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## Dementia

Public health stakeholders must plan now for the forecast tidal wave of cases

### Awake craniotomy

KFSH&RC neurosurgeon discusses this advanced intervention for epilepsy and brain tumours

### Korean MedTech

Innovative companies to showcase their cutting-edge developments in Abu Dhabi

### In the News

- Saudi Arabia launches National Institute of Health to advance clinical research
- AI in BioMed forecast to reach \$6 trillion by 2027
- WHO launches new Global Initiative on Digital Health
- Longevity gene from naked mole rats extends lifespan of mice
- Researchers create synthetic human embryo from stem cells without egg or sperm
- UAE approves novel gene therapy for Duchenne muscular dystrophy

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# Prognosis

## Mitigating the coming tidal wave of dementia

Dementia is a significant global health challenge, and it is expected to increase in prevalence in the coming decades. Forecast increases in dementia in the MENA region published in 2022 <<https://bit.ly/31KORwW>> by *The Lancet Public Health* are staggering. In the MENA region, cases are predicted to grow by 367%, from almost 3 million in 2019 to nearly 14 million by 2050, with disturbingly large increases in Qatar (1926%), the United Arab Emirates (1795%), and Bahrain (1084%).

Key reasons for this expected increase include an ageing population, increasing life expectancy, lifestyle factors and, to some extent, improved diagnosis and awareness.

One of the primary factors contributing to the rise in dementia cases is the ageing of the global population. As people live longer, the risk of developing dementia, particularly in individuals over the age of 65, increases significantly. This demographic shift is expected to continue over the coming decades.

Advances in healthcare and improved living conditions have led to increased life expectancy in many parts of the world. With longer life comes a greater likelihood of age-related conditions, including dementia.

Lifestyle factors such as diet, physical activity, and exposure to certain environmental factors can influence the risk of dementia. Changes in modern lifestyles, including diets high in processed foods and sedentary behaviour, have been associated with an increased risk of dementia.

There are efforts to address the growing dementia risk and these include research into treatments, interventions to reduce modifiable risk factors, and support for caregivers and individuals living with dementia.

It's important for governments, healthcare systems, and communities to plan for the increasing number of dementia cases and develop strategies to provide quality care and support for affected individuals and their families.

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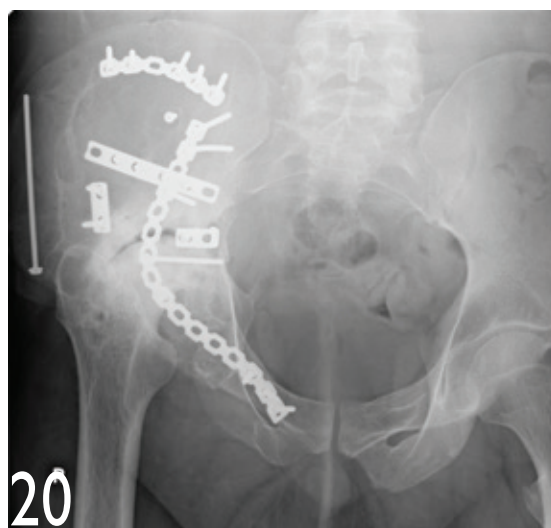
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16



20



22



26

## NEWS

- 6 Middle East Monitor
- 12 Worldwide Monitor
- 16 The Laboratory

## FOCUS

- 20 **Orthopaedics:** Global hip fractures forecast to double by 2050, IOF urges action for prevention
- 21 **Orthopaedics:** Experts issue important update on use of trabecular bone score in clinical practice
- 24 **Qatar Report**
- 42 **Neurology:** Middle East faces tidal wave of dementia cases
- 44 **Neurology:** Researchers identify new genetic variant protective against Alzheimer's disease

## INTERVIEWS

- 48 **Awake craniotomy:** Dr Afnan Alkhotani, Associate Consultant in Neurosurgery at King Faisal Specialist Hospital & Research Centre, Jeddah



30



48

# Deep Resolve

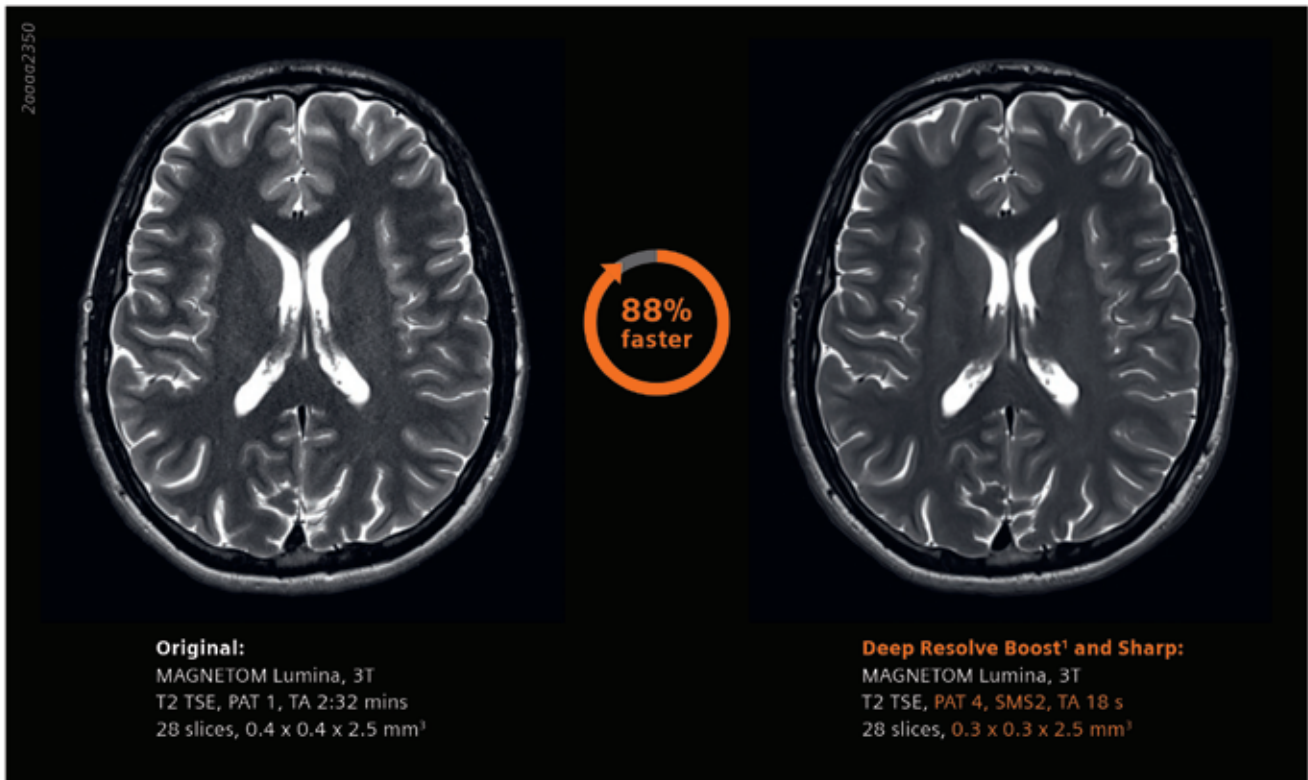
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Deep Resolve is a deep learning image reconstruction technology that takes advantage of neural networks that accelerate MR scans, making them faster than ever before. Shorter scans boost workflow efficiency while improving the patient experience. Deep Resolve's raw data-to-image reconstruction and very fast acquisition are game changers in MRI, helping generate actionable insights that can be diagnostically relevant.

- Deep Resolve is a raw data-to-image deep learning reconstruction technology that enables high SNR and radically accelerated image acquisition.
- Enabling all relevant contrasts in one go with multi-shot EPI and deep learning reconstruction for a total neuro exam in two minutes scan time.



<sup>1</sup> MAGNETOM Lumina with Deep Resolve Boost is not commercially available in some countries. Due to regulatory reasons the future availability cannot be guaranteed.



# middle east monitor

Update from around the region

## UAE Ministry of Climate Change and PureHealth sign MoU to study the impact of air quality on public health

The UAE Ministry of Climate Change and Environment (MOCCA) has signed a memorandum of understanding (MoU) with PureHealth, the largest healthcare platform in the Middle East, to evaluate the impact of air quality on public health with a focus on the factors affecting the longevity and quality of life of the people in the UAE.

The MoU was signed 9 August 2023 in the presence of Her Excellency Mariam Almhiri, Minister of Climate Change and Environment, and attended by Her Excellency Eng. Othaiba Al Qaydi, Acting Assistant Undersecretary for Sustainable Communities, Farhan Mallik, Managing Director and Chief Executive Officer at PureHealth Group and Marwan Ali Al Kaabi, Chief Infrastructure Officer at PureHealth.

The MoU builds on PureHealth’s commitment to work towards boosting research and other efforts to enhance longevity in people.

Almhiri commented: “This partnership marks a significant step forward in our commitment to enhancing the quality of life for



the people of the UAE. By evaluating the impact of air quality on health, we can make informed decisions that contribute to effective climate action, community health, and overall sustainability. As we prepare to host COP28 later this year at Dubai Expo City, during this Year of Sustainability, the MoU underscores our focus on fostering a sustainable future for our nation and the world through strategic partnerships.”

Malik said: “Our goal is clear – to advance the science of longevity, and ensuring people live longer, healthier, happier, and fuller lives. Through the research and assessment of the impact of air quality on

public health, we can work towards building a healthier, more resilient future for the people of the UAE.”

As part of the MoU, a Joint Working Committee, comprising representatives from both entities, will be set up to oversee the implementation of the activities outlined in the agreement. The committee will meet periodically to review progress, share information, and address any challenges.

This partnership between MOCCA and Abu Dhabi-based PureHealth is a testament to the UAE’s commitment to addressing the challenges of climate change and enhancing the health and well-being of its people. **MEH**

## Saudi Arabia launches National Institute of Health to advance clinical research

Saudi Arabia’s cabinet announced 15 August the establishment of the Saudi National Institute of Health (SNIH). Aiming to facilitate medical research and clinical trials on a national scale.

The institute will oversee and support all translational research and clinical trials, Minister of Health Fahad Aljalajel said. It will gain added value from research by transforming the results into health and economic benefits to raise the quality of life.

Aljalajel added that the institute will aid in the prevention of health emergencies, one of the goals of Saudi Arabia’s

Vision 2030 and the Health Sector Transformation Program. This will be achieved through research, development, and innovation to improve health policies and strategies, he said.

SNIH will contribute to raising national income by developing locally manufactured products for prevention, diagnosis, and treatment.

“The Cabinet’s decision to establish the SINH has been made to support health sector researchers and creative competencies in translational research and clinical trials to improve the health sector in Saudi

Arabia,” Aljalajel said.

The institute will help pharmaceutical and medical device manufacturers to develop innovative products.

Furthermore, it will reduce overall healthcare costs, by attracting global investors and raising research funding.

SNIH is one of the Health Sector Transformation Program initiatives, launched with Vision 2030. It was preceded by the launch of the Saudi Patient Safety Center, the National Public Health Laboratory, and the National Health Emergency Operations Center. **MEH**





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## Pulsar Capital takes controlling stake in TruDoc to advance telehealth

Pulsar Capital has taken a controlling stake in TruDoc, UAE's leading telehealth and virtual primary care provider. Pulsar Capital is a prominent regional private equity firm specializing in the healthcare, e-commerce and fintech sectors. The investment marks a significant milestone in TruDoc's mission to redefine healthcare delivery and expand its reach to benefit patients across multiple regions.

Pulsar Capital invested in TruDoc with the vision to enhance its product offerings and accelerate its growth across South Asia, the GCC, and Africa. This new investment comes a year after an initial investment in 2022 which saw the private equity firm own a minority share of TruDoc.

TruDoc strives to bridge the gap in accessibility and affordability, the two the big-

gest challenges facing global healthcare by offering comprehensive end-to-end care for healthy individuals and those dealing with acute and chronic illnesses. At present, TruDoc serves diverse geographies, including the UAE, Kingdom of Saudi Arabia as well as Nigeria and other parts of Africa.

Established in 2011, TruDoc is at the forefront of delivering innovative and accessible healthcare solutions. Its commitment to reimagining healthcare delivery has made the company the trusted provider of 24/7 access to licensed telemedicine along with its homecare doctors, labs and diagnostics, e-pharmacy services, and personalized wellness programmes. TruDoc has close to one million paid subscribers in UAE and two million globally,

TruDoc innovative approach enables patients to proactively manage their health in the convenience of their own home, ultimately creating a more intimate and

user-friendly healthcare experience.

Characterized by a commitment to value-based care and evidence-based medicine, TruDoc's team of dedicated medical professionals prioritizes patients' needs, ensuring that each individual receives tailored and comprehensive care that addresses their unique health requirements.

Vish Narain, Managing Partner of Pulsar Capital, will assume the new role of Executive Chairman of TruDoc. He commented: "The acquisition of TruDoc represents our continued commitment to deliver quality care to patients with an emphasis on convenience, affordability and accessibility. Technology is going to significantly change the way primary care is going to be delivered. TruDoc has cutting edge tools using the latest technology in electronic patient record management, home health, telemonitoring, wearables and generative AI which will benefit our payors and end-consumers." MEH

## UAE's Mediclinic Parkview Hospital provides early access to new revolutionary ALS therapy

Mediclinic Parkview Hospital in Dubai is the first hospital in the UAE to offer Tofersen, a revolutionary medication for a rare subset of Amyotrophic Lateral Sclerosis (ALS), Superoxide Dismutase 1 (SOD1) gene mutation-mediated ALS.

Dr Fatmah Al Zahmi, Consultant Neurologist at Mediclinic Parkview Hospital, Dubai, explained: "ALS is a debilitating neurodegenerative disease that affects thousands of individuals worldwide. SOD1 mutations account for approximately 20% of all familial ALS cases and 2% of all ALS cases.

"This medication is designed to bind to SOD1 mRNA, effectively reducing the production of toxic SOD1 protein in motor neurons. By addressing the underlying cause of ALS in this subset. We aim to slow down the progression of the disease and offer new hope to patients, particularly those with familial ALS."

Dr Mohammed Sallam, Pharmacy Manager at Mediclinic Parkview Hospital, commented: "The therapy received FDA approval for the treatment of ALS secondary to SOD1 mutation on 25 April 2023,



Dr Fatmah Al Zahmi, Consultant Neurologist at Mediclinic Parkview Hospital, Dubai



Dr Mohammed Sallam, Pharmacy Manager at Mediclinic Parkview Hospital

and was administered on 17 August 2023 for the first time in the UAE at Mediclinic Parkview Hospital. This approval marks a significant breakthrough in ALS treatment and underscores our commitment to bringing cutting-edge treatments to our patients."

Dr Sallam added: "This achievement would not have been possible without the unwavering dedication and unique ex-

perience of our team, led by Dr Fatmah Al Zahmi. Her relentless efforts to understand the underlying cause of ALS in her young patients and explore the most up-to-date treatments have resulted in timely access to this recently FDA-approved breakthrough therapy. Dr Fatmah emphasises that her patients shall always receive the highest standard of care available in the most reputable hospitals worldwide." MEH

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## Novel gene therapy for Duchenne muscular dystrophy approved in UAE

Delandistrogene Moxeparvovec, a ground-breaking novel gene therapy for the treatment of Duchenne muscular dystrophy (DMD), has been approved by the United Arab Emirates Ministry of Health and Prevention (MOHAP).

DMD is one of the most severe forms of inherited muscular dystrophies and also the most common hereditary neuromuscular disease. It affects about one in 5,000 males at birth. Although life expectancy has increased due to improvements in standard of care, DMD still leads to early death often before or during a patient's 30s due to respiratory impairment and cardiomyopathy.

Delandistrogene Moxeparvovec, a novel gene transfer therapy, is approved for ambulatory paediatric patients aged 4 through 5 years with DMD who have a

confirmed mutation in the DMD gene.

The MOHAP approval is the first regulatory approval outside the U.S. FDA, which approved the treatment in June this year, meaning that DMD patients in UAE may be the first to receive the treatment outside the U.S.

In the UAE the treatment is being commercialised by Roche Pharmaceuticals.

The treatment is expected to be available at UAE hospitals this year thanks to the fast-tracked approval by MOHAP.

Delandistrogene Moxeparvovec is designed to deliver a gene that makes a shortened functional form of the dystrophin protein with the aim of improving muscle function via a one-time administration. Dystrophin provides structural integrity in muscle cells.

Clinical data to date suggest Delandistrogene Moxeparvovec has the potential to

transform the lives of patients living with the condition.

Results from the pivotal Phase 3 EMBARK study (ClinicalTrials.gov Identifier: NCT05096221) to evaluate the safety and efficacy of Delandistrogene Moxeparvovec are expected by the end of the year.

Mohammed Elshaarawy, General Manager, UAE, Roche Pharmaceuticals, said: "We welcome the approval of Delandistrogene Moxeparvovec for children aged 4-5 years. Living by our purpose of 'doing now what patients need next', we are working with urgency to support our partners in ensuring the UAE healthcare system is ready to bring this promising gene therapy to people with Duchenne and their families this year."

• MOHAP approval code: YVP9K-T7F-300823.

## UAE Multiple Sclerosis Society praises WHO approval of essential medication

Dr Fatima Al Kaabi, Vice Chair of the UAE's National MS Society Board of Trustees and Executive Director of the Bone Marrow Transplant Programme at the Abu Dhabi Stem Cells Center (AD-SCC) has praised the World Health Organization's (WHO) decision to approve three Multiple Sclerosis Disease-Modifying Therapies – A.10 Cladribine, glatiramer, and rituximab – as part of its Essential Medicines List (EML), calling it a "significant milestone for the global MS community" – especially for those living in resource-limited settings.

Led by one of the National Multiple Sclerosis Society's (NMSS) key global partners, the London-based Multiple Sclerosis International Federation (MSIF), this marks the first-ever successful application to the WHO Expert Committee on Essential Medicines on the addition of an MS-dedicated section into the EML.

Earlier this year, Dr Al Kaabi issued a statement of support on behalf of NMSS to supplement the MSIF application. Com-



Dr Fatima Al Kaabi, Vice Chair of the UAE's National MS Society Board of Trustees and Executive Director of the Bone Marrow Transplant Programme at the Abu Dhabi Stem Cells Center

menting on the development, she said: "The approval by WHO represents the start of a significant chapter for the global MS community and one that will provide those that are living with MS with increased availability and disbursement of therapies across the globe. This is particularly important for those in resource-limited settings.

"Since its inception, NMSS has been guided by a mission to build a world that is free of MS, and advocates for better access to treatment for all people living with MS in the UAE and beyond.



"As the UAE continues to develop its healthcare system, the country is also committed to providing a variety of MS treatments, with medical professionals proactively building domestic capabilities for hematopoietic stem cell transplantation.

"We are going in the right direction, and WHO's announcement is a moment that we should all celebrate. While progress continues to be made, we are acutely aware that much more is required going forward if we are to impact people's lives and give them a better future. NMSS is committed to continuing to work with local and international partners to improve diagnosis and access to treatment, and ultimately to finding a cure."

Established in 2022 under the Ministry of Community Development, the National Multiple Sclerosis Society (NMSS) is a UAE-based NGO created to better the lives of people living with Multiple Sclerosis (MS) and their communities in the UAE through education, advocacy and advancing global efforts to finding a cure for MS.



## KFSH&RC marks regional milestone with robotic-assisted neurosurgery procedure


King Faisal Specialist Hospital and Research Centre (KFSH&RC) has achieved a remarkable milestone by successfully employing advanced robotic technology to implant electrodes into the brain of a patient with refractory epilepsy, unresponsive to conventional treatments. This groundbreaking procedure marks the Middle East's inaugural use of robotic assistance in identifying epilepsy foci.

The patient, who had endured unyielding epilepsy for years, underwent a transformative surgical intervention. A cutting-edge robotic system facilitated a minimally invasive approach, wherein minute apertures (no more than 2 mm in diameter) were discreetly created within the cranial framework to implant the electrodes. This method enabled the precise measurement of cerebral electrical activity, accurately identifying seizure origins.

The robotic system is a more accurate and efficient alternative to the traditional Leksell frame method, which requires more time and effort to calculate the measurements and determine the correct placement of the holes. Furthermore, the system augments patient well-being and extends to a broader spectrum of neurosurgical interventions, further underscoring its transformative potential.

This historic achievement stands as testament to KFSH&RC's commitment to harnessing cutting-edge technologies in its pursuit of enhanced patient outcomes, experience, and operational efficacy.

Renowned for its exemplary neurosciences department, KFSH&RC has consistently delivered exceptional care to adult and paediatric patients facing complex and refractory epilepsy. Recent breakthroughs include successfully implanting electrodes in an 11-year-old child's brain and a historic brain hemispherectomy on a 14-day-old infant, marking global milestones and reaffirming the hospital's pioneering spirit.

Ranked among the world's premier healthcare institutions, KFSH&RC secured 20th position in the 2023 world rankings, emerging as the Middle East and Africa's definitive leader in specialized healthcare, according to Brand Finance. 



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Update from around the globe

## AI in BioMed forecast to reach \$6 trillion by 2027

The most comprehensive mapping of companies, investors, trends, technologies and industry leaders in the AI in BioTech and HealthTech Industry Ecosystem<sup>[1]</sup> – 14,000 organizations in total – was released recently by Global AI Ecosystem, with the support of AI Industry Analytics (AiiA) and Deep Knowledge Group.

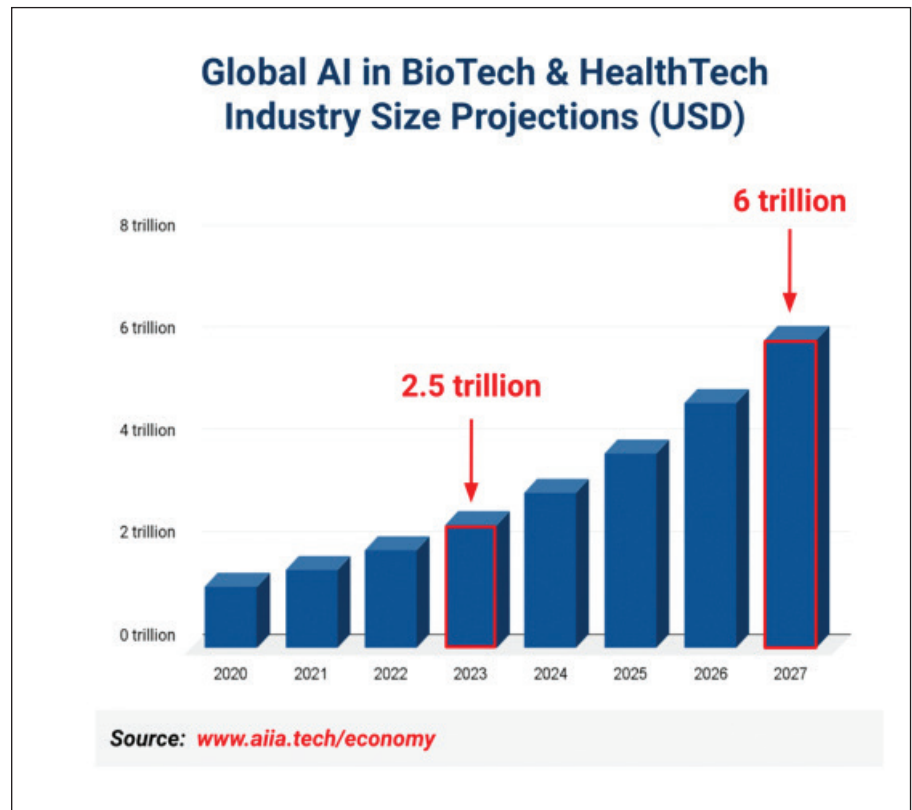
The AI in BioMed platform contains searchable and filterable profiles of 4,700 HealthTech companies, 2,300 BioTech companies, 6,000 investors, more than 250 hubs, and 600 industry leaders, alongside interactive ecosystem mindmaps and industry databases, all centred around the applications at the intersection of AI with biomedicine and healthcare.

Paradigm-shifting use-cases of AI in BioTech and HealthTech can no longer be questioned, with a wide variety of applications and high rates of AI adoption across science, industry and medicine, and strong levels of penetration in many distinct healthcare sectors covering the entire spectrum of healthcare, from basic science to clinical practice.

The platform also contains two individual sub-platforms on the AI in BioTech<sup>[2]</sup> and AI in HealthTech<sup>[3]</sup> Industry Ecosystems, outlining and visualising distinct players, technologies and sectoral distributions, each containing searchable, interactive and filterable mindmaps and industry databases of their constituent companies, investors, hubs and leaders.

### AI in BioTech

The AI in BioTech Ecosystem sub-platform has been established to highlight the evolving synergy between AI and biotechnology. It provides access to pioneering AI frameworks, influential investors, industry experts, and cutting-edge research facilities. It covers diverse topics from Biomarkers and Drug Discovery to NeuroTech and Space Medicine. Embodying the future of BioTech, the platform serves as the definitive gateway to insights and advancements shaping the BioPharma industry.



### AI in HealthTech

Meanwhile, the AI in HealthTech Ecosystem sub-platform explores the dynamic convergence of AI and health technology. It offers a window into innovative AI methodologies, key opinion leaders, established organizations, and innovative research institutes. AI in HealthTech addresses a wide array of topics from Deep Early-Stage Diagnostic and Precision Medicine to Healthy Longevity and Healthcare InsurTech, showcasing current trends and predicts emerging ones reinforced by AI. The platform aims to provide access to knowledge and progress that defines and propels the HealthTech sector.

On order to profile the full scope of the global AI in Biomedicine industry ecosystem, AI Industry Analytics (which supported the development of the project) had first of all to develop specially-designed analytical frameworks suitable

for this purpose, and then to deploy their unique suite of specialised AI algorithms to identify, extract and segregate AI in Biomedicine companies from their less technologically-proactive peers.

### Global AI Ecosystem

Alongside the AI BioMed platform itself, Global AI Ecosystem has also released a first-of-its-kind *Global AI in BioMed Economy Size Assessment* report<sup>[4]</sup>. The study's unique findings reveal the AI in BioMed Economy has surpassed \$2.5 trillion in 2023 and is projected to reach \$6 trillion by 2027. The report charts the key analyses that underlie these figures, as well as sectoral and regional economic analysis.

Substantial portions of the data utilised for specific ecosystem subsectors were provided by a number of Deep Knowledge Group life sciences subsidiaries, including Deep Pharma Intelligence, Aging An-



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alytics Agency, and FemTech Analytics.

Commenting on the report, Dmitry Kaminskiy, Founder of AI Industry Analytics and General Partner of Deep Knowledge Group, said: “AI holds substantial potential across many industries and domains, but when it comes to healthcare, it transcends its role as a mere support tool or industry segment. Whereas just five years ago AI was considered an exotic, small sector in BioTech, today it has reached the scale of \$2.5 trillion and has become a fundamental pillar of healthcare, all the way from basic science to real-world clinical applications.

“But what is much more important than

the tremendous financial growth of AI in healthcare is the fact that AI in Medicine is far beyond business. Its true value must be measured not in dollars but in Quality-Adjusted-Life-Years, tangibly improved outcomes in real-world human patients, and saved lives. And in this regard we are only at the beginning, with AI quickly becoming the major engine driving the paradigm shift towards preventive and precision medicine and, eventually, Healthy Longevity.”

The AI in BioMed platform was developed by Global AI Ecosystem <sup>[5]</sup>, an innovative, open-access platform designed to foster knowledge and collaboration

within the AI industry. Providing access to advanced analytics, open-source libraries, interactive mindmaps, and community building infrastructure, its aim is to promote efficient cooperation and discussion among a variety of stakeholders, including companies, investors, non-profits, academic labs, R&D hubs, governmental bodies, and policy makers in the international AI community. 

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## Malaria vaccine candidate appears safe and produces promising immune response in infants

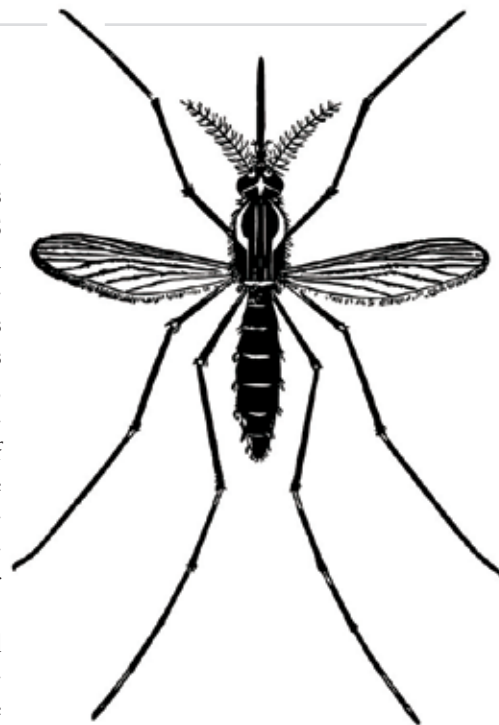
An experimental malaria vaccine appears safe and promotes an immune response in African infants, one of the groups most vulnerable to severe malaria disease. There is currently only one malaria vaccine, “RTS,S” that is approved by the World Health Organization and offers partial disease protection. However, in the results of the early-stage phase Ib trial conducted in Tanzania and published on August 11 in the journal *Med*<sup>[1]</sup>, researchers find that targeting RH5 – a protein that the malaria pathogen *Plasmodium falciparum* uses to invade red blood cells – can generate a promising immune response that is most pronounced in an infant cohort.

“Anti-sporozoite vaccines such as RTS,S need to be 100% effective in stopping the parasite from invading the liver to prevent disease,” says senior author Angela Minasian, a clinician scientist at the University of Oxford. “Even if just one parasite slips through the net, this will then go on to multiply in the liver, burst out into the bloodstream, and then infect red blood cells where the parasites then grow at an exponential rate. Having a blood-stage vaccine like RH5 on board gives you a second line of defence once the parasite has entered the bloodstream, allowing a second chance to stop malaria before it causes illness.”

A person is infected with malaria when bitten by an infected mosquito, which releases *Plasmodium falciparum* into the body. RTS,S and many other vaccine candidates teach the immune system how to target the parasite at this sporozoite stage, before it invades the liver. Once the parasite matures and is released from the liver into the bloodstream, *Plasmodium falciparum* displays RH5 and infects red blood cells, which causes disease. If an anti-sporozoite and an anti-RH5 vaccine were used in combination in the future, individuals could potentially experience more effective protection against malaria for a longer period of time.

“The data in the phase 1b trial reported here confirm, for the first time, that substantial anti-RH5 immune responses can be achieved safely by vaccination in infants from a malaria-endemic area,” say the authors.

The researchers conducted the vaccine trial in Bagamoyo, Tanzania, where the average malaria prevalence throughout the population is 13%. 63 participants aged 6 months to 35 years were enrolled and randomized to receive either the experimental malaria vaccine, called “ChAd63-MVA RH5,” or a control rabies vaccine. The trial was also double-blinded, meaning that neither the participants nor the vaccine administrators knew who received the malaria vaccine or



the control. All participants were given the second dose of vaccine two months later and followed for four months after this.

The primary purpose of this study was to evaluate the safety of this vaccine in a population where malaria is endemic. Participants in both the control and treatment group reported pain at the injection site and a mild fever shortly after vaccination, but overall the vaccine was well tolerated and there were no safety concerns.

A secondary outcome of the study was whether the vaccine would promote an im- ▶



## WHO launches a new Global Initiative on Digital Health supported by the G20 Presidency

The World Health Organization (WHO) and the G20 India presidency announced a new Global Initiative on Digital Health<sup>[1]</sup> (GIDH) at the recent Health Minister's Meeting of the G20 Summit hosted by the Government of India.

The new GIDH initiative (pronounced "guide" for short) will operate as a WHO-managed network and platform to support the implementation of the Global Strategy on Digital Health 2020–2025. WHO serves as the Secretariat for the strategy implementation to converge and convene global standards, best practices and resources to fast track digital health system transformation.

"We thank the G20 countries and the India G20 Presidency for recognizing WHO's unique role and strengths in this area and supporting the establishment of the new GIDH network," said Dr Tedros Adhanom Ghebreyesus, WHO Director-General. "Continued support and collaboration of the G20, development partners and international organizations will be necessary to accomplish together what none of us can do alone. WHO is committed to working with countries to strengthen their capacities and to improve access to quality-assured digital solutions for a

healthier, safer, fairer future."

Speaking at the launch, India's Union Health Minister Dr Mansukh Mandavaya said: "Today was a momentous day in the history of the G20 Health Working Group, wherein G20 countries not only identified a priority for its relevance but collectively worked towards its launch."

The new Global Initiative on Digital Health is one of the key deliverables of India's G20 Presidency.

Since the first WHO resolution on ehealth in 2005 that led the pathway for development and adoption of the WHO Global Strategy on Digital Health, over 120 WHO Member States have developed a national digital health policy or strategy.

While recent experiences during the COVID-19 pandemic resulted in a boost in digital health use, many countries express the need for support to move from product-focused and pilot digital health initiatives to establishing national digital health infrastructure with appropriate governance, policy and a competent health workforce needed to select, maintain and adapt digital health interventions.


The GIDH initiative aims to bring countries and partners together to achieve measurable outcomes by:

- developing clear priority-driven in-

vestment plans for digital health transformation;

- improving reporting and transparency of digital health resources;
- facilitating knowledge exchange and collaboration across regions and countries to accelerate progress;
- supporting whole-of-government approaches for digital health governance in countries; and
- increasing technical and financial support to the implementation of the Global Strategy on Digital Health 2020–2025 and its next phase.

WHO and partners announced substantial commitments in cash and kind from multiple stakeholders to support the launch of this new initiative.

Digital health is a proven accelerator to advance health outcomes towards achieving Universal Health Coverage and the health-related Sustainable Development Goals by 2030. Digital health interventions improve health care in many ways, from supporting individuals in managing their health and wellness journeys, to enabling care providers to adhere to guidelines and provide high quality care, to strengthening health systems by improving supply chains and workforce management. 

### • Reference:


1. <https://www.who.int/initiatives/global-initiative-on-digital-health>

mune response. Researchers found that participants who received the malaria vaccine developed antibodies against RH5 in their blood upon follow-up. In the laboratory, these antibodies were able to inhibit the growth of the malaria parasite at high levels that are associated with disease protection. "These data justify onward progression to phase IIb field efficacy trials to determine whether parasite growth-inhibition levels of this magnitude can ultimately protect against clinical malaria." say the authors.

### • Reference:

1. doi: <http://dx.doi.org/10.1016/j.medj.2023.07.003>

The authors note that they observed the strongest immune responses in infants under 11 months, followed by children aged 1-6 years, then adults. "Why the infants and young children vaccinated with ChAd63-MVA RH5 induced such high levels of antibody remains to be fully understood," say the authors. "Given that both anti-sporozoite and blood-stage malaria vaccine strategies necessitate very high levels of antibody to protect against parasite infection, current efforts remain focused on infants and young children."

The researchers note that this was a small study that followed participants for only four months after receiving their full vaccine schedule. They recommend that additional phase Ia/Ib trials should be conducted to optimize the recommended age range, boosting schedule, and delivery platform for anti-RH5 vaccines. Currently, a phase 1b trial is planned in the Gambia which will look at the effects of combining an anti-RH5 vaccine with an anti-sporozoite vaccine. 

# the laboratory

Medical research news from around the world

## Longevity gene from naked mole rats extends lifespan of mice

In a groundbreaking endeavour, researchers at the University of Rochester have successfully transferred a longevity gene from naked mole rats to mice, resulting in improved health and an extension of the mouse's lifespan.

Naked mole rats, known for their long lifespans and exceptional resistance to age-related diseases, have long captured the attention of the scientific community. By introducing a specific gene responsible for enhanced cellular repair and protection into mice, the Rochester researchers have opened exciting possibilities for unlocking the secrets of ageing and extending human lifespan.

“Our study provides a proof of principle that unique longevity mechanisms that evolved in long-lived mammalian species can be exported to improve the lifespans of other mammals,” says Vera Gorbunova, the Doris Johns Cherry Professor of biology and medicine at Rochester. Prof. Gorbunova, along with Andrei Seluanov, a professor of biology, and their colleagues, report in a study published in *Nature*<sup>[1]</sup> that they successfully transferred a gene responsible for making high molecular weight hyaluronic acid (HMW-HA) from a naked mole rat to mice. This led to improved health and an approximate 4.4 percent increase in median lifespan for the mice.

### A unique mechanism for cancer resistance

Naked mole rats are mouse-sized rodents that have exceptional longevity for rodents of their size; they can live up to 41 years, nearly ten times as long as similar-size rodents. Unlike many other species, naked mole rats do not often contract diseases – including neurodegeneration, cardiovascular disease, arthritis, and cancer – as they age. Professors Gorbunova and Seluanov have devoted decades of research to understanding the unique mechanisms that naked mole rats use to protect themselves against ageing and diseases.

The researchers previously discovered<sup>[2]</sup> that HMW-HA is one mechanism responsible for naked mole rats' unusual resistance to cancer. Compared to mice and humans, naked mole rats have about ten times more HMW-HA in their bodies. When the researchers removed HMW-HA from naked mole rat cells, the cells were more likely to form tumours.

Profs. Gorbunova, Seluanov, and their colleagues wanted to see if the positive effects of HMW-HA could also be reproduced in other animals.

### Transferring a gene that produces HMW-HA

The team genetically modified a mouse model to produce the naked mole rat version of the hyaluronan synthase 2 gene, which is the gene responsible for making a protein that produces HMW-HA. While all mammals

#### • Reference:

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2. Tian, X., Azpurua, J., Hine, C. et al. High-molecular-mass hyaluronan mediates the cancer resistance of the naked mole rat. *Nature* 499, 346–349 (2013). <https://doi.org/10.1038/nature12234>



University of Rochester photo / Adam Fenster

University of Rochester researchers successfully transferred a longevity gene from naked mole rats to mice, resulting in improved health and an extension of the mouse's lifespan.

have the hyaluronan synthase 2 gene, the naked mole rat version seems to be enhanced to drive stronger gene expression.

The researchers found that the mice that had the naked mole rat version of the gene had better protection against both spontaneous tumours and chemically induced skin cancer. The mice also had improved overall health and lived longer compared to regular mice. As the mice with the naked mole rat version of the gene aged, they had less inflammation in different parts of their bodies – inflammation being a hallmark of ageing – and maintained a healthier gut.

While more research is needed on exactly why HMW-HA has such beneficial effects, the researchers believe it is due to HMW-HA's ability to directly regulate the immune system.

### A fountain of youth for humans?

The findings open new possibilities for exploring how HMW-HA could also be used to improve lifespan and reduce inflammation-related diseases in humans.

“It took us 10 years from the discovery of HMW-HA in the naked mole rat to showing that HMW-HA improves health in mice,” Prof. Gorbunova says. “Our next goal is to transfer this benefit to humans.”

They believe they can accomplish this through two routes: either by slowing down degradation of HMW-HA or by enhancing HMW-HA synthesis.

“We already have identified molecules that slow down hyaluronan degradation and are testing them in pre-clinical trials,” Prof. Seluanov says. “We hope that our findings will provide the first, but not the last, example of how longevity adaptations from a long-lived species can be adapted to benefit human longevity and health.” MEH



## International collaboration identifies new genes associated with breast cancer

A large-scale international collaboration has identified new genes associated with breast cancer that could eventually be included in tests to identify women at increased risk of the disease. The study, published in *Nature Genetics* <sup>[1]</sup>, was led by teams at the University of Cambridge and Université Laval, Quebec.

Current genetic tests for breast cancer only consider a few genes, such as BRCA1, BRCA2, and PALB2. However, these only explain a minority of the genetic risk, suggesting that more genes remain to be identified.

Researchers looked at genetic changes in all genes in 26,000 women with breast cancer and 217,000 women without breast cancer. These included women from eight countries in Europe and Asia.

Professor Douglas Easton, Director of the Centre for Cancer Genetic Epidemiology at the University of Cambridge, who co-led the study, said: “To our knowledge, this is the largest study

of its kind. It was made possible through the use of data from multiple collaborators in many countries, as well as publicly available data from the UK Biobank.”

The team found evidence for at least four new breast cancer risk genes, with suggestive evidence for many others. The team say identification of these new genes will contribute to our understanding of the genetic risk of breast cancer and help improve risk prediction by better identifying those women at higher risk of the disease.

The findings will better inform approaches to breast screening, risk reduction and clinical management. The aim is to integrate this information into a comprehensive risk prediction tool currently used worldwide by health professionals.

“Improving genetic counselling for high-risk women will promote shared decision-making regarding risk reduction strategies, screening and determination of treatment options,” said Professor Jacques Simard of Université Laval, co-lead of the study.

“Although most of the variants identified in these new genes are rare, the risks can be significant for women who carry them. For example, alterations in one of the new genes, MAP3K1, appear to give rise to a particularly high risk of breast cancer.”

Before this information can be used in a clinical setting, scientists need to validate the results in further datasets.

“We need additional data to determine more precisely the risks of cancer associated with variants in these genes, to study the characteristics of the tumours, and to understand how these genetic effects combine with other lifestyle factors affecting breast cancer risks,” added Prof. Easton.

The discovery of these novel genes also provides crucial information on the biological mechanisms underlying cancer development, potentially opening the way to identifying new treatments. MEH

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1. Wilcox, N et al. Exome sequencing identifies breast cancer susceptibility genes and defines the contribution of coding variants to breast cancer risk. *Nat Gen*; 17 Aug 2023; doi: <https://doi.org/10.1038/s41588-023-01466-z>

## Sedentary time in children linked with heart damage in young adulthood

Hours of inactivity during childhood could be setting the stage for heart attacks and strokes later in life, according to research presented at ESC Congress 2023. <sup>[1]</sup> The study found that sedentary time accumulated from childhood to young adulthood was associated with heart damage – even in those with normal weight and blood pressure.

“All those hours of screen time in young people add up to a heavier heart, which we know from studies in adults raises the likelihood of heart attack and stroke,” <sup>[2]</sup> said study author Dr Andrew Agbaje of the University of Eastern Finland, Kuopio, Finland. “Children and teenagers need to move more to protect their long-term health.”

This was the first study to investigate the cumulative effect of smartwatch-assessed sedentary time in young people and cardiac damage later in life. It was conducted as part of the Children of the 90s study, which began in 1990/1991 and is one of the world’s largest cohorts with lifestyle measurements from birth. <sup>[3]</sup>

At 11 years of age, children wore a smartwatch with an activity tracker for seven days. This was repeated at 15 years of age and again at 24 years of age. The weight of the heart’s left ventricle was assessed by echocardiography at 17 and 24 years of age and reported in grams relative to height (g/m<sup>2.7</sup>). The researchers analysed the association between sedentary time between

11 and 24 years of age and heart measurements between 17 and 24 years of age after adjusting for factors that could influence the relationship including age, sex, blood pressure, body fat, smoking, physical activity and socioeconomic status.

The study included 766 children, of whom 55% were girls and 45% were boys. At 11 years of age, children were sedentary for an average of 362 minutes a day, rising to 474 minutes a day in adolescence (15 years of age), and 531 minutes a day in young adulthood (24 years of age). This means that sedentary time increased by an average of 169 minutes (2.8 hours) a day between childhood and young adulthood.

Each one-minute increase in sedentary



time from 11 to 24 years of age was associated with a 0.004 g/m<sup>2.7</sup> increase in left ventricular mass between 17 to 24 years of age. When multiplied by 169 minutes of additional inactivity this equates to a 0.7 g/m<sup>2.7</sup> daily rise – the equivalent of a 3 gram increase in left ventricular mass between echocardiography measurements at the average height gain. A previous study in adults found that a similar

increase in left ventricular mass (1 g/m<sup>2.7</sup>) over a seven-year period was associated with a two-fold increased risk of heart disease, stroke, and death.<sup>141</sup>

Dr Agbaje said: “Children were sedentary for more than six hours a day and this increased by nearly three hours a day by the time they reached young adulthood. Our study indicates that the accumulation of

inactive time is related to heart damage regardless of body weight and blood pressure. Parents should encourage children and teenagers to move more by taking them out for a walk and limiting time spent on social media and video games. As Martin Luther King Jr. once said, ‘If you can’t fly, run. If you can’t run, walk. If you can’t walk, crawl. But by all means keep moving.’” **MEH**

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2. Armstrong AC, Gidding S, Gjesdal O, et al. LV mass assessed by echocardiography and CMR, cardiovascular outcomes, and medical practice. *JACC Cardiovasc Imaging*. 2012;5:837-848.
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## Researchers create synthetic human embryo from stem cells without egg or sperm

A research team headed by Prof. Jacob Hanna at the Weizmann Institute of Science has created complete models of human embryos from stem cells cultured in the lab – and managed to grow them outside the womb up to day 14. As reported in *Nature*,<sup>11</sup> these synthetic embryo models had all the structures and compartments characteristic of this stage, including the placenta, yolk sac, chorionic sac and other external tissues that ensure dynamic and adequate growth.

Cellular aggregates derived from human stem cells in previous studies could not be considered genuinely accurate human embryo models because they lacked nearly all the defining hallmarks of a post-implantation embryo. Not only did they fail to contain several cell types that are essential to the embryo’s development, such as those that form the placenta and the chorionic sac, but they also did not have the structural organization characteristic of the embryo and revealed no dynamic ability to progress to the next developmental stage.

Given their authentic complexity, the human embryo models obtained by Hanna’s group may provide an unprecedented opportunity to shed new light on the

embryo’s mysterious beginnings. Little is known about the early embryo because it is so difficult to study, for both ethical and technical reasons, but its initial stages – from the point it implants into the womb on day seven to the point it becomes a well-structured embryo with body organs three to four weeks later – are crucial to its future development.

“The drama is in the first month. The remaining eight months of pregnancy are mainly lots of growth,” Hanna says. “But that first month is still largely a black box. Our stem cell-derived human embryo model offers an ethical and accessible way of peering into this box. It closely mimics the development of a real human embryo, particularly the emergence of its exquisitely fine architecture.”

#### The embryo is self-driven

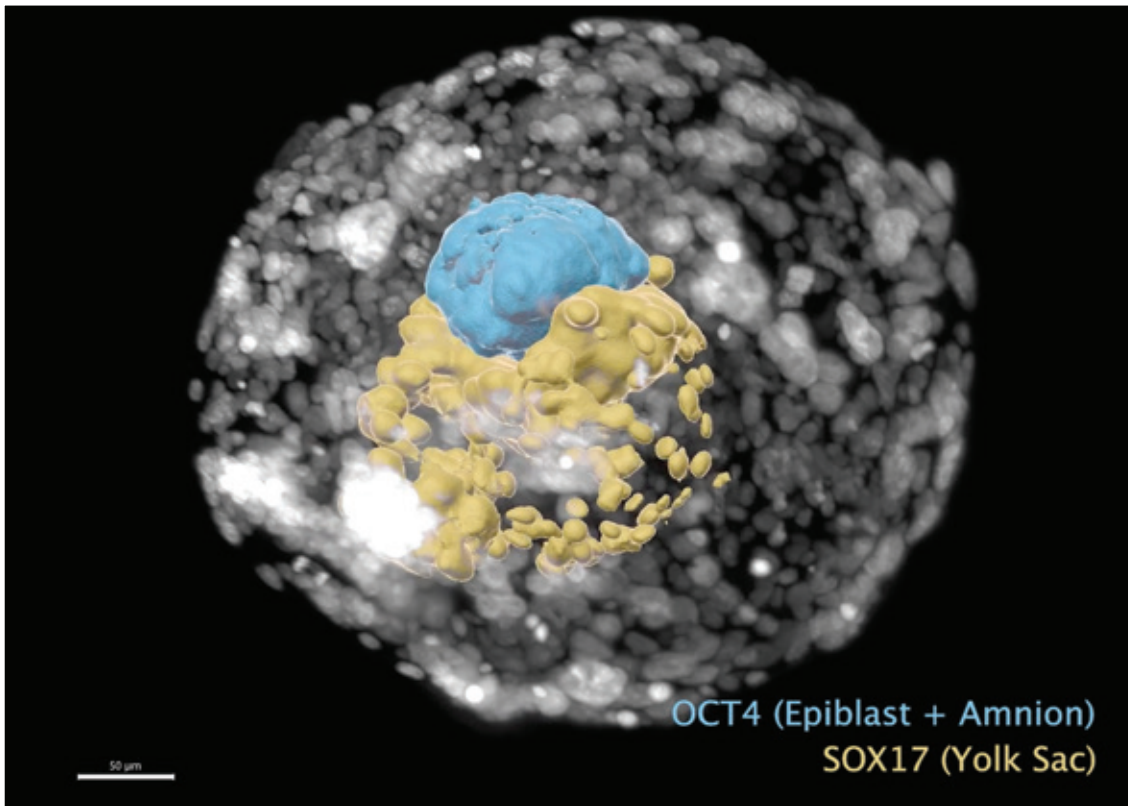
Hanna’s team built on their previous experience creating synthetic stem cell-based models of mouse embryos, once again making no use of fertilized eggs or a womb. Instead, they started out with pluripotent stem cells, which are human cells that have the potential to differentiate into many cell types. Some were derived from adult skin cells that had been

reverted to “stemness”, while others were the progeny of human stem cell lines that had been cultured for years in the lab.

The researchers then used Hanna’s recently developed method to reprogram pluripotent stem cells so as to turn the clock further back: to revert these cells to an even earlier state – known as the naïve state – in which they are capable of specializing into any type of cell. This stage corresponds to day seven of the natural human embryo, which is the time at which it implants itself in the womb. Hanna’s team was the first to start describing methods to generate human naïve stem cells back in 2013, and they continued to improve these methods over the years.

For this current project, the scientists divided the cells into three groups. In one, the cells intended to develop into the embryo were left as is. In the other two, the cells were treated with chemicals to turn on certain genes, causing them to differentiate toward one of three tissue types needed to sustain the embryo: placenta, yolk sac, or the extraembryonic mesoderm membrane that ultimately creates the chorionic sac.

Soon after being mixed together under



optimized, specifically developed conditions, the cells formed clumps, about one percent of which self-organized into complete embryo-like structures. “An embryo is self-driven by definition; we don’t need to tell it what to do – we must only unleash its internally encoded potential,” Hanna says. “It’s critical to mix in the right kinds of cells at the beginning, which can only be derived from naïve stem cells that have no developmental restrictions. Once you do that, the embryo-like model itself says, ‘Go!’”

The stem cell-based embryo-like structures (SEMs) developed normally outside the womb for eight days, reaching a developmental stage equivalent to day 14 in human embryonic development. That’s the point at which natural embryos acquire the internal structures that enable them to proceed to the next stage: developing the progenitors of body organs.

#### Human embryo models match classic diagrams

When the researchers compared the in-

ner organization of their stem cell-derived embryo models with illustrations and microscopic anatomy sections in classical embryology atlases from the 1960s, they found an uncanny structural resemblance between the models and the natural human embryos at the corresponding stage. Every compartment and supporting structure existed in the right place, size, and shape. Even the cells that make the hormone used in pregnancy testing were evident and active; when the scientists applied cell secretions to a commercial pregnancy test, it yielded a positive result.

This implied that their models faithfully emulated the process by which an early embryo gains all the structures it needs for beginning its transformation into a foetus.

#### New embryonic development finding

In fact, the study has already produced a finding that may open a new direction of research into early pregnancy failure. The researchers discovered that if the embryo is not enveloped by placenta-forming

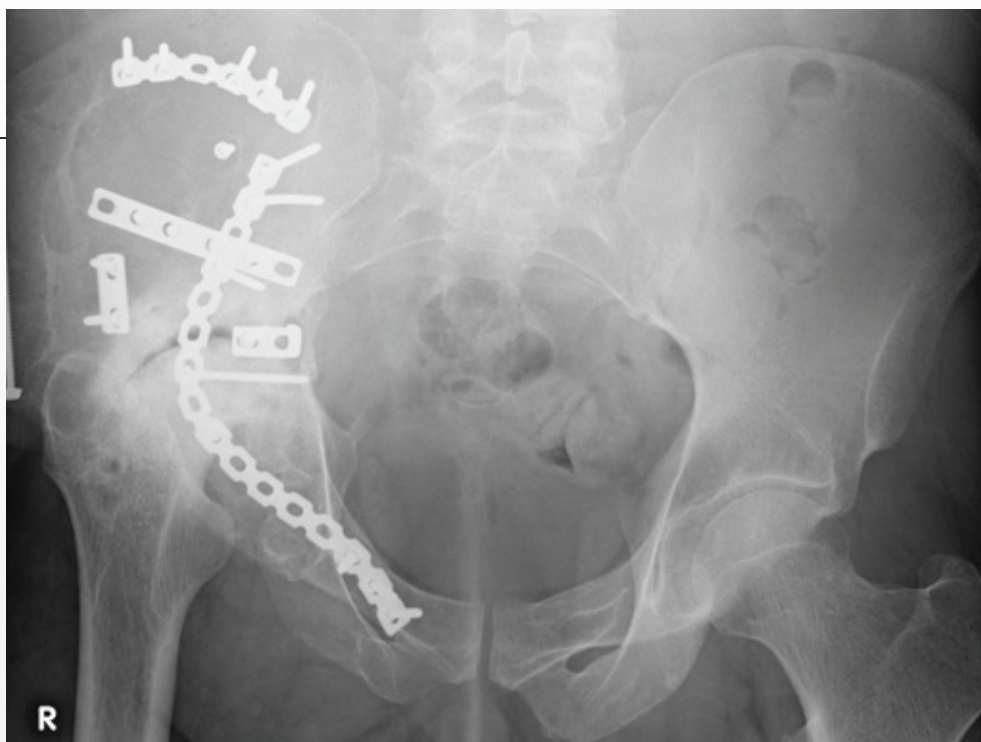
cells in the right manner at day three of the protocol (corresponding to day 10 in natural embryonic development), its internal structures, such as the yolk sac, fail to properly develop.

“An embryo is not static. It must have the right cells in the right organization, and it must be able to progress – it’s about being and becoming,” Hanna says. “Our complete embryo models will help researchers address the most basic questions about what determines its proper growth.”

This ethical approach to unlocking the mysteries of the very first stages of embryonic development could open numerous research paths. It might help reveal the causes of many birth defects and types of infertility, or it could lead to new technologies for growing transplant tissues and organs. It also could offer a way around experiments that cannot be performed on live embryos – for example, determining the effects of exposure to drugs or other substances on foetal development. MEH

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# Global hip fractures forecast to double by 2050, IOF urges action for prevention

Of all osteoporosis-related fractures, hip fractures cause the most morbidity with reported mortality rates up to 20-24% in the first year after a hip fracture. Loss of function and independence among survivors is profound, with 40% unable to walk independently, and 60% requiring assistance a year later. Hip fractures represent a major global public health concern, which places a heavy burden on patients, and their families, and represents a significant cost burden to healthcare systems.

In a recently published study in the *Journal of Bone & Mineral Research*<sup>[1]</sup>, an international group of researchers evaluated the secular trends in hip fracture incidence, post-fracture treatment, and all-cause mortality in 19 countries across five regions from 2005 to 2018. The study reveals that while the age- and sex-standardised hip fracture incidence rates decreased in most regions, the number of hip fractures worldwide is projected to nearly double by 2050 compared to 2018. A significant post-fracture treatment gap in fracture prevention was also observed for both sexes in all countries and regions, particularly in men. Males also had higher rates of all-cause mortality and a larger increase in the projected number of hip fractures by 2050.

Commenting on the study, Professor Cyrus Cooper, President of the International Osteoporosis Foundation (IOF) and a co-author of the global study, said: “The findings of this important study highlight the urgent need for improved strategies in hip fracture prevention and care. This should be seen as both a warning and a call to action for healthcare systems worldwide. Past studies have shown that five to 10 % of hip fracture patients go on to ex-

perience a recurrent hip fracture, and of these, as many as 23% occur in the year following their first hip fracture, and 70% within the first five years. Clearly, the enormous osteoporosis treatment gap, which the study found to be even higher in men than in women, is unacceptable. Healthcare systems must act. A first step is to prioritize the implementation of post-fracture care coordination programmes, such as Fracture Liaison Services<sup>[2]</sup>, to ensure that any older adult who has sustained a first hip fracture receives the needed treatment and management to prevent further, potentially life-threatening fractures.”

## Study analyses data from 19 countries

The international study analysed data from a large representative cohort involving 19 countries in Oceania, Asia, Europe, and North- and South America. It examined the incidence of hip fractures, post-fracture treatment, and all-cause mortality following hip fractures, among patients aged 50 years and older, from 2005 to 2018. The study is unique in that, in contrast to previous reports on hip fracture incidence which are based on data with heterogeneity in data sources, study pe-

riods, and analytical approaches, it applied a standardised protocol and a common data model across all sites to provide comparable data. Age- and sex-standardised incidence rates of hip fracture were estimated using the 2020 United Nations world population as a standard. The number of hip fractures in 2030, 2040, and 2050 were projected based on the trends in the incidence rates and the World Bank data. Within 12 months following hip fractures, post-fracture treatment (defined as the proportion of patients receiving anti-osteoporosis medication), and the all-cause mortality rates were estimated.

The study identified 4,115,046 hip fracture cases in the cohort, with the following key findings:

- The reported age- and sex-standardized incidence rates of hip fractures ranged widely, from 95.1 (Brazil) to 315.9 (Denmark) per 100,000 population.
- Most countries and regions showed a decreasing trend in hip fracture incidence, with the most pronounced declines in Denmark (2.8% per year), Singapore (2.8%), and Hong Kong (2.4%). The largest increases were noted in the Nether-

# Experts issue important update on use of trabecular bone score in clinical practice

A new position paper presents an up-to-date review and expert recommendations using the GRADE methodology to inform the implementation of trabecular bone score (TBS) in clinical practice for the management of primary and secondary osteoporosis <sup>[1]</sup>.

TBS is a grey-level scale textural measurement acquired from dual-energy X-ray absorptiometry lumbar spine images that correlates with bone microarchitecture and which can be used alongside FRAX and bone mineral density measurements to enhance the assessment of fracture risk and to inform treatment initiation and monitoring.

The position paper <sup>[1]</sup> was authored by an international Expert Working Group appointed by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the International Osteoporosis Foundation (IOF) under the auspices of the WHO Collaborating Center for Epidemiology of Musculoskeletal Health and Aging (Liège). It encompasses a comprehensive systematic review of 96 high-quality clinical studies from over 20 coun-

tries published since 2015, which provide information on the use of TBS for:


- fracture risk prediction in postmenopausal and male osteoporosis
- initiation of treatment and monitoring of treatment effect in postmenopausal osteoporosis
- prediction of fracture risk associated with secondary osteoporosis
- treatment monitoring in secondary osteoporosis

## The role of TBS in clinical practice

Based on the review, the experts authored 22 statements supporting the role of the TBS software in fracture risk prediction, treatment initiation and monitoring of osteoporosis. The position paper additionally incorporates a more practically focused clinician guide to the incorporation of TBS into clinical pathways for the management of osteoporosis and high fracture risk.

Professor Jean-Yves Reginster, co-author and Director of the WHO Collaborating Center for Epidemiology of Musculoskeletal Health & Aging commented: "Assessing information related to bone microarchitecture in addition to bone density and clinical risk factors provides a more complete assessment

to inform management decisions for the benefit of the patient. As there has been considerable new research since the publication of our comprehensive review of TBS in 2015 <sup>[2]</sup>, we judged it was time for a systematic update of the evidence on the clinical use of TBS, via expert consensus to inform practical clinical guidance. As such we have provided a helpful appendix with concise operational guidance that facilitates the integration of TBS in clinical practice, in alignment with clinical workflow."

Professor Nicholas Harvey, joint-senior author and Chair of the IOF Committee of Scientific Advisors, noted: "This position paper documents the role of TBS in clinical practice, synthesising a wide range of evidence across risk assessment, treatment initiation and monitoring, in the context of postmenopausal osteoporosis, osteoporosis in men and secondary causes. The work demonstrates the value of drawing together global expertise to generate what is an evidence-based, but very practical, guide to implementing TBS in the management of osteoporosis and high fracture risk." 

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2. Harvey, N. C., Glüer, C. C., Binkley, et al. (2015). Trabecular bone score (TBS) as a new complementary approach for osteoporosis evaluation in clinical practice. *Bone*, 78, 216-224. doi: <https://doi.org/10.1016/j.bone.2015.05.016>.

lands (+2.1%), and South Korea (+1.2%).

- Despite the overall decline in hip fracture incidence, the total number of hip fractures is estimated to nearly double from 2018 to 2050.


- Within 1 year following a hip fracture, post-fracture treatment remained low, ranging from 11.5% in Germany to 50.3% in United Kingdom.

- One-year all-cause mortality rates following hip fracture ranged from 14.4% (Singapore) to 28.3% (United Kingdom),

while mortality trends varied from 5.3% to +18.4% per year.

- Males had lower use of anti-osteoporosis medication than females, higher rates of all-cause mortality, and a larger increase in the projected number of hip fractures by 2050.

Professor Nicholas Harvey, Chair of the IOF Committee of Scientific Advisors, noted: "One of the study's key takeaways is that the decrease in age-and sex-specific hip fracture incidence observed in numerous countries over the past few years will

not compensate for the global impact of ageing populations. The burden of hip fracture will thus continue to grow, leading to increased dependency, morbidity, and mortality, and resulting in immense socio-economic costs for resource-strapped healthcare services worldwide. The time for action is now. IOF urges healthcare systems to address the treatment gap through targeted policy and multidisciplinary intervention to reduce the impact of the hip fracture in the coming decades." 

## References:

1. Sing CW, Lin TC, Bartholomew S, et. al. Global Epidemiology of Hip Fractures: Secular Trends in Incidence Rate, Post-Fracture Treatment, and All-Cause Mortality. *Journal of Bone & Mineral Research*. April 29, 2023. doi: <https://doi.org/10.1002/jbmr.4821>
2. Fracture Liaison Service: [www.capturethefracture.org/what-is-a-pfc](http://www.capturethefracture.org/what-is-a-pfc)



# The solution to achieving healthy longevity

If you're not in a hurry to grow old, get moving! Exercise is key to healthy longevity.

Only part of our life expectancy is pre-defined and 'written' in our genes. One of the main ways that science points out to act on our ageing process, **getting old healthy and fit** (healthy longevity) is committing to a structured physical exercise plan.

Proper physical exercise is a subcategory of physical activity (any state of unrest) and it includes all activities that require the movement of the human body, carried out with a particular purpose and following specific criteria in terms of duration, intensity and frequency.

When we talk about physical exercise being extraordinarily effective in maintaining a healthy body and helping us to "age well", we're talking about both aerobic and anaerobic activities. If your exercise sessions aren't just a one-off, but are continued over time in a systematic and structured way, the body will undergo **positive changes in the long term**.

In recent times, we have seen a huge reassessment of resistance training (or **strength training**), also for the senior demographic: it turns out to be a particularly useful and effective activity for counteracting the natural loss of muscle mass and strength that occurs with age. Strength training also increases bone density, improves the metabolism, general posture, the condition of ligaments, tendons and joints and of the cardiovascular and nervous systems.

## Technogym solutions for staying effectively active

Technogym has made both physical and mental well-being its mission, and so it's



no surprise that it is a trailblazer in offering training options, both equipment and digital, to facilitate and encourage the maintenance of a training routine, at any age:

- **Technogym App** is the ideal solution for achieving your fitness goals (losing weight, increasing muscle mass, improving sports performance, etc.): whether you're at home, travelling, at the park or in the gym, the digital coach suggests the workout most suited to your profile, combining scientific research, artificial intelligence, and engaging and challenging video content.

- The robust and highly customisable **Biocircuit** offer (both cardio and strength) has been chosen by numerous clubs and rehabilitation-medical centres around the world: By simply logging in, the stations au-

tomatically adapt to the individual user, the user's profile and selected fitness goals. **Biocircuit** registers the user profile (age, physical details, fitness goal), and sets up all the stations in the circuit accordingly (weight, duration, pace, rest, etc.).

- As far as strength training is concerned, **Biostrength** allows training with the right load, the right range of motion, the correct posture, the most suitable speed for the goal, and also indicates the number of sets, reps and optimum recovery time. The patented Biodrive system provides six different types of resistance (isotonic, no inertia, eccentric reduction, eccentric overload, viscous, and elastic), improving the effectiveness of the exercise according to the goal the user wants to reach. **MEH**



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## NEUROMUSCULAR ACTIVATION

Increased neuromuscular activation



## BIODRIVE SYSTEM

PATENTED

## PERSONALISED ROM

Right ROM and speed



## OPTIMAL WORKLOAD

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## CORRECT POSTURE

Automatic posture setup



Biostrength™ helps you avoid the most common strength training mistakes to get up to 30% more results from your workout. Thanks to the patented Biodrive System, you can easily and automatically:

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- Train with the correct workload
- Find the proper range of motion
- Set the right tempo and number of reps
- Get the correct rest time

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**TECHNOGYM**

# Sidra Medicine scientist publishes groundbreaking case study on monogenic obesity

A groundbreaking case study on monogenic obesity by the Endocrinology Department at Sidra Medicine, a member of Qatar Foundation, has been published June 15, 2023 in the prestigious *New England Journal of Medicine* <<https://doi.org/10.1056/NEJMoa2204041>>.

Monogenic obesity is a rare, early-onset, and severe form of obesity resulting from a mutation or deficiency of a single gene. It is caused by changes in leptin, a hormone that helps it maintain normal body weight. Children affected by monogenic obesity generally experience delayed pubertal development and recurrent severe infections. They often show a decreased sensation of satiety in early childhood and suffer from a constant feeling of hunger.

The study was led by Prof. Khalid Hussain, Division Chief of Endocrinology at Sidra Medicine and Professor of Clinical Pediatrics at Weill Cornell Medicine-Qatar, in collaboration with the German Research Foundation (DFG).

Prof. Hussain and his team from the Obesity Clinic at the hospital, were presented with a young child, aged 19 months, with severe obesity; the signs of which began at just three months of age. Patients with monogenic obesity typically

lack leptin and respond well to leptin replacement therapy. However, the patient exhibited high levels of circulating leptin in her blood, but was resistant to treatment, indicating an issue with the signaling mechanism.

“Over the period of 18 months, we discovered that by markedly increasing the dose of leptin by nearly 50 percent we could successfully overcome the effects of the antagonist leptin and reduce her weight to a normal, healthy level,” said Prof. Hussain.

## Monogenic obesity may be undiagnosed in MENA

Previous studies on monogenic obesity were conducted on patients in Europe or North America, but research on the regional population was lacking, according to Prof. Hussain.

“This is the first study on monogenic obesity from the MENA region to be published and we hope it can provide insights into what is triggering the problem and what might help reverse it. Our research indicates there may be other children with this genetic disorder that are undiagnosed, and that measuring leptin levels can provide the key to understanding some genetic malfunctions or deficiencies. Childhood



Prof. Khalid Hussain

obesity is a challenging clinical condition, and our research can help drive new discoveries and new treatments, not just in young people, but for adults as well, which will have implications for public health in Qatar and worldwide.”

By tracing the family history of the patient, the team at Sidra Medicine were also able to identify the same condition in two of the patient’s aunts. The family members are currently under treatment at Hamad Medical Corporation, and have shown remarkable progress, underscoring the importance of genetics in understanding and treating complex medical cases. MCH

## Dr Jassim Mohammed Al Suwaidi appointed HMC’s new Chief of Scientific, Academic and Faculty Affairs

Hamad Medical Corporation (HMC) has appointed Dr Jassim Mohammed Al Suwaidi as Chief of Scientific, Academic and Faculty Affairs in addition to his current role as Senior Consultant, Cardiology. Dr Al Suwaidi assumed the position in July.

Dr Al Suwaidi started his career at HMC in 1991 after graduating from the Royal College of Surgeons in Ireland (Honours) and subsequently rejoined HMC in 2000 after completing post-graduate training at Mayo Clinic, USA

and becoming American Board certified in Internal Medicine, Cardiovascular Diseases and Interventional Cardiology. Dr Al Suwaidi has been actively involved in HMC’s academic strategies and developments as Executive Director of Cardiovascular Research since 2013.

He has also been a Professor of Clinical Medicine at Weill Cornell Medicine - Qatar since 2018, is Past President of the Gulf Heart Association and to date has more than 300 peer reviewed publications in addition to research presenta-



tions at several prestigious international cardiology meetings. MCH




# Weill Cornell Medicine-Qatar

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At Weill Cornell Medicine-Qatar, we know that the talented people of this region have the potential to make a great impact in the medical field – when given the right tools. That's why we provide our researchers with world-class training programs and state-of-the-art laboratories to find cures and treatments for the most formidable health challenges facing the region. To discover how you can join a research program making Qatar a global centre for medical innovation, please visit our website.

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[www.qatar-weill.cornell.edu](http://www.qatar-weill.cornell.edu)

**Care. Discover. Teach.**



# QU Health at Qatar University: a journey of collaboration, innovation and inspiration

QU Health at Qatar University (QU) established in 2017 in line with the Qatar National Vision 2030, is the national provider of higher education in health and medicine and is the largest academic cluster in the region. QU Health works to address Qatar's evolving needs and healthcare system. It strives to be recognized as a leader in health profession education, research, clinical care, and community engagement through interprofessional collaboration and partnership. The institution aims to inspire and empower individuals, ultimately driving excellence and innovation for healthier communities.

QU Health is comprised of five colleges: Pharmacy, Medicine, Health Sciences, Dental Medicine, and Nursing. It offers nine undergraduate programmes in health professions, including Pharmacy, Medicine, Dental Medicine, Nursing, Biomedical Sciences, Human Nutrition, Physiotherapy, Public Health and Speech and Language Pathology.

QU Health is passionate about ensuring excellence at every level in the institution. In 2023, QU made big progress in its rankings. According to the prestigious QS World University Rankings, QU soared to an impressive position at 173<sup>rd</sup> worldwide. Notably, QU's outstanding performance extends beyond the global stage. In the Arab region, it proudly holds the title of being the second top university. It jumped from the 250<sup>th</sup> spot in 2022 to the top 150<sup>th</sup> globally in the field of Pharmacy & Pharmacology in the QS Subject Ranking. In the fields of Life Sciences & Medicine, it places in the top 300, and in Medicine, the top 350.

### The tapestry of excellence at QU Health

With a total of 1,484 enrolled students, QU Health serves as a diverse hub where talents and perspectives from around the world converge. Its dedication to excellence shines through the diverse range of programmes. With two graduate certificate programmes, six master's programmes, and one PhD programme, QU Health offers a wide array of opportunities for academic growth. The 89

dedicated, nationally and internationally recognized faculty, who serve as educators and researchers, exemplify the cluster's commitment to excellence in education and research. QU Health is at the forefront of cutting-edge research, collaborating locally and globally to enhance health outcomes. It emphasizes experiential education, providing students with hands-on learning experiences that extend beyond the classroom, enriching their education and preparing them for success.

### QU Health's commitment to excellence and empowering minds

At QU Health, the strategic objectives are deeply woven into the commitment to quality, believing that a strong healthcare system hinges on solid education and research. QU Health colleges have achieved several important accreditations, including Accreditation Council for Education in Nutrition and Dietetics, USA (ACEND) for the BSc Nutrition programme, National Accrediting Agency for Clinical Laboratory Sciences, USA (NAACS) for the BSc Biomedical Sciences programme, and the Canadian Council for Accreditation of Pharmacy Programs (CCAPP) for both the Bachelor and PharmD pharmacy degree programmes. QU has also recently obtained the institutional accreditation from the WASC Senior College and University Commission (WSCUC). This reflects QU's commitment to delivering top-tier education and research, aligning with the highest academic standards.

These accreditations underscore QU's commitment to maintaining high standards in education and healthcare. QU has a major goal to pursue accreditation for all the degree programmes for which there are accrediting agencies.

QU Health focuses on an integrated campus to encourage collaboration among students, faculty, and researchers, fostering innovation and preparing graduates for interprofessional health teams. Additionally, it is dedicated to creating a University Hospital System, offering practical training and advanced healthcare research opportunities, ensuring graduates are aca-




QU Health aims to be recognized as a leader in health profession education, a symbol of inspiration, collaboration, and innovation in the healthcare arena.

demically and clinically proficient.

Partnerships stand at the core of QU Health's journey towards academic and healthcare brilliance, benefiting students, faculty, and the institution as a whole in several ways. QU Health fosters extensive collaborations with both national and international healthcare institutions. These collaborations encompass a wide range of activities, including research initiatives, clinical training, knowledge exchange, joint research projects, faculty and student exchanges, and collaborative educational programmes, which contribute to QU Health's commitment to excellence in health profession education, research, clinical care, and community engagement.

### All Together Better Health conference

In November 2023, QU Health will host the prestigious All Together Better Health (ATBH) conference, which aligns with its mission to lead in health profession education and innovation.

Join QU, as it sets higher standards, breaks new boundaries, and illuminates the path to a healthier, brighter future for all. 



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# HMC surgeon develops innovative 'Qatar Flap' for reconstructing injured fingertips

Hamad Medical Corporation (HMC) has achieved a scientific milestone and surgical innovation in the field of reconstructive microsurgery and hand surgery. This new surgical innovation given the name, 'Qatar Flap', facilitates the functional and cosmetic restoration of various fingertip injuries, restoring the natural function of the finger without any disability or disfigurement.

Dr Saleem Al-Lahham, a Specialist in the Department of Plastic Surgery at HMC said: "Hand injuries are common and the Department of Plastic Surgery at HMC receives many hand injuries that require a precise surgical intervention to restore the finger's functional and anatomical state. Given the

different types of finger injuries, the surgical procedures available may vary, but these surgeries often leave painful scars on the fingers and some require sacrificing major blood vessels in the fingers, making them undesirable options for patients."

Dr Al-Lahham, the innovator of the Qatar Flap, explained that this surgical innovation is based on functionally and cosmetically repairing fingertip injuries through a single surgical procedure that involves one of the small secondary arterial branches, which contributes to restoring the fingers to their natural shape without any disability or deformity.

"More than 100 surgical procedures have been successfully performed using this surgi-

cal innovation, and we perform five surgical procedures of this kind per week. It is expected that this innovation will become the preferred option for fingertip restoration surgeries worldwide, in addition to the medical and scientific value it adds to various surgical specialties," said Dr Al-Lahham.

The surgical innovation was covered in a scientific article published in the journal *Plastic & Reconstructive Surgery-Global Open*<sup>[1]</sup>. The journal described HMC's innovation as a brilliant breakthrough that will enhance the outcomes of finger restorative and cosmetic surgeries, considering it a reliable option to be performed in a single surgical procedure while preserving the finger's arteries. **MEH**

### Reference:

1. Al Lahham, Salim MD; Aljasssem, Ghanem MD; Alyazji, Zaki MD; et. al. The Qatari Flap for Fingertip Reconstruction: Versatility, Reliability, Clinical Applications, and Review of Literature. *Plastic & Reconstructive Surgery-Global Open* 11(7):p e5128, July 2023.

doi: <https://doi.org/10.1097/GOX.0000000000005128>

## Women Wellness and Research Center establishes new Level 2 ICU for high-risk obstetric patients

Qatar's Women Wellness and Research Center (WWRC) has established a new level 2 Intensive Care Unit in its labour suite to provide continuity of care for pregnant women who are at high risk of severe morbidity or mortality.

The new level 2 ICU sets an example for leading tertiary maternity centres around the world.

At the new ICU unit, high-risk pregnant women will be assessed and followed by the same healthcare team from their induction to delivery and throughout their immediate post-partum care.

The ICU is one of the initiatives in WWRC's strategic plan to improve current service standards in order to enhance the management of high-risk obstetric patients. A multidisciplinary team of obstetricians, anaesthetists, intensivists, and nurses will provide care for this category of patients.

"We are aiming to improve outcomes and experience of critically ill pregnant women

in labour by establishing a level 2 ICU in the labour room and it is our expectation that this labour ICU will enable high-risk patients who are eligible for normal vaginal delivery to be closely monitored and supervised. This initiative is expected to set the standards for similar services in the region and an example to be followed by leading tertiary maternity centres around the world," explained Dr Hilal Amin Al Rifai, WWRC's Chief Executive Officer and Medical Director.

"The vision of WWRC is to deliver the safest, most effective, and most compassionate care to our patients. Improved patient experience is a priority. Upholding high standards of safety in a tertiary maternity hospital is imperative. Particular attention needs to be directed towards the high-risk pregnant population who are at risk of severe morbidity or mortality. The intrapartum phase for high risk and critically ill pregnant women is paramount. Improving the care provided to this population will

impact the outcome and experience."

He said that although the hospital currently provides this level of care for antenatal and postnatal patients, the period of maximum risk – the intrapartum period – has, however, not been covered for the same patients by a proper ICU service. The new ICU will fill this gap.

Dr Al Rifai, added: "Other important advantages of creating this new unit are early recognition and prompt treatment of deteriorating patients; easier accessibility to an operating theatre in case of emergency; easier accessibility to a level 3 ICU should the need arise; better patient and family experience; improved staff satisfaction using blended care, midwives and critical care nurses; cost reduction as optimization of a patient's condition pre-admission leads to shorter stay and better outcomes; the need for a level 3 ICU can be reduced; and the patient's experience can be improved through continuity of care and fewer transfers." **MEH**

# Exercising with heart conditions



Exercise has many well-recognised health benefits. It reduces the risk of heart problems and improves mental and physical wellbeing.

“Patients with existing heart problems are encouraged to exercise. Studies show it can help strengthen the heart and extend life expectancy,” explains Dr Sabiha Gati, consultant cardiologist and specialist in sports cardiology at Royal Brompton and Harefield hospitals, London.

The European Society of Cardiology recommends that people with heart problems complete at least 150 minutes of moderate intensity exercise each week. This is the same recommendations as for all healthy adults.

Moderate intensity exercise means increasing your heart and breathing rate but still being able to hold a conversation.

“For patients with heart disease, it is important to talk to your doctor before starting any kind of physical activity. This includes competitive exercise as well as leisurely activities. They will be able to assess the condition of your heart and guide on how to exercise safely,” explains Dr Gati.


## Heart screening for athletes of all abilities

“For people that have an existing heart problem, their doctor is usually already ad-

vising them to ensure they are exercising safely. However, if people don't know they have a heart problem, there could be a risk with exercise.”

Risk factors for coronary heart disease include smoking, a family history of heart attacks and high blood cholesterol. It can also include conditions like diabetes and high blood pressure.

Royal Brompton and Harefield sports cardiology assessments start with an initial consultation with one of our world-leading cardiologists.

If you require diagnostics tests for your heart following your initial consultation, these will be tailored to your needs. 

- For more information on Royal Brompton and Harefield hospitals' sports cardiology service visit: [www.rbhh-specialistcare.co.uk/diagnostic-services/sports-cardiology](http://www.rbhh-specialistcare.co.uk/diagnostic-services/sports-cardiology)



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Part of  Guy's and St Thomas' Specialist Care





# Samsung Medical Centre, a leading innovator in Korea's healthcare sector

Samsung Medical Center (SMC) is one of Korea's most renowned hospitals committed to excellence in providing the highest quality, compassionate care and service to patients with 2,000 beds, 1,400 physicians, and 3,100 nurses. Since its opening in 1991, it has been leading the innovation of the healthcare sector by advocating a high-tech intelligent hospital, and now it has the highest grade in three areas (INFRAM, DIAM, EMARM) of HIMSS as the best smart hospital in Korea.

## Product profile

Samsung Medical Center has initiated Digital Transformation (DX) to eliminate inefficiencies in the hospital and create an environment where medical staff can provide the best treatment to patients. As part of this digital transformation, Samsung Medical Center defines the concept of DX strategy as 'Connect & Thru', and is trying to realize differentiated patient services.



bot, along with a Connected Command Center which operates all these robots.



In particular, Samsung Medical Center developed the I.R.O Platform, which consists of Hardware (Product) and Software (System). Trends and needs were analyzed in five categories: eCare Robots, Special Specimen Robots, Multipurpose Bulk Delivery Robots, Service Delivery Robots, and Guide & Sanitization Ro-

The business model is subdivided from consulting to platform and tool sales according to the current status of institutions that want to introduce the DX model at Samsung Medical Center. **MEH**

- For more information, visit: [www.samsunghospital.com/english](http://www.samsunghospital.com/english)





## Lunit's AI solutions assist in interpreting chest radiography, mammography images

Lunit, abbreviated from “learning unit” is an AI software company dedicated to developing advanced medical image analytics and data-driven imaging biomarkers via cutting-edge deep-learning AI technology.

With AI, Lunit aims to make data-driven medicine the new standard of care. The company is especially focused on conquering cancer, one of the leading causes of death worldwide.

Lunit develops AI solutions for precision diagnostics and therapeutics, to find the right diagnosis at the right cost, and the right treatment for the right patients.

### Shaping the future

Founded in 2013, Lunit has been internationally acknowledged for its advanced, state-of-the-art technology and its application in medical imaging. Lunit has been named by CB Insights as one of the “AI 100” startups transforming the healthcare industry and “Digital Health 150” companies. Lunit has been chosen by the World Economic Forum as one of the “Technology Pioneers” that is shaping the future.

Lunit seeks to provide AI solutions that open a new era of data-driven precision medicine. Through AI solutions for diagnostic and therapeutic biomarkers, the company aims to solve the most critical issues in cancer care, reduce medical costs and prolong survival.

Lunit's technology has been recognized at international competitions, such as ImageNet (5th place, 2015), TUPAC 2016 (1st place), and Camelyon 2017 (1st place), surpassing top companies like

Google, IBM, and Microsoft.

As a medical AI company, Lunit places great value on building clinical evidence by publishing their research in major peer-reviewed journals. Their findings in AI detection on chest x-ray and mammography are published in *Radiology*, *The Lancet Digital Health*, *JAMA Network Open*, *Clinical Infectious Diseases*, and other prestigious scientific journals.

### Product profile

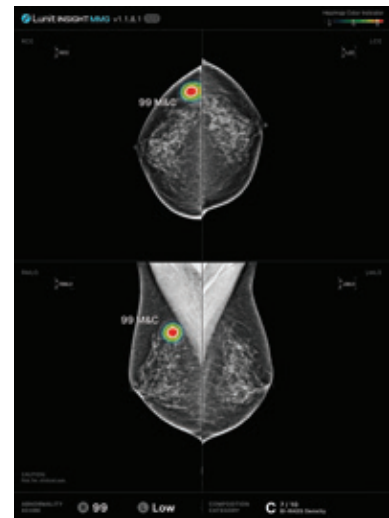
**Lunit INSIGHT CXR** is a software solution that assists physicians in the interpretation of chest radiography images. The solution has been designed to automatically analyze chest radiographs via deep-learning technology. The device helps identify abnormal-looking areas on chest radiography with 97-99% accuracy, such as: atelectasis, calcification, cardiomegaly, consolidation, fibrosis, mediastinal widening, nodule, pneumothorax, pleural effusion and pneumoperitoneum.

Validated by published clinical studies, Lunit INSIGHT CXR can improve a physician's reading performance, especially for critical and urgent findings such as nodule, pneumoperitoneum, pneumothorax, and consolidation.

Relying on its proven accuracy, a physician can focus specifically on abnormalities, ultimately saving time and addressing the excessive workload and shortage of radiologists in chest X-ray interpretation.

### Lunit INSIGHT MMG

Lunit INSIGHT MMG is a software solution that assists physicians in the interpretation of



mammograms. The device has been designed to automatically analyze digital mammograms via deep-learning technology.

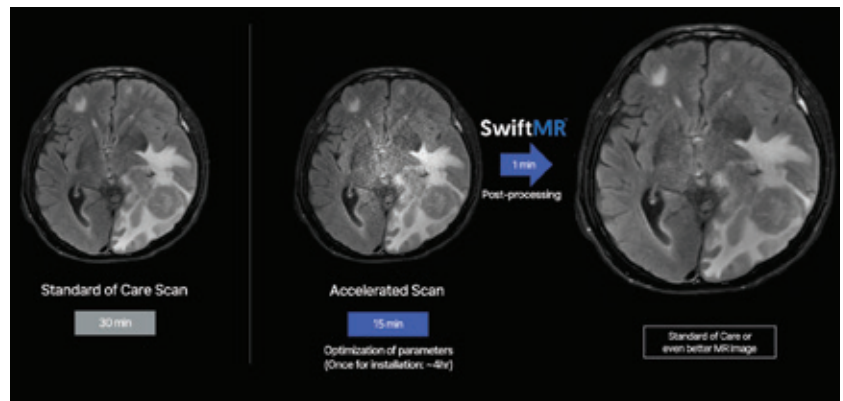
The device identifies and classifies suspect areas for breast cancer on mammograms with 96% accuracy. The solution enables visualization and quantitative estimation of the likelihood of the presence of a malignant lesion.

Validated by published clinical studies, Lunit INSIGHT MMG can improve a physician's diagnostic performance especially for dense breast and early breast cancers.

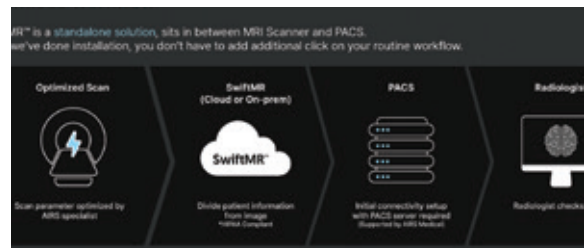
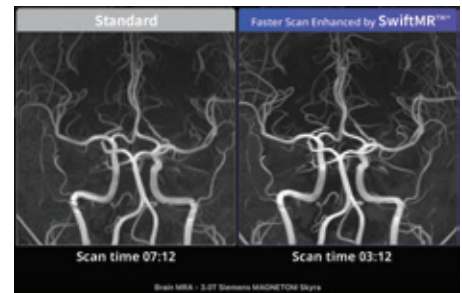
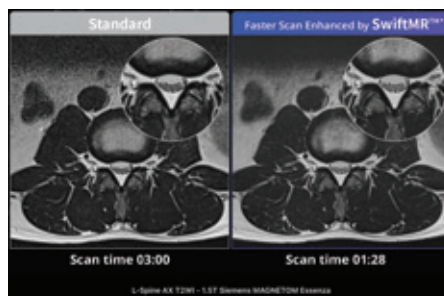
Based on its proven accuracy, physicians can reduce false-negative cases and recall rates, which ultimately addresses the shortage of mammography specialists in a single- and double-reading environment. **IMEH**

- For more information, visit: <https://www.lunit.io/en>

# AIRS Medical's SwiftMR AI solution reduces MRI scan time by enhancing image quality



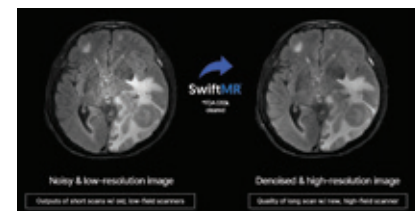
AIRS Medical Co. is a Korean medical AI startup company which aims to reduce inefficiencies in the healthcare industry through digital transformation of the medical experience. Founded in 2018 by five co-founders from Seoul National University, the company now consists of around 100 talented people and succeeded in attracting 30 billion won (about US\$25 million) in a Series B investment last year. AIRS Medical's first product, SwiftMR, is currently in more than five countries including South Korea and the United States with more than 250 install bases around all the world. AIRS Medical plans to expand market coverage to 10 more countries this year.



## Product profile

SwiftMR is a standalone medical software that helps reduce the scan time of MRI by enhancing the quality of MRI images using elaborate deep-learning AI technology. SwiftMR allows hospitals to maximize their productivity and sales by reducing MRI scan time by up to 50%. SwiftMR benefits medical practices, as well as helping to improve the patient experience. SwiftMR is used by more than 250 customers around the world and is registered in more than 10 countries including Korea, US, and UAE.

Case #1 Birtum Hospital (MSK)				Case #2 KMI (Imaging center)			
Body part	Scan time (before)	Scan time (after)	Reduction %	Body part	Scan time (before)	Scan time (after)	Reduction %
C-spine	20:03	15:30	-39%	Brain MRA	7:23	4:30	-38%
L-spine	10:45	10:45	-36%	Brain MRI	11:12	8:54	-29%
Shoulder	20:01	12:45	-36%	C-spine	14:13	7:26	-48%
Ankle	18:22	11:48	-36%	L-spine	13:10	8:43	-48%
Knee	19:24	12:04	-34%				



## Faster scans, better image quality

MRI scans have a critical trade-off between shorter scan times and higher image quality. SwiftMR breaks this rule by enhancing the image quality of fast-scanned MRI, using its sophisticated deep learning AI algorithm.

## Obtain best quality images from your old, low-field scanners

SwiftMR can make the best out of older scanners through denoising and resolution-enhancing technology to generate MR images that look like they were scanned by the latest high-field MRI machines.

## More than 250 customers globally, now expanding to the Middle East

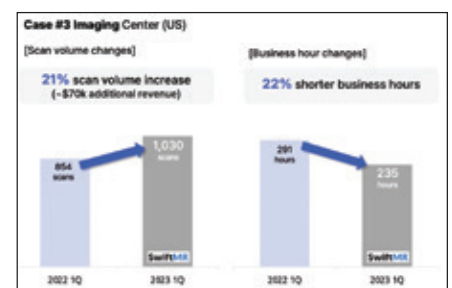
Since its market launch in 2022, SwiftMR has been able to satisfy more than 250 customers globally. In this time, SwiftMR has processed around 787,000 MRI scans and now is ready to serve customers in the Middle East, including the UAE, KSA, Egypt, and Kuwait.

## Seamless workflow, vendor-neutral software

SwiftMR does not require any hardware upgrades to existing MRI machines. Connected to the MRI and PACS, it seamlessly enhances fast-scanned MRI images and automatically sends them to the PACS.

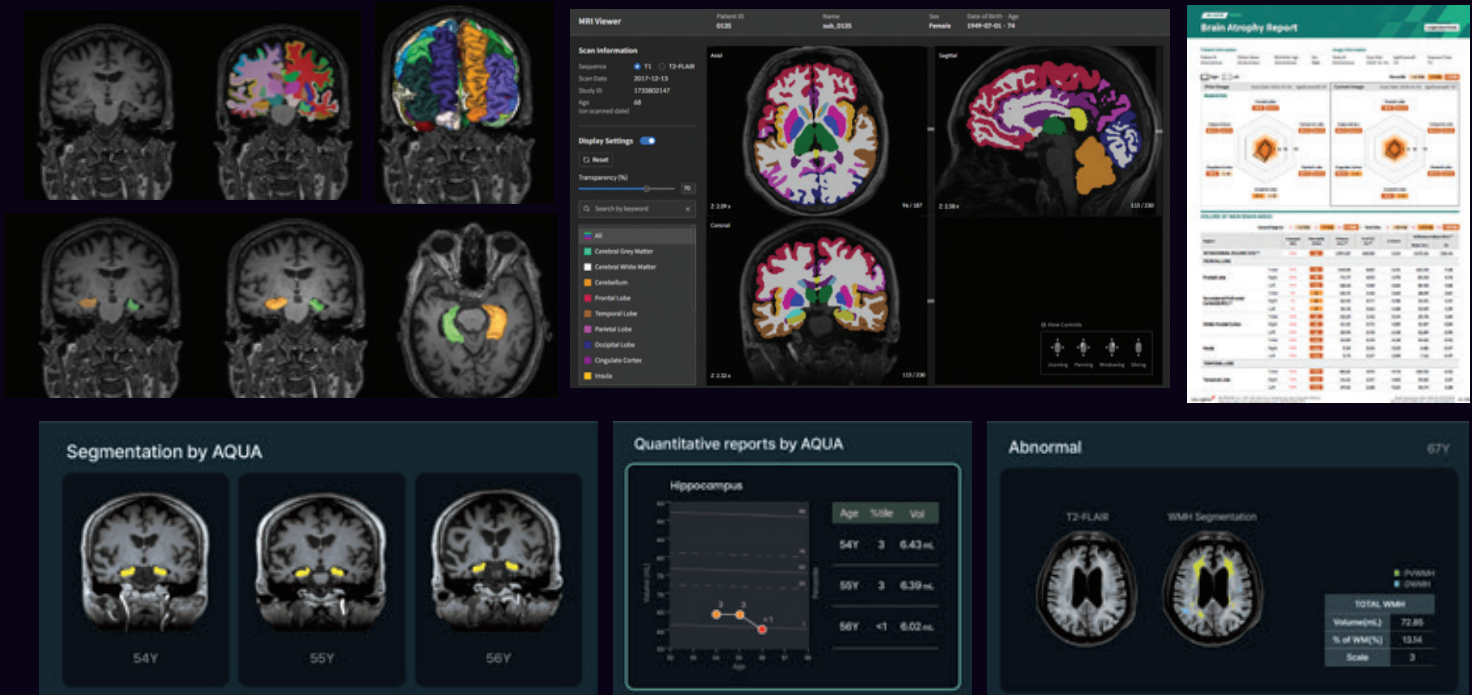
## Faster scans for patients and hospitals

SwiftMR can reduce scan time by up to 50%, which not only reduces the patient's



time in the MRI scanner, but also increases hospital productivity with larger scan volumes and revenue.

- For more information, visit: <https://airsmed.com/>



# Neurophet develops AI solutions for neurodegenerative diseases

Neurophet Inc., with expertise in neuroscience, has been focusing on developing and providing innovative medical solutions for helping patients suffering from neurological disorders. To achieve this mission, the company has applied state-of-the-art AI technologies to their expertise in neuroimaging, brain modelling and neuromodulation. They have been conducting research in imaging-based biomarkers for Alzheimer’s disease, which will be a valuable tool for clinical trials (surrogate biomarkers for drug response, disease progression and efficacy/safety monitoring) and prescription decisions for Alzheimer’s therapeutics, such as Lecanemab and Donanemab.

Neurophet provides medical-grade solutions including brain MRI imaging analysis and interpretation (brain atrophy, white matter hyperintensity) software “Neurophet AQUA” and brain PET scan analysis (Amyloid/Tau/FDG PET tracer deposition) software “Neurophet SCALE PET”, approved by international regulatory bodies including US-FDA, CE, Japanese PMDA and Korean MFDS.

Neurophet has set its top priority to

helping patients suffering from neurological diseases. Based on expertise in neuroscience, Neurophet will continue to challenge and grow to explore the human brain’s health and pioneer solutions for brain diseases with AI technology.

## Product profile

Neurophet AQUA is a medical-grade AI software that assists neuroradiologists and clinicians in the accurate diagnosis of neurodegenerative diseases, including dementia, by providing brain MRI analysis for brain atrophy and white matter hyperintensity within five minutes.

It encompasses two primary functions: firstly, it offers brain segmentation into 126 regions of interest (ROI) from T1-weighted images, facilitating brain volume quantification and atrophy assessment, which is a key indicator of neurodegenerative diseases, such as Alzheimer’s. Additionally, it provides a longitudinal feature for tracking changes in brain volume over time. Secondly, from T2-FLAIR images, it accurately segments and quantifies white matter hyperintensity (WMH) caused by

vascular degeneration, while also providing a severity score based on the Fazekas scale. The brain MRI analysis can support precise diagnosis of neurodegenerative disorders and contribute to time-saving for the neuroimaging interpretation with comparable accuracy.

The solution has been validated through various peer-reviewed published studies and provides a diverse range of nine report formats and normative percentile information derived from both Asian and Western populations. Furthermore, it is compatible with various MRI scanners – validated across 16 different models – making it a versatile tool for neuroimaging analysis. The software can be fully integrated with PACS in radiology departments.

New features for Alzheimer’s therapeutics-related (e.g. Lecanemab and Donanemab) neuroimaging technologies, including Amyloid-Related Image Abnormalities (ARIA) and MRI-based amyloid-PET positivity prediction, are under development and will become a valuable tool for prescription decisions and screening of subjects for Alzheimer’s therapeutics. **MEH**

- For more information, visit: <https://www.neurophet.com>

# Heuron's comprehensive AI solutions for stroke and neurodegenerative diseases

Heuron Co., Ltd. is a medical AI startup founded in 2017 that focuses on developing innovative AI-based solutions and advanced image analysis methods to enhance the diagnosis and treatment of neurodegenerative diseases and emergency stroke care.

Heuron software is easily integrated into any medical system to facilitate the accurate and early diagnosis of neurodegenerative diseases such as Alzheimer's and Parkinson's diseases. In emergency settings, the StroCare Suite™ tools can reduce the time of treatment by several crucial hours, saving lives and reducing post-stroke physical complications.

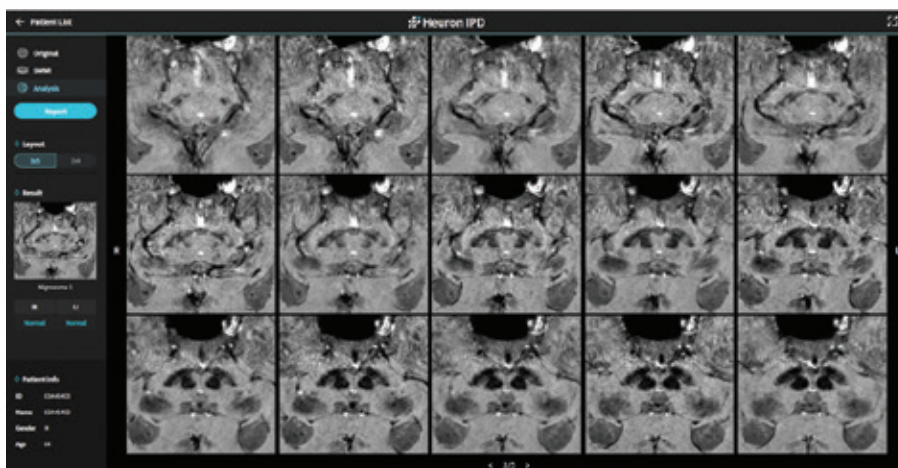
The company is dedicated to protecting people's brain health by combatting the impact of age-related neurodegenerative diseases on ageing populations around the world through AI-based diagnostic assistance tools. To achieve this, Heuron collaborates with numerous medical institutions and partners in Asia, the United States and is now in the process of expanding to the Middle East.

## Prioritizing healthy ageing

Heuron AgingCare Suite™ combines tailored software solutions for neurodegenerative diseases such as Parkinson's and Alzheimer's. Heuron Parkinson's tools, including Heuron IPD and Heuron NI, enable the visualisation and quantification of the Nigrosome area based on MR images through the innovative SMWI (susceptibility map-weighted imaging) sequence. This method not only reduces examination costs and time, but also eliminates potential risks of radiation exposure from PET scans in Parkinson's diagnosis.

Heuron Alzheimer's tools include Heuron AD, a software developed for quick, fully automated and accurate volumetric quantification of over 90 brain regions on routine MR images, and Heuron Brain PET, a tool designed to detect, map and quantify protein deposits common in Alzheimer's patients. Users can combine it with 10 different tracers and adjust the settings to their needs.

Heuron AgingCare Suite provides a de-



tailed report for each patient and is helpful for early diagnosis and tracking of the disease progression. Users can customize the settings to suit their specific requirements.

## Time is brain

Stroke is a life-threatening emergency condition that occurs when there is a disruption in blood flow to a part of the brain. It is the second leading cause of death globally. It can result from either a blocked blood vessel, known as an ischemic stroke, or bleeding within the brain, referred to as a haemorrhage. In stroke cases, time is of the essence; the faster stroke is addressed, the greater the likelihood of a full recovery without lasting disability.

Heuron StroCare Suite™ is a dedicated so-

lution designed to address the most crucial aspect of stroke management, which is reducing the response time for emergency patients. It is an integrated AI solution that generates comprehensive patient classifications in emergency situations for patients with suspected intracranial haemorrhage and large vessel occlusion using non-contrast CT scans.

The software scans for any potential haemorrhages and large vessel occlusions and calculates the ASPECT Score in under three minutes to facilitate rapid decision-making and minimize treatment duration. This tool reduces the need for a contrast agent and is particularly helpful when transferring patients from facilities where contrast CT or thrombectomy procedures are not available to those where

- For more information, visit: <https://iheuron.com/>

# Waycen's WAYMED Endo uses AI to analyze endoscopy video in realtime

Korean company Waycen was founded by a team of eminent clinicians and AI experts with the mission of creating the next generation of AI-enabled applications for healthcare.

Waycen researches and develops healthcare AI technologies based on realtime applications.

Their vision is to create a full-cycle precision medical platform through their cutting-edge AI technology.

Waycen was recognized for competitive-

ness with four Innovation Awards at CES 2023, the world's largest IT exhibition.

## Product profile

WAYMED Endo is a world-class AI software solution for analyzing endoscopy video in real-time during an endoscopy procedure. It is compatible with all existing endoscopy suites and has very simple installation, so that any hospital can use their product with no limiting factors.

It serves as a second observer in the

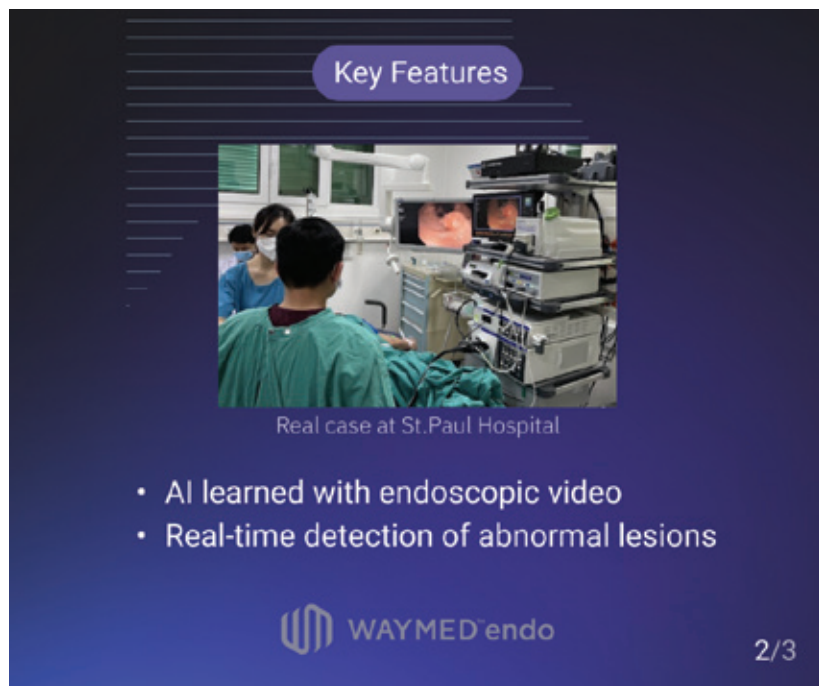
endoscopy suite. It serves as a clinical assistant to the doctor and helps to shorten the time spent analysing endoscopy video.

WAYMED Endo was recognized as a breakthrough medical device in South Korea.

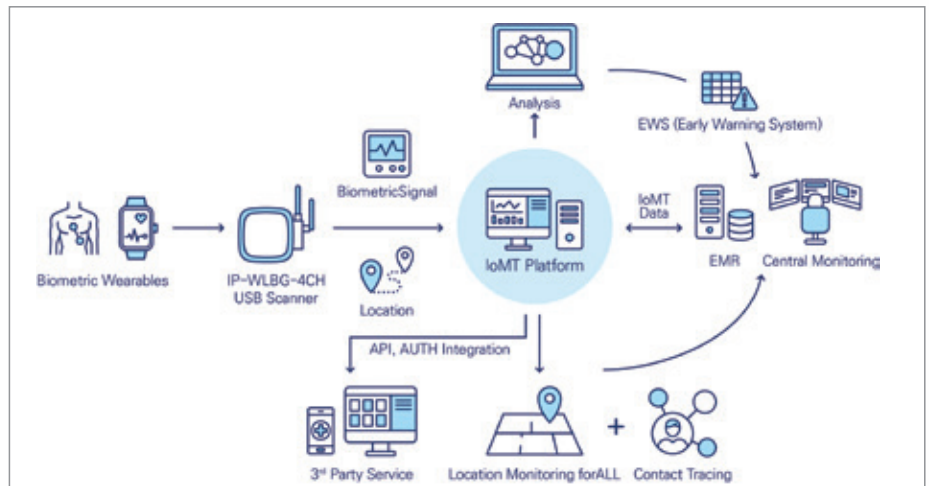
## User benefits

- Improves accuracy and quality of endoscopic exams
- Helps reduce fatigue of endoscopists
- Maintains consistent quality of endoscopic exams.

- For more information, visit: [www.waycen.com/en](http://www.waycen.com/en)



# People and Technology specialises in healthcare IoT



Korean company People and Technology collects, connects, and monitors various data generated by hospitals, such as location information of patients, medical staff, and biometric information from medical devices.

People and Technology has developed IndoorPlus+ Smart Care as a solution to enhance efficiency, automation, and digitization of hospital operations. The healthcare DX (Digital Transformation) company specialises in developing and providing healthcare IoT solutions.

Since its establishment in 2013, the company has been developing and supplying solutions for hospitals, factories, and buildings. It has more than 100 customers in Korea and globally.

In particular, in the hospital digitization sector, they developed a leading smart hospital model project in 2020, and have since secured a positive track record of supplying and operating solutions to about 35 medium and large hospitals in Korea. As a result, People and Technology has been recognised as the leading supplier of healthcare IoT for smart hospitals in Korea.

In 2018, the company established an overseas subsidiary (People and Technology AG) which actively focuses on foreign expansion. Currently they have 10 customer references in the Middle East and Europe. Through active business activities in the Middle East, including KSA and UAE, the company achieved remarkable overseas expansion in 2022, and are aiming for more than 100% growth in 2023.

As a result of their efforts to enter the global market, the company was selected as a “notable vendor” in the IoT/IoMT field by Gartner for 2019 and 2020, demonstrating the excellence of their solutions.

## Product profile

The IndoorPlus+ SmartCare solution is an integrated IoT/IoMT (Internet of Medical Things) platform that utilizes collected location positioning and biometric data through BLE (Bluetooth Low Energy) signal collection devices to enhance the protection, operation, and management of medical assets and individuals (patients, staff, and visitors) more effectively. Through the IoMT platform, various manual tasks within healthcare institutions are automated, digitized, and transformed into efficient services. By connecting diverse data generated at hospital sites, the solution addresses unmet needs in the healthcare field and ultimately provides a Smart Hospital solution that aims to enhance medical quality.



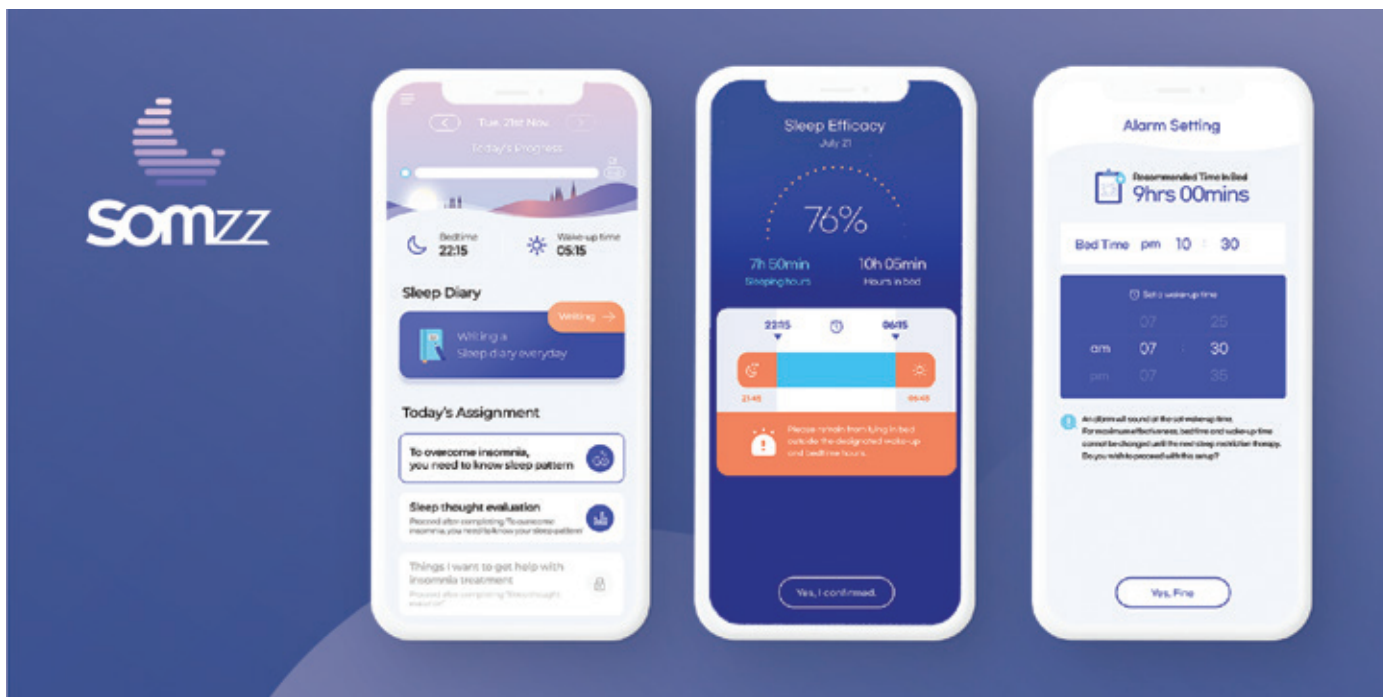
## Typical IndoorPlus+ use cases:

- Find equipment you need instantly
- Locate a patient for treatment
- Control and track asset utilization
- Monitor and optimize workflows
- Control access to restricted areas
- Improve staff safety
- Check patient safety
- Facilitate way-findings
- Monitor environmental conditions
- Comply with regulations
- Support patient monitoring
- Enhance response to emergencies.

## Key benefits

- No application silos: One platform supports multiple use cases combining sensor data and location
- Reuse of network communication infrastructure for cost-effective deployment
- Multi-vendor environment with BLE avoiding vendor lock-in and fostering innovation
- Highly scalable, performant, open system
- Flexible deployment choice: Cloud or On Premises. MEH

• For more information, visit: <https://pntbiz.com>



## AIMMED's Digital Therapeutics, Somzz helps relieve insomnia with Cognitive-Behavioural Therapy

AIMMED Corp. is a leading digital therapeutics company based in Seoul, South Korea. AIMMED creates digital healthcare systems as a frontrunner in South Korea's DTx (Digital Therapeutics) industry as well as the field of the healthcare platforms and senior care.

Since 2019, AIMMED has consistently expanded its product pipeline across a broad-spectrum of disease areas. It continues to discover, develop, and improve software-based therapeutics with the aim of creating more effective and personalized products for patients and convenient products for clinicians to manage treatment.

AIMMED uses evidence-based medicine (EBM) to ensure the safety and clinical effectiveness of its products to achieve better outcomes for patients worldwide.

### Product profile

Somzz is a digital therapeutics mobile app designed for adults suffering from insomnia. Somzz applies and implements the protocols of Cognitive-Behavioural Therapy for Insomnia (Stimulus Con-

trol Therapy, Sleep Restriction Therapy, Sleep Hygiene Education, Relaxation Techniques, and Cognitive Therapy) through a mobile app.

In clinical practice, this is considered the first-line treatment recommended for insomnia. Somzz provides education, real-time feedback, behaviour intervention, and algorithm-based push notifications to patients with insomnia over 6 to 9 weeks.

### Indications for use

Somzz is a Software as a Medical Device (SaMD) intended to improve insomnia symptoms by delivering a medical intervention (Cognitive-Behavioural Therapy for Insomnia, CBT-I) in the form of a mobile app.

### Prescription status

A prescription from a qualified healthcare provider is required.

### Unique features

- **Expanded treatment options:** Introducing a new treatment in addition to traditional medications and face-to-face CBT-I

- **Remote access:** Available via online access without physical constraints of space and time
- **Real-time feedback:** Making it easy to track progress and engage patients actively in their treatment
- **Safety:** Non-invasive and non-pharmacological, which makes it less prone to safety issues.

### Clinical outcomes

In a clinical trial, the efficacy of Somzz for patients with chronic insomnia was proven superior to a placebo device, which consisted of a sleep diary and sleep hygiene education. It demonstrated statistically significant improvement in insomnia severity scores at the end of treatment. The efficacy of Somzz was also observed in the assessment scales, which measure dysfunctional beliefs about sleep, depressive symptoms, fatigue, daytime sleepiness, health related quality of life, as well as sleep quality which includes sleep efficiency and sleep onset latency.

In particular, 46.81% of the patients reached remission at the end of the treatment program. [MEDI](#)

# Add Able's Smart Breathe devices enable personalised respiratory rehabilitation

Add Able is a South Korean respiratory medical device startup company that provides data-based, customized respiratory rehabilitation solutions.

In the field of rehabilitation and medical care, Add Able solves social problems together and seeks growth together, developing products under the slogan of "Being Healthier".

The respiratory rehabilitation solution developed by the Add Able research team connects a breathing training device and mobile app to improve health and immunity by increasing lung capacity through respiratory training. It is effective in reducing dementia and improving health in elderly dementia patients.

During the design and manufacture process, the team collaborated with physical therapists, occupational therapists, elderly care professors, and IT experts to ensure the reliability and efficacy of the device.

With the motif of "making life healthier", Add Able is making products that anyone can use. The basis of life is breathing.

Add Able says they will change the paradigm of respiratory training by constantly researching and improving their Smart Breathe series.

## Product profile

Add Able's respiratory training system is divided into two types:

- Motorized functional recovery devices that connect a respiratory measurement device to a mobile device and are used through a dedicated application, and
- Manual functional recovery devices that can be used in daily life while performing aerobic exercises, such as running.

According to the user's breathing volume and condition, the air volume is adjusted through the load control mechanism mounted on the device. During breathing exercises, by placing the mouth on the mouthpiece, spirometry and respiratory muscle measurements are acquired. Reports on related breathing data are provided,



ed, and unlike existing analog breath training methods (blowing balloons, blowing out candles), it is possible to continuously train by inducing user interest through games.

Add Able's respiratory training system can reduce the time from pulmonary function tests in hospitals to the application of respiratory rehabilitation therapy. It provides a new paradigm in the respiratory rehabilitation market by increasing user motivation through AI-based lung disease diagnosis and customized respiratory rehabilitation guides currently under development. **IMEH**

- For more information, visit: <http://www.smartbreathe.co.kr/en>



# Meet ezCaretech's Global All-in-one HIS, BESTCare 2.0

ezCaretech was established to improve patient care and innovate the medical service environment with their Hospital Information Systems. Over 20 years, ezCaretech has carried out medical digital transformation and IT projects in Korea and the global market. ezCaretech is now a major healthcare IT company with business operations around the world, including Korea, Japan, the United States and the Middle East (KSA and UAE).

## Product profile

BESTCare 2.0 is the next-generation Hospital Information System (HIS) designed and developed with the help of medical doctors to enable hospitals to provide patient-centric medical services. It caters to the various needs of medical facilities and helps provide high-quality medical services as well as enhancing the efficiency of management.

## Features

- Supports the international standard codes (ICD, SNOMED CT, LOINC)
- Supports the international interface protocols (HL7, API, SSO, DICOM, CDA, FHIR)
- Secures patients safety and provides patient-centric care (CDSS, CLMA, CVR)
- Includes a system for optimal work process (clinical core functions, clinical enhancement functions, ancillary functions, administrative functions, etc.)



## Benefits

BESTCare 2.0 is a value-based all-in-one HIS. The solution enables hospitals to provide patient-centric care with the improved safety and efficiency. The HIS interfaces with other smart solutions, such as CDW (Clinical Data Warehouse), CLMA (Closed Loop Medication Administration), as well as a mobile EMR and e-Consent which optimizes work flow so that medical providers can focus on the patient and the treatment.

Utilizing BESTCare 2.0 is the first step to setting up an environment which supports digital health and a personal healthcare information ecosystem. **MEH**

- For more information, visit: <https://www.ezcaretech.com/en/>

## Leading Korean MedTech companies to be showcased in UAE

Event to be held in Abu Dhabi in October

The Korea Health Industry Development Institute (KHIDI) UAE office, the Embassy of the Republic of Korea to the UAE, the Department of Health – Abu Dhabi, and G42 Healthcare will jointly hold a conference to introduce future medical technologies at Dusit Thani Abu Dhabi on October 31, 2023.

Global information technology companies such as Google and Facebook in the US, and Naver and Kakao in South Korea, are pioneering new medical markets by collecting and analyzing medical data by combining health information and information technology, which will open a new medical era.

Currently, we are at a level where health information and artificial intelligence (AI) can interact to analyze patients' diseases and support physicians' work. In addition, robotic technology can deliver medicine and medical information to a patient on behalf of medical personnel in the hospital.

In the near future, early diagnostic information, such as for cancer diagnoses, will be obtained by analyzing human DNA. This is expected to enable future medical care to move from disease diagnosis and treatment to disease prevention.

Therefore, AI and digital medical technologies are expected to contribute to patients receiving highly personalised medi-

cal services that enable people to enjoy healthier and better quality lives.

### Opportunity for business partnerships

The "Medical Korea 2023 in U.A.E." conference will introduce clinical cases using digital & AI technology in hospitals in Korea and the UAE, and digital medical technology companies from Korea. Mr. Lee Young Ho, director general of the KHIDI UAE office said there will be opportunities to develop business partnerships at company exhibition booths at the conference. **MEH**

- Register for the event here: <https://mco.ae/khidi/>

Medical Korea 2023 in U.A.E.

**KHIDI**  
Korea Health Industry  
Development Institute



## ADOPTING DIGITAL & AI TECHNOLOGY IN MEDICAL SERVICES

📍 Dusat Thani Abu Dhabi, UAE

📅 31 October, 2023

As a rise of digital and artificial intelligence technology in medical field, "Med-Tech" will bring together regional and international experts, policy drivers, and healthcare professionals to facilitate knowledge and experience sharing. We will present a special session and exhibition to introduce Traditional Korean Medicine(TKM) with demonstration of TKM practice as well.

**Title:** Medi-Tech: Cancer Diagnosis and Treatment Using Digital and AI Technology

**Hosted by:** Embassy of the Republic of Korea to United Arab Emirates,  
Department Of Health, Abu Dhabi (DOH), G42 Healthcare

**Organized By:** Korea Health Industry Development Institute (KHIDI), UAE Office

**Online Session** 1,2 (Online for overseas participants only) / **Offline Session** 1,2,3 and Special Session



### Session 1: Policy Development

Hall: Onyx 2&3

Korean and UAE government policies on digital and AI technology will be introduced. This session will bring the past, present and future trends in digital medical trends in government policy

- For Governments officials & Medical Doctors
- Presentation: UAE (DOH, G42 Healthcare)/ Korea (KHIDI)



### Session 2: Clinical Cases

Hall: Onyx 2&3

Clinical cases utilizing digital and AI technology from Korean & UAE hospitals will be introduced.

- For Governments officials & Medical Doctors



### Session 3: Business Partnership

Hall: Sapphire

Will bring business partnership opportunities for digital medical technology companies. There will be business presentations & networking opportunities

- Business Presentations



### Special Session : Introduction of Traditional Korean Medicine(TKM)

Hall: Onyx 1

Will introduce Traditional Korean Medicine focusing on Clinical Practice with a demonstration.

- Public Event



### Exhibition:

- Healthcare Digital and AI Technology
- Traditional Korean Medicine(TKM)

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STRATEGIC PARTNERSHIP





# DUPHAT



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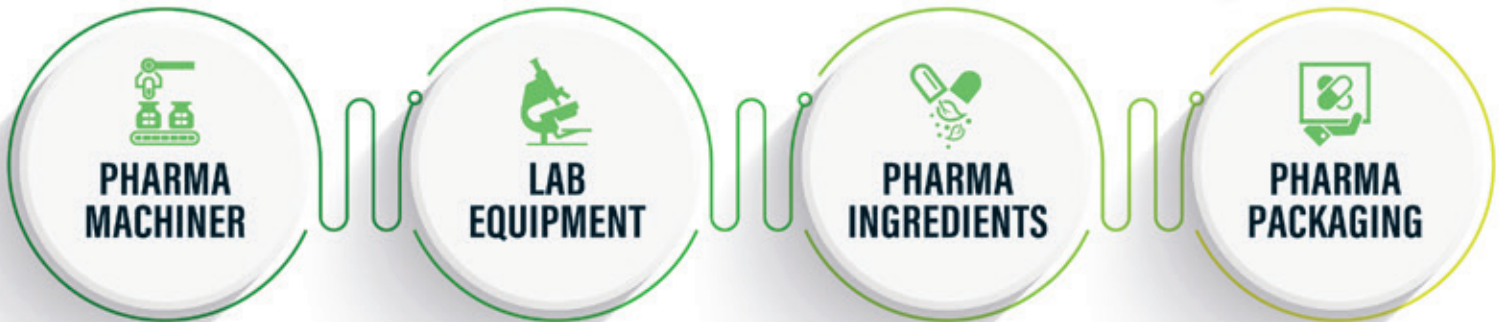
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## FEATURE OF DUPHAT 2024



**36,591**  
Square meters



**1,147**  
Brand & Exhibiting  
Companies



**1,000**  
Pre-fixed  
B2B meetings



**26,400**  
Total Visitors

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# Middle East faces tidal wave of dementia cases

Countries in the Middle East will face a tidal wave of dementia cases by 2050 if nothing is done to prevent it. This disturbing forecast by research scientists was published in *The Lancet Public Health* in 2022. Qatar and the UAE, for example, will see unprecedented increases in cases of dementia by 2050, which are projected to rise from current levels by a massive 1926% and 1795% respectively. Other countries in the region are also forecast to experience exceptionally large increases in dementia. *Middle East Health* speaks to **Paolo Barbarino**, CEO, Alzheimer's Disease International, to find out more about these forecasts and what can be done to mitigate these distressing projections.



Paolo Barbarino, CEO Alzheimer's Disease International.

The number of adults (aged 40 years and older) living with dementia worldwide is expected to nearly triple, from an estimated 57 million in 2019 to 153 million in 2050, due primarily to population growth and population ageing, according to a Global Burden of Disease study published in *The Lancet Public Health*<sup>[1]</sup>.

In the Middle East and North Africa (MENA), cases are predicted to grow by 367%, from almost 3 million to nearly 14 million, with worryingly large increases in Qatar (1926%), the United Arab Emirates (1795%), and Bahrain (1084%).

Paolo Barbarino, CEO, Alzheimer's Disease International (ADI), said these distressing figures are credible and are similar to their own forecasts. However, she added, the MENA forecasts are probably predicated on a low base figure due to under-reporting of dementia in the region.

"Dementia may have been severely under-reported," said Barbarino. "We know this happens in other countries where governments are in denial about dementia. Although that's not the case in the Middle East where governments in general are aware that it exists, it may still have been under-reported. This is not unusual, since the care for persons with dementia would have happened primarily in the home and

would not have been recorded."

She said that more research is needed to show why there has been under-reporting. "Is it due to home-based care or a lack of awareness, for example?"

Regarding potential lack of awareness, Barbarino referred to a global survey ADI conducted in 2019 in which 62% of the healthcare professionals surveyed around the world did not consider dementia a disease, but rather that dementia was caused by normal ageing.

"62% is a massive figure," Barbarino emphasised. It speaks volumes to the lack of attention this disease has been afforded in the recent past.

## More dementia research needed

Although there has been an increase in research on dementia in general and Alzheimer's Disease in particular, it is still relatively small. Barbarino referred to a report by ADI in 2017 that showed that for every 12 studies on cancer worldwide there was only one on neurodegenerative diseases.

"This highlights the disproportionate knowledge we have about dementia compared to cancer. And even though there has been an increase in funding for dementia research, the bulk of this fund-

ing is being used to find a pharmacological treatment for the disease, when actually we need all kinds of research – research on risk-reduction, research on care, and research on psychosocial intervention, for example," said Barbarino.

At government level, the United States is putting the most money into research by a long way, she said. This is followed by the UK, Australia and Canada. There is a research in all high-income countries, but on a relatively small scale.

"At ADI we advocate for 1% of the societal cost of the disease to be spent on research – which we have estimated for each country. However, only the United States comes close to this," she pointed out.

"We need research on all aspects of dementia. However, diagnostics research is particularly important. We recently published a report on this, because at the moment you can only get a confirmatory diagnosis of Alzheimer's by doing a PET scan and by doing a lumbar puncture. A lumbar puncture is painful and invasive and people generally don't like them. A PET scan is, in many cases, prohibitively expensive if it is available at all. So we need more research in this area."

She noted that there has been some progress on the development of blood-

based biomarkers for diagnosis, which show a lot of promise. “But they are not quite there yet,” she added.

### Early warning signs and risk reduction

Barbarino explained that there are early warning signs for dementia and they can help people prepare for the onset of dementia and potentially delay its onset through various lifestyle or behavioural changes.

Early signs and symptoms of dementia include: memory impairment, such as difficulty remembering events; difficulty concentrating, planning or problem-solving; problems finishing daily tasks at home or at work, such as writing or using eating utensils.

“In Japan they diagnose people at risk as young as the late 30s, or at least in their 40s. The earlier the diagnosis, the better. There seems to be no doubt in the scientific community that you can start lifestyle interventions to reduce your risk of dementia, such as changing your physical habits, doing more exercise, and changing your eating habits to eat more healthy food.

“There are ongoing studies that indicate that early interventions can lower the risk factors for dementia.

“For example, there is evidence that traumatic brain injury causes dementia. So for sportspeople who have been playing football or rugby for many years, stopping playing the sport may help.

“Can you do anything to reverse it? This is not known. So really all we have at this stage is risk reduction. Risk reduction seems to slow it down.”

Barbarino advised that public health stakeholders and governments in the Middle East, who are facing this impending tidal wave of dementia over the next few decades, should now start promoting early diagnosis of risk at the level of primary care so that early interventions can be implemented to reduce the risk and slow the onset of dementia.

### The role of ADI

Talking about the role of ADI, Barbarino

### References:

1. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health* 2022 Published online January 6 2022. <https://bit.ly/31KORuW>

Public health stakeholders and governments in the Middle East, who are facing this impending tidal wave of dementia over the next few decades, should now start promoting early diagnosis of risk at the level of primary care so that early interventions can be implemented to reduce the risk and slow the onset of dementia.

explained that the organisation “exists to increase awareness of dementia at all levels, including the public, healthcare workers, governments and the people who make the policies. We help dementia-related organizations in countries around the world become stronger, so they can advocate better. But fundamentally, we also exist to spread awareness of the best way for people with dementia and their families to live their lives after they’ve been diagnosed.

“We also exist to provide clarity, to provide information about what is real and what is disinformation with regards dementia.”

She explained there is a lot disinformation about treatments and cures which have to be corrected as there is no evidence to support them. There is no cure, she emphasised.

“When requested to, we also provide advice and recommendations to government about dementia.” For example, she said Ukraine had approached ADI for recommendations on the best way to design care homes to cater for people with dementia.

“However, usually we advise governments to work with our local member, the local Alzheimer’s organisation in that specific country. We believe the local organisation will have the best local knowledge.”

- To learn more about ADI, visit: [www.alzint.org](http://www.alzint.org)

## Early warning signs of dementia

These are some common early symptoms that may appear some time before a diagnosis of dementia. They include:

- memory loss
- difficulty concentrating
- finding it hard to carry out familiar daily tasks, such as getting confused over the correct change when shopping
- struggling to follow a conversation or find the right word
- being confused about time and place
- mood changes

These symptoms are often mild and may get worse only very gradually.

It’s often termed “mild cognitive impairment” as the symptoms are not severe enough to be diagnosed as dementia.

## Symptoms specific to Alzheimer’s disease

The most common cause of dementia is Alzheimer’s disease. Common symptoms of Alzheimer’s disease include:

- memory problems, such as regularly forgetting recent events, names and faces
- asking questions repetitively
- increasing difficulties with tasks and activities that require organisation and planning
- becoming confused in unfamiliar environments
- difficulty finding the right words
- difficulty with numbers and/or handling money in shops
- becoming more withdrawn or anxious

Source: NHS UK

<<https://www.nhs.uk/conditions/dementia/symptoms-and-diagnosis/symptoms/>>

# Researchers identify new genetic variant protective against Alzheimer's disease

A single patient can spark new research questions and provide answers about a disease. And when a new case is identified, investigators can make connections between them that can lead to even more powerful and persuasive ideas about cause and treatment. In a publication in May this year in *Nature Medicine*<sup>[1]</sup>, an international team led by investigators from two Mass General Brigham hospitals – Massachusetts General Hospital (MGH) and Mass Eye and Ear – reports on a new case of a patient with a genetic predisposition for developing early-onset Alzheimer's disease who remained cognitively intact until his late 60s.

Through clinical assessments led by investigators at the University of Antioquia in Colombia, genetic and molecular studies performed at Mass Eye and Ear, and Children's Hospital Los Angeles, neuroimaging and biomarker studies conducted at MGH, and neuropathological studies carried out by investigators at University Medical Center Hamburg-Eppendorf in Germany, the team identified a new genetic variant that provides protection from Alzheimer's disease. The variant occurs in a different gene than in a case from the same family reported in 2019 [2], but points to a common disease pathway. Insights from their findings also pinpoint a region of the brain that may provide an optimal treatment target in the future.

"The genetic variant we have identified points to a pathway that can produce extreme resilience and protection against Alzheimer's disease symptoms," said co-senior author Joseph F. Arboleda-Velasquez, MD, PhD, an associate scientist at Mass Eye and Ear. "These are the kinds of insights we cannot gain without patients. They are showing us what's important when it comes to protection and challenging many of the field's assumptions about Alzheimer's disease and its progression."

## Paisa mutation

The case that caught the investigators' at-

tention involved a family member of the world's largest-known kindred with a genetic variant called the "Paisa" mutation (Presenilin-1 E280A). Carriers of this variant usually develop mild cognitive impairment at a median age of 44, dementia at age 49, and die from complications of dementia in their 60s.

Francisco Lopera, MD, director of the Neuroscience Group of Antioquia in Medellín, Colombia, a co-first author of the *Nature Medicine* paper, is the neurologist who discovered this family and has been following them for the last 30 years. This team of investigators previously studied a woman from this family who remained unimpaired until her 70s and whose case was reported in 2019. In their new *Nature Medicine* paper, the investigators describe a case of a male carrier of the Paisa mutation who remained cognitively intact until age 67. He progressed to mild dementia at age 72 and died at 74 – decades after most people with the Paisa mutation typically do.

"Extraordinary cases like this one illustrate how individuals and extended families with Alzheimer's disease can help advance our understanding of the disease and open new avenues for discovery," said co-senior author Yakeel T. Quiroz, PhD, a clinical neuropsychologist and neuroimaging researcher, director of the Familial Dementia Neuroimaging Lab in the Departments of Psychiatry and Neurology at Massachusetts General Hospital. "The insights we are gaining from this second case may guide us on where in the brain we need to look to delay and stop disease progression and will help us form new hypotheses about the series of steps that may actually lead to Alzheimer's dementia."

"What we have done with the study of these two protected cases is to read mother nature," said. "The most exciting thing is that nature has revealed to us both the cause of Alzheimer's and the cure for it. Mother nature did an exceptional experiment with these two subjects: it endowed them both with a gene that causes AL-

zheimer's and at the same time with another gene that protected them from the symptoms of the disease for more than two decades. Therefore, the solution is to imitate nature by developing therapies that mimic the mechanism of protection of these genetic variants in subjects at risk of suffering from the disease."

Dr Lopera added: "A great door has been opened for the prevention and treatment of incurable diseases."

## Reelin-COLBOS gene variant

The male patient was enrolled in the Mass General Colombia-Boston biomarker study (COLBOS), which brings members of an extended family group of 6,000 individuals with the known Paisa mutation to Boston for advanced neuroimaging, biomarker and genetic examinations. The same study previously detected a case in which a female patient carried two copies of a rare Christchurch genetic variant, which affects APOE3 – a protein that is heavily implicated in Alzheimer's disease. However, the researchers ruled out the presence of the APOE Christchurch genetic variant in the male patient.

The team performed genetic and molecular analyses at Mass Eye and Ear in collaboration with Xiaowu Gai Ph.D. and colleagues from Children's Hospital Los Angeles to identify other variants that could have been protecting him from Alzheimer's disease. The most promising candidate was a new and rare variant, never before reported in the Reelin gene. The team named it Reelin-COLBOS. In studies led by co-senior author Diego Sepulveda-Falla, MD, a principal investigator at the Institute of Neuropathology at the University Medical Center Hamburg-Eppendorf, the team further verified the protective role of the Reelin-COLBOS variant in mouse models and neuropathological studies.

## A re-evaluation of neurodegeneration

"Each of the protected cases, the APOE Christchurch and the Reelin-COLBOS case, shows a distinctive protective pattern



that can modify or manipulate gene expression, understanding what region of the brain to focus on for delivery will become increasingly important.

Many treatments for Alzheimer's disease, including drugs recently approved by the U.S. Food and Drug Administration and other drugs currently in clinical trials, target reducing amyloid plaque buildup. The study's results point to potential new avenues for treatment because the two patients with protection had extremely high levels of amyloid in their brains and yet they were protected.

#### Academic collaboration

"These exciting findings demonstrate the power of academic collaboration, where a retinal disease genetics expert working with a local neuroimaging authority can team up with leading neurologists and neuropathologists around the world to power scientific discovery," said Joan W. Miller, MD, chair of Ophthalmology at Mass Eye and Ear, Mass General Hospital and Brigham and Women's Hospital, and David Glendenning Cogan Professor and chair of Ophthalmology at Harvard Medical School. "Alzheimer's disease remains a devastating disease with an immense global burden, and this work opens the door to further investigation into how this resilience pathway may lead to an effective therapeutic strategy."

The researchers note that they cannot completely rule out that other factors, including additional gene variants, may have contributed to the patient's resilience against Alzheimer's disease symptoms. But their experimental evidence in preclinical studies strongly implicate the Reelin-COLBOS variant.

Dr Arboleda-Velasquez and Quiroz, together with Drs Lopera and Sepulveda-Falla, plan to continue their work to identify additional protected patients from these Colombian families, learning from each extraordinary case. They are also conducting research looking at treatments to target this protective pathway.

"It is a huge privilege to have these genetic cases to work on," said Dr Arboleda-Velasquez. "We are honoured to be a part of the team that has made this discovery." MEH

in the postmortem analyses, one global and the other very localized," said Dr Sepulveda-Falla. "These outstanding cases are teaching us that Alzheimer's protection can take different shapes, and that perhaps a therapy can be successful just by targeting key brain structures such as the entorhinal cortex. They are forcing us to revise our previous concepts about neurodegeneration and cognitive decline. These are exciting times for us, and hopefully for the Alzheimer's research field as well."

The researchers describe Reelin as a "cousin" of the more famous APOE. Both Reelin and APOE compete to bind to similar cellular receptors, essentially jostling to occupy the same seat. When Reelin sits in the receptor seat, it diminishes the phosphorylation of tau, a protein known to form pathological tangles in brains with Alzheimer's disease. When APOE binds the receptor, it has the opposite effect.

Reelin is a protein with a pivotal role in the regulation of brain cell development and function. In fact, previous reports have linked mutations in Reelin to diseases like autism, schizophrenia, epilepsy, and bipolar disorder. However, mutations linked to disease are different because they diminish the protein's function, whereas, in the case of Reelin-COLBOS, the protective variant increases the function of the protein.

"When we saw that one of our top candidates for the variant sat in Reelin, it was a bit shocking," said Dr Arboleda-Velasquez. "The fact that the first case showed us a variant affecting APOE and the second case affects Reelin tells us that this signaling pathway that controls the phosphorylation of tau, among other effects, may be key to understanding why these patients were protected. This is critical to guide therapies because it clearly tells us that more Reelin could potentially have beneficial effects."

#### Amyloid-beta plaque

The most recent patient underwent neuroimaging exams at Massachusetts General Hospital at age 73. These scans revealed that while the patient's amyloid-beta plaque burden was high and he had tau tangles in some regions of his brain, his entorhinal cortex had notably very limited tau pathology. The entorhinal cortex plays a critical role in memory and learning, and its degeneration is known to lead to cognitive impairment and dementia. Studies in a mouse model also showed that the Reelin-COLBOS variant protected against tau pathology.

"This case indicates that the entorhinal region may represent a tiny target that's critical for protection against dementia," said Quiroz.

As investigators pursue gene therapies that may in the future deliver treatments

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# Best U.S. hospital has unique model of care

Patients from more than 150 countries travel to Mayo Clinic for treatment

Mayo Clinic is the world's largest integrated, not-for-profit medical group practice. *Newsweek* magazine ranks Mayo Clinic as the best hospital in the world. Additionally, *U.S. News & World Report* has ranked it No. 1 in more specialties than any other hospital in the U.S. for seven consecutive years. Mayo Clinic has locations in Rochester, Minnesota, Phoenix, Arizona and Jacksonville, Florida in the United States and a speciality clinic in London, England.

What sets Mayo Clinic apart from other hospitals is Mayo Clinic's Model of Care. Dr. Mohamad Bydon, Professor of Neurosurgery at Mayo Clinic and Executive Medical Director for Europe, the Middle East, India, Africa and International Academic Affairs, describes the Mayo Clinic Model of Care as "a set of principles that have guided our organization since its earliest days. They are the reason patients come to Mayo. Many healthcare facilities offer high-quality care, but these principles set Mayo Clinic apart."

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Under the Mayo Clinic Model of Care,



Dr. Mohamad Bydon, Professor of Neurosurgery at Mayo Clinic and Executive Medical Director for Europe, the Middle East, India, Africa and International Academic Affairs.



patient care begins with an unhurried examination with time to listen to the patient. From there, a physician takes personal responsibility for directing patient care over time in a partnership with the local physician. Collegial, cooperative staff teamwork with multispecialty integration is utilized, and a team of specialists is available and appropriately used.

Mayo Clinic believes in the highest-quality patient care provided with compassion and trust, respect for the patient, family and the patient's local physician. A decisive diagnosis and treatment can be determined through a comprehensive, timely and efficient assessment.

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Effective treatment depends on getting the right diagnosis as soon as possible.

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Interview

# Saudi neurosurgeon performs awake brain surgery to treat epilepsy

King Faisal Specialist Hospital & Research Centre in Saudi Arabia has been offering awake craniotomy, an exceptionally advanced brain surgery procedure, for several years. *Middle East Health* speaks to Afnan Alkhotani, MD, Associate Consultant in Neurosurgery at King Faisal Specialist Hospital & Research Centre, Jeddah, about the awake craniotomy procedure, indications for the procedure, as well as the challenges and potential complications of the intervention. Dr Alkhotani is subspecialized in Stereotactic Functional, Pain and Epilepsy Neurosurgery.

**Middle East Health:** What are the main indications for performing an awake craniotomy, and what types of brain conditions or tumours are typically addressed with this procedure?

■ **Dr Afnan Alkhotani:** An awake craniotomy is a remarkable surgical intervention specifically designed for the treatment of brain conditions residing within eloquent areas. Eloquent areas refer to the regions of the brain that are intricately involved in vital functions, in stark contrast to the silent counterparts. These functions encompass critical components such as speech centres within the dominant hemisphere, motor abilities encompassing facial expressions, limb movements, and the perception of bodily sensations.

Primarily employed for the resection of tumours, epileptic foci, and specific vascular or congenital malformations, the technique of awake craniotomy offers an unparalleled opportunity for surgeons to meticulously map the intricate landscape of the brain. By actively engaging the patient during the procedure, the surgical team can effectively identify and delineate the boundaries of

these crucial functional areas, allowing for their preservation while adeptly removing tumours located in their proximity.

This innovative approach stands as a testament to the remarkable progress and sophistication achieved in the realm of neurosurgery. By delicately balancing the imperative of eradicating diseased tissue with the paramount importance of safeguarding essential brain functions, the awake craniotomy reflects the commitment of medical professionals to redefine the boundaries of possibility in their pursuit of enhanced patient outcomes and improved quality of life.

**MEH:** What are the main challenges and risks associated with performing awake craniotomy compared to traditional craniotomy under general anaesthesia?

■ **AA:** Performing an awake craniotomy presents a multitude of challenges and risks when compared to the traditional craniotomy under general anaesthesia. These challenges include:

- **Patient cooperation:** Maintaining



Dr Afnan Alkhotani, Associate Consultant in Neurosurgery at King Faisal Specialist Hospital & Research Centre. Dr Alkhotani is subspecialized in Stereotactic Functional, Pain and Epilepsy Neurosurgery.

patient cooperation throughout the surgery is essential but can be challenging. Some patients may experience anxiety or discomfort during the procedure. To address this, thorough explanation, rehearsal, and mental preparation are undertaken to ensure the patient understands and feels as comfortable as possible.

- **Psychological impact:** The unique na-



Dr Afnan Alkhotani (centre) and her surgical team assess medical imaging for a neurosurgical procedure.

ture of an awake craniotomy, wherein patients can hear and see parts of the surgery, can have a significant psychological impact. The patients may experience fear or distress during the procedure. To mitigate this, a comprehensive neuropsychological baseline assessment before surgery and appropriate follow-up care can help alleviate anxiety and fear.

- **Pain management:** While local anaesthesia numbs the scalp and dura, effective pain management and anxiety medications are crucial to ensure the patient's comfort and cooperation. Adequate measures are taken to ensure that the patient is not experiencing unnecessary pain or discomfort during the procedure.

- **Intraoperative seizures:** Brain tumours or lesions can trigger seizures during surgery, which can impair consciousness and patient cooperation. Sensitive electrical recorders are employed to detect seizures before they spread, and topical irrigation with cold water can be utilized to abort the seizure if necessary.

- **Neurological deficits:** The primary goal of an awake craniotomy is to minimize the risk of postoperative neurological deficits, such as weakness or sensory changes, compared to traditional craniotomy. However, despite meticulous care, there is still a

chance of post-operative weakness, which can be attributed to the disconnection of brain cell fibres, cellular swelling, or direct injury. Every effort is made to assess and protect critical brain areas, but the potential for complications remains.

- **Surgical precision:** A high degree of surgical precision is required during an awake craniotomy to avoid damaging vital motor, sensory, and language functions. Surgeons employ emerging technologies and utilize all available resources to accurately delineate the diseased areas and ensure minimal disruption to critical brain functions.

**MEH: How do you ensure patient comfort and cooperation during an awake craniotomy, especially considering the potentially stressful and invasive nature of the solutions include:?**

- **AA:** Awake craniotomies require patient comfort and cooperation. Some advisable solutions:

- Pre-operative education about the procedure, what to expect, and why their participation is important. This reduces emotional stress and boosts cooperation.

- While awake, the patient receives local freezing to numb the skin incision. Sedatives also calm the patient and reduce anxiety.

- The surgical team clearly communicates with the patient throughout the procedure. Patients should voice their concerns; the head position should be as comfortable as surgically possible, where the patient can swallow sips from an ice chip if his/her feels too dry to vocalize. Some may need voice augmentation microphones.

- Awake craniotomy can stress patients. Patients may receive psychological support before, during, and after the procedure. Counselling or other methods may help manage anxiety.

By implementing these strategies, healthcare professionals can prioritize patient comfort and ensure their active participation in the awake craniotomy process. Through a multidimensional approach encompassing education, communication, and psychological support, the surgical team can navigate the challenges of the procedure while fostering an environment of empathy and care for the patient's well-being.

**MEH: Can you explain the process of brain mapping during an awake craniotomy and its significance in preserving critical brain functions while removing tumours or treating epilepsy?**

- **AA:** The process typically begins during the clinic visit, days before the sur-

gery. Evaluation by the process of brain mapping during an awake craniotomy is a meticulous and critical step in preserving crucial brain functions while removing tumours or treating epilepsy. The significance of brain mapping lies in its ability to identify and delineate the boundaries of functional areas within the exposed brain, enabling surgeons to navigate and operate with precision.

The process typically begins well before the actual surgery, during the clinic visit. During this evaluation phase, the patient undergoes an assessment by an anaesthesiologist, and if necessary, any blood thinners they are taking may be temporarily stopped. Additionally, necessary laboratory tests and structural or functional imaging studies are requested to aid in surgical planning.

On the day of the surgery, the patient's scalp is numbed with local anaesthesia. The head is then secured in a three-point head holder to ensure stability during the procedure. The patient is informed about the vibrations that may be felt during the drilling of the skull bone. It is important for the patient to keep their mouth slightly open to avoid teeth clenching, and the infiltration of local anaesthesia into the dura can help alleviate mild headaches.

Once the dura, the protective covering of the brain, is opened, the surgeon proceeds with brain mapping. This involves stimulating different areas of the exposed brain using a mild electrical current. The stimulation helps elicit specific responses or movements from the patient, providing valuable information about the functional areas being activated.

For example, when the right motor area is stimulated, the patient may experience twitches or movements in the left-sided limbs or face. Similarly, stimulating a language area in the dominant hemisphere of the brain may cause the patient to have difficulty speaking or understanding words. By mapping these responses, the surgeon can precisely identify the boundaries of critical brain regions and avoid inadvertently damaging them during the surgical procedure. This meticulous approach minimizes the risk of postoperative neurological deficits or impairments by choosing the

safest path of surgical resection.

In addition to direct electrical stimulation, other adjunctive techniques may be employed for brain mapping during an awake craniotomy. These may include neuronavigation, which uses imaging data to precisely locate tumour boundaries, diffusion tensor imaging (DTI) to assess white matter tracts and connectivity, functional magnetic resonance imaging (fMRI) to identify language and motor areas, or electrocorticography (ECoG) to monitor brain activity during the procedure.

By combining these sophisticated mapping techniques, surgeons can achieve an enhanced understanding of the individual patient's brain organization, ensuring a more targeted and precise approach to surgical intervention. The integration of brain mapping during an awake craniotomy underscores the commitment to preserving critical brain functions while effectively addressing tumours or treating epilepsy, leading to improved patient outcomes and quality of life.

### **MEH: What are the most common neurological complications that can arise during or after an awake craniotomy, and how are they managed or minimized?**

■ **AA:** During or after an awake craniotomy, some common neurological complications that can arise include seizures, neurological deficits, or infections.

- Seizures can occur during the procedure due to stimulation of the brain tissue which can be aborted with direct cold solution irrigation. Also, to minimize the risk of seizures, antiseizure medications may be administered before and during the surgery.
- Damage to critical brain structures during surgery can cause neurological deficits. Pre-operative brain mapping reduces the risk of neurological deficits. Functional mapping helps the surgeon avoid damaging critical brain areas.
- Any craniotomy carries a risk of infections. Sterile surgery practices reduce infection risk. Antibiotics can also be given before, during, and after the procedure to reduce infection risk.
- In addition to these complications there is the potential for pain, bleeding,

and swelling. Painkillers, close monitoring, and postoperative care manage these.

Close attention to infection control, diligent monitoring, and utilizing advanced mapping techniques allows for a more precise and meticulous surgical approach, minimizing the risks and maximizing the benefits of this specialized procedure.

### **MEH: How do you handle communication with the patient during the procedure to ensure their safety and provide necessary feedback about potential changes in neurological function?**

■ **AA:** Ensuring effective communication with the patient during an awake craniotomy is vital for their safety and to provide necessary feedback regarding potential changes in neurological function. The following methods are employed to facilitate communication and maintain patient well-being:

- **Speech Mapping:** To assess language function, the patient may be asked to perform tasks such as counting, naming objects, or reading aloud while specific brain areas are stimulated. This allows the surgical team to evaluate potential changes in speech and language function and make informed decisions accordingly.
- **Motor Mapping:** The patient may be instructed to move their fingers or toes while specific brain areas are stimulated. This enables the surgical team to assess motor function and detect any alterations that may occur during the procedure.
- **Verbal Communication:** Throughout the surgery, the surgeons engage in ongoing conversation with the patient. The patient is encouraged to actively communicate and promptly report any changes in sensation, motor function, or speech they may experience. This real-time feedback allows the surgical team to address concerns immediately and make necessary adjustments to ensure patient safety.
- **Neurological Assessments:** The surgical team continuously monitors the patient's cognitive function, motor strength, sensation, and speech during the procedure. Any changes in these parameters are evaluated promptly. In the event of unexpected deficits, further evaluation, such as an instant CT scan, may be requested



Dr Afnan Alkhotani performs brain surgery on one of her patients.

to assess the situation and rule out major bleeding or complications.

- **Anaesthesia Management:** While the patient is awake during the craniotomy, local anaesthesia is administered to numb the scalp and skull, ensuring their comfort and minimizing pain.

By employing these communication strategies and closely monitoring the patient's neurological status throughout the procedure, the surgical team can maintain patient safety, promptly address and stabilize any changes in function,

**MEH:** What specific technologies or techniques do you employ to monitor the patient's neurological function in real time during an awake craniotomy?

- **AA:** During an awake craniotomy, several technologies and techniques are employed to monitor the patient's neurological function in real time. These monitoring methods play a crucial role in ensuring patient safety and the effectiveness of the procedure. Here are some specific technologies and techniques utilized:

- **Electrocorticography (ECoG):** Electrodes placed on the surface of the brain record electrical activity. ECoG helps identify brain function and detect any seizure activity that may arise during the surgery.

- **Electromyography (EMG):** EMG measures muscle electrical activity. It is used to monitor facial muscles during the procedure, allowing for the detection of any potential damage to the facial motor cortex.

- **Motor Evoked Potentials (MEP):** MEP involves stimulating specific brain areas and monitoring the corresponding muscle responses. This technique assesses the integrity of the motor pathways and aids in the detection of any surgical damage.

- **Somatosensory Evoked Potentials (SSEP):** SSEP involves stimulating peripheral nerves and monitoring the electrical responses in the brain. SSEP is used to assess the integrity of sensory pathways throughout the surgery and identify any abnormalities.

- **Intraoperative MRI (iMRI):** Real-time brain imaging is conducted during the surgery using an MRI machine. This technology provides immediate feedback on tumour removal and helps identify any potential complications or residual tumour tissue.

- **Awake Brain Mapping:** This technique involves stimulating specific regions of the brain while the patient is awake. It allows for the identification and preservation of critical language and motor regions, ensuring their protection during tumour removal or other surgical interventions.

- **Continuous Neuromonitoring:** Various parameters such as blood pressure, heart rate, oxygen levels, and intracranial pressure are continuously monitored throughout the procedure. Any significant changes in these parameters may indicate potential complications and allow for prompt intervention.

**MEH:** What kind of team dynamics and coordination are required for ensuring a successful awake craniotomy procedure, considering the need for close collaboration between neurosurgeons, anaesthesiologists, and other healthcare professionals?

- **AA:** Successful awake craniotomy procedures rely on strong team dynamics and close collaboration among healthcare professionals involved, including neurosurgeons, anaesthesiologists, neurophysiologists, and nurses. The following practitioners are crucial for ensuring a well-coordinated and successful procedure:

- **Neurosurgeons:** Neurosurgeons lead the surgical team, performing the procedure, identifying the target area, and implementing surgical techniques. They work closely with the anaesthesiologists to determine the appropriate level of sedation required for the patient's comfort and cooperation. Effective communication between the neurosurgeon and anaesthesiologist is essential throughout the procedure.

- **Anaesthesiologists:** Anaesthesiologists play a pivotal role in managing pain, sedation, and the overall well-being of the patient. They closely monitor the patient's neurological function in collaboration with the neurophysiologists. Anaesthesiologists must strike a delicate balance between providing adequate sedation to keep the patient calm and cooperative while ensuring they remain awake and responsive.

- **Neurophysiologists:** Neurophysiologists are responsible for monitoring

the patient's neurological function in real time during the awake craniotomy. They utilize techniques such as EEG (electroencephalography), EMG, and SSEP to assess brain and nervous system function. Their findings and observations are communicated promptly to the neurosurgeon and anaesthesiologist, enabling them to make informed decisions during the procedure.

- **Nursing staff:** The nursing team plays a crucial role in supporting both the patient and the surgical team. They monitor vital signs, ensure patient comfort, and assist during the surgery. Effective communication and coordination between the nursing staff, neurosurgeon, anaesthesiologist, and neurophysiologist are essential for seamless patient care.

**MEH: Can you briefly discuss any recent advancements or emerging technologies that have helped overcome some of the challenges associated with awake craniotomy, improving patient outcomes or reducing procedure-related complications?**

- **AA:** Awake craniotomy has indeed witnessed significant advancements and the integration of emerging technologies, leading to improved patient outcomes and a reduction in procedure-related complications:

- **Intraoperative and functional MRI:** The utilization of intraoperative and functional MRI during awake craniotomy represents a noteworthy advancement. Real-time imaging allows surgeons to visualize the tumour and surrounding brain tissue, facilitating precise identification and preservation of critical brain areas responsible for speech, movement, and sensation. This enables more effective tumour resection while minimizing damage to vital functional brain tissue.

- **Neurophysiological monitoring:** The emergence of neurophysiological monitoring techniques has greatly contributed to enhancing patient safety and reducing postoperative neurological deficits during awake craniotomy. By placing electrodes on the patient's scalp or brain, surgeons can monitor electrical activity, allowing for the real-time assessment of the patient's brain responses during the surgery. This proactive monitoring approach enables timely adjust-

ments and interventions to safeguard vital brain functions.

- **Advancements in anaesthesia:** The continuous improvement of anaesthesia practices has significantly enhanced the safety and comfort of awake craniotomy procedures. Local anaesthetics, sedatives, and analgesics are employed to minimize pain and anxiety during the procedure, facilitating a state of wakefulness and cooperation while ensuring the patient's overall well-being.

By leveraging these innovations, healthcare professionals continue to push the boundaries of possibility, achieving greater success in treating brain conditions while prioritizing patient safety and well-being.

**MEH: What is the history of awake craniotomy at KFSH&RC and can you tell us about some of the successful cases of awake craniotomy at KFSH&RC?**

- **AA:** At King Faisal Specialist Hospital & Research Centre (KFSH&RC), the practice of awake craniotomy has been firmly established for several years. Recognizing the numerous benefits of this procedure in specific cases, we began offering it as an option to patients who would derive significant advantages from its implementation.

One remarkable success story from KFSH&RC involved a 20-year-old girl with a tumour located in the region of the brain responsible for speech and language function on the left side. By performing an awake craniotomy, we meticulously

mapped her brain, precisely locating the tumour while meticulously preserving her speech function. This altered the surgical plan, allowing us to choose a safer entry point, resulting in the successful removal of the entire tumour with minimal to zero damage to the surrounding healthy tissue. Following the procedure, the patient experienced a favourable recovery, with preserved speech and language function intact.

Another notable case at our centre involved a patient suffering from epilepsy, with seizures originating from the left side of the brain. During the awake craniotomy, we employed cortical mapping techniques to identify the precise location of the epileptic focus, enabling us to successfully resect the abnormal tissue. This intervention led to a substantial reduction in the frequency and severity of the patient's seizures, significantly improving their overall quality of life without compromising the integrity of the surrounding vital brain structures.

These cases exemplify the positive outcomes and improved quality of life achieved through the implementation of awake craniotomy at KFSH&RC. We have consistently demonstrated exceptional results, which can be attributed to our experienced and well-supported team, state-of-the-art technology, and patient-centred approach. These factors synergistically contribute to making this transformative advancement readily accessible, ensuring optimal patient care and outcomes. **MEH**

### About Dr Afnan Alkhotani

Dr Afnan Alkhotani is an accomplished neurosurgeon specializing in Stereotactic Functional, Pain, and Epilepsy Neurosurgery. Her clinical journey includes a Senior Registrar position and Fellowships in Epilepsy Neurosurgery and Stereotactic Functional Neurosurgery. Dr Alkhotani obtained her Saudi Board of Neurosurgery and holds an MBBS degree with honours. Her dedication to advancing medical knowledge is evident through her numerous research contributions, including studies on epilepsy treatments, tremor therapy, and cerebrospinal fluid leaks. She has presented at prestigious conferences and published papers in esteemed medical journals. Dr Alkhotani is actively involved in ongoing research projects and collaborative clinical trials. Her commitment to patient care and innovative research establishes her as a respected and valuable member of the medical community. **MEH**

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# Generative AI's business impact will be slow, then slow, then big



By **Vikram Savkar**

In the months since ChatGPT first broke into global consciousness, extreme hype about its transformational possibilities was met with extreme doomsaying about its potential risks. Which is correct?

As always at such points of disruption, the answer is neither. ChatGPT represents

a powerful new application of advanced technology, but it appears its impact on the larger business world will be gradual. ChatGPT is not as much of a *sui generis* innovation as it is sometimes made to seem, and it won't instantly reinvent a hundred occupations. True, the fluidity and naturalness of the text that ChatGPT creates is superior to that of previous versions of generative AI, but it's a difference of degree rather than kind. OpenAI regards ChatGPT-3 as simply one in a series of iterative releases and were taken aback by its astonishing cultural reception. In fact, they just recently launched GPT-4 as a new and improved successor. That should tell us something important. The events of the previous few months are ultimately a waystation in a long-term journey towards integration of AI into everyday life. We may have arrived at a significant moment in terms of public interest

in AI, but generative AI technology itself has much farther to go before it becomes fundamentally disruptive to industries like finance, media, education, and so on.

That said, there are industry niches where ChatGPT will start to have an immediate impact. Professionals have long used AI technology for spellchecking and grammar review of their emails. It's easy to envision that ChatGPT will quickly become a tool for drafting emails from a series of background information. Grammarly's recent product launch in this vein is likely just the first of many such in the upcoming months.

## Workflow integration

Behind the scenes, it's likely that ChatGPT will be integrated into workflow tools, such as the electronic health record (EHR) systems that hospitals use. Clinicians have to quickly assimilate a massive amount of information from EHRs about



their patients, including their medical history, comorbidities, genetics, and more when diagnosing them, and as patient volumes grow, the need to do this quickly rises in importance as well. In the same way that AI-based voice-to-text tools like Nuance helped transform how clinicians write up patient notes, ChatGPT will likely transform how they ingest info from EHRs. And there are places in the media landscape where ChatGPT will probably start to make an immediate (and possibly hidden) impact – with the volume of articles published on the internet always rising and the number of professional writers and journalists employed by newspapers, magazines, and other publications always shrinking, it doesn't take a lot of imagination to picture how some media organizations will look to square the circle.

But the deeper ramifications of ChatGPT will play out over a period of years, not months, as mature industries turn ideas into experiments, experiments into products, and products into markets. Healthcare software companies, like my own, will find ways to significantly accelerate their impact on patient outcomes and clinician education through generative AI, but will do it methodically and carefully, because they understand that the information and solutions they provide address matters of quality of life and even survival for patients around the world. As this dynamic plays out – as the potential of generative AI is filtered through the structural rigor and deep customer focus of companies that have decades of expertise and reputation in various professional markets – I'm confident we'll find that the net impact is quite positive.

### Credible concerns

It's not that the doomsayers don't have viable concerns. Of course, if students start to use AI to write their essays, then they won't actually learn. Of course, if medical textbooks are written with AI, they will be riddled with life-threatening errors. If

news articles are written only by AI, the scale of disinformation in the world will expand exponentially. We don't want any of those things.

But I think the structures that underpin most industries are robust enough to put necessary guardrails in place. Already, higher education institutions are experimenting with in-class essays, rather than take-home essays, to eliminate the role of ChatGPT, or are considering how to redesign curricula to place less emphasis on essays and more on dialogue and argumentation. Medical publishers are working with established technologies to develop tools that accurately identify when text is sourced from AI rather than a person. Disinformation is, sadly, a harder solve but the traditional companies through whom most people get their news will put rigorous editorial standards around their work – because their brand depends on it – and one can hope that social media companies will, under pressure from society and the government, turn the corner on emphasizing trust over scale. Overall, the doomsday scenarios are overblown.

### The butterfly effect


What is more worth thinking about are the surprising “butterfly effect” ways in which generative AI could spread its benefits across industries. One example, close to home for me, is medical research. Today, clinicians from every country in the world submit potentially significant research papers on medical topics ranging from obstetrics to oncology to prestigious journals, but the reality is that most published papers still come from the U.S., Europe, and China<sup>[1]</sup>. Why are so few papers published from outside of those regions? There are structural causes, of course, but a surprisingly big part of the reason why is the quality of English in many papers from outside of traditional research powerhouse countries. The inside baseball on this is that in some journals 50-70% of submit-

ted research papers are rejected by editors out of hand, independently of the quality of the research itself, because of the papers' poor English writing style (and English is the standard international language of medical communication).

Could generative AI help researchers from low- and middle-income countries turn viable research into professional quality papers that would stand a better chance of being accepted in prestigious journals? I think the answer is clearly yes – a recent study<sup>[2]</sup> indicated that 20% of researchers already access the previous generation of AI-enabled language improvement tools to improve the clarity of their research output --- and the result would be a material improvement not just in the global inclusiveness of medical research exchange but also in patient outcomes around the world, because groundbreaking clinical insights are not confined to a handful of countries. This is one potentially exciting example from my own space; experts in other spaces will I'm sure have comparable scenarios of their own.

When the smoke clears, I think we'll find that ChatGPT is, counterintuitively, more meaningful than its hype.

### The author

**Vikram Savkar** is the senior vice president and general manager for the Medicine Segment at Wolters Kluwer. In his role, Savkar leads product innovation to advance the digital evolution of information and productivity solutions for medical researchers, clinicians, medical students and faculty to inform evidence-based decisions on care and outcomes. He has been with Wolters Kluwer for ten years, serving as general manager for several businesses in the Legal & Regulatory division before joining the Health division. Prior to joining Wolters Kluwer, he held senior positions at Nature Publishing Group and Pearson Education. 

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# Target-Controlled Infusion anaesthesia: New more universal models



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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 pharmacodynamic (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 Remifentanyl is generally achieved with 3-6 ng/ml. A Remifentanyl 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 compart-

ment 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 Remifentanyl 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 de-

creasing 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 Remifentanyl, and the Kim-Obara-Egan Remifentanyl 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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