and stop adversaries before they can execute their attack – if the team lacks the time or skills to do this in house, outsource to a Managed Detection and Response (MDR) specialist
- Prepare for the worst. Know what to do if a cyber incident occurs and keep the plan updated MEH

International team awarded $25 million to research genesis of cancer

A team of researchers co-led by UC San Francisco's Allan Balmain, PhD, FRS, has been selected to receive a $25 million Cancer Grand Challenges award to investigate the very early stages of cancer development. Cancer Grand Challenges is a global funding platform, co-founded by Cancer Research UK (CRUK) and the National Cancer Institute (NCI) in the U.S., that supports a community of diverse, global teams in taking on some of cancer's toughest challenges.

Balmain, with Kim Rhoads, MD, MS, MPH, and Luke Gilbert, PhD, both of UCSF, will lead the team, called PROMINENT (PROMotion to INform prevENTion) alongside Paul Brennan, PhD, from the International Agency for Research on Cancer and Nuria Lopez-Bigas, PhD, Institute for Research in Biomedicine Barcelona, in seeking answers to fundamental questions about the very early stages of tumor development.

"As a research community, we're on the verge of a major leap forward in our understanding of the factors that contribute to the risk of cancer, which could help to find new, informed ways to stop cancer before it even starts," said Balmain, a professor in cancer genetics at UCSF and an acclaimed scientist at UCSF's Helen Diller Family Comprehensive Cancer Center (HDFCCC).

The researchers will build on recent findings that suggest cells can remain seemingly "normal" despite carrying many cancer-causing mutations in their DNA, aiming to develop a picture of underlying forces that keep cells healthy or turn them cancerous.

"This investment in team science encourages diverse thinking to problems that have long hindered research progress," said David Scott, PhD, Director of Cancer Grand Challenges, Cancer Research UK (CRUK). "Cancer Grand Challenges provides the multidisciplinary teams the time, space and funding to foster innovation and a transformative approach."

The PROMINENT team unites advocates and scientists with expertise in epidemiology, genetics, imaging and more, across five institutions in the U.S., Spain and France.

"We're really excited to be part of this multifaceted group investigating the most foundational questions about cancer," said Gilbert, a member of the HDFCCC. "These kinds of collaborative efforts to tackle grand challenges in cancer biology are at the heart of science at UCSF and we hope our team's effort will transform our understanding of these very complex problems." MEH

World Bank board approves new fund for pandemic prevention, preparedness and response

The devastating human, economic, and social cost of COVID-19 has highlighted the urgent need for coordinated action to build stronger health systems and mobilize additional resources for pandemic prevention, preparedness, and response (PPR).

The World Bank's Board of Executive Directors on 30 June approved the establishment of a financial intermediary fund (FIF) that will finance critical investments to strengthen pandemic PPR capacities at national, regional, and global levels, with a focus on low- and middle-income countries. The fund will bring additional, dedicated resources for PPR, incentivize countries to increase investments, enhance coordination among partners, and serve as a platform for advocacy. The FIF will complement the financing and technical support provided by the World Bank, leverage the strong technical expertise of WHO, and engage other key organizations.

Developed with leadership from the United States, and from Italy and Indonesia as part of their G20 Presidencies, and with broad support from the G20 and beyond, over US$1 billion in financial commitments have already been announced for the FIF, including contributions from the United States, the European Union, Indonesia, Germany, the United Kingdom, Singapore, the Gates Foundation and the Wellcome Trust.

"I'm pleased by the broad support from our shareholders for a new Financial Intermediary Fund at the World Bank," David Malpass, World Bank Group President, said. "The World Bank is the largest provider of financing for PPR with active operations in over 100 developing countries to strengthen their health systems. The FIF will provide additional, long-term funding to complement the work of existing institutions in supporting low- and middle-income countries and regions to prepare for the next pandemic."

The goal of the FIF is to provide financing to address critical gaps in pandemic PPR to strengthen country capacity in areas such as disease surveillance, laboratory systems, health workforce, emergency communication and management, and community engagement. It can also help address gaps in strengthening regional and global capacity, for example, by supporting data sharing, regulatory harmonization, and capacity for coordinated development, procurement, distribution and deployment of countermeasures and essential medical supplies. MEH

the laboratory

Medical research news from around the world

AI detects autism speech patterns across different languages

A new study led by Northwestern University researchers used machine learning AI to identify speech patterns in children with autism that were consistent between English and Cantonese, suggesting that features of speech might be a useful tool for diagnosing the condition.

Undertaken with collaborators in Hong Kong, the study yielded insights that could help scientists distinguish between genetic and environmental factors shaping the communication abilities of people with autism, potentially helping them learn more about the origin of the condition and develop new therapies.

Children with autism often talk more slowly than typically developing children, and exhibit other differences in pitch, intonation and rhythm. But those differences (called "prosodic differences" by researchers) have been surprisingly difficult to characterize in a consistent, objective way, and their origins have remained unclear for decades.

However, a team of researchers led by Northwestern scientists Molly Losh and Joseph C.Y. Lau, along with Hong Kong-based collaborator Patrick Wong and his team, successfully used supervised machine learning to identify speech differences associated with autism.

The data used to train the algorithm were recordings of English- and Cantonese-speaking young people with and without autism telling their own version of the story depicted in a wordless children's picture book called "Frog, Where Are You?"

The results were published in the journal *PLOS One* on June 8, 2022.

"When you have languages that are so structurally different, any similarities in speech patterns seen in autism across both languages are likely to be traits that are strongly influenced by the genetic liability to autism," said Losh, who is the Jo Ann G. and Peter F. Dolle Professor of Learning Disabilities at Northwestern.

"But just as interesting is the variability we observed, which may point to features of speech that are more malleable, and potentially good targets for intervention."

Lau added that the use of machine learning to identify the key elements of speech that were predictive of autism represented a significant step forward for researchers, who have been limited by English language bias in autism research and humans' subjectivity when it came to classifying speech differences between people with autism and those without.

"Using this method, we were able to identify features of speech that can predict the diagnosis of autism," said Lau, a postdoctoral researcher working with Losh in the Roxelyn and Richard Pepper Department of Communication Sciences and Disorders at Northwestern.

"The most prominent of those features is rhythm. We're hopeful that this study can be the foundation for future work on autism that leverages machine learning."

The researchers believe that their work has the potential to contribute to improved understanding of autism. Artificial intelligence has the potential to make diagnosing autism easier by helping to reduce the burden on healthcare professionals, making autism diagnosis accessible to more people, Lau said. It could also provide a tool that might one day transcend cultures, because of the computer's ability to analyze words and sounds in a quantitative way regardless of language.

Because the features of speech identified via machine learning include both those common to English and Cantonese and those specific to one language, Losh said, machine learning could be useful for developing tools that not only identify aspects of speech suitable for therapy interventions, but also measure the effect of those interventions by evaluating a speaker's progress over time.

The results of the study could also inform efforts to identify and understand the role of specific genes and brain processing mechanisms implicated in genetic susceptibility to autism, the authors said. Ultimately, their goal is to create a more comprehensive picture of the factors that shape people with autism's speech differences.

"One brain network that is involved is the auditory pathway at the subcortical level, which is really robustly tied to differences in how speech sounds are processed in the brain by individuals with autism relative to those who are typically developing across cultures," Lau said.

"A next step will be to identify whether those processing differences in the brain lead to the behavioural speech patterns that we observe here, and their underlying neural genetics. We're excited about what's ahead."

• doi: *https://doi.org/10.1371/journal.pone.0269637*

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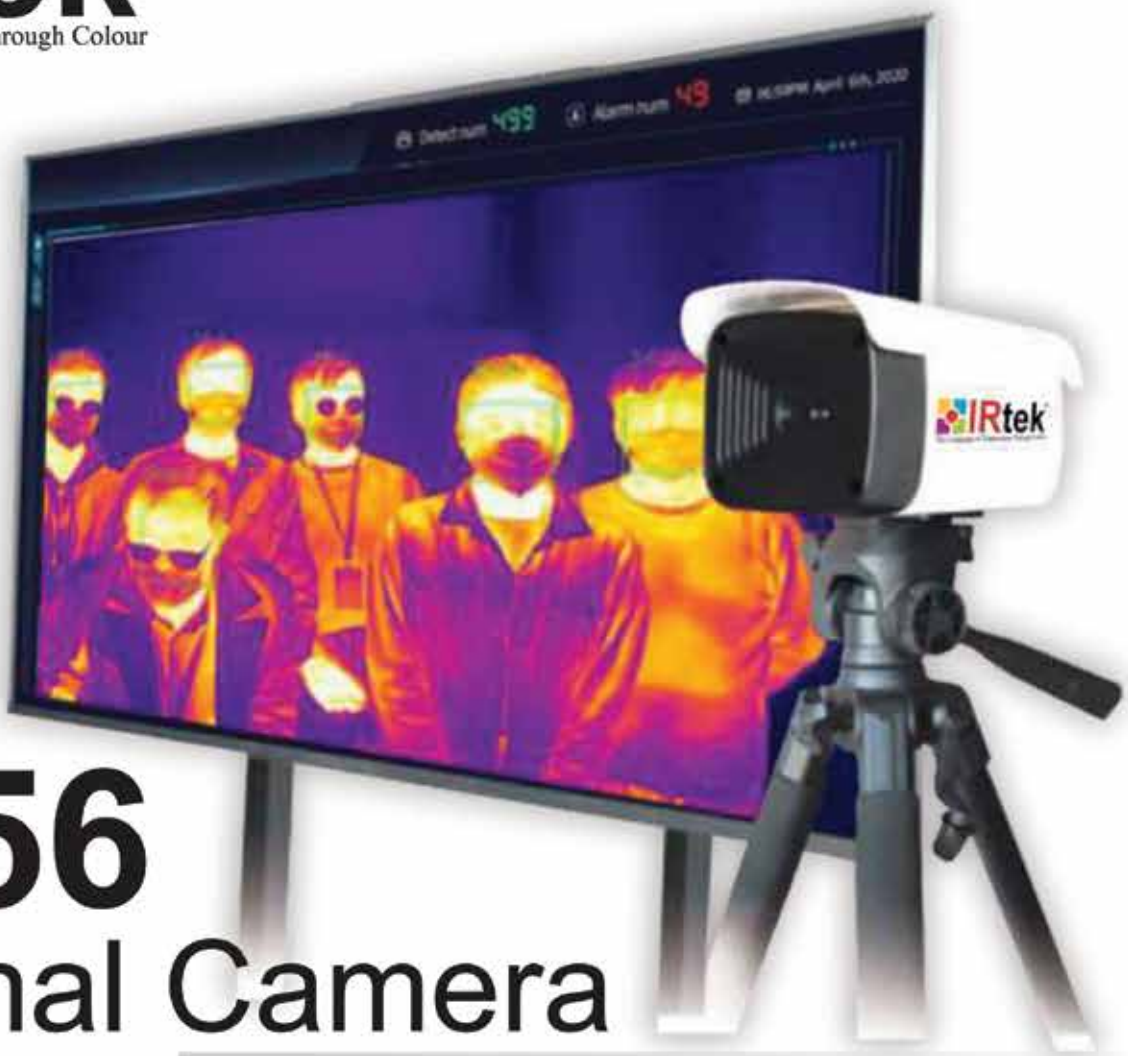

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New work upends understanding of how blood is formed

The origins of our blood may not be quite what we thought. Using cellular "barcoding" in mice, a groundbreaking study finds that blood cells originate not from one type of mother cell, but two, with potential implications for blood cancers, bone marrow transplant, and immunology. Fernando Camargo, PhD, of the Stem Cell Program at Boston Children's Hospital led the study, published in *Nature* on June 15.

"Historically, people have believed that most of our blood comes from a very small number of cells that eventually become blood stem cells, also known as hematopoietic stem cells," says Camargo, who is also a member of the Harvard Stem Cell Institute and a professor at Harvard University. "We were surprised to find another group of progenitor cells that do not come from stem cells. They make most of the blood in foetal life until young adulthood, and then gradually start decreasing."

The researchers are now following up to see if the findings also apply to humans. If so, these cells, known as embryonic multipotent progenitor cells (eMPPs), could potentially inform new treatments for boosting ageing people's immune systems. They could also shed new light on blood cancers, especially those in children, and help make bone marrow transplants more effective.

Camargo's team applied a barcoding technique they developed several years ago. Using either an enzyme known as transposase or CRISPR gene editing, they inserted unique genetic sequences into embryonic mouse cells in such a way that all the cells descended from them also carried those sequences. This enabled the team to track the emergence of all the different types of blood cells and where they came from, all the way to adulthood.

"Previously, people didn't have these tools," says Camargo. "Also, the idea that stem cells give rise to all the blood cells was so embedded in the field that no one attempted to question it. By tracking what happened in mice over time, we were able to see new biology."

Through barcoding, the researchers found that eMPPs, as compared with blood stem cells, are a more abundant source of most lymphoid cells important to the immune responses, such as B cells and T cells. Camargo believes the decrease in eMPPs that they observed with age may explain why people's immunity weakens as they get older.

"We're now trying to understand why these cells peter out in middle age, which could potentially allow us to manipulate them with the goal of rejuvenating the immune system," says Camargo.

In theory, there could be two approaches: extending the life of eMPP cells, perhaps through growth factors or immune signalling molecules, or treating blood stem cells with gene therapy or other approaches to make them more like eMPPs.

Camargo is also excited about the potential implications for better understanding and treating blood cancers. For example, myeloid leukaemia's, striking mostly older people, affect myeloid blood cells such as granulocytes and monocytes. Camargo thinks these leukaemias may originate from blood stem cells, and that leukaemias in children, which are mostly lymphoid leukaemias, may originate from eMPPs.

"We are following up to try to understand the consequences of mutations that lead to leukaemia by looking at their effects in both blood stem cells and eMPPs in mice," he says. "We want to see if the leukaemias that arise from these different cells of origin are different – lymphoid-like or myeloid-like."

Improving bone marrow transplant?

Additionally, the recognition that there are two types of mother cells in the blood could revolutionize bone marrow transplant.

"When we tried to do bone marrow transplants in mice, we found that the eMPPs didn't engraft well; they only lasted a few weeks," says Camargo. "If we could add a few genes to get eMPPs to engraft long term, they could potentially be a better source for a bone marrow transplant. They are more common in younger marrow donors than blood stem cells, and they are primed to produce lymphoid cells, which could lead to better reconstitution of the immune system and fewer infection complications after the graft."

• doi: *https://doi.org/10.1038/s41586-022-04804-z*

'Cellular brake' offers clue to autoimmune response during immunotherapy

A 'cellular brake', which could prevent lung cancer patients from developing a dangerous autoimmune response during immunotherapy treatment, has been identified by scientists at the University of Birmingham.

The finding, published in *Nature Communications*, is the first clue to the cause of autoimmune toxicity, in which patients develop dangerous additional conditions during treatment.

Immunotherapy works by enabling the body's immune cells (T cells) to engage with and kill tumour cells. They do this by suppressing proteins called immune checkpoints. These exist to prevent an immune response from being so strong that it destroys healthy cells in the body.

Autoimmune toxicity, which includes conditions such as pneumonitis, or inflammation of the lungs, can affect lung cancer patients undergoing immunotherapy treatment. Pneumonitis is responsible for around 35% of treatment-related deaths in lung cancer patients.

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Given the increasing use of immunotherapy treatment against cancer, the management of these reactions has become a significant healthcare challenge. Most commonly, clinicians will recommend discontinuing the treatment and exploring other options.

Led by Professor Gary Middleton, the team, in the University's Institute of Immunology and Immunotherapy pinpointed a specific biological response among patients who develop autoimmune toxicity. They found a 'cellular brake' – a protein which would normally limit the activity of the T cells – is missing or not functioning properly.

By identifying patients who lack this cellular brake, it may be possible to recognise patients at high risk of developing severe autoimmune complications.

Lead author Dr Akshay Patel said: "Immunotherapy is an extremely important weapon in cancer treatment and so identifying people who are at particular risk of developing these potentially life-threatening autoimmune conditions is key to weighing the risks and benefits of different treatments. It would enable clinicians to closely monitor high-risk patients, develop preventative strategies, or pursue alternative treatments altogether."

- doi: *https://doi.org/10.1038/s41467-022-30863-x*

New study offers first evidence of replay during sleep in the human motor cortex

Why do we sleep? Scientists have debated this question for millennia, but a new study by researchers at Massachusetts General Hospital (MGH), conducted in collaboration with colleagues at Brown University, and several other institutions, adds new clues for solving this mystery. Their findings, published in the *Journal of Neuroscience*, may help explain how humans form memories and learn, and could eventually aid the development of assistive tools for people affected by neurologic disease or injury.

Scientists studying laboratory animals long ago discovered a phenomenon known as "replay" that occurs during sleep, explains neurologist Daniel Rubin, MD, PhD, of the MGH Center for Neurotechnology and Neurorecovery, the lead author of the study. Replay is theorized to be a strategy the brain uses to remember new information. If a mouse is trained to find its way through a maze, monitoring devices can show that a specific pattern of brain cells, or neurons, will light up as it traverses the correct route. "Then, later on while the animal is sleeping, you can see that those neurons will fire again in that same order," says Rubin.

Scientists believe that this replay of neuronal firing during sleep is how the brain practices newly learned information, which allows a memory to be consolidated – that is, converted from a short-term memory to a long-term one.

However, replay has only been convincingly shown in lab animals. "There's been an open question in the neuroscience community: To what extent is this model for how we learn things true in humans? And is it true for different kinds of learning?" asks neurologist Sydney S. Cash, MD, PhD, co-director of the Center for Neurotechnology and Neurorecovery at MGH and co-senior author of the study. Importantly, says Cash, understanding whether replay occurs with the learning of motor skills could help guide the development of new therapies and tools for people with neurologic diseases and injuries.

To study whether replay occurs in the human motor cortex – the brain region that governs movement – Rubin, Cash, and their colleagues enlisted a 36-year-old man with tetraplegia (also called quadriplegia), meaning he is unable to move his upper and lower limbs, in his case due to a spinal cord injury. The man, identified in the study as T11, is a participant in a clinical trial of a brain-computer interface device that allows him to use a computer cursor and keyboard on a screen.

The investigational device is being developed by the BrainGate consortium, a collaborative effort involving clinicians, neuroscientists, and engineers at several institutions with the goal of creating technologies to restore communication, mobility, and independence for people with neurologic disease, injury, or limb loss. The consortium is directed by Leigh R. Hochberg, MD, PhD, of MGH, Brown University, and the Department of Veterans Affairs.

In the study, T11 was asked to perform a memory task similar to the electronic game Simon, in which a player observes a pattern of flashing colored lights, then has to recall and reproduce that sequence. He controlled the cursor on the computer screen simply by thinking about the movement of his own hand. Sensors implanted in T11's motor cortex measured patterns of neuronal firing, which reflected his intended hand movement, allowing him to move the cursor around on the screen and click it at his desired locations. These brain signals were recorded and wirelessly transmitted to a computer.

That night, while T11 slept at home, activity in his motor cortex was recorded and wirelessly transmitted to a computer. "What we found was pretty incredible," says Rubin. "He was basically playing the game overnight in his sleep." On several occasions, says Rubin, T11's patterns of neuronal firing during sleep exactly matched patterns that occurred while he performed the memory-matching game earlier that day.

"This is the most direct evidence of replay from motor cortex that's ever been seen during sleep in humans," says Rubin. Most of the replay detected in the study occurred during slow-wave sleep, a phase of deep slumber. Interestingly, replay was much less likely to be detected while T11 was in REM sleep, the phase most commonly associated with dreaming.

- **See video:** *https://youtu.be/NfvKKdb6u2A*
- **doi:** *https://doi.org/10.1523/JNEUROSCI.2074-21.2022*

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Hospitals can reduce antibiotic overuse by avoiding unnecessary blood draws in critically ill children, study shows

When a patient in the paediatric intensive care unit (PICU) develops a fever, physicians often routinely order a blood culture to identify the cause, particularly if they have reason to worry about sepsis, a life-threatening condition that occurs when chemicals released by immune system cells in the bloodstream to fight an infection trigger inflammation and shock throughout the body.

"Repeated blood draws, especially those from venous catheters, along with use of antibiotics while awaiting culture results just in case of a bacterial infection, are practices that contribute to a rise in antibiotic resistance, lead to additional testing and can prolong a child's hospital length of stay," says paediatric infectious diseases specialist Aaron Milstone, M.D., M.H.S., who is also a professor of paediatrics at the Johns Hopkins University School of Medicine and an expert on systems designed to prevent hospital-acquired infections and improve patient safety.

In an effort to reduce those unwanted consequences, researchers at Johns Hopkins Children's Center and elsewhere report they have developed and demonstrated the safety of a decision support programme that appears to substantially reduce the number of blood draws in the PICU, and is likely to reduce antibiotic prescriptions without increasing the risk of sepsis.

The findings of the study, which was a collaborative of 14 institutions in the United States and their experts, were published May 2 in *JAMA Pediatrics* [1].

"Patients in the PICU are usually the sickest of the sick, and you want to do everything you can to help," says Milstone, who is the senior author on the paper.

"But when you perform a blood culture, anything can grow – whether it's the reason behind the concerning symptom or possible contamination of the sample. Collecting a blood culture when it's not needed can lead to unnecessary antibiotic use, unwanted side effects from additional medications, and additional blood tests."

30% of antibiotics unnecessary

According to data from the U.S. Centers for Disease Control and Prevention, about 30% of antibiotics used in hospitals are unnecessary or prescribed incorrectly. Previous studies from other researchers have found that more than half of patients in the PICU often receive antibiotics for

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symptoms such as fever that may arise from noninfectious illnesses or even weaning from some medications.

Milstone, who is also an epidemiologist and member of the Johns Hopkins Armstrong Institute for Patient Safety and Quality, says the new study builds on programs already in place that have safely reduced the use of other diagnostic tests, such as urine cultures.

In their study, the research team at Johns Hopkins Children's Center led a national multidisciplinary collaborative of experts in paediatric infectious diseases, critical care medicine, quality improvement and other fields called BrighT STAR (Testing STewardship to reduce Antibiotic Resistance) [2]. The goal was to explore and compare existing studies and practices, and produce guidance recommendations to reduce blood draws in patients with low suspicion or risk for sepsis, and to measure the impact of the algorithm on blood culture rates, broad-spectrum antibiotic use and other patient outcomes.

The 14 participating sites were diverse with respect to institution size, patient population and geographic area. Johns Hopkins Medicine investigators provided each site, which had its own team of experts, with a pre-implementation assessment tool while coaching them to launch their own quality improvement programs and strategies to execute the plans.

"With our support, the different sites created a clinical algorithm to help front-line providers evaluate patients with fevers, optimize decisions and consider questions like: 'How do I think about that patient? Do they need a blood culture? Did they have a blood culture already?'" says Charlotte Woods-Hill, M.D., M.S.H.P., former paediatric critical care fellow at the Johns Hopkins University School of Medicine and lead author of the paper, who is now a senior fellow at Leonard Davis Institute of Health Economics with the University of Pennsylvania and critical care physician at Children's Hospital of Philadelphia.

While the composition of the clinical support tools varied, each institution sought to standardize practices across its unit and reduce variability in decisions in ordering blood cultures, as well as highlight patient safety considerations. Blood culture rates, along with other measures, were tracked and reported monthly. The coordinating team held regular calls with individual sites and the larger collaborative throughout all steps of the project, conducted between 2017 and 2020.

Blood culture rate reduction

In the 24-month period prior to implementation of the quality improvement algorithms, 41,731 blood cultures were performed at all 14 sites, compared with 22,408 cultures in the 18-month post-implementation period. Across sites, the median blood culture rate dropped from 146 per 1,000 patient days/month before implementation to 99 per 1,000 patient days/month after. Overall, 13 of 14 sites reduced their blood culture rates in the post-implementation period between 15% and 58%. Across the 14 sites, the blood culture rate was reduced by an average of 34% between the study's pre- and post-implementation time frames (156.9 blood cultures per 1,000 patient days/month to 104.1 blood cultures per 1,000 patient days/month).

In the 11 sites that reported on antibiotic use, results showed a 13% overall average reduction in the amount of antibiotics prescribed (506.0 versus 440.3 total days per 1,000 patient days/month).

Bloodstream infections

At all 14 sites, central line-associated bloodstream infections decreased by 36% (1.79 to 1.14 per 1,000 central line days/month). There was no significant change in the rates of one of the most frequent and dangerous hospital-acquired infections, *Clostridioides difficile* (0.38 vs 0.36 infections per 1,000 patient days/month).

Mortality rates, length of stay and readmission in the PICU, as well as overall hospital readmissions, were similar before and after program implementation.

"These findings suggest that multidisciplinary efforts to standardize blood culture collection and avoid unnecessary testing in the PICU can be done successfully and safely in diverse settings, and that reducing blood culture use can, in turn, reduce broad-spectrum antibiotic use," Milstone says.

These findings suggest that multidisciplinary efforts to standardize blood culture collection and avoid unnecessary testing in the PICU can be done successfully and safely in diverse settings, and that reducing blood culture use can, in turn, reduce broad-spectrum antibiotic use.

The research team cautioned that the study may have missed instances in which antibiotics were prescribed without collecting blood cultures, which could have increased the amount prescribed. Also, all sites enrolled in the study had clinicians and others experienced in quality improvement. The researchers additionally say their analyses do not account for variations in individual site implementation plans.

However, they believe their concept will help change clinician decision-making and, ultimately, benefit patients. "It means that patients will hopefully get higher value and more precise care safely that avoids unintended harm and getting antibiotics and tests that they don't need," Woods-Hill says.

The researchers say they are seeking to expand and implement a similar approach at all hospitals across the United States. They are also investigating ways to scale this concept to other hospital units, including those caring for adults.

References

[1] https://doi.org/10.1001/jamapediatrics.2022.1024
[2] https://bit.ly/3ydWYhU

New understanding of congenital heart disease progression opens door to improved treatment options

A team of investigators from Texas Heart Institute, Texas Children's Hospital and Baylor College of Medicine uncovered new insights into the mechanisms underlying the progression of congenital heart disease (CHD) – a spectrum of heart defects that develop before birth and remain the leading cause of childhood death.

The research published in *Nature*[1] represents the first reported single-cell genomics evidence of unique differences in heart muscle cells and immune systems of CHD patients. Uncovering these key differences and how these diseases progress provides an opening for researchers to devise new ways to treat CHD.

While the eventual outcome of heart failure in CHD is well documented, the underlying cause of declining heart function in these patients is still poorly understood. That knowledge gap in understanding has led to roadblocks in developing new therapies capable of extending a patient's life.

To address these unanswered questions, Texas Heart Institute and Baylor College of Medicine's James F. Martin, MD, PhD, collaborated with Iki Adachi, MD, Director of the Mechanical Circulatory Support Program at Texas Children's and Associate Professor at Baylor College of Medicine, and Diwakar Turaga, MD, PhD, a Texas Children's Hospital paediatric cardiac critical care specialist and Assistant Professor at Baylor College of Medicine, to profile heart and blood samples from CHD patients. The team studied patients with hypoplastic left heart syndrome (HLHS), Tetralogy of Fallot (TOF) and dilated (DCM) and hypertrophic (HCM) cardiomyopathies undergoing heart surgery.

Dr Martin is an internationally recognized physician-scientist who has made numerous fundamental contributions to our understanding of cardiac developmental and disease pathways, as well as tissue regeneration.

"Using several exciting new technologies such as single-cell RNA sequencing, we were able to interrogate samples from congenital heart disease patients at the single cell level. One of our goals is to improve the natural history of this terrible disease afflicting children," said Dr Martin, Director of the Cardiomyocyte Renewal Laboratory at the Texas Heart Institute and Vivian L. Smith Professor in the Department of Integrative Physiology at Baylor College of Medicine. "There is still a lot of work to do as the team, including co-first authors Drs Matthew C. Hill, Zachary A. Kadow and Hali Long, heads toward that goal."

Dr Turaga is a physician-scientist dedicated to bringing cardiac regenerative medicine therapies to the bedside.

Cell atlas of congenital heart disease

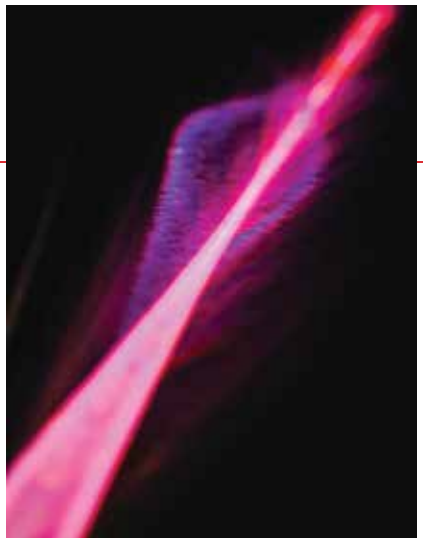
"This is the first step in developing a comprehensive cell atlas of congenital heart disease," said Dr Turaga, physician in the Cardiac Intensive Care Unit at Texas Children's, as well as an expert in genomics and microscopy. "We are creating a roadmap for therapies targeting individual cell types and unique gene pathways in CHD that include both the heart and the immune system, something that had not been reported before. As the technology matures, this will become the standard of care in treatment of CHD."

Dr Adachi is a congenital heart surgeon at Texas Children's Hospital who is specialized in reconstructive surgical procedures of CHD lesions including those analyzed in this study.

"What we achieved with this study is absolutely exciting but represents just the beginning," said Dr Adachi, director of the world's largest paediatric Heart Transplant and Ventricular Assist Device Program. "The collaboration between the extremely sophisticated laboratory at the Texas Heart Institute and the top paediatric heart centre at Texas Children's definitely has the potential to go further."

The findings of the study not only provide a new roadmap to develop personalized treatments for CHDs, but also provide the scientific community with a critical resource of rare paediatric heart samples that can be used to make further discoveries and deepen our understanding of CHD. MEH

Reference:
doi: *http s://doi.org/10.1038/s41586-022-04989-3*



New super-pulsed thulium fibre laser improves treatment results in paediatric patients with urinary stones

A new thulium fibre laser system may provide improved outcomes in the treatment of urinary stones for paediatric patients, compared to the current standard for laser lithotripsy, reports a study in *The Journal of Urology*[1], an official journal of the American Urological Association (AUA). The journal is published in the Lippincott portfolio by Wolters Kluwer.

Based on their experience as early adopters of the new technology for treatment of paediatric urinary stones (urolithiasis), Christopher Jaeger, MD, and colleagues of Boston Children's Hospital found a higher "stone-free rate" with the SuperPulsed Thulium Fibre (SPTF) laser, compared to standard low-power holmium:yttrium-aluminum-garnet (Ho:YAG) lasers.

The researchers evaluated their initial experience with the SPTF laser system in paediatric patients with urinary stones (located in the kidney and/or ureter) undergoing treatment with laser lithotripsy. In this minimally invasive procedure, an optical fibre is placed in the urinary system through an instrument called a ureteroscope. Laser energy is then delivered through the fibre to break up the stones into pieces small enough to pass in the urine.

The analysis included a total of 125 laser lithotripsy procedures in 109 patients, performed between 2016 and 2021. Ninety-three patients were treated using low-power Ho:YAG lasers and 32 using the recently introduced thulium fibre laser. The two groups were similar in terms of age, sex, and number, size, and location of stones.

On their first imaging scan after treatment, 62% of children were free of any residual stone fragments. The stone-free rate was significantly higher for children treated with the SPTF laser: 70%, compared to 59% with the Ho:YAG lasers.

Residual fragments

On analysis adjusting for other factors, the odds of having a residual fragment after treatment was about 60% lower in the SPTF laser group. That's likely to be an important advantage over time, as residual stone fragments of any size can eventually cause problems requiring further treatment.

Total operating time was similar between groups, although laser time was longer in the SPTF group. The two laser groups had similar complication rates.

The authors note that they were early adopters of the SPTF laser system noting its technical advantages over Ho:YAG technology, including a shorter wavelength leading to "superior stone ablation efficiency." The beam can be delivered in continuous or pulsed modes across a wide range of energy and frequency settings. The SPTF is also more energy-efficient than Ho:YAG lasers, which can require a complex refrigeration system to dissipate heat. In contrast, the thulium fibre laser unit requires only a fan, resulting in a smaller and much quieter machine.

Previous studies have shown the clinical advantages of the SPTF laser system for treatment of urinary stones in adults. The new study is the first to evaluate the safety and effectiveness of thulium fibre lasers in paediatric patients. While more common in adults, urinary stones appear to be occurring more frequently in children.

"The SPTF laser using thulium fibre laser technology is an effective alternative to the low-power Ho:YAG laser for treatment of urolithiasis in paediatric patients," Dr Jaeger and co-authors conclude. They emphasize the need for further studies to determine the optimal STPF settings and compare its performance to high-power Ho:YAG lasers. MEH

Reference:

[1] https://doi.org/10.1097/JU.0000000000002666

Paediatric liver disease increases risk of developing type 2 diabetes

Nonalcoholic fatty liver disease (NAFLD) is the most common paediatric liver disease, affecting 5 to 8 million children in the United States. In NAFLD, the cells of the liver store large fat droplets, which can affect the function of the liver. Physicians have long observed a relationship between NAFLD and type 2 diabetes in adults, but much less is known about a similar connection in children.

Rates of type 2 diabetes have doubled in children over the past 20 years. Children with NAFLD have features of insulin resistance, a key characteristic of type 2 diabetes, and so may be at risk for developing the disease.

"There is a growing public health crisis as children with diabetes mature into adults with diabetes. We need to better understand how NAFLD contributes to type 2 diabetes risk in children so that we can actively work to prevent it," said Jeffrey Schwimmer, MD, professor of paediatrics at University of California San

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Diego School of Medicine and director of the Fatty Liver Clinic at Rady Children's Hospital-San Diego.

In a new study, published June 13, 2022 in *Clinical Gastroenterology and Hepatology* [1], a team of researchers, led by senior author Schwimmer, provide hard numbers describing the connection between NAFLD and diabetes risk, finding that among 892 children with NAFLD enrolled in the Nonalcoholic Steatohepatitis Clinical Research Network, type 2 diabetes was present in 6.6% of the children at initial assessment, with the incidence rate increasing 3% annually over the next four years.

By the end of the study, one in every six children had developed type 2 diabetes.

"This is alarming because type 2 diabetes in youth is a much more aggressive disease than in adults, with more immediate and serious complications and outcomes," said Schwimmer.

The authors also identified specific factors that increase the risk of type 2 diabetes in children with NAFLD: sex (females were more likely to develop type 2 diabetes), severity of obesity and the amount of fat and scar tissue in the liver.

"These findings have clinical implications for gastroenterologists caring for children with NAFLD," Schwimmer said. "They should be aware of the risk and provide monitoring, anticipatory guidance and lifestyle interventions that help their patients avoid developing type 2 diabetes." MEH

New research yields valuable evidence regarding the assessment of Health-Related Quality of Life in children

Value in Health[1] the official journal of ISPOR – the professional society for health economics and outcomes research, has recently published a series of articles providing new insights on measuring and valuing children's health-related quality of life. The collection of papers was published in the July 2022 issue of *Value in Health* [2].

"Evaluating the effectiveness and cost-effectiveness of treatments for children is essential to support good healthcare decisions," said Nancy J. Devlin, PhD, Centre for Health Policy, University of Melbourne, Parkville, Victoria, Australia in her commentary on the three full-length papers. "Yet the evidence on child health-related quality of life (HRQoL) submitted to health technology assessment (HTA) has, in general, been very poor. In fact, no HTA body anywhere in the world currently provides guidance on how to measure and value HRQoL in younger populations."

Part of the challenge facing researchers seeking to value child HRQoL is that there are additional methodological issues involved, including the complexity of asking adults to value the health states of children. The papers in Value in Health engaged one of these important issues: what age should be specified when we ask adults to value child HRQoL – and what effect will the specified age exert on the values?

Devlin's introductory commentary, "Valuing Child Health Isn't Child's Play," includes an overview of the topic and introduces the 3 articles in the series:

1. "Why Do Adults Value Eq-5D-Y-3L Health States Differently for Themselves Than for Children and Adolescents: A Think-Aloud Study," by Vivian Reckers-Droog, PhD, et. al. [3].
2. "Exploration of the Reasons Why Health State Valuation Differs for Children Compared to Adults: A Mixed Methods Approach," by Sarah Dewilde, PhD, et. al. [4].
3. "Does Changing the Age of a Child to Be Considered in Eq-5D-Y-3L DCE Based Valuation Studies Affect Health Preferences?," by Juan M. Ramos-Goñi, PhD, et. al. [5].

"Valuation of child HRQoL underscores the importance of identifying and being transparent about all value judgements involved in methods choices," said Devlin. "These should reflect the principles and values of decision makers who use this evidence. There may not be a 'one-size-fits-all' set of methods for valuing child HRQoL that are acceptable to all HTA bodies, so consultation with local decision makers is crucial."

An ISPOR Emerging Good Practices Task Force on paediatric HRQoL values, planned to commence before the end of 2022, will build on this growing evidence base to promote consistent and improved practices.

"In the end," concluded Devlin, "while methods questions remain, considerable progress is now being made in valuing child HRQoL. These efforts will support greater use of these instruments in clinical trials and other studies. The growing body of evidence around methods, greater awareness of the normative issues, and availability of value sets will help HTA bodies to establish methods guidance, which will give greater clarity to those planning paediatric clinical trials." MEH

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[1] www.ispor.org/publications/journals/value-in-health
[2] www.ispor.org/publications/journals/value-in-health/issue/Volume-25--Issue-7
[3] https://bit.ly/3ymgvwp
[4] https://bit.ly/3OOVp0H
[5] https://bit.ly/3Rb8ZNJ

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World class paediatric health system ranked in top 10 in the U.S. for paediatric cardiology & cardiac surgery

In the 2021-22 *U.S. News & World Report* rankings of the Best Children's Hospitals, Ann & Robert H. Lurie Children's Hospital of Chicago continues to be the top-ranked paediatric hospital in all 10 specialties for nearly 10 years. It provides superior paediatric care in a setting that offers the latest benefits in medical technology, breakthroughs in research innovations and family focused services for over 224,000 individual patients in fiscal year 2020, including nearly 400 patients from outside the United States. Lurie Children's is among the best children's hospitals in the U.S.

Top 10 U.S. News & World Report ranked Heart Center

Lurie Children's Heart Center is ranked 9th in the nation for child cardiology and heart surgery by *U.S. News & World Report*. It brings the spectrum of cardiac specialists together to care for patients with the most complex and serious heart conditions from foetal cardiology to adult congenital heart disease. The Heart Center uses the most comprehensive tests and treatments to deliver the highest quality care from admission, to discharge, to follow-up. Each year, Lurie Children's cardiologists see more than 17,000 paediatric patients in outpatient diagnostic visits and more than 700 inpatient admissions.

Lurie Children's Heart Center is nationally and internationally renowned for the diagnosis and treatment of irregular heart rhythms (arrhythmia), and for helping pioneer the treatment of paediatric congenital heart disease. This year, the team performed the hospital's 400th paediatric heart transplant. Heart transplant patients at Lurie Children's experience 1 month, 1 year and 3-year outcomes at or greater than the U.S. average for paediatric heart transplant. The Heart Center team has also successfully pioneered a total artificial heart transplantation in the world's smallest patient. Lurie Children's experienced, multidisciplinary teams of paediatric cardiologists and surgeons make it easier for patients to see every specialist they may need under one health system.

Cardiac Care Unit

Due to increased demand for paediatric services, Lurie Children's opened the 44-bed state-of-the-art Regenstein Cardiac Care Unit (CCU). The CCU is one of the few paediatric units of its kind in the U.S. and has many features including high-tech rooms to adapt to the intensity of care the patient needs, allowing children to stay in the same room, with the same care team.

Foetal & Neonatal Cardiology Program

Specialists from Lurie Children's Heart Center and The Chicago Institute for Fetal Health ensure that families expecting a new baby with heart concerns receive the best diagnostic and counselling care available. The team provides specialized ultrasound imaging of the heart during pregnancy and, each year, performs more than 2,000 foetal echocardiograms with a diagnostic accuracy that exceeds 95%.

Single Ventricle Center of Excellence

The Single Ventricle Center of Excellence at Lurie Children's offers long-term comprehensive treatment for patients born with single ventricle heart defects in an environment that supports the whole family. The complex anatomy of the heart and its chambers makes each single ventricle defect different and each child's journey unique. Children born with these complex hearts need specialized treatment, evaluation, and lifelong follow-up care. Lurie Children's is dedicated to improving patient surgical, medical, neurodevelopmental, and psychosocial outcomes so their patients can lead meaningful and active lives.

Priority Second Opinion Program

Designed for children with existing heart defects, Lurie Children's Priority Second Opinion Program provides families and referring physicians searching for the best possible medical management and surgical treatment with the second or third opinion. The multidisciplinary program brings together the opinions of a diverse team of healthcare specialists, providing patients the most holistic evaluation.

International Patient Services Department

Our International Patient Services (IPS) Department works with families around the world seeking specialized paediatric healthcare services. We're committed to providing family-centred care through every interaction, from referrals through treatment and the journey home. Our team provides immediate access to interpreters through a combination of an in-person interpreter, video, or telephonic interpretation.

Learn more

To contact IPS, call +1 312.227.4550 or e-mail *IPS@luriechildrens.org*.

To learn more about Lurie Children's, the Heart Center, and the International Patient Services, visit: *luriechildrens.org/international*

Great Ormond Street Hospital for Children: 170 years of leadership

Great Ormond Street Hospital (GOSH) is a globally renowned children's hospital, championing innovation across more than 60 clinical specialties and providing groundbreaking treatments for the rarest and most complex conditions. Located in the heart of London, GOSH is a British institution with royal patronage and 170 years of history.

As a pioneer of cutting-edge and innovative medical technology, GOSH works at the forefront of the field to continuously deliver the medicine of the future. As well as world-class clinical treatment and care, we also have a commitment to delivering a nurturing and family-centred experience.

GOSH has 19 highly specialised national services. Our expert teams of over 300 world-leading consultants deliver 360-degree, multi-specialty care with the child at the centre. As champions of the highest calibre of paediatric care, our teams are dedicated to quality, integrity, and safety.

We are part of Europe's largest academic centre for research and education in children's health and disease. We are committed to achieving the best possible results by consistently measuring outcomes and value against the highest international standards, and our collaborative approach to international partnerships means we are dedicated to sharing best practice in a transparent and empowering way.

Our world-leading expertise includes:

- One of the largest heart transplant centres for children in the world and the largest paediatric cardiac programme in the UK
- The leading centre in the world for gene therapy in children
- One of the three largest centres for children with cancer/leukaemia in the western world and the largest in Europe
- One of the two largest centres in Europe for paediatric bone marrow transplantation (BMT)
- The largest epilepsy surgery centre in Europe and the largest centre for paediatric brain surgery in the UK
- The leading centre in Europe for the management of conjoined twins
- The largest paediatric centre for Interventional Radiology in Europe
- The largest paediatric centre in the UK for intensive care
- The largest paediatric centre in the UK for craniofacial reconstruction
- The largest paediatric centre in the UK for renal transplantation.

As the global pioneer in children's rare disease studies and treatments, GOSH has extensive experience and knowledge in the clinical treatments of rare diseases in children and developed a mature multidisciplinary diagnosis and treatment model. At GOSH, we treat over 28,000 children with rare & ultra-rare diseases and have more than 500 research projects looking into rare and complex diseases.

Established in 2019, Zayed Centre for Research into Rare Disease in Children is the world's first purpose-built centre dedicated to paediatric research into rare diseases. The Centre houses circa 500 researchers and clinicians. It brings together pioneering research and clinical care under one roof and drives forward new treatments and cures for seriously ill children from across the UK and international patients.

GOSH has a longstanding relationship with the Middle East providing high quality and safe care for patients in a family-centred environment. A dedicated Gulf office ensures that children and families being referred to the hospital receive the very best experience possible as well as providing a local point of contact. The unit is tailored to the referral and treatment of international patients with a dedicated, multi-lingual team ensuring a smooth and efficient patient experience. MEH

Want to know more about Great Ormond Street Hospital in London?

We've been helping children overcome rare and complex conditions ever since we opened our doors in 1852. Stronger than ever, our team is made up of 300 exceptional and dedicated consultants across over 60 specialties. We are a driving force in medical technology and research so we can provide much needed treatment for children across the world.

Our International and Private Care service supports over 5,000 children from over 80 countries every year. We have a compassionate and multi-lingual team to help our international patients and their families feel at home.

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New-York Presbyterian: Providing a direct connection to first-class medical care

When most people hear the term "GPS" – they might think of a global positioning system that directs them to their desired destination. It is fitting, then, that GPS also stands for the Global Patient Services programme at New-York Presbyterian (NYP), which assists patients and their families throughout the Middle East and around the world to make it their destination – for state-of-the-art medical care and the best in-patient experience.

NewYork-Presbyterian is the only academic medical centre in the nation affiliated with two world-class medical schools, Weill Cornell Medicine and Columbia University Vagelos College of Physicians and Surgeons. Its longstanding reputation for clinical excellence has put the hospital at the forefront in terms of medical education, groundbreaking research, and patient-centric treatment.

Global Services Program: 24/7 "concierge" service – for when it matters most

Each year, more than 5,000 international patients travel to NewYork-Presbyterian with assistance from its Global Services Program, which gives them access to the hospital's world-renowned Columbia University and Weill Cornell Medicine physicians.

NYP has a long history of caring for patients in the Middle East and North Africa, and our regional "ambassadors" collaborate closely with local governments and private institutions in those regions to provide access to our services and making the entire process a smooth one for patients. Our GPS team of multilingual professionals is dedicated to assisting families, 24 hours a day, 7 days a week, to help manage the many logistics involved in planning for care far from home, including:

- scheduling physician visits and clinical appointments
- escorting patients to appointments
- explaining and interpreting medical information, instructions, and procedures
- facilitating communication between physicians, administrators and patients
- organizing global air ambulance, ground ambulance, or other emergency transport services for critically ill patients
- helping to arrange for hotels or furnished apartments, including NYP's on-site facilities
- assisting families in understanding the cost of care.

Innovative treatments

Cancer Care: NYP is home to two major cancer centres – the National Cancer Institute-designated Herbert Irving Comprehensive Cancer Center at Columbia, and the Weill Cornell Medicine Meyer Cancer Center at NewYork-Presbyterian. Patients benefit from the latest anti-cancer drugs, targeted therapies, advanced radiation therapies, and emerging minimally-invasive surgical procedures.

> Our GPS team...helps manage the many logistics involved in planning for care far from home.

Cardiology: NYP is renowned for its latest interventional therapies and pioneering cardiac surgery techniques, including heart transplants. NewYork-Presbyterian is one of the leading centres in the United States for innovative treatment of adult heart conditions and for paediatric cardiology.

Neurosciences: NYP continues to make clinical advances for conditions such as glioblastoma and complex epilepsy, as well as offering new applications for high-intensity-focused ultrasound for neurological conditions.

Orthopaedics: We treat patients of all ages, from newborns to older adults, for virtually every type of orthopaedic injury, disease, or disorder to relieve symptoms and restore comfort, function, and mobility.

Paediatrics: For more than a decade, NewYork-Presbyterian has been at the forefront of more paediatric treatments than any other New York City metropolitan area. MEH

Contact
NewYork-Presbyterian's Global Patient Services Program starts you on your journey to the very best medical care that you or your loved one deserve. For more information, contact:

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UCLH offers specialist care for teenagers and young adults with cancer and blood disorders

The teenage and young adult cancer and blood disorder service at University College Hospital, London, UK, is the main treatment centre for teenage cancer in London and is also the largest teenage and young adult service in the UK.

The hospital's highly specialised haematology service is dedicated to patients aged 13-18 years old who have been diagnosed with a blood-related cancer such as acute leukaemia or Hodgkin's lymphoma. It is also a national and international centre for the treatment of teenagers with other non-malignant blood disorders including aplastic anaemia, sickle cell anaemia and thalassaemia.

UCLH provides all aspects of state-of-the-art cancer care and is a highly specialist centre for advanced treatments, including haemopoietic stem cell transplantation, radio-isotope therapy and CAR-T cell therapy. Clinical services are also enhanced by exceptional clinical and translational research, based within University College London and the Institute of Child Health, and it is a leading European centre for CAR-T cell treatment research.

Patients are cared for by a highly skilled multidisciplinary team led by a named consultant, with the input of their consultant colleagues and the wider clinical team, which may include clinical nurse specialists, physiotherapists, occupational therapists, dieticians, psychologists, psychotherapists and psychiatrists.

Tailored care for patients

The clinical team meets regularly to review each patient's tailored care plan which is revised when needed to meet each individual's medical and holistic needs. They have vast experience in managing autologous and allogenic transplants for patients with either malignant or non-malignant blood disorders; from acute leukaemia and high-grade lymphomas to hemoglobinopathies. The UCLH team were pioneers in the development of delivering gene therapy to thalassemia patients in the UK, which can potentially offer a cure to patients whilst delivering a less toxic treatment plan, leading to a vastly improved patient experience.

As well as providing world-class care, the ward has been specifically tailored to the needs of teenagers and young adults, and is designed to make their stay in hospital as comfortable and enjoyable as possible. This includes entertainment systems for TV and gaming, webcams to help patients stay in touch with friends and family, a recreational area and a small kitchen. An additional bed can also be provided for a family member when required.

For outpatients, there is also a large recreational area in the nearby Macmillan Cancer Centre known as 'the hub' which has a range of recreational, social and educational options including a gym, DJ booth, computer, gaming space, education zone and pool table, and provides an environment where young people can meet others in a similar situation.

Patients and their families also have access to a psych-oncology team, to help make sense of what has happened to them.

Patients from the Middle East

Advocates are available to help with the specific needs of Middle Eastern patients seeking treatment in the UK as well as the wider needs of any family members travelling with them. A team member will be able to help from initial enquiry through to first consultations and follow-up care plans. They will also be able to help translate and answer any questions.

Where to find University College Hospital

University College Hospital is based in leafy Bloomsbury; a short walk from Oxford Street and the West End of London, with quick and easy transport links including buses, tubes and mainline stations.

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Neurosurgery team performs laser hemispherectomy on child with epilepsy

The patient, Zachary Kurek, with his mother Amanda Morey.

For only the second time in the world, doctors at the University of Chicago Medicine Comer Children's Hospital and the Department of Neurosurgery used a minimally invasive surgery to disconnect the right and left sides of the brain and the left epilepsy-generating zones in a boy with epilepsy, stopping his seizures.

Neurosurgeon Peter Warnke, MD, performed the 8-hour laser functional hemispherectomy surgery in February 2021. The patient, 11-year-old Zachary Kurek, suffered a stroke at birth, causing him to lose most of the function of the left side of his brain. His epilepsy was getting worse as he got older, causing dozens of seizures a day that medication couldn't control.

Anything startling, such as a loud noise or a barking dog, could trigger a seizure, causing his body to lock up and fall. He suffered countless bad bruises, a few broken bones and teeth, embarrassment, stress and the inability to do many normal activities. His mother said he was becoming depressed, angry and unable to sleep.

With Zachary facing a lifetime of these seizures and with very limited function in his left cerebral hemisphere as a result of the stroke, Warnke and his team studied the boy's case. They determined that they could completely disconnect the right and left sides of his brain, and separate any epileptogenic tissue in the left hemisphere, without worsening his verbal or physical functioning.

That way, if seizure activity occurred in the left side of his brain, it would be unable to send signals to the right side of the brain or to the fibres that transmit seizure activity, and Zachary's body wouldn't react.

The surgery

A laser hemispherectomy is a highly complex, risky and challenging operation to help people with epilepsy. UChicago Medicine, which is a Level IV Pediatric Epilepsy Center, has performed about 250 laser surgeries, Warnke estimated.

But to completely disconnect a whole hemisphere with implanted laser fibres was a new challenge. Warnke and his team drew on their previous research, suggesting that interstitial lasers could be used to disconnect the two hemispheres of the brain.

"If we could replace open surgery with this, that would be a major breakthrough," said Warnke, UChicago Medicine's Director of Stereotactic and Functional Neurosurgery. "We've entered uncharted territory, but added a new level of safety as the surgery is carried out in the MRI scanner. It provides continuous vision and real-time monitoring of the brain temperature and imaging of the cell damage produced."

"Where we're at now is amazing," said his mother Amanda Morey. "Not only have the seizures stopped, but his whole attitude has changed. He's optimistic and happy now."

Laser epilepsy surgery at Comer Children's is now done using a new state-of-the-art robot. The robot is able to insert the laser fibres in the brain with greater speed and precision, shortening the surgery time.

When medications weren't working, Julia Henry, MD, Zachary's neurologist and epileptologist, told Zachary's mother about different surgical treatment options available to him.

While a laser hemispherectomy might not be appropriate for every patient with epilepsy, Henry said the risk of death is less than 1%, and between 73% and 83% of children have their seizures cured by surgery.

"This surgery is a big and scary procedure. Disconnecting half my child's brain? That's a lot for any parent to process. But the results can be so dramatic," Henry said. "The kids come to us so impaired. They have bad, frequent seizures. There are a lot of patients who might be good candidates for this, and this minimally invasive approach might open up the option for them."

"There was so much that he went through, and I was very hesitant to do this surgery at first. I kept thinking about all the 'what ifs'," Amanda said. "Knowing what I know now, I wouldn't have hesitated, and I wouldn't have waited this long. It worked out perfectly for him."

- For more information, visit *https://uchicagomedicine.org/global*.

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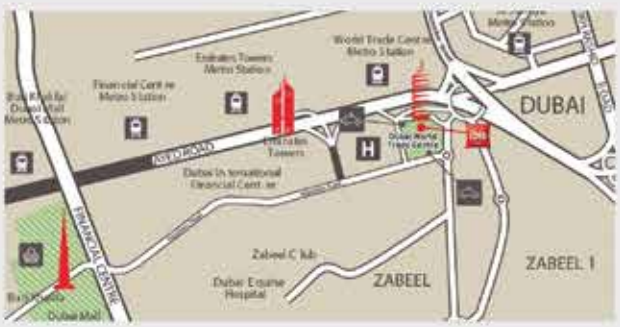

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The two founders of Purenum GmbH in the lab: Prof. Ingo G[illegible] a[illegible] ht).

Researchers develop hydrogel to remove kidney stone fragments

Kidney stones are often removed via an endoscopic procedure. If a stone is too large, the urologists break it into pieces using a laser. The larger pieces can be removed with a grasping instrument, but this is not possible for the smaller fragments – instead, they remain in the kidney in the hope that they will leave the body naturally. In the future, doctors will be able to remove even the smallest of stone fragments from the kidney during endoscopy using a hydrogel. This biocompatible 2-component system was developed by Purenum GmbH, a spin-off of the Fraunhofer Institute for Manufacturing Technology and Advanced Materials (IFAM). *Middle East Health* reports.

Nephrolithiasis occurs in all parts of the world. The annual incidence of urinary tract stones in the industrialized world is estimated to be 0.2%. A lifetime risk of 2-5% has been noted for Asia, 8-15% for the West, and 20% for Saudi Arabia. [1] Kidney stones are hard deposits of minerals and are classified into calcium oxalate, calcium phosphate, uric acid, cysteine, struvite, and mixed stones types, depending on the material of the stones. Calcium stones account for almost 70–80% of all kidney stones [2].

The size of the stones varies – at their worst, they can be as large as a walnut. The risk factors that can lead to the formation of a kidney stone include an unbalanced diet, a lack of exercise and insufficient fluid intake.

Kidney stones can be treated with medication or with minimally invasive therapies; as the technical possibilities continue

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mediNiK® in use: the hydrogel with encapsulated kidney stone fragments following removal from the kidney.

to evolve, urologists are opting more and more frequently for endoscopic procedures. The endoscope is inserted into the kidney via the urinary tract in order to locate the stones and remove them in a targeted manner. If the kidney stone is larger than five millimetres – i.e., larger than the natural urinary tract – it must be broken into pieces using a laser. These pieces vary in size: The larger ones can be removed with a grasping instrument, but the smaller ones are too tiny to be grasped. Within a few months, the fragments that remain in the kidney can grow into a large stone and cause complications once again.

> The term "stone-free" is not precisely defined – there are various definitions. There have not been any systematic studies conducted among patients to provide information about the size of the stones retrieved during operations.

Purenum decided to tackle this problem. Manfred Peschka and Prof. Ingo Grunwald founded the company as a spin-off of Fraunhofer IFAM in Bremen in December 2017. By participating in the GO-Bio funding programme for biotechnology start-ups offered by the German Federal Ministry of Education and Research (BMBF), they were able to secure the funding they needed to launch their company successfully.

Biocompatible hydrogel

The two researchers developed a hydrogel made from biocompatible materials to help remove the tiny stone fragments. It consists of two liquid components that are dyed blue and yellow to ensure a good colour contrast. This allows the surgeon to control dispensing in an extremely precise manner. The blue component is applied first, then flows around and wets the stone fragments. Following this, the yellow component is added. Application is extremely straightforward as the two components do not need to be mixed. Within a few seconds, the addition of the yellow component produces a gel that is solid enough to hold the small stone fragments inside. It is also elastic enough to be grasped with a grasping instrument and pulled through narrow channels (such as an endoscope). This makes it easy for the surgeon to pull the gel containing the stone fragments out of the kidney via the endoscope. After the operation, it can be dissolved easily in order to analyze the stones.

"We intend to launch the gel on the German market in the second quarter of this year under the name mediNiK-basic," said Peschka, CEO of Purenum GmbH.

100% stone removal

Commenting on the possibility of 100% stone removal, Prof. Grunwald said: "The term "stone-free" is not precisely defined – there are various definitions. There have not been any systematic studies conducted among patients to provide information about the size of the stones retrieved during operations."

Prof. Grunwald, CTO at Purenum, continued: "To that end, we are currently conducting a study at five different locations. Once it has been completed, this study will underpin our promise that, with mediNiK, we can remove more small stone fragments than would be possible without the use of our hydrogel."

The product is also attracting international interest, with Purenum receiving inquiries from all over the world.

"There are no comparable products out there at the moment – mediNiK is a world first in the field of urology," said Prof. Grunwald, a biologist.

His colleague, Peschka, added: "Our success is due in no small part to Fraunhofer IFAM. Without the exceptional support of Institute Director Prof. Bernd Mayer, Purenum would not exist." MEH

References

[1] https://www.medscape.com/answers/437096-155528/what-is-the-global-prevalence-of-nephrolithiasis
[2] https://doi.org/10.22037/jpn.v4i3.13121

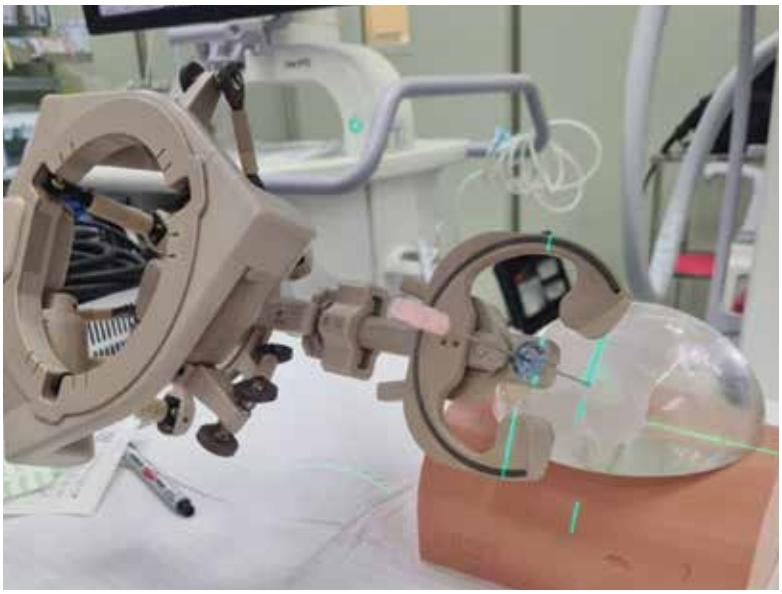
Automating renal access in kidney stone surgery using AI-enabled surgical robot

A novel AI-empowered robotic device has successfully undergone a clinical trial for assisting in percutaneous nephrolithotomy. *Middle East Health* reports.

Percutaneous nephrolithotomy (PCNL) is an efficient, minimally-invasive, gold standard procedure used for removing large kidney stones. Creating an access from the skin on the back to the kidney – called renal access – is a crucial yet challenging step in PCNL. An inefficiently created renal access can lead to severe complications including massive bleeding, thoracis and bowel injuries, renal pelvis perforation, or even sepsis. It is therefore no surprise that it takes years of training and practice to perform this procedure efficiently.

There are two main renal access methods adopted during PCNL – fluoroscopic guidance and ultrasound (US) guidance with or without fluoroscopy. Both approaches deliver similar postoperative outcomes but require experience-based expertise.

Many novel methods and technologies are being tested and used in clinical practice to bridge this gap in skill requirement. While some offer better imaging guidance, others provide precise percutaneous access. Nonetheless, most techniques are still challenging for beginners. This inspired a research team led by Assistant Professors Kazumi Taguchi and Shuzo Hamamoto, and Chair and Professor Takahiro Yasui from Nagoya City University (NCU) Graduate School of Medical Sciences (Nephro-urology), to question if artificial intelligence (AI)-powered robotic devices could be used for improved guidance compared with conventional US guidance. Specifically, they wanted to see if the AI-powered device called the Automated Needle Targeting with X-ray (ANT-X), which was developed by the Singaporean medical start-up, NDR Medical Technology, offers better precision in percutaneous renal access along with automated needle trajectory.



Nagoya City University Graduate School of Medical Sciences

This is the Automated Needle Targeting with X-ray (ANT-X), which was utilized for the robotic-assisted fluoroscopic guidance in percutaneous nephrolithotomy. This study presents the results of the clinical trial using the ANT-X.

The team conducted a randomized, single-blind, controlled trial comparing their robotic-assisted fluoroscopic-guided (RAF) method with US-guided PCNL. The results of this trial were published on June 13, 2022 in *The Journal of Urology* [1].

"This was the first human study comparing RAF with conventional ultrasound guidance for renal access during PCNL, and the first clinical application of the ANT-X," said Dr Taguchi.

The trial was conducted at NCU Hospital between January 2020 and May 2021 with 71 patients – 36 in the RAF group and 35 in the US group. The primary outcome of the study was single puncture success, with stone-free rate (SFR), complication rate, parameters measured during renal access, and fluoroscopy time as secondary outcomes.

Trial results

The single puncture success rate was ~34% and 50% in the US and RAF groups, respectively. The average number of needle punctures were significantly fewer in the RAF group (1.82 times) as opposed to the US group (2.51 times). In 14.3% of US-guided cases the resident was unable to obtain renal access due to procedural difficulty and needed a surgeon change. However, none of the RAF cases faced this issue. The median needle puncture duration was also significantly shorter in the RAF group (5.5 minutes vs. 8.0 minutes). There were no significant differences in the other secondary outcomes. These results revealed that using RAF guidance reduced the mean number of needle punctures by 0.73 times.

Multiple renal accesses during PCNL are directly linked to postoperative complica-

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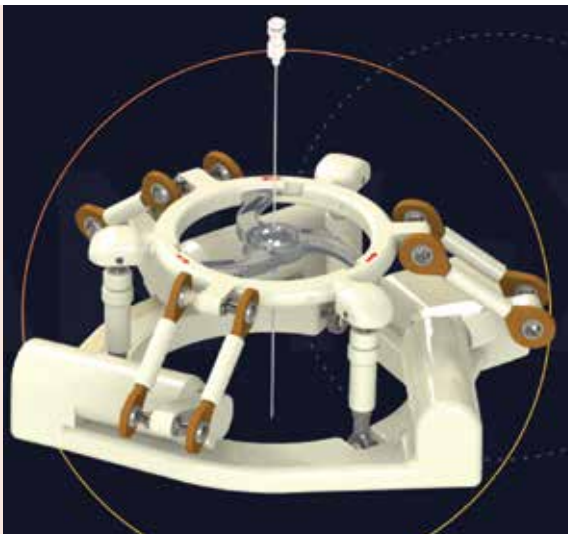
tions including, decreased renal function. Therefore, the low needle puncture frequency and shorter puncture duration, as demonstrated by the ANT-X, may provide better long-term outcome for patients. While the actual PCNL was performed by residents in both RAF and US groups, the renal access was created by a single, novice surgeon in the RAF group, using ANT-X. This demonstrates the safety and convenience of the novel robotic device, which could possibly reduce surgeons' training load and allow more hospitals to offer PCNL procedures.

Outlining the potential advantages of their RAF device, Dr Taguchi said: "The ANT-X simplifies a complex procedure, like PCNL, making it easier for more doctors to perform it and help more patients in the process. Being an AI-powered robotic technology, this technique may pave the way for automating similar interventional surgeries that could shorten the procedure time, relieve the burden on senior doctors, and perhaps reduce the occurrence of complications." MEH

ANT-X

ANT-X is NDR Medical Technology's first interventional robot that integrates C-arm fluoroscopy and AI software to help clinicians achieve safe and accurate percutaneous needle placement. ANT-X fully automates its system calibration and the needle alignment with a single x-ray image and allows clinicians to focus solely on controlling the depth of insertion.



Reference

[1] doi: https://doi.org/10.1097/JU.0000000000002749

D-Serine is useful for the rapid and precise measurement of kidney function

A team of researchers led by the Japan's National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN) and Osaka University has established a new method to measure glomerular filtration rate (GFR), a primary kidney function, by calculating the clearance of D-serine. Their research was published in the January 1, 2022 issue of *eClinicalMedicine* [1].

The research group evaluated the clearance of D-serine when assessing GFR through the inulin clearance measurement in living kidney transplant donors and recipients. Consequently, they found that the D-serine clearance strongly correlated with GFR and was less biased than the creatinine clearance, a conventional marker for renal function.

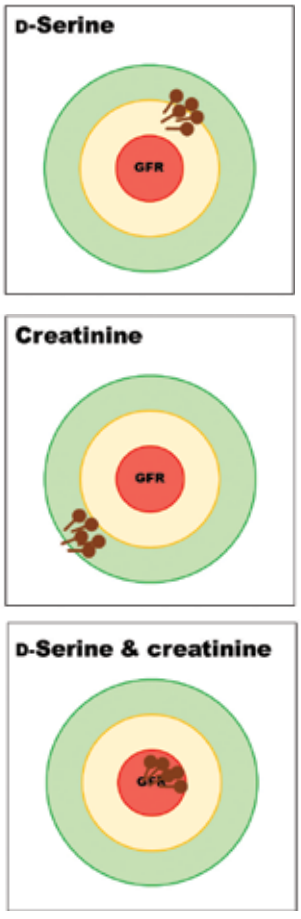
Chronic kidney disease is a global problem, and its frequency is increasing with the ageing population. Evaluation of GFR is essential for better clinical practice to reduce the number of dialysis patients; however, the current evaluation of GFR has several limitations, including a labour-intensive procedure for the inulin clearance (the gold standard of GFR), a major bias for the creatinine clearance, and imprecise estimation of estimated GFR (eGFR). Endogenous molecules potentiating the precise assessment of kidney function with low biases are still necessary for important clinical decisions, including drug administration design, transplant donor selection, and staging of kidney disease.

L- and D-amino acids are mirror-image enantiomers, and L-amino acids are exclusively present in the human body. "A trace amount of D-serine is present in human blood and reflects kidney function," says study lead author Masataka Kawamura. "We are investigating the potential of D-serine for the precise assessment of kidney function."

The research group evaluated the urinary excretion rate (clearance) of D-serine in living kidney transplant donors and recipients. The clearance of D-serine was calculated based on the D-serine levels in the blood and urine, measured using a two-dimensional high performance liquid chromatography system, which is the most accurate and sensitive system for measuring D-amino acids.

Remarkably, the clearance of D-serine agreed well with GFR. The low bias as a measure of GFR was an advantage for the D-serine clearance. The degree of bias against GFR was smaller than that of the creatinine clearance. Additionally, the combinational analysis of clearances of D-serine and creatinine could measure GFR with high performance, say the authors.

"D-Serine turned out to be of great clinical importance," says the study senior author of the study, Tomonori Kimura. "D-Serine may solve the problem of kidney disease with more than 800 million patients in the world. Measuring D-serine is applicable in a wide range of clinical fields and for drug development." MEH



Tomonori Kimura

D-Serine is useful for the measurement of glomerular filtration rate (GFR). The clearance of D-serine has an advantage of lower bias against GFR compared to that with the creatinine clearance. Combinational clearance measurement of D-serine and creatinine can serve as a measure of GFR with precision and low bias.

Reference:

[1] doi: https://doi.org/10.1016/j.eclinm.2021.101223

Improving prognosis in chronic kidney disease

Researchers from Osaka University identify an association between mineralocorticoid receptor antagonist use and improved renal outcomes in patients with chronic kidney disease. *Middle East Health* reports.

Just as a water filtration system acts to filter contaminants from the water you drink, your kidneys act to filter waste and excess fluid from your blood. In chronic kidney disease (CKD), kidney function is impaired over time, and the resultant build-up of excess fluid and waste has harmful repercussions on overall body function. Researchers in Japan conducted a study of real-world data from patients with CKD to evaluate the impact of a commonly prescribed medication on disease outcome.

In a study published in the January 14, 2022 issue of *Hypertension* [1], researchers from Osaka University have demonstrated an association between the use of mineralocorticoid receptor antagonists (MRAs), a class of medicines that acts by suppressing the action of the steroid hormone aldosterone, and an improved renal prognosis in individuals with CKD.

As CKD progresses, the initiation of renal replacement therapy (RRT), which includes dialysis and kidney transplantation, may be necessary for life support in kidney failure. MRAs, which include spironolactone, eplerenone, and potassium canrenoate, are commonly used to reduce swelling, blood pressure, and urine protein levels in people with CKD. However, the association between MRA treatment and the initiation of RRT has not been fully explored in a real-world population, which spurred the research team from Osaka University to undertake a large-scale retrospective study of MRA use in people with CKD.

"We conducted a retrospective analysis of clinical data from over 3100 individuals with CKD," says lead author Tatsufumi Oka. "We evaluated MRA treatment in various populations of people with CKD, including those with diabetes, heart disease, and severely impaired renal function."

The research team employed a marginal structural model to analyze the association between MRA use and the initiation of RRT across multiple patient subgroups.

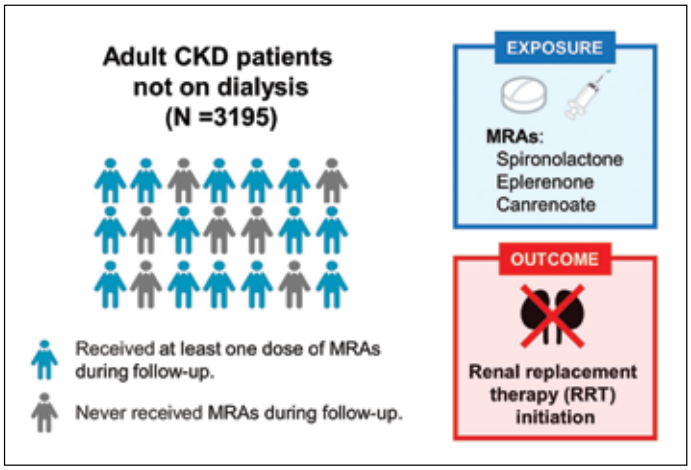


Figure 1. Overview of the present study.

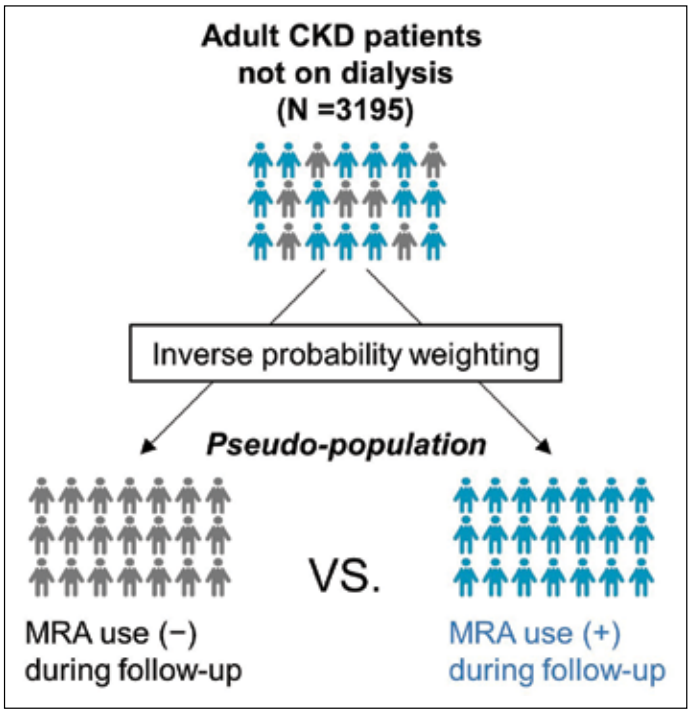


Figure 2. Marginal structural model.

"Our analysis showed that MRA use was associated with a 28% lower rate of RRT initiation and a 24% lower rate of the combined outcomes of RRT initiation and death," says senior author Jun-Ya Kaimori.

The research team observed a reduced risk for RRT initiation across various subgroups of people with CKD, including those with and without diabetes and those with severely impaired renal function. These findings highlight the association of MRA use and improved renal outcomes in a real-world population of CKD patients with varying health backgrounds. Overall, this study supports the use of MRAs in treatment plans for various groups of people with CKD who are not undergoing dialysis. MEH

Reference:

[1] doi: *https://doi.org/10.1161/HYPERTENSIONAHA.121.18360*

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Enhancing our global reputation is an active research programme that keeps us at the vanguard of clinical research and developing new technologies and therapeutic interventions for the benefit of all patients.

Our achievements

- Guy's and St Thomas' pioneered robotic technology in the UK
- Our transplant surgeons were the first in the world to use 3D printing to support an adult donor kidney transplantation successfully into a child
- Our renal team spearheaded the use of da Vinci technology in the UK to undertake full kidney transplants and perform keyhole surgery to implant donor kidneys in patients
- One of the first three centres in the UK to have a laparoscopic (keyhole) donor programme.

Kidney transplants

Our renal unit's expertise in adult and paediatric complex cases means we can provide transplants for many patients for whom transplantation would otherwise be impossible. It is supported by a network of specialists in living donation, cardiology, urology, infectious disease and pharmacology.

The living donor transplantation programme is one of the largest, most active in the UK and one of the most successful in Europe, with a one-year graft survival rate of 98%.

Our paediatric renal service is also the largest in Europe. We operate from Evelina London Children's Hospital and provide blood group compatible kidney transplants for private patients. In addition, we specialise in managing complex nephrotic syndrome, reno-vascular patients and transplant urology for adolescents.

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Our multidisciplinary approach assures private patients of excellent clinical care from dedicated expert teams working together to provide personalised care at every stage of treatment or surgery.

The multidisciplinary team include renowned consultants, such as transplant surgeons, urological surgeons and nephrologists who look after all renal conditions and are supported by nurses and specialists with extraordinary knowledge and expertise in complex care.

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Our surgeons perform many vascular access operations, including standard arteriovenous fistulae, complex grafts and revision surgeries supported by an expert interventional radiology service. We also provide an outstanding paediatric vascular access service to children in London and beyond who require haemodialysis and other therapies. Our consultants are involved in several national studies at the frontiers of dialysis access and novel approaches such as endovascular fistula formation.

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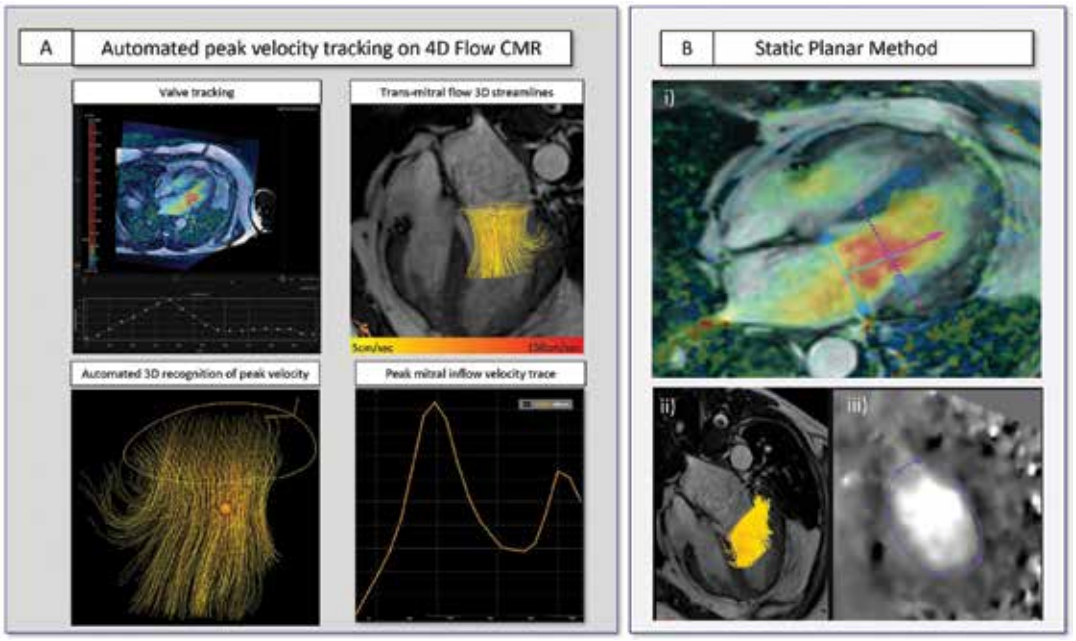

Mitral inflow peak velocity tracking on CAAS MR using two novel methods: A) Automated dynamic method and B) static-plane method. Image A (Top-left) Semi-automated mitral valve-tracking schematics - the two attachments of the mitral valve leaflets are manually selected at a single point in the cardiac cycle. The software performs automated tracking of the valve in motion throughout the cardiac cycle. 3D streamlines produced showing mitral inflow. Automated peak velocity tracking is indicated by a yellow sphere within the streamlines. 4-chamber orthogonal long-axis cine view showing mitral inflow as 3D streamlines on 4D flow CMR during diastole (Top-right) (Bottom-left). Peak velocity tracings demonstrating E-wave and A-wave velocity peaks (Bottom-right). Image B (Top image) Static method using the alternative plane to illustrate colour-coded 4D flow CMR. Mitral inflow velocity detection (purple arrow). (Bottom-left) Mitral forward flow shown as 3D streamlines on 4D flow CMR. (Bottom-right) 4D flow CMR velocity mapping of mitral flow showing the contour (purple ring) which is manually adjusted to outline the region of mitral inflow depicted as the hyperdense opacity.

Cutting-edge 4D flow MRI scans could revolutionise blood flow assessment in the heart

Researchers at the University of East Anglia have developed cutting-edge imaging technology to help doctors better diagnose and monitor patients with heart failure.

The state-of-the-art technology uses magnetic resonance imaging (MRI) to create detailed 4D flow images of the heart.

The study published in the *International Journal of Cardiology* on June 27, 2022 [1], shows how this non-invasive imaging technique can measure the peak velocity of blood flow in the heart accurately and precisely.

The 4D heart MRI scan takes just six to eight minutes and can provide precise imaging of the heart valves and the flow inside the heart in three-dimension, helping doctors determine the best course of treatment for patients.

Cardiology patients at the Norfolk and Norwich University Hospital were the first to trial the new technology. The team hope their work will revolutionise how heart failure is diagnosed.

Lead researcher Dr Pankaj Garg, from University East Anglia's Norwich Medical School, said: "Heart failure is a dreadful condition resulting from rising pressures inside the heart. The best method to diagnose heart failure is by invasive assessment, which is not preferred as it has risks.

"An ultrasound scan of the heart called echocardiography is routinely used to measure the peak velocity of blood flow through the mitral valve of the heart.

"However, ultrasound assessment is dependent on the operator and can be unreliable.

"In our study, we used one of the most cutting-edge methods of flow assessment inside the heart called 4D flow MRI.

"In 4D flow MRI, we can look at the flow in three directions over time, the fourth dimension.

"We applied automated methods to hunt for the peak velocity in the chamber of the heart and showed that it is similar to echocardiography assessment, but with much greater precision."

The team tested the new technology with 50 patients at the Norfolk and Norwich University Hospital and at the Sheffield Teaching Hospitals NHS Foundation Trust in Sheffield.

Patients with suspected heart failure were assessed using both echocardiography and the new advanced 4D flow heart MRI.

The team collaborated with industry partner Pie Medical Imaging from the Netherlands to develop prototype software

New MRI technique could improve diagnosis and treatment of multiple sclerosis

It is important that multiple sclerosis (MS) is diagnosed and treated as early as possible in order to delay progression of the disease. The technique of magnetic resonance imaging (MRI) plays a key role in this process. In the search for ever better methods, a new MRI technique has been used at MedUni Vienna as part of a research project that could pave the way to quicker assessment of disease activity in MS. The study was conducted by a research team led by Wolfgang Bogner at MedUni Vienna's Department of Biomedical Imaging and Image-guided Therapy and was is published in the journal *Radiology* [1].

Multiple sclerosis is a disease of the central nervous system that manifests itself in lesions primarily in the brain. As yet, there is no cure for MS, but it can be effectively treated. Early diagnosis is critical to the prognosis, with highly detailed imaging techniques playing a major role. Although conventional MRI can detect brain lesions, scientists are researching methods to detect the changes at an earlier microscopic or biochemical stage. The method known as proton MR spectroscopy has been identified as a promising tool for this purpose.

Using this technique, the research group led by Eva Niess and Wolfgang Bogner from MedUni Vienna's Department of Biomedical Imaging and Image-guided Therapy, working with scientists from MedUni Vienna's Department of Neurology, went one step further in their recently published study. The team used MR spectroscopy with a 7-tesla magnet to compare the neurochemical changes in the brains of 65 MS patients with those of 20 healthy controls. This particularly powerful imaging tool was co-developed by MedUni Vienna researchers and has been used for scientific studies, e.g., of the brain, at MedUni Vienna's Center of Excellence for High-Field MR since it was commissioned in 2008.

Identifying and predicting changes

Using 7-tesla MRI, MedUni Vienna researchers have now been able to identify MS-relevant neurochemicals, i.e. chemicals involved in the function of the nervous system.

"This allowed us to visualize brain changes in regions that appear normal on conventional MRI scans," says study leader Bogner, pointing to one of the study's main findings. According to the study's lead author, Niess, these findings could play a significant role in the care of MS patients in the future: "Some neurochemical changes that we've been able to visualize with the new technique occur early in the course of the disease and might not only correlate with disability but also predict further disease progression."

More research is needed before these findings can be incorporated into clinical applications, explained Niess and Bogner. They said that the results already show 7-tesla spectroscopic MR imaging to be a valuable new tool in the diagnosis of multiple sclerosis and in the treatment of MS patients.

"If the results are confirmed in further studies, this new neuroimaging technique could become a standard imaging tool for initial diagnosis and for monitoring disease activity and treatment in MS patients," said Bogner, looking to the future. The method is currently only available on the only 7-Tesla MRI scanner in Austria at MedUni Vienna and only for research purposes. However, the scientific team led by Niess and Bogner is working on refining the new method for use in routine clinical MRI scanners.

Reference:

[1] **doi:** *https://doi.org/10.1148/radiol.210614*

to automate the process of measuring the peak velocity of blood flow inside the heart.

Dr Garg said: "This work is very important because the heart's inability to relax leads to a rise in pressures inside the heart, and this causes heart failure with preserved ejection fraction.

"Peak velocity of the blood flow inside the heart is a very important assessment for patients, and our findings show that by using a state-of-the-art 4D flow MRI imaging, we can do this accurately and with a high degree of repeatability.

"This advanced imaging offers an alternative to ultrasound methods and may even be better than ultrasound in the future."

This research project was funded by the Wellcome Trust.

- **Watch a heart in 4D:** *https://youtu.be/U6_izjU4n90*

Reference:

[1] **doi:** *https://doi.org/10.1016/j.ijcard.2022.06.032*

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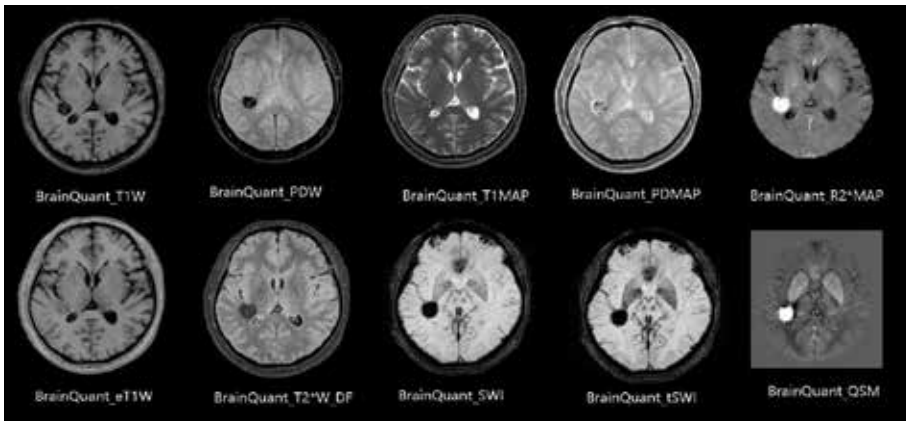

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T1W image can provide a good histological image, while contrast-enhanced T1-weighted eT1W has better gray and white matter contrast than conventional T1W image; T1 quantitative image can be used in the study of multiple sclerosis and other diseases.

The PDW image reflects the amount of hydrogen protons in the tissue and is used for the measurement of tissue water content; the PD quantitative image can be used to detect changes in tissue water content caused by brain tumors.

T2* image can reflect the changes of tissue iron content and oxygen content through the influence of tissue susceptibility differences on the signal and can be used in the diagnosis of neurological diseases.

BrainQuant clinical value exploration: Stroke value research; Value research in neurodegenerative diseases: Evaluation of efficacy in Alzheimer's disease and Parkinson's disease; Calcification and hemorrhage Identification; Tumor screening, etc.

CT: Various low-dose technologies to ensure patient safety

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O-dose platform is an integrated approach for dose management from Neusoft Medical. It encompasses a set of techniques, programs and practices based on ALARA (As Low As Reasonably Achievable) principle and supports outstanding image quality at low dose. It is incorporated in every aspect of scanning. It provides a full range of low dose solutions for everyone involved to preserve the image quality while delivering more care to patients and operators.

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Target-Controlled Infusion anaesthesia: New more universal models

By **James Waterson**, RN, M.Med.Ed. MHE. Becton Dickinson. Medical Affairs Manager, Middle East & Africa

In simple terms Target-Controlled Infusion (TCI) means that instead of setting a dose-rate on the pump, the pump is programmed to target a required plasma concentration or effect-site concentration. A TCI pump automatically calculates how much drug is needed during induction and maintenance to maintain the desired effect-site or plasma concentration.

A TCI algorithm (the 'target' and plan on which the pump relies to deliver appropriate induction and maintenance rates to maintain anaesthesia without overdosing the patient) is based on pharmacokinetic (PK) and pharmodynamic (PD) models and on Absorption, Distribution, Metabolism, and Excretion of medications by the body.

For example, the effect-site concentration of Propofol required to produce loss of consciousness is about 3 to 6 mcg/ml, depending on the patients' demographics. Patients waking from anaesthesia generally have a blood concentration of around 1- 2 mcg/ml, although this is dependent on other drugs given during anaesthesia.

Adequate analgesia with Remifentanil is generally achieved with 3-6 ng/ml. A Remifentanil infusion of 0.25-0.5 mcg/kg/min in an 'average' man – 70 kg, 170 cm, 40 years old – produces a blood concentration of around 6ng/ml after 25 minutes.

PK models are based on body compartments

Conventionally the body compartment that the drug is injected into is V1 (plasma/blood), the next compartment is the 'vessel-rich' or 'fast re-distribution' compartment and is characterized as V2 (heart, liver, etc.). The final compartment, which is anatomically 'vessel-poor' and 'slow' in terms of re-distribution, is V3 (fatty tissue).

Drug distribution and the metabolism/elimination of each drug in each compartment is also part of each TCI model, as is the pharmacodynamics of the time taken between the plasma and effect-site effect.

Computer simulations and mathematical modelling of infusion schemes based on the above theories of compartments and clearances give models for both Target Plasma Concentration (Cpt) and Target Effect Concentration (Cet) and these can be incorporated into specialist infusion pumps.

The Marsh model for Propofol requires only age and weight to be programmed in the pump. The Schnider model is an alternative model for Propofol and has advantages in elderly patients as it is based on a lean body mass (LBM) calculation for each patient. Elderly patients receive a lower induction and maintenance dose, which can assist with hemodynamic stability.

The Remifentanil Minto model uses age, height, gender and weight, and determines LBM for its calculations.

TCI pumps deliver the infusion at a constantly altering rate, but it is useful to think of this one infusion as being a mean-average of three continually calculated infusion rates: a constant rate to replace drug elimination and two exponentially decreasing infusions to match drug removed from central compartments to other peripheral compartments of distribution.

Key features of an ideal TCI infusion system or pump are:

- Critical information such as decrement time, current Cet or Cpt and respective targets, current dose rate and concentration and type of agent being infused can be displayed at the same time on one screen.
- Patient parameters used during the setting-up of infusions appear on one screen to avoid the need for shuttling through multiple screens to check vital information.
- An Induction Time adjustable from seconds to minutes to allow for a gentle induction for patients with cardiovascular conditions or established hypotension.

Obese patients have previously presented a problem for 'classic' TCI, and the physiological differences between paediatrics and adults had required separate models for children.

Now, however, we have the Eleveld model for both Propofol and Remifentanil, and the Kim-Obara-Egan Remifentanil model which are much more universal and can potentially allow TCI in age ranges from 6 months to 99 years of age, and from 2.5 to 215 kg.

TCI, with its emphasis on evidence-based anaesthesia, and new near-universal patient models seems primed to change our approach to the management of all patients receiving sedatives and analgesic agents. MEH

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Reimagining nursing for the future: 6 ways to improve communication for nurses

Nursing holds a critical and unique place in the world's healthcare infrastructure. Without nurses, patient care and safety would be at risk, but their impact is much greater. The safety and well-being of communities, nations, and the world would be at risk without nurses, which is why we must protect them and the nursing profession.

The future of nursing is threatened today by many variables, including a staffing shortage that is beyond anything ever seen in the industry. In a survey by Nurse.org of 1,500 nurses worldwide from September to November of 2021, 80% of nurses said their units are inadequately staffed.

Unfortunately, we cannot backfill our way out of the current crisis because we simply do not have enough nurses in the funnel. The World Health Organization estimates that by 2030, there will be a need for 36 million nurses practicing around the globe with a potential global shortage of 13 million nurses.

To reverse these trends, we must, first, listen to nurses describe their experiences, and second, implement innovations to improve their working environment. At the centre of both is better communication.

Communication: Every hospital's foundation

Communication is at the heart of nursing work. When communication is difficult, everything slows down. When nurses must take extra steps, spend more time, and use cognitive resources searching for the right person or information, they lose valuable time and resources that could be used caring for their patients at the bedside.

As vacancies leave gaps in shifts and add additional pressures to already fatigued and stressed nurses , the healthcare industry must find ways to use technologies to simplify clinical workflows and processes to improve patient care and safety. Nurses are asking for help. Here are six ways to address nurses' calls for innovation to improve their work environment:

1. **Simplify and unify communication workflow:** Streamlining workflows for nurses starts with improving communication. A single, unified communication platform is essential.
2. **Connect mobile care teams:** In response to staffing pressures, many hospitals are turning away from primary nursing and moving to team nursing where one nurse manages a team of healthcare assistants. For such a team to function effectively, effective communication and workflows designed for mobility are imperative.
3. **Transform the hospital's systems into nurse extenders:** A nurse extender is a technology, tool, process, or protocol that extends a nurse's reach and influence. Start with the patient in the bed. Many hospitals use smart, connected beds that can be integrated with a communication system that notifies the correct caretaker when a patient is in a compromised state and at risk for injury.
4. **Innovate care models:** Two of the most time-consuming tasks a nurse has are admission assessment and discharge teaching. Hospital leaders should consider enabling virtual nurses to assist with admissions and discharges using video.
5. **Identify tasks to offload from the nurse:** Nurses should not have to spend their valuable time performing tasks that patients can do for themselves if the patient has the cognitive capabilities to perform these functions. Hospitals can give patients the means to document their own intake and output, blood sugar, ambulation in the room, and the like.
6. **Empower nurses to manage the patient and family experience:** Keeping patients' families informed and at ease can be a time-consuming task. Give nurses greater control of this communication by equipping them with mobile technology that helps automate the process as part of their rounding process.

Nurses remain the largest work group in the healthcare system and their impact on the safety and well-being of patients is immeasurable. Difficult times have presented never-before challenges. Nurse leaders must listen and respond to nurses' appeals to change the work environment and innovate care models to improve systems, technologies and processes that will ensure quality patient care. The future of nursing is in peril if we ignore them.

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