

Made to measure

The growing trend for wearable MRI

DOTAREM

Gadoteric acid

DOTAREM 0.5 mmol/mL, solution for injection. **Composition:** For 100 mL of solution: active ingredient: Gadoteric Acid 27.932 g corresponding to: DOTA 20.246 g corresponding to gadolinium oxide 9.062 g. **Indications (*):** Medicinal product for diagnostic use only: Magnetic Resonance Imaging for cerebral and spinal disease, diseases of the vertebral column, and other whole-body pathologies (including angiography). Dotarem should be used only when diagnostic information is essential and not available with unenhanced magnetic resonance imaging (MRI). **Posology and method of administration:** The recommended dose is 0.1 mmol/kg, i.e. 0.2 mL/kg in adults and children. The lowest dose that provides sufficient enhancement for diagnostic purposes should be used. The dose should be calculated based on the patient's body weight, and should not exceed the recommended dose per kilogram of body weight detailed in this section. In angiography, depending on the results of the examination being performed, a second injection may be administered during the same session if necessary. Angiography with Gadoteric acid is not recommended in children (0-18 years). In Encephalic and spinal MRI, in some exceptional cases, as in the confirmation of isolated metastasis or the detection of leptomeningeal tumours, a second injection of 0.2 mmol/kg may improve tumor characterisation and facilitate therapeutic decision making. For patients with impaired renal function and paediatric population (0-18 years) more than one dose should not be used during a scan, injections should not be repeated unless the interval between injections is at least 7 days. The product must be administered by strict intravenous injection. Depending on the amount of gadoteric acid to be given to the child, it is preferable to use gadoteric acid vials with a single use syringe of a volume adapted to this amount in order to have a better precision of the injected volume. In neonates and infants the required dose should be administered by hand. **Contraindications:** Hypersensitivity to gadoteric acid, to meglumine or to any medicinal products containing gadolinium. **Special warnings and precautions for use:** Dotarem must not be administered by subarachnoid (or epidural) injection. The usual precaution measures for MRI examination should be taken such as exclusion of patients with pacemakers, ferromagnetic vascular clips, infusion pumps, nerve stimulators, cochlear implants or suspected intracorporal metallic foreign bodies, particularly in the eye. **General particulars corresponding to all gadolinium contrast agents:** All gadolinium based contrast media can cause minor or major hypersensitivity reactions that can be life-threatening. These can occur immediately (within 60 minutes) or be delayed (within 7 days) and are often unpredictable. Because of the risk of major reactions, emergency resuscitation equipment should be available for immediate use. Hypersensitivity reactions can be aggravated in patients on betablockers and particularly in the presence of bronchial asthma. These patients may be refractory to standard treatment of hypersensitivity reactions with beta agonists. Impaired renal function: Prior to administration of gadoteric acid, it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests. There have been reports of Nephrogenic Systemic Fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with severe renal impairment (GFR < 30 ml/min/1.73 m²). As there is a possibility that NSF may occur with Dotarem, it should only be used in these patients after careful consideration. CNS disorders: As with other contrast agents containing gadolinium, special precautions should be taken in patients with a low seizure threshold. Precautionary measures, e.g. close monitoring, should be taken. All equipment and drugs necessary to counter any convulsions which may occur must be made ready for use beforehand. **Interactions with other medicinal products and other forms of interaction:** No interactions with other medicinal products have been observed. Formal drug interaction studies have not been carried out. **Fertility, pregnancy and lactation:** Gadoteric acid should not be used during pregnancy unless the clinical condition of the woman requires use of gadoteric acid. Continuing or discontinuing breast feeding for a period of 24 hours after administration of gadoteric acid, should be at the discretion of the doctor and lactating mother. **Effects on ability to drive and use machines:** No studies on the effects on the ability to drive and use machines have been performed. Ambulant patients while driving vehicles or operating machinery should take into account that nausea may incidentally occur. **Undesirable effects:** Uncommon ($\geq 1/1000$ to <1/100): hypersensitivity, headache, dysgeusia, dizziness, somnolence, paraesthesia (including burning sensation), hypotension, hypertension, nausea, abdominal pain, rash, feeling hot, feeling cold, asthenia, injection site reactions (extravasation, pain, discomfort, oedema, inflammation, coldness). Rare ($\geq 1/10\ 000$ to <1/1 000): anxiety, presyncope, eyelid edema, palpitations, sneezing, throat tightness, vomiting, diarrhea, salivary hypersecretion, Urticaria, pruritus, hyperhidrosis, chest pain, chills. Very rare (<1/10 000): anaphylactic reaction, anaphylactoid reaction, agitation, coma, convulsion, syncope, tremor, parosmia, conjunctivitis, ocular hyperaemia,

Stab

Upon the co
in order to r
gadoterate

Dotarem® s

- Macrocycli
- Patented n
- More than
- unconfoun
- No visible
- even in cas

Guerbet | 

 COMMITTED



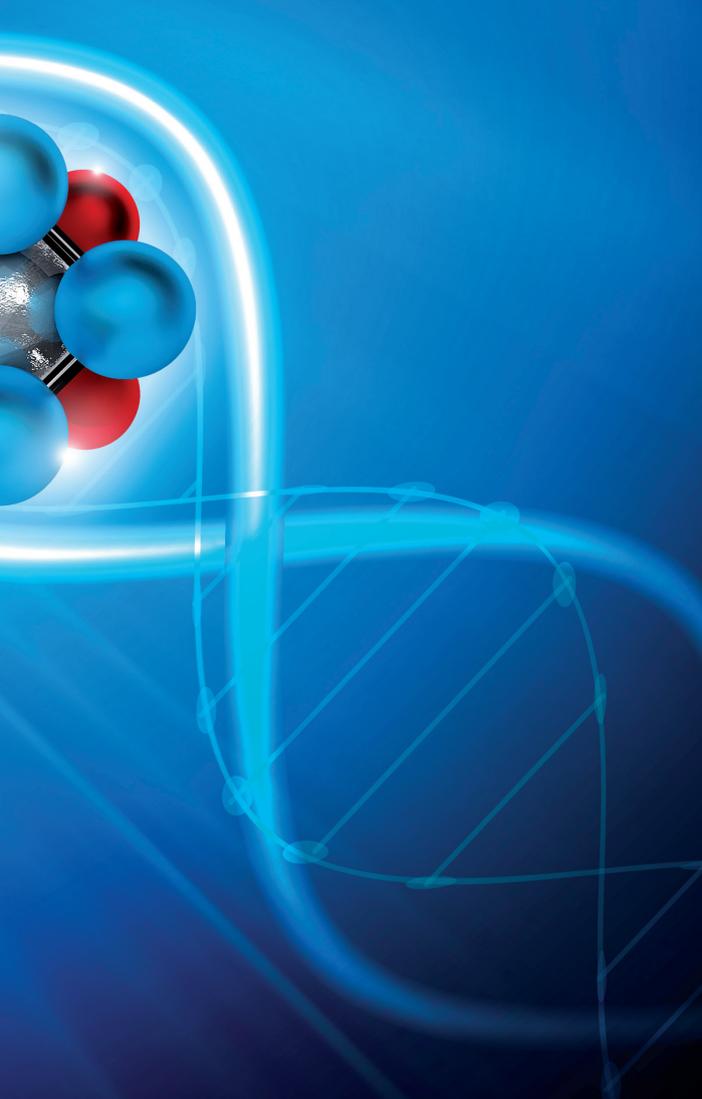
Stability is in its DNA

Conception of Dotarem[®], Guerbet's research team, minimize the release risk of gadolinium, designed the meglumine molecule to provide high chemical stability.¹

Shows a unique profile based on its original features: a cyclic & ionic molecule developed by Guerbet's researchers through a unique manufacturing process

Over 70 million global injections with zero confirmed neurological cases of NSF²⁻⁴

No brain hyperintensities related to dechelated Gd, even after multiple doses of repeated injections⁵⁻⁸



vision blurred, lacrimation increased, tachycardia, cardiac arrest, arrhythmia, bradycardia, flushing, pallor, vasodilatation, hot flush, cough, dyspnoea, nasal congestion, respiratory arrest, bronchospasm, throat irritation, laryngospasm, pharyngeal oedema, dry throat, pulmonary oedema, erythema, angioedema, eczema, muscle cramps, muscular weakness, back pain, arthralgia, malaise, chest discomfort, pyrexia, face oedema, injection site necrosis (in case of extravasation), phlebitis superficial, decreased oxygen saturation, Not known : nephrogenic systemic fibrosis. **Overdose:** Gadoteric acid can be removed by haemodialysis. However there is no evidence that haemodialysis is suitable for prevention of nephrogenic systemic fibrosis. **Please note:** The peel-off tracking label on the vials or syringes should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record. **Pharmacological properties:** Pharmacotherapeutic group: paramagnetic contrast media for MRI, ATC code: V08CA02. **Presentation (*):** 5, 10, 15, 20, 60 & 100 mL in vial (glass) and 10, 15 & 20 mL in a prefilled syringe (glass). **Marketing authorization holder: (*) Information:** Guerbet - BP 57400 - F-95943 Roissy CdG cedex - FRANCE. Tel: 33 (0) 1 45 91 50 00. **Date of revision of this document:** February 2018

For current and complete prescribing information refer to the package insert and/or contact your local Guerbet organization.

(*) Indications, presentations and marketing authorization holder may differ from country to country.

Reporting of suspected adverse reactions is important as it helps to continuously assess the benefit-risk balance. Therefore, Guerbet encourages you to report any adverse reactions to your health authorities or to our local Guerbet representative. Not intended for US healthcare professionals.

1. Meyer D et al. Gd-DOTA, a potential MRI contrast agent. Current status of physicochemical knowledge. Invest Radiol. 1988 Sep;23 Suppl 1:S232-5.
2. Internal data as of December 2017.
3. Dotarem[®] USA PI as of December 2017.
4. de Kerviler E et al. Adverse reactions to gadoterate meglumine: review of over 25 years of clinical use and more than 50 million doses. Invest Radiol. 2016 Sep;51(9):544-51.
5. Radbruch A et al. Gadolinium retention in the dentate nucleus and globus pallidus is dependent on the class of contrast agent. Radiology. 2015 Jun;275(3):783-91.
6. Eisele P et al. Lack of increased signal intensity in the dentate nucleus after repeated administration of a macrocyclic contrast agent in multiple sclerosis: An observational study. Medicine (Baltimore). 2016 Sep;95(39):e4624.
7. Radbruch A et al. No signal intensity increase in the dentate nucleus on unenhanced T1-weighted MR images after more than 20 serial injections of macrocyclic gadolinium-based contrast agents. Radiology. 2017 Mar;282(3):699-707.
8. Radbruch A et al. Pediatric brain: no increased signal intensity in the dentate nucleus on unenhanced T1-weighted MR images after consecutive exposure to a macrocyclic gadolinium-based contrast agent. Radiology. 2017 Jun;283(3):828-36.

INTEGRATED AND CONNECTED DIAGNOSTIC SOLUTIONS



Guerbet | 

COMMITTED

www.guerbet.com

On the web...

Keep up with the latest developments across the medical industry by visiting www.practical-patient-care.com



Medical Imaging Technology

Vol. 22 2018

EDITORIAL

Editor Emma Green

emmag@compelo.com

Chief sub-editor Thom Atkinson

Sub-editor Dale Hogan

Senior writer Greg Noone,

Feature writers Grace Allen, Tim Gunn

Production manager Dave Stanford

Group art director Henrik Williams

Designers Sandra Boucher

COMMERCIAL

Copy coordinator Melissa Parkinson

Sales manager Martin John

Business development manager Shamraiz Ayub

shamraiz.ayub@compelo.com

Head of sales Richard Jameson

Subscriptions marketing manager

Mariella Salerno

Publisher William Crocker



Medical Imaging Technology is published by Compelo, a member of the Audit Bureau of Circulations.

John Carpenter House, John Carpenter Street,
London, EC4Y 0AN, UK

Tel: +44 20 7936 6400 Fax: +44 20 7411 9800

www.compelo.com

www.practical-patient-care.com

ISSN 1757-5982 © 2018 Compelo. Registered in England No. 09901510. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, photocopying or otherwise, without prior permission of the publisher and copyright owner. While every effort has been made to ensure the accuracy of the information in this publication, the publisher accepts no responsibility for errors or omissions.

The products and services advertised are those of individual authors and are not necessarily endorsed by or connected with the publisher. The opinions expressed in the articles within this publication are those of individual authors and not necessarily those of the publisher.

SUBSCRIPTIONS

Single issue price: UK £31 EU €49 US \$65 RoW \$65

One year: UK £48 EU €76 US \$99 RoW \$100

Two year: UK £77 EU €120 US \$158 RoW \$159

Customer services: cs@compelo.com

Subscription hotline: +44 845 073 9607 (local rate)

Subscription fax: +44 207 458 4032

Address: Compelo Customer Subscriptions, Riverbridge House, Ground Floor, South Tower, Anchor Boulevard, Crossways, Kent, DA2 6SL

Printed by Stephens & George Print Group

Emma Green
Editor



Hot off the press

Medical imaging modalities are experiencing a period of rapid growth, having progressed from black and white to colour, from 2D to 3D – and most recently even 4D. They are becoming more powerful and able to diagnose and treat an increasingly wider range of diseases. These developments have occurred in parallel with the emergence of 3D printing and related technologies, which can transform medical imaging from the virtual to the physical. This evolution is thus changing not only the potential applications of imaging but also the nature of the technologies themselves.

Although such developments are hugely promising for medical imaging, they also bring a number of challenges to be navigated. They require additional knowledge and skills in order to be successfully implemented, potentially demanding an advanced or extended role for radiographers. An early adopter must invest heavily in its own development, as this expertise is likely to be soon incorporated into the normal medical imaging workflow, facilitating a new pathway of using 3D printing and related technologies as a further step to achieve

and maintain higher levels of patient care. These challenges are only going to increase in the next few years, demanding greater collaboration and discussion with individuals involved in all aspects of imaging. As the new editor of *Medical Imaging Technology*, I am hugely excited about driving these conversations forward. With a keen interest in the continual developments within the area, combined with a long-standing passion for the central role of publications, such as ours, in taking the lead in these important dialogues, it is a responsibility I do not take lightly.

In my role as editor, I will ensure that each and every edition combines analysis of current and future developments with insights from the industry's key figures to provide best practice and innovative solutions. This will help our readers continually evolve their patient-care strategies for the better, improving health outcomes while reducing costs. I hope you enjoy this issue and I look forward to meeting with many of our readers to also carry out these exciting and important discussions in person. In the meantime, I welcome your feedback on this issue and your ideas for future editions.



Also in this issue

Page 20: A look into 'X-ray-triggerable liposomes', a significant new development for cancer treatment.

Page 28: Results from the Tomosynthesis Mammographic Imaging Screening Trial to determine an industry standard.

Page 40: Leaders behind a new technique for 3D models of MRI and CT scans divulge about the approach.

Visit www.practical-patient-care.com

PHILIPS

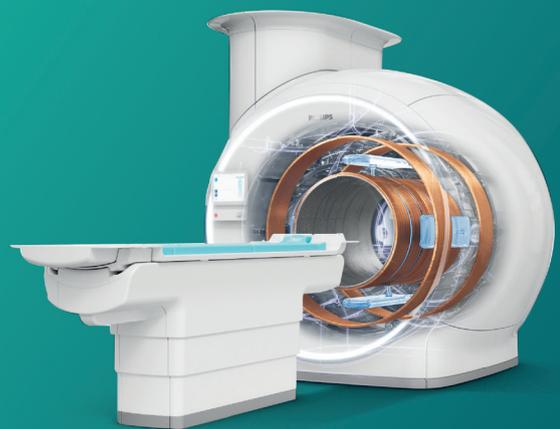
Ingenia Ambition 1.5T



MR services. Helium-free.

The Philips Ingenia Ambition offers cutting-edge MR imaging techniques to help you excel clinically every day. Based on its new, revolutionary fully sealed BlueSeal magnet, the solution lets you experience more productive¹ helium-free MR operations. Get superb image quality even for challenging patients, and perform your MRI exams up to 50% faster with Compressed SENSE acceleration for all anatomies in both 2D- and 3D scanning². Fast overall exam-time is achieved by simplifying patient handling at the bore with the touchless guided patient setup. There's always a way to make life better.

innovation  you



Discover our latest innovations at
www.philips.com/thenextmrwave

1. Compared to the Ingenia 1.5T ZBO magnet.
2. Compared to Philips scans without Compressed SENSE.

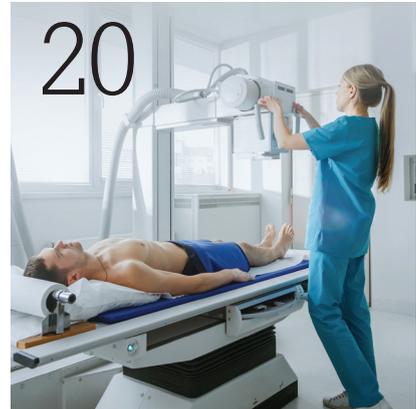
In this issue

Cover story

13



The potential of wearable MRI devices is deduced, in respect to 3D printing and sensor technology.



Lowering X-ray in cancer treatment for better results.



A potential new industry standard for mammography.

The intelligence

8 News

An update on the latest developments in the world of medical imaging.

12 The best of both worlds

The European Society of Radiology and GE Healthcare are partnering on artificial intelligence for the upcoming European Congress of Radiology, to be held on 27 February to 3 March 2019 in Vienna, Austria.

for wearable MRI devices. Paul Miller hears from research teams at NYU School of Medicine, the University of Nottingham, and University College London who are leading the charge.

17 Triumph in ambition

Philips

18 Brains behind the operation

Brainreader

activated by an X-ray. Tim Gunn takes a look at this procedure, which combines two cancer treatments with immense precision and has the potential to be more effective at lower doses than either could be on its own.

23 Innovative electronic X-ray ruler redefines precision

QUART

MRI

13 The start of something

Developments in areas such as 3D printing and sensor technology are ushering in a new era of MRI design, with two current projects highlighting the growing potential

20 A ray of hope

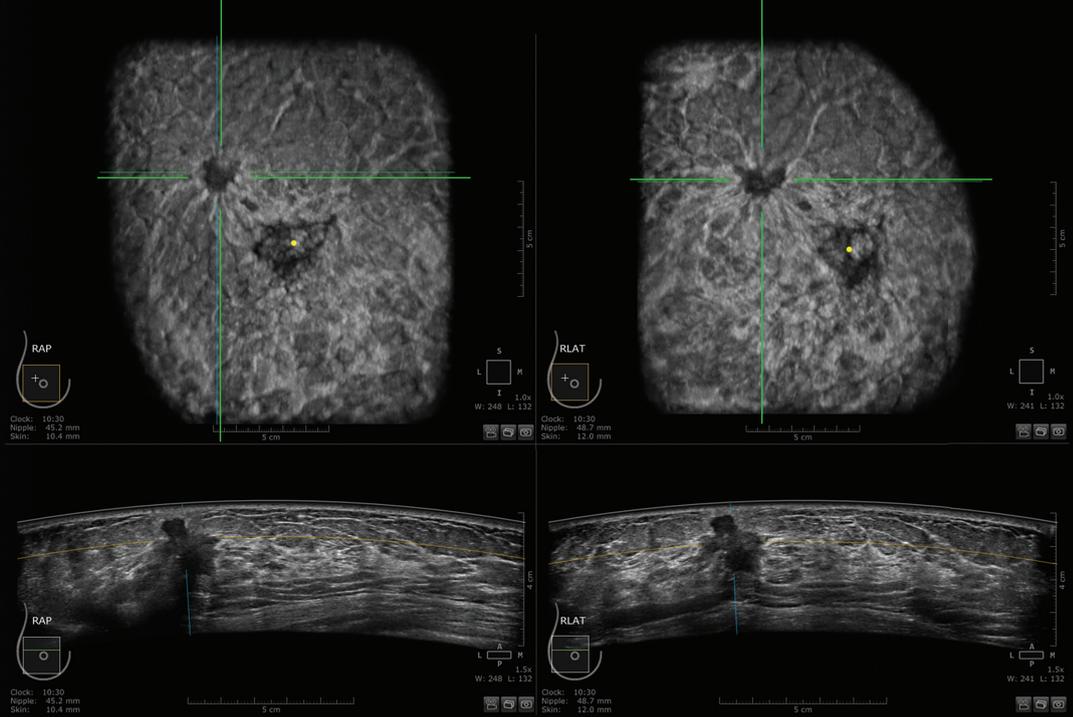
In a significant development for the use of X-rays in cancer treatment, a group of Australian scientists have engineered 'X-ray-triggerable liposomes'. These tiny bubbles, filled with chemotherapy drugs, are injected into the body and release their payload when

24 A scanner sharply

Despite widespread use, conventional ultrasound devices have their drawbacks – they are bulky and cannot be used in conjunction with other imaging modalities. University College London have developed an optical ultrasound imager

X-Ray

Ultrasound



Top portion of the image displays the coronal view of a biopsy proven invasive ductal carcinoma with multiple satellite lesions. Bottom portion of the image displays the axial view of the selected lesion. Location, size and depth of the lesion can be identified in relationship to skin surface, nipple or satellite lesions.

Designed to help find more cancer in dense breast tissue over mammography alone, Invenia™ ABUS provides a global view of the breast.

3D ABUS volumes enable full evaluation of the breast and the unique ability to interpret exams utilizing the coronal view. The reproducible, wide field-of-view acquisition method also enhances prior exam comparisons – including correlation of multi-modality breast exams.

Learn more about how Invenia ABUS is used to improve breast care for patients with dense breast tissue for screening, diagnostic and surgical applications.



GE Healthcare Call for Prospective Research Proposals

Four \$100,000 (USD) awards.
Deadline to apply is October 26, 2018

Visit <https://gex.brightidea.com/ABUSResearch>

Learn more



Contact your GE Healthcare Representative if you would like to arrange a demonstration. Contact us at www.gehealthcare.co.uk/contact_us.

Invenia ABUS is part of the GE Healthcare suite of personalized breast care solutions.

that can be used at the same time as an MRI scanner. *Medical Imaging Technology* gets an insight into its findings.

27 PC-based ultrasound scanners and OEM components

Telemed

Mammography

28 Take it to another dimension?

100 sites across the US are participating in a clinical trial to determine the best method of mammography. The Tomosynthesis Mammographic Imaging Screening Trial (TMIST) will compare 2D and 3D mammograms in a bid to determine whether the latter should be the industry standard.

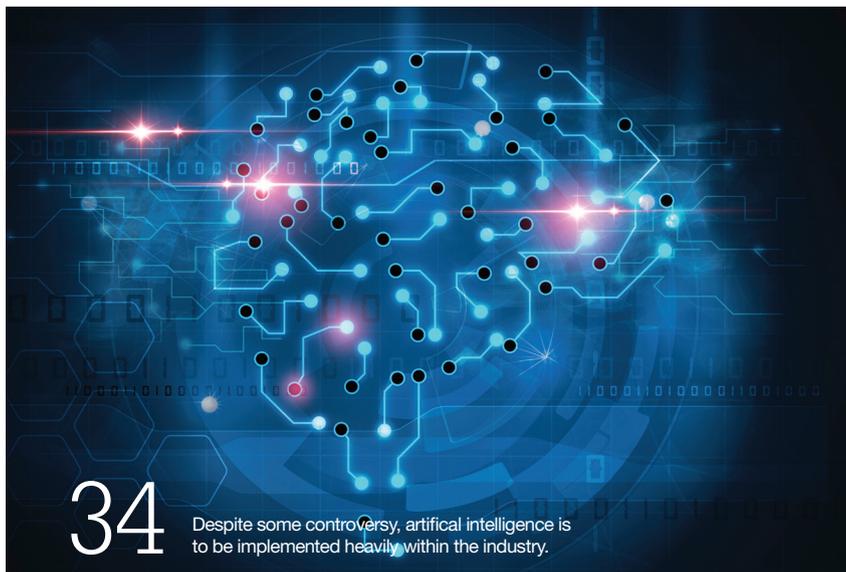
33 Reliable adjunct screening

GE Healthcare

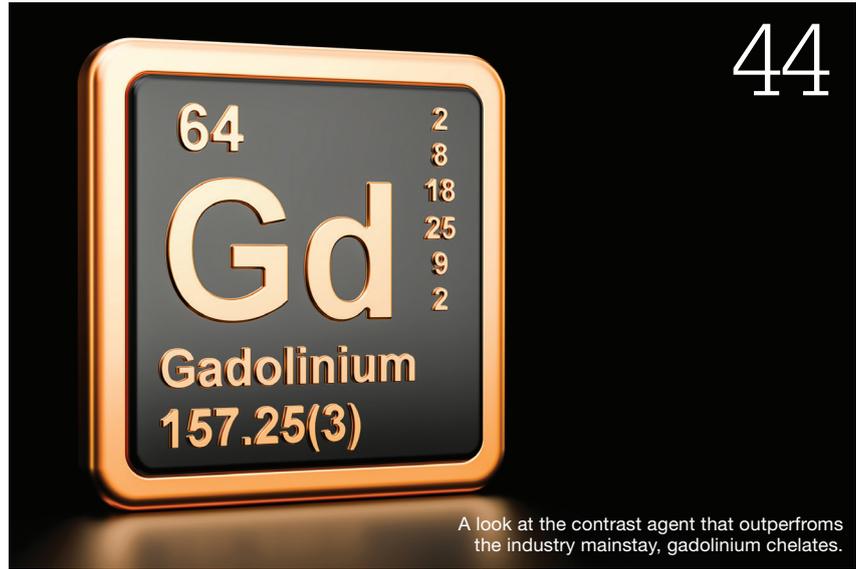
CT & PET

34 The future of discipline

Artificial intelligence is rapidly moving from an experimental phase to implementation in many fields, including medicine.



34 Despite some controversy, artificial intelligence is to be implemented heavily within the industry.



A look at the contrast agent that outperforms the industry mainstay, gadolinium chelates.

It is anticipated that the implementation of AI in the field over the next decade will significantly improve the quality, value and depth of radiology's contribution to patient care and population health, as well as revolutionise radiologists' workflows. Here, the Canadian Association of Radiologists ask how best we can handle the transition to standards.

39 Innovation is afoot

Planned

40 Fresh ideas

A new technique for quickly and affordably creating incredibly detailed 3D models of MRI,

CT and other scans promises to add significant value to the medical community and empower patients. Leaders behind the development speak to Lindsay Brownell.

Contrast agents

44 An air of distinction

Nanoscience at Rice University have demonstrated a method for loading iron inside nanoparticles to create MRI contrast agents that outperform gadolinium chelates, the mainstay contrast agent that is facing increased scrutiny due to potential safety concerns. James Sanderson hears from the team.

Dose management

48 Bit by bit

In ongoing efforts to reduce radiation exposure, how big a role might a new generation of radiation dose-monitoring software have to play? The UK's National Institute for Health and Care Excellence (NICE) has developed a Medtech innovation briefing, inviting input from industry specialists.

News



The Mariana project uses 3D ultrasound technology for improved navigation and control during lung biopsies.

Innovation award for ultrasound technology

A project that uses 3D ultrasound technology to develop more effective navigation and bronchoscope control when taking biopsies from the lungs has been given an innovation award at the recent Innovation Expo 2018 held in Rotterdam, in the Netherlands.

Named Mariana, the project is the result of collaboration between researchers and doctors at institutions including Norway-based independent research organisation SINTEF and

St Olav's Hospital in Trondheim. The technology has the potential to improve the diagnosis of lung cancer.

"We have collaborated to develop a system which improves navigation and our ability to reach the most deep-seated parts of the lungs. We are doing this by combining state-of-the-art tracking technology, cloud-based 3D image management technology and the design of controllable instruments," said Thomas Langø, senior research scientist at SINTEF.

A future for CT in the diagnosis of coronary heart disease

A trial conducted on behalf of the European Cardiovascular Research Institute (ECRI) has highlighted the potential of computer tomography as a diagnostic tool for coronary artery disease, possibly providing a non-invasive substitute for angiography.

The SYNTAX III trial featured 223 subjects with left main or three-vessel coronary artery disease; they first underwent an invasive angiography and then a multislice CT scan. Two heart teams (comprising a radiologist, an interventional cardiologist and a cardiac surgeon) made treatment recommendations, each team using only the angiography or the CT scan results. The trial showed a high overlap in treatment decisions between the two teams.

"The implications of these trial results for the future are tremendous," commented Professor Patrick W Serruys, the principal investigator and study chairman. "In the next five to ten years, with its increasing accuracy, I think we are going to see the new generation of multislice CT scans play an increasingly important role in diagnosing and treating CAD."

Test leads to improved assessment of mild cognitive impairment

Researchers at Boston University School of Medicine have created a framework using machine learning that uses models from medical imaging and neuropsychological testing to predict mild cognitive impairment (MCI), a symptom of Alzheimer's disease.

The researchers used data from 386 subjects with either normal cognition or mild cognitive impairment, all of whom had undergone the Mini-Mental State Examination (MMSE), the Wechsler Memory Scale (WMS) test and an MRI scan. The combination model was more successful than the individual models in predicting cognitive impairment, displaying an overall accuracy of higher than 90%.

"Our findings indicate that this framework can better predict MCI as it has the capability to combine needed information from multimodal data resource," said corresponding author Vijaya B Kolachalama, assistant professor of medicine.

PET/CT diagnoses better than biopsy

Pairing PET and CT has good diagnostic accuracy compared with temporal artery biopsy in patients newly suspected of having giant cell arteritis (GCA), according to new research findings.

GCA is a type of vasculitis, a disease involving blood vessel inflammation, most often in the arteries of the scalp and head – which is why it is also known as ‘temporal arteritis’.

PET/CT is often used for imaging of the aorta and primary arterial branches, but newer-generation scanning technology can also detect inflammation in the smaller temporal, occipital, maxillary or vertebral arteries.

Researchers in Australia conducted a new study to assess the accuracy of a PET/CT time-of-flight scanner compared with temporal artery biopsy (TAB) for the diagnosis of giant cell arteritis in suspected patients, showing that the PET/CT protocol has good diagnostic accuracy in patients suspected of having GCA.

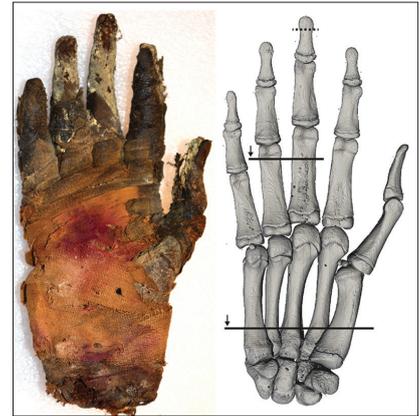
“Patients and their doctors increasingly seek non-invasive, timely, accurate and low-risk diagnostic tests. This is especially important for GCA, where symptoms are often non-specific, and a delay in diagnosis can lead to permanent vision loss,” said Anthony M Sammel, a rheumatologist at Royal North Shore Hospital in Sydney, and the study’s lead author.

“While temporal artery biopsy is well established for GCA, it can give a falsely negative result in a proportion of patients due to the small amount of artery that is sampled. Furthermore, biopsy is invasive and uncomfortable for patients, and may occasionally be complicated by bleeding, scalp and/or nerve damage. PET/CT is a non-invasive scan.”

Tomography technique used on mummified hand

Researchers at KTH Institute of Technology in Stockholm have used phase-contrast computer tomography to produce detailed images of the hand of a 2,400-year-old mummy. While the traditional CT scan techniques used on ancient remains make examining soft tissues difficult, the phase-contrast CT allowed the researchers to image blood vessels, nerves and layers of skin.

“Even though conventional CT has been used to study mummies since its invention in the 1970s, phase-contrast imaging had never been tried in this context,” said KTH doctoral student Jenny Romell, who conducted the research with colleagues. “The idea was to produce images with better contrast and higher resolution,



The scan offers improved soft tissue imaging, especially for the soft tissues of the ancient specimens.” Phase-contrast computer tomography is normally used in material science and biomedical research.

Lung cancer screening in London supermarket car parks

A pilot scheme aiming to increase the early detection of lung cancer is planned for London, with mobile CT scan units using new wireless technology to be set up in supermarket car parks in two London boroughs.

Funded by the NHS, the scheme is focused on current or former smokers between the ages of 60–75, and follows a similar programme established in Manchester. “What we are looking for is a complete change in

the landscape, something called a stage shift,” Dr Anand Devaraj, consultant thoracic radiologist at Royal Brompton Hospital and leader of the pilot, told London’s *Evening Standard*. “At the moment, large numbers of patients only present at stages three and four of the disease because the earlier stages can be asymptomatic. We are trying to increase the number that present at stages one and two, and screening can help achieve that.”

FDA to update mammography regulations

FDA is set to propose new regulations to improve mammogram quality, by taking new technology and updated screening recommendations into account, the agency has announced. It will be the first such reform in more than 25 years.

The aim is to improve the delivery of mammography services and allow more informed decision-making by strengthening the communication of breast density information.

FDA commissioner Scott Gottlieb, said the upcoming proposal takes into account “increased use of digital imaging devices, revised screening

recommendations from CDC and others, the need for more uniform, nation-wide breast density reporting in lieu of the patchwork of reporting requirements that has been implemented in various states, and the increasing clinical value of breast density information in informing medical practice and effective patient care”.

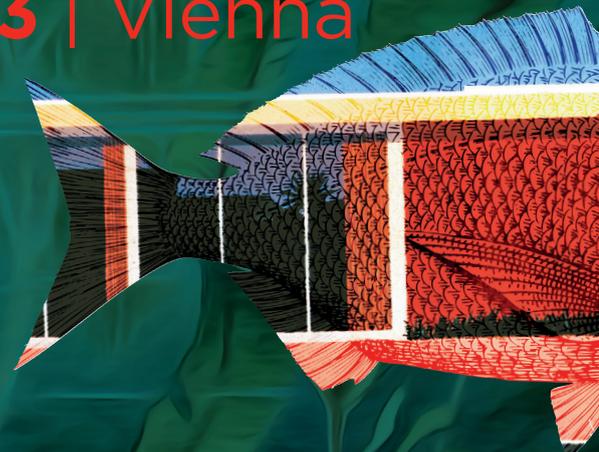
“We believe this proposal will have significant health benefits given its potential to provide women and healthcare providers with more consistent, comprehensive, scientifically relevant information about mammography results,” he added.



ECR2019

the bigger picture

February 27 – March 3 | Vienna

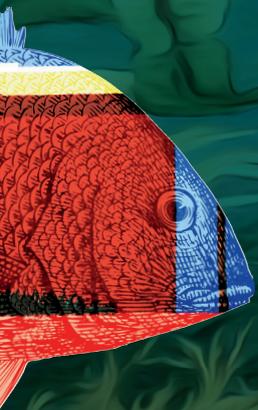


the annual meeting of

ESR
EUROPEAN SOCIETY OF RADIOLOGY



**REGISTER
NOW!**



myesr.org/registration

The best of both worlds

The European Society of Radiology and GE Healthcare are partnering on artificial intelligence for the upcoming European Congress of Radiology, to be held from 27 February to 3 March, 2019 in Vienna, Austria.

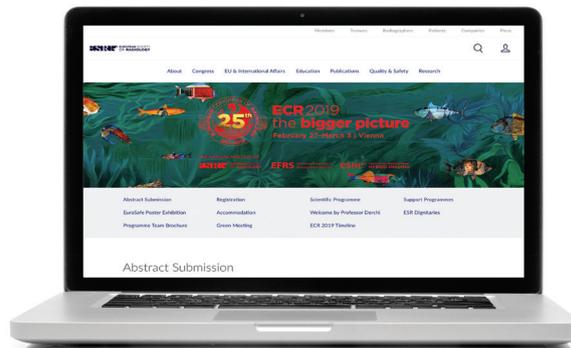
The partnership between the European Society of Radiology (ESR) and GE Healthcare is to include joint sessions on artificial intelligence and a 300m² dedicated space on GE Healthcare's 850m² booth, where visitors can experience the AI transformation through interactive tools.

The average hospital generates 50PB of data annually. This encompasses clinical notes, lab tests, medical images and genomics among much more. However, less than 3% of the overall amount of data is actually used. Artificial intelligence has the potential to make sense of the data and to generate actionable insights that would help improve provider efficiency, increase diagnostic accuracy, personalise treatment, improve patient experience and enable remote and predictive maintenance. GE Healthcare has over 200 imaging applications and is working with partners like Nvidia, Microsoft, Amazon and Intel to embed analytics, cloud capability and AI into devices, workflows and technologies already used by healthcare providers today.

Strength in numbers

The European Congress of Radiology (ECR) is the annual meeting of the ESR, which represents more than 82,000 members worldwide. The ECR is one of the largest medical congresses on the planet, attracting more than 28,000 congress participants. With 300 companies exhibiting, its one of the largest in Europe.

GE Healthcare is the \$19-billion healthcare business of GE. As a leading provider of medical imaging, monitoring, biomanufacturing, and cell and gene therapy technologies, GE Healthcare



The collaboration between GE Healthcare and ESR is sure to make ECR 2019 a landmark event.

enables precision health in diagnostics, therapeutics and monitoring through intelligent devices, data analytics, applications and services. The company boasts over 100 years of experience in the healthcare industry and more than

Genoa, Italy. "Through our joint efforts, congress participants will be able to witness AI excellence on the highest level, making next year's exhibition an event no one should miss," he concludes. "We are honoured to partner with the

“Through our joint efforts congress participants will be able to witness AI excellence on the highest level, making next year's exhibition an event no one should miss.”

- Professor Lorenzo Derchi, ESR

50,000 employees globally.

This reach helps improve outcomes more efficiently for patients, healthcare providers, researchers and life sciences companies around the world.

Combined force for good

"AI will be one of the leading topics at next year's ECR and this exclusive partnership with GE Healthcare is a major step in making ECR 2019 the leading event on artificial intelligence for radiologists and related medical professionals," says Professor Lorenzo Derchi, president of ESR, who hails from

European Society of Radiology for the leading European radiology event," says Catherine Estrampes, president and CEO of GE Healthcare (Europe). "AI is one of the most exciting developments in healthcare today and a key enabler to achieve precision health. Done right, it can be the technology of the decade, perhaps the century, in healthcare." But there's still much work to do. Sound data science and eliminating data siloes are absolutely key to eventual success. Europe and the European radiology community have a key role to play in the AI transformation. ■

The start of something

Developments in areas such as 3D printing and sensor technology are ushering in a new era of MRI design, with two current projects highlighting the growing potential for wearable MRI devices. Paul Miller hears from research teams at NYU School of Medicine, the University of Nottingham and University College London who are leading the charge.

Densely packed resonant structures used for magnetic resonance imaging (MRI), such as nuclear magnetic resonance phased array detectors, suffer from resonant inductive coupling, which restricts the coil design to fixed geometries, imposes performance limitations and narrows the scope of MRI experiments to motionless subjects.

Now, a new kind of MRI component in the shape of a glove promises to deliver the first clear images of bones

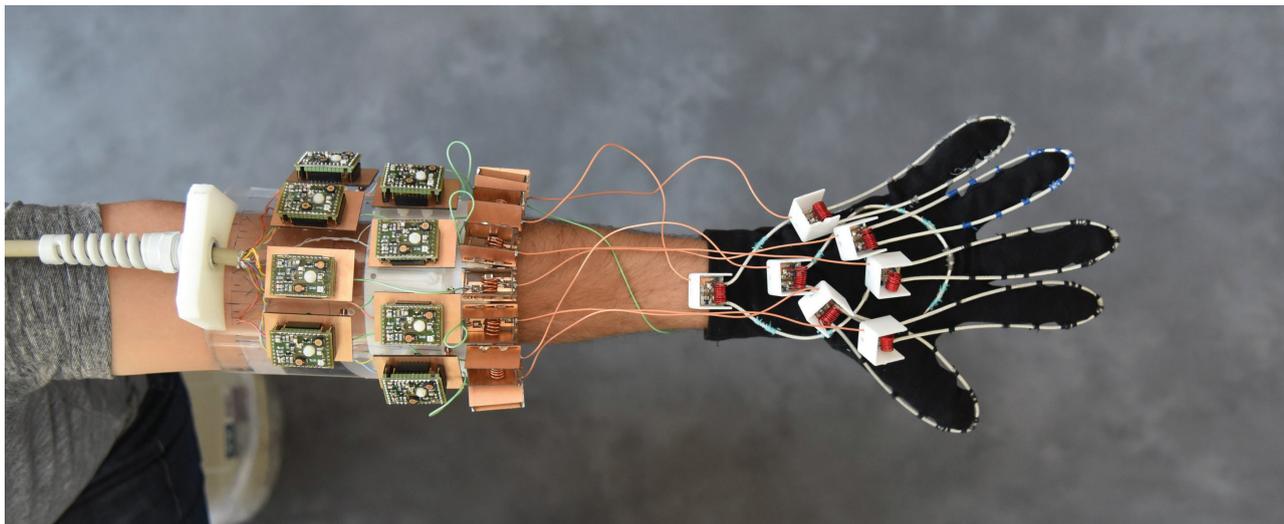
and ligaments moving together. Led by NYU School of Medicine and recently published in *Nature Biomedical Engineering*, the study shows how a new MRI element design woven into garment-like detectors can capture high-quality images of moving joints.

The study authors say their MRI glove prototype promises to become useful in the future diagnosis of repetitive strain injuries like carpal tunnel syndrome in office workers, athletes, and musicians. Because the

invention shows how different tissue types impinge on each other as they move, the team believes it could enable the construction of a more versatile atlas of hand anatomy, guide surgery with hand images in more realistic positions, or aid in the design of better prosthetics.

“Our results represent the first demonstration of an MRI technology that is flexible and sensitive enough to capture the complexity of soft-tissue mechanics in the hand,” says lead





Researchers have found that placing coils within cotton gloves allows impeccable images to be processed of muscles, tendons and ligaments in motion.

author Bei Zhang, research scientist at the Center for Advanced Imaging Innovation and Research (CAI2R), within the Department of Radiology at NYU Langone Health.

Past and current trends

Since its emergence in the 1970s, MRI has given physicians a better look inside tissues, helping to diagnose millions of maladies per year, from brain tumours to internal bleeding to torn ligaments.

The technology works by immersing tissues in a magnetic field such that any hydrogen atoms present align to create an average magnetic force in one direction in each tissue slice. These little magnets can then be tipped out of equilibrium by waves of electromagnetic force, or 'radio waves'. Once tipped, they spin like tops and emit radio signals, which reveal their positions and can be rebuilt into images.

Another factor that is fundamental to MRI is the ability of radiofrequency coils to convert radio waves into a detectable electric current. Despite this impact, the technology has long struggled with a basic limitation.

the captured 'spinning top radio waves' produce little currents inside receiver coils, which in turn create their own magnetic fields and prevent nearby coils from capturing clean signals.

Over the past 30 years, attempts to manage interactions between

neighbouring coils have resulted in state-of-the-art MRI scanners in which receiver coils are painstakingly arranged to cancel out magnetic fields in neighbouring coils. Once the best arrangement is set, coils can no longer move relative to one another, constraining the ability of MRI to complex, moving joints.

As all current MRI scanners measure signals that create currents in receiver coils (detectors), such coils have always been designed as low impedance structures that let the current flow easily. The leap made by the study authors was to design a high impedance structure that blocks current, and then measures how hard the force in magnetic waves pushes (the voltage) as it attempts to establish a current in the coil.

With no electric current created by the MR signal, the new receiver coils no longer create magnetic fields that interfere with neighbouring receivers, removing the need for rigid structures. The researchers found that their system, with the new coils stitched into a cotton glove, generated exquisite images of freely moving muscles, tendons and ligaments in a hand as it played piano and grabbed objects.

The MRI signal is produced by hydrogen atoms (protons), and so this technology excels at imaging soft tissue structures rich in water, each molecule of which includes two atoms of hydrogen. For this reason, MRI is

great at capturing muscles, nerves, and even cartilage, which are difficult to study using other non-invasive methods. Tendons and ligaments, however, which are made of dense proteins, remain difficult to see independently, because they appear as black bands alongside bone.

The next verb generation

The study found that, in visualising fingers as they flexed, the new coils revealed how the black bands moved in concert with the bones, which could help to catalogue differences that come with injury.

"We wanted to try our new elements in an application that could never be done with traditional coils, and settled on an attempt to capture images with a glove," says senior author Martijn Cloos, assistant professor from the CAI2R institute in the Department of Radiology at NYU Langone Health. "We hope that this result ushers in a new era of MRI design, perhaps including flexible sleeve arrays around injured knees, or comfy beanies to study the developing brains of newborns."

This movement towards wearable or mobile MRI devices is gathering pace elsewhere. In the UK, scientists have carried out the first study of human cognition using a new generation of brain scanner that can be worn like a helmet, marking an important step forward in the translation of their new technique from the laboratory bench to

a genuinely useful tool for cognitive neuroscience and clinical application. The study was undertaken in collaboration by researchers at the Sir Peter Mansfield Imaging Centre, University of Nottingham and the Wellcome Centre for Human Neuroimaging, University College London. It is part of a five-year Wellcome-funded project that has the potential to revolutionise the world of human neuroimaging.

Brain cells operate and communicate by producing electrical currents. These currents generate tiny magnetic fields that are detected outside the head. Researchers use magnetoencephalography (MEG) to map brain function by measuring these magnetic fields. This allows a millisecond-by-millisecond picture of which parts of the brain are engaged when we undertake different tasks, such as speaking or moving.

Here, subjects wearing the MEG scanner were shown nouns on a screen and told to think of related words without speaking. They were instructed to continue doing this until the word disappeared from the screen after a three-second period.

Each verb generation period was followed by a period of two seconds where the subject was asked to do nothing. Images captured exactly how the language network was engaged when subjects undertake the task.

"This is the first study of human cognition using this new scanner and it highlights this technology's potential as a tool for cognitive neuroscience," says Dr Matt Brookes, who leads MEG work in the School of Physics and Astronomy at the University of Nottingham. The study shows the potential of our system to improve the accuracy of surgical planning, via mapping eloquent cortex.

"If we can map, for example, the language network, then that will provide useful information for surgeons who may be planning resections in, for example, epilepsy. We hope the methods will be particularly beneficial for young children, who are often difficult to scan accurately using the fixed scanners which rely on the patient staying very still for long

periods of time. This therefore represents an exciting step forward as it demonstrates the utility of a new generation of wearable MEG sensors for cognitive and clinical neuroscience."

Potential in development

Conventional MEG scanners are large and weigh around 0.5t. This is because the sensors used to measure the brain's magnetic field need to be kept very cold (-269°C), which requires bulky cooling technology. With current scanners, the patient must remain very still while being scanned, as even a 5mm movement can make the images unusable. This means it is often difficult to scan people who find it hard to remain still, such as young children or patients with movement disorders.

The new OPM-MEG system uses quantum sensors, mounted in a 3D-printed prototype helmet. As the new sensors are very light in weight and can work at room temperature, they can be placed directly onto the scalp surface. Positioning the sensors much closer to the brain increases the amount of signal that they can pick up.

"From a neuroscience perspective, this work is very exciting as it allows us to study tasks that we could never have contemplated before with conventional

scanners where the head has to remain fixed," says Professor Gareth Barnes of the Wellcome Centre for Human Neuroimaging.

"For example, people interacting naturally or people navigating through virtual worlds and laying down memories. Importantly, we can do this throughout the lifespan—allowing us to understand how key functions like memory or language develop and how they degrade in dementia. We soon expect delivery of even smaller sensors, which we should be able to put within a bicycle helmet and we are building a new room where subjects are free to move around naturally. We will be able to allow people to interact with one another or within virtual worlds where we can study how they make decisions and lay down memories. This will mean we will be able to study natural human movement and how it is compromised in diseases, such as Parkinson's."

These projects remain at the developmental stage, but they clearly highlight the potential for smaller, wearable forms of imaging technology to transform what is possible in the imaging sphere. As more of these similar developments come to the fore, it is clear the trend is unlikely to go out of fashion any time soon. ■



The OPM-MEG system uses a 3D-printed helmet to place sensors closer to the patient's scalp.

PHILIPS

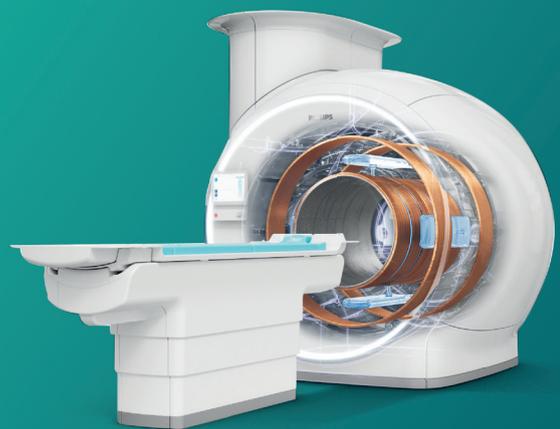
Ingenia Ambition 1.5T



MR services. Helium-free.

The Philips Ingenia Ambition offers cutting-edge MR imaging techniques to help you excel clinically every day. Based on its new, revolutionary fully sealed BlueSeal magnet, the solution lets you experience more productive¹ helium-free MR operations. Get superb image quality even for challenging patients, and perform your MRI exams up to 50% faster with Compressed SENSE acceleration for all anatomies in both 2D- and 3D scanning². Fast overall exam-time is achieved by simplifying patient handling at the bore with the touchless guided patient setup. There's always a way to make life better.

innovation  you



Discover our latest innovations at
www.philips.com/thenextmrwave

1. Compared to the Ingenia 1.5T ZBO magnet.
2. Compared to Philips scans without Compressed SENSE.

A triumph in ambition

Philips' healthcare division launches an industry first in its Ingenia Ambition 1.5T magnetic resonance system. The new solution combines fully sealed BlueSeal magnet technology and workflow innovations for a step change in productivity and helium-free operations.

The Ingenia Ambition 1.5T is the latest advance in the Ingenia MR portfolio, which comprises digital MRI systems, healthcare informatics, and a range of maintenance and life-cycle services for integrated solutions that aim to enable improved outcomes, lowered cost of care delivery and enhanced patient and staff experience. The first commercial installation of the Ingenia Ambition 1.5T was recently completed at Uster Hospital, a major provider of extended primary healthcare in the canton of Zurich, Switzerland. The Ingenia Ambition 1.5T is CE-marked and has received 510k clearance from FDA in the US.

Out with the old

The perception is often that MR represents a trade-off between productivity and image quality. The Ingenia Ambition 1.5T provides leading MR imaging capabilities while helping to increase overall productivity. It combines its revolutionary BlueSeal magnet with features that can help reduce downtime, enable single-operator workflow and speed up exam times with Compressed SENSE by up to 50% (compared to Philips exams without Compressed SENSE).

"MRI provides exceptional diagnostic and therapy guidance capabilities, but it also places substantial operational demands on the hospital or imaging centre. This is due to requirements for installation, footprint and service," says Arjen Radder, global business leader for MR at Philips. "BlueSeal is breakthrough MRI technology and we are proud to be first to market. The fully sealed magnet dramatically reduces the amount of liquid helium needed to cool to about seven litres. This results in significant operational benefits for our customers."

Practical makes perfect

Incorporating this breakthrough fully sealed magnet, the Ingenia Ambition 1.5T is the world's first MR system to enable helium-free operations, reducing the chance of potentially lengthy and costly disruptions, and virtually eliminating dependency on an unpredictable commodity. The fully sealed system does not require a vent pipe and is approximately 900kg lighter than its predecessor. This significantly reduces the siting challenges presented by conventional magnets and lowers construction costs.

"Our siting space was an issue, but fortunately the Ingenia Ambition 1.5T is well designed for this," says Dr Christoph Juli, CT and MR Lead, Uster Hospital, Switzerland. "From the first scan, we have been positively surprised by the field homogeneity and the quality of the images coming from the



Philips' groundbreaking BlueSeal technology is the world's first fully sealed magnet to enable helium-free operations.

Ingenia Ambition 1.5T. This new platform supports us everyday to deliver high quality MR services to both our referring physicians and patients."

The Ingenia Ambition 1.5T includes a range of features that combine to deliver a step-change in productivity. With Philips' EasySwitch solution, the BlueSeal's magnetic field can be easily turned off if an item is trapped in the bore.

“ This new platform supports us everyday to deliver high quality MR services to both our referring physicians and patients. ”

– Dr Christoph Juli, Uster Hospital

Once the problem is resolved, an in-house or Philips technician can initiate an automated ramp-up to bring the magnet back to field, minimising operational downtime.

Philips' Compressed SENSE is an advanced acceleration application that reduces exam times by up to 50%. In addition, Philips' VitalEye is a unique approach to detecting patient physiology and breathing movement.

VitalEye technology and algorithms intelligently extract signs of breathing – allowing routine exam set-up time to occur in less than a minute, even for less experienced operators. These allow clinicians to focus on the patient. ■

Further information

Philips
www.philips.com/ambition





Brains behind the operation

The challenges that the field of radiology currently faces are increasingly demanding. Namely, a shortage of radiologists, along with an increasing interest and use of MRI scans, creates ripples throughout the healthcare ecology. However, the Neuroreader software from **Brainreader** supports the subjective measurements of brain volume with quantifiable metrics, which allows greater efficiency in procedure.

The current shortfalls of the field of radiology affect radiologists, who primarily rely on the time-demanding processes of manual analysis of MRI scans and subjective measurement, but also referrals, such as neurologic and psychiatric practitioners, and purchase departments on administrative levels, as well as patients and their relatives.

Recent developments in neurological computer-assisted analysis could, however, prove a valuable tool in counteracting the current trends. By substituting subjective-based decision-making processes with quantifiable metrics for brain volume, radiologists may have found the tool to increase productivity, optimise distribution of resources, reduce subjectivity and establish a new standard of radiological reading ensuring greater assessment confidence. The effects of this could benefit not only radiologic practices but also those that are directly or indirectly affected by it.

Current challenges

In most countries, there is a shortage of radiologists to meet the ever-increasing demand for imaging and diagnostic services. Future prospects are not too bright, as imaging volumes are increasing at a faster rate than new radiologists are entering the field.

This results in a skewed distribution of the experience of the radiologists; with the majority of radiologists still pertaining to manual analysis of brain MRI analysis, a balanced distribution of resources is hard to obtain, especially for the younger and less experienced radiologists. The effects are also seen in more remote places, where there are often less radiological subspecialist experts, such as neuroradiologists.

The current challenges also stem from the fact that the field of neuroradiology still has not fully adopted the possibilities brought along by neurological computer-assisted analysis. Perhaps neuroradiology could seek inspiration from the field of mammography, which, within the past decade, has seen a steady increase in the use of computer-assisted analysis. Using automated techniques for the diagnosis and grading of breast cancer images has resulted in earlier detection of diseases and an improvement in survival rate.

Radiological best practice procedures, in terms of analysis and diagnosis, still rely heavily on individual experience and subjective measurements. As a result, radiologists cannot always fully exploit their expertise or quantify their results. The increased demand for radiological services, along with the global shortage of educated radiologists, means less time

for radiological coretasks, such as analysing and assessing brain MRIs and determining diagnoses.

For patients, the stakes are even higher, dealing with repeatable revisitations in the healthcare system. They also suffer from late detection and diagnosing of diseases, which makes treatment less likely to succeed and reduces the chances of recovery.

On a larger scale, continuous revisitations of patients affect the economic stability of the health system, causing higher costs for hospitals, insurance companies and purchase departments.

While the current state of affairs requires more than quick fixes, recent advances in neurological computer-assisted analysis may prove valuable in mitigating a number of challenges by optimising and supporting radiologic resources and work processes.

Mitigating challenges

Computer-assisted analysis of brain MRI scans aims at releasing the full potential of MRI scans by providing a better decision-making foundation for radiologists. Software tools, such as Danish Neuroreader, support subjective measurements of brain volume with quantifiable metrics, thereby supporting a more holistic and objective assessment. Neuroreader enables radiologists to compare readings with images and outcomes of similar cases, ensuring a decision-making foundation independent of individual experience.

“Neuroreader gives us easy, reliable, reproducible volume measurements and takes the guesswork out of analysing structures in our patients’ brains,” says Professor Barton Branstetter, from the University of Pittsburgh Medical Center.

The ability to compare readings makes it easier for the radiologist to direct attention to specific areas of interest. This allows a swifter and more effective analysis, with a more knowledgeable and precise focus. For radiologists, this could mean a reduction of the need for second opinions and second-guessing, thereby increasing productivity and optimising workflow.

Leading the pack

“Neuroreader stands out from the crowd by its comprehensive approach, as it performs a fully automated analysis of 45 visually identifiable brain structures in ten minutes,” says Professor John L Ulmer, from the Medical College of Wisconsin. “This enables the analysis of patterns of neurodegeneration in patients with MCI. Significant diagnostic benefits have already been realised, such as earlier detection of disease, supporting clinical diagnoses, and the subsequent coherent and more personalised treatment plans.

“Neuroreader has established itself as an essential diagnostic aid in our memory disorders programme. It may also have positive implications for patients depending on radiologic services, as well as those neurologic and psychiatric practitioners who interact with the patients on a regular basis. Finally, the healthcare purchase departments that pay for the services may experience positive consequences,” he concludes.

For patients, an early and correct diagnosis is naturally essential, promising fewer revisitations in the healthcare system and, ultimately, better chances of recovery and maintenance of life quality for as long as possible. Computer-assisted brain MRI analysis software points to a potential near future where patients, as well as their physicians, are provided with the possibility to track individual health development over time. In turn, patients may have a more complete understanding of their health situation, in the case of negative and positive changes. In this sense, computer-assisted brain MRI analysis software could have a health-promoting angle, assuring patients if nothing is wrong or building motivation in showing that efforts to stabilise or reverse symptoms are paying off.

“Neuroreader has established itself as an essential diagnostic aid in our memory disorders programme.”

– Professor John L Ulmer, Medical College of Wisconsin

For the neurologist or psychiatrist, computer-assisted analysis of brain MRI scans could, among the already mentioned benefits, also prove valuable as a communication frame for conveying technical information to patients and relatives about their health development over time. One could imagine visual representations of, for example, hippocampus growth or regress being used as a concrete and tangible tool in demonstrating current disease or health development to patients.

Finally, hospital administration or purchase departments could benefit from the advances made with computer-assisted brain MRI analysis software. Higher productivity, efficiency and accuracy in brain MRI analysis could amount to reduced costs in terms of less revisitation of patients and a higher number of referred patients to the clinic or hospital due to positive reputation and strengthened image. Brain MRI analysis software, such as Neuroreader, can be applied regardless of the individual radiologist’s experience level. This could allow a more nuanced hiring policy where younger radiologists could execute tasks that were previously reserved for more experienced physicians.

The field of radiology is, like everything else, always evolving alongside technological developments. The current challenges require the best from all radiologists, and radiologists should therefore also be supported in the best possible way.

A tight integration of computer-assisted brain MRI analysis software, such as Neuroreader, in radiologic processes may be the next natural step that the field should take. ■

Further information

Brainreader
<https://brainreader.net>



A ray of hope

In a significant development for the use of X-rays in cancer treatment, a group of Australian scientists have engineered 'X-ray-triggerable liposomes'. These tiny bubbles, filled with chemotherapy drugs, are injected into the body and release their payload when activated by an X-ray. Tim Gunn takes a look at this procedure, which combines two cancer treatments with immense precision and has the potential to be more effective at lower doses than either could be on its own.

For almost as long as doctors have known about X-rays, they have been using them to treat cancer. Although Emil Grubbe pioneered radiotherapy after observing its damaging effects on his skin, he thought that damage was superficial, something cleared up with little more than petroleum jelly and time. By contrast, chemotherapy did not figure

in treating the same conditions until its associated dangers were indisputable. It took the horror wrought by chemical weapons in the First World War, and the study of their effects in the Second World War, for scientists to realise the breakthrough chemical treatments heralded in their ongoing battle with cancer.

Now, researchers at Australia's ARC Centre of Excellence for Nanoscale BioPhotonics have developed a method to deliver chemotherapy drugs with 'X-ray-triggerable liposomes', combining the two treatments in a way that can increase their effectiveness and minimise their side effects.

"Our method makes it possible to perfectly synchronise both treatments



so they can be given simultaneously,” explains Ewa Goldys, a senior researcher on the project. “This enables enhanced therapeutic outcomes with potentially reduced doses of drug and/or radiation required because of this exquisitely precise timing of drug release.”

As the team’s research paper – ‘Controlled gene and drug release from a liposomal delivery platform triggered by X-ray radiation’, published in *Nature Communications* – rather less elegantly recommends, “From a clinical point of view, it would be beneficial to have access to this multimodality treatment, given our evidence of better therapeutic effect (or, potentially, equal therapeutic effect) at diminished toxicity, in the case when single modality treatment options alone can only produce desired therapeutic effects at a significant cost of short and long-term toxicity.”

The key ingredients

Injectable liposomes are the most established nanomaterial vehicles for targeted drug delivery. As the name indicates, their aqueous core is surrounded by a lipid bilayer, which facilitates cellular uptake of the liposome’s content due to its similarity to cell membranes. Biocompatible, biodegradable and able to isolate hydrophilic and hydrophobic drugs from the surrounding environment, liposomes are extremely well-qualified drug delivery systems. In fact, one of their few limitations is the lack of tuneable triggers they offer to control drug release. That is precisely the issue this research solves.

“We have ensured that the liposomes release their drug payload at exactly the right time and in exactly the right place to ensure the most effective treatment,” explains Dr Wei Deng.

Whereas previous triggering approaches have made liposomes sensitive to changes in pH, externally applied heat, or light, Deng’s team attuned their liposomes to react to X-ray radiation using gold



Researchers at the ARC Centre of Excellence for Nanoscale BioPhotonics in Australia have developed a new method of delivering chemotherapy drugs with ‘X-Ray-triggerable liposomes’.

nanoparticles and the photosensitive molecule verteporfin (VP).

“The radiation from the X-ray causes the verteporfin to react and to produce highly reactive singlet oxygen (1O_2) that then destabilises the liposomal membrane, causing the release of the drug,” Deng explains. “The gold nanoparticles are added into the mix as they focus the X-ray energy. This enhances the singlet oxygen generation and hence improves the speed of the membrane break-up.”

More specifically, gold reacts so strongly with X-rays that gold nanoparticles are highly effective ‘radiosensitisers’ able to amplify the radiation doses in tumour tissue. As the paper highlights, these nanoparticles can also “selectively scatter or absorb the high-energy X-ray radiation, leading to enhanced energy transfer from X-ray to photosensitisers. With such contribution, the VP molecules in the presence of gold nanoparticles are able to interact more strongly with ionising radiation than the VP on its own, causing enhanced 1O_2 generation”. As such, the team’s tests demonstrate that liposomes ‘doped’ with gold nanoparticles and VP molecules aid drug delivery by generating by far the highest amounts of destabilising 1O_2

under X-ray, approximately 79% more than unenhanced liposomes.

Target cancer

So much for the mechanism; all that 1O_2 generation is only relevant as far as it impacts treatment. As Deng indicated above, the destabilising effect works to release an antisense oligonucleotide for gene silencing and the chemotherapy drug doxorubicin (Dox) from inside the liposome (LipoDox). When used for in-vitro testing, the effects were dramatic. Without X-ray triggering, the LipoDox was found to kill about 10% of human colorectal cancer cells. When it was triggered, however, that proportion rose to 50%. Equally encouraging is the fact that assessments of X-ray-induced damage in genetic materials indicated that the levels of X-ray radiation and doxorubicin did not cause obvious damage to DNA molecules.

Similarly, once released, the antisense oligonucleotide prevented the translation of the PAC1R mRNA by blocking the translation initiation complex, thus helping to stop the cancer spreading. Its effects were less pronounced – but still notable. 24 hours after X-ray exposure, the density of PAC1R decreased by around 45%, compared with a 30% decrease in cells that received the liposomes without X-ray triggering. >>

If anything, the results of in vivo tests were even more impressive. Whereas bowel tumours in mice treated with liposomes and X-rays grew by 2.9-fold and 3.4-fold respectively in the two weeks after treatment, in the group treated with X-ray-triggered liposomes the tumours actually shrunk. There was a 74% reduction in tumour volume compared with the control group, and the X-ray-triggered liposome treatment also achieved the largest amount of tumour necrosis.

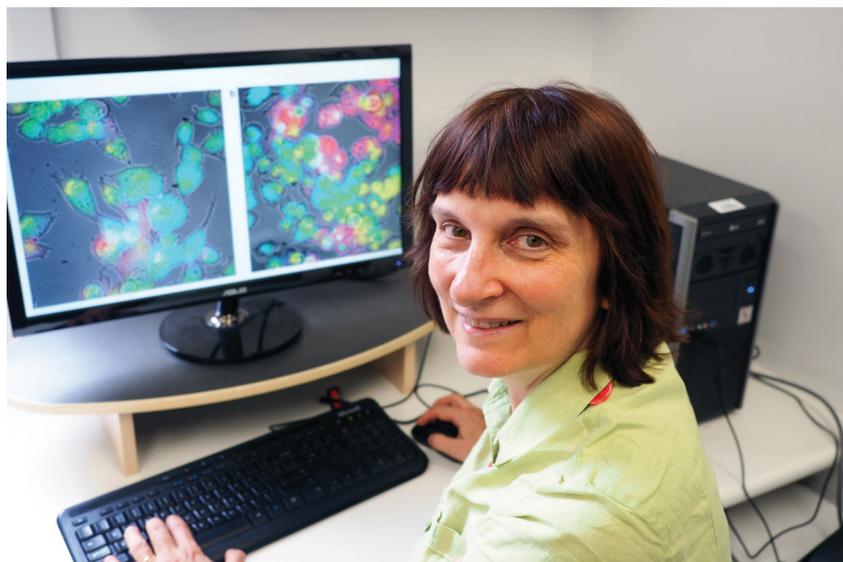
Moreover, no mortality was observed during 14 days after treatment with X-ray-triggered liposomes, and no weight loss of treated mice was observed compared with the control, suggesting that this combined technique is well tolerated by mice under the present conditions. If she was not a doctor, Goldys' assertion that this is an extremely encouraging result might be considered an understatement.

Minimise side effects

Of course, there are reasons for the research team to remain level-headed – no cancer treatment is without its side effects. It took time, but the pioneers of X-ray gradually came to realise that the radiation they worked with had the potential not merely to fight the condition, but cause it. The first related death took place nine years after X-rays were discovered. Charles Madison Dalley was Thomas Edison's glassblower. Both of his arms were amputated in a futile attempt to stop his cancer spreading before it killed him at 39.

In 1951, the radiotherapy pioneer Grubbe was asked to move out by his landlord: he had been so disfigured by X-ray-related facial tumours that he was scaring away other tenants. The side effects of chemotherapy are less ghoulish, but we are all aware of the difficulty of dealing with the hair loss, exhaustion, nausea and vomiting, to name just a few of its debilitating impacts.

In the case of X-ray-triggerable liposomes, one of the most troubling possible dangers is the fact that simultaneous chemo and radiotherapy may result in damage to the heart. This



The common use of VP, lipids, Dox and X-rays in tumour treatment suggests that using X-ray-triggerable liposomes to deliver drugs should work effectively in the clinical context.

fact prompted the team to test the same approach using the chemotherapy drug etoposide (ETP), which is associated with reduced incidence of cardiotoxicity, instead of Dox. These tests also indicate that chemotherapy drugs are more effective when triggered with X-ray radiation.

Similarly, the harmful effects of singlet oxygen – the primary cytotoxic agent released as part of this drug delivery technique – are limited by its short lifespan, which means it cannot travel beyond a very limited area. On top of that, the reaction by which the $^1\text{O}_2$ destabilises liposome membranes consumes $^1\text{O}_2$ radicals, further minimising any adverse effects.

Although the common use of VP, lipids, Dox and X-rays in the treatment of tumours suggests the strategy of using X-ray-triggerable liposomes to deliver drugs should translate well to the clinical context, gold nanoparticles are not yet approved by all regulatory agencies. Even so, the study notes that the size of gold nanoparticles is compatible with the requirements of renal clearance, which means that long-term nanoparticle toxicity is likely to be minimised, if not eliminated, as the body flushes them out. Tumour-specific targeting ligands could also be grafted onto the particles, ensuring they interact with the tumour without coming into contact with the rest of the body. In fact,

the paper makes clear that “the ease of conjugation of targeting ligands to liposome surface with appropriate linkers would be an added advantage when applied to the targeted therapy, in particular for tumour treatment”.

Future modalities

The team is now working to further optimise the X-ray-triggered liposomes while they scale up their processes and develop the clinical protocols necessary to get clinical approval for their first in-human trials.

As with almost all cancer treatments, it feels like that approval can't come soon enough. An estimated 9.6 million people will die from cancer in 2018. By 2030, that number is predicted to reach 13 million. Even more monumentally, statistics suggest that half of all people in the UK will get cancer in their lifetime. Appropriately, then, the crux of Deng and Goldys' work is that combinatory cancer treatments have a better therapeutic effect than single-modality approaches, as they make it possible to cure or manage cancers while doing far less damage to the patient's quality of life. Beyond that, however, their approach shows an elegant genius in finding a specific meeting point for two modalities. Humanity has come a long way from the hideous, tragic beginnings of chemotherapy and X-ray use. ■

Innovative electronic X-ray ruler redefines precision

QUART, a leading German X-ray QA solution specialist, has debuted an innovative ruler set to imbue the industry with a new benchmark for efficiency and accuracy.

X-ray QA solution specialist QUART has introduced an electronic X-ray ruler with enhanced features. The new and improved QUART nonius ruler now provides added measurement capabilities for user benefit and increased labour efficiency.

The QUART nonius is an easy-to-use but sophisticated measuring instrument to verify size and geometrical properties of X-ray fields in radiography, fluoroscopy and CBCT. It analyses characteristics of fanned X-ray beams as used in CT or dental panoramic X-ray. The device can be applied with digital and conventional X-ray applications. In any case, its precision is an absolute strong point – as it is accurate to 0.1mm.

Originally, screen-film was used for checks on X-ray beam properties. But digitisation in X-ray technology makes traditional screen-films less available. Here, the QUART nonius is able to step in. Yet, it provides even more substantial features, such as verification technology that ascertains if the light visor matches the actual radiation field.

That applies to radiology or fluoroscopy application including CR or DR mammography. It can verify a concentric radiation field in a dental intra-oral tube beam applicator. Moreover, the nonius provides the option to assess the position of a fanned beam relative to the image receiving detector or verify the nominal width to the total width of a fan beam as used in dental panoramic or CT X-ray modalities.

Added value of the device is provided by its graphic user interface (GUI). As the device is coupled up to a Windows operated laptop or tablet, measured data is displayed as radiation profile of an edge or a waveform. The powerful nonius software incorporates a database feature to add and manage customer data, and to create automated protocols to follow soft or hard-copy requirements. ■

Further information

QUART
www.quart.de



30+ Years of Innovation for X-Ray Quality Control and Service

QUART
Quality Assurance in Radiological Technologies

X-Ray Control Instrumentation
X-Ray Phantoms + Test Objects
Dosimetry Items + Accessories

made
in
Germany



www.quart.de

QUART GmbH • Kirchenweg 7 • D-85604 Zorneding • Germany • Phone: +49(0)8106/249118 • Skype: quartxrayqc • info@quart.biz



A scanner sharply

Despite widespread use, conventional ultrasound devices have their drawbacks – they are bulky and cannot be used in conjunction with other imaging modalities. Now a research team from University College London have developed an optical ultrasound imager that can be used at the same time as an MRI scanner. This could enable true multimodal imaging, with versatile low-cost components. Here, *Medical Imaging Technology* present an edited extract of their findings.

All-optical ultrasound is an emerging imaging modality that shows great promise for biomedical imaging. With this modality, optically absorbing structures convert pulsed or modulated light into ultrasound via the photoacoustic effect. Compared with conventional electronic systems comprising piezoelectric or capacitive ultrasound transducer elements, optical transducers have been shown to yield similar or higher pressures and bandwidths.

The researchers present a new paradigm for all-optical ultrasound

imaging that enables real-time, video-rate 2D imaging at a frame rate of 15Hz.

Whereas electronic transducer elements are defined through electrode patterning or physical separation, in this work optical ultrasound sources are shaped and positioned by means of optical confinement achieved using lenses and scanning optics.

This allowed the synthesis of dynamically reconfigurable source arrays of arbitrary geometry, thus enabling 1D source arrays exhibiting non-uniform source spacing and reduced image artefacts. In addition, a combination

of innovations was used to achieve a sensitivity suitable for imaging weak reflections from deep within biological tissue in real time. Among these innovations were a centimetre-scale ultrasound generation surface comprising carbon nanotubes and an elastomeric polymer that was suspended in free space, eccentric optical excitation achieved through the use of cylindrical optics and a high-finesse Fabry-Pérot cavity for ultrasound reception. The sensitivity of the system was demonstrated on different biological tissues, with its real-time dynamic capabilities demonstrated

through the imaging of pulsating blood vessel sections and acoustic contrast agent injections.

Potential to overcome all possible limitations

In this work, an all-optical ultrasound imaging paradigm is presented that allows real-time, video-rate 2D imaging of soft tissue. This was achieved through the use of an optical ultrasound generator, a highly sensitive fibre-optic receiver, eccentric illumination resulting in acoustic sources exhibiting constrained acoustic radiation patterns, a modest excitation pulse repetition rate and pulse energy, fast sequential scanning of a source aperture using a galvo mirror exhibiting low inertia, source arrays exhibiting non-uniform source spacing and partially overlapping sources.

A wire phantom was used to determine the resolution of the system (axial: 75µm, lateral: 100µm), and the penetration depth (up to at least 6mm) and dynamic range (up to 30dB) were determined using tissue samples. In addition, the high frame rate (15Hz) was used to capture the dynamics of a pulsating vessel phantom and the injection of an acoustic contrast agent.

All-optical ultrasound has the potential to overcome several fundamental limitations of its electronic counterparts. Electronic ultrasound transducers typically derive their sensitivity from mechanical resonance at a fixed frequency and bandwidth, resulting in a fixed spatial resolution and penetration depth. In addition, electronic ultrasound imaging probes typically comprise transducer elements that are spatially fixed and arranged in a periodic array, which can result in image artefacts.

As a result, electronic imaging probes are optimised for specific applications, and typically multiple probes are required for versatility. In contrast, optical ultrasound sources do not rely on resonance, and hence can be tuned to either high-resolution imaging or large imaging depth through temporal modulation of the excitation light. In addition, the position and spatial confinement of

optically generated ultrasound sources can be varied dynamically using optical methods to avoid imaging artefacts and tailor the source aperture to a wider range of applications.

Compared with conventional ultrasound imaging arrays comprising piezoelectric or capacitive transducers, the all-optical ultrasound set-up achieved a lower dynamic range of 30dB that was limited by comparatively high image artefact levels and relatively low signal-to-noise ratios.

Improve the dynamic range

The image artefact levels were due to the use of a low number of acoustic sources and a single receiver, combined with the delay-and-sum image reconstruction algorithm, and could be reduced in various ways. First, multiple fibre-optic ultrasound receivers can be distributed across the aperture.

“ In this work, an all-optical ultrasound imaging paradigm is presented that allows real-time, video-rate 2D imaging of soft tissue. ”

This is similar to conventional electronic linear arrays comprising a multitude of electronic transducers that can each transmit and receive acoustic signals. This way, the back-scattered acoustic field can be recorded in multiple locations in parallel, resulting in the detection of a larger fraction of the back-scattered energy at the same frame rate. This will decrease the artefact levels and alleviate the observed limited-view artefacts, at the expense of a significant increase in complexity.

Second, subsequent ultrasound sources can exhibit spatial overlap without exhibiting cross-talk, and an arbitrary number of sources can be positioned within the aperture. Consequently, the image quality could be improved by using more source locations. However, currently the image acquisition and reconstruction rate is limited by the computational cost of the reconstruction and the inertia of the galvo mirror, and hence faster mirrors

(for instance resonant galvo mirrors) and parallelised reconstruction algorithms would be required to accommodate the higher pulse repetition rate required to maintain high frame rates.

Third, the artefact levels could be further reduced by implementing different source density apodisation (SDA) schemes. While the schemes studied in this work achieved a significant improvement in image quality, alternative SDA schemes might yield even further improvements. Further research is required to determine the most effective SDA schemes.

Finally, different image reconstruction algorithms that better exploit the spatial coherence of consecutive A-scans, such as delay, multiply and sum (DMAS) or short-lag spatial coherence (SLSC), might result in reduced artefact levels.

The dynamic range of the images could be improved further by increasing the signal-to-noise ratio of the data.

It has previously been shown that the presence of a rigid backing can improve the efficiency of optical ultrasound sources, thus improving the A-scan signal-to-noise ratio. However, the presence of a rigid backing introduced spurious ringing artefacts that decreased the acoustic bandwidth and the image quality; hence, in this work, an ultrasound-generating membrane was suspended in free-space.

Alternatively, increasing the optical fluence would result in larger pressures to be generated in the ultrasound-generating membrane. However, as the fluence used in this work (38mJ/cm²) approached the damage threshold of the membrane (approximately 175mJ/cm²), the pressure increase achievable using a pulsed light source is limited.

However, alternative optical excitation schemes, such as coded excitations or temporally modulated pulses, could be employed to deliver more optical energy over an extended period of time without



Multimodal imaging is just one of several benefits of the new approach to ultrasound.

exceeding the optical damage threshold. The optical ultrasound sources distributed across the source aperture were found to consistently generate a wide bandwidth ranging 4–31MHz. However, the lateral extent of the sources ($224 \pm 53\mu\text{m}$) was too large to fully exploit this bandwidth: the sources were highly directional for higher frequencies, and thus only the lower frequencies contributed to the images. Hence, in this work, signals were band-pass filtered 2–15MHz, which limited the achieved resolution. To use the generated bandwidth, acoustic sources of reduced lateral extent should be used.

These can be achieved through a change in optics, for instance using a lens with a shorter focal length. However, to avoid damaging the ultrasound-generating membrane, the pulse energy should be decreased when decreasing the optical spot size, thus reducing the generated pressure amplitude and signal-to-noise ratio.

In addition, in the set-up presented in this work, the lens focuses excitation light onto the ultrasound-generating membrane through the transparent wall of a water bath and a layer of water, resulting in a wall-reflection artefact in the images at a depth of approximately 3.5cm. Decreasing the focal length reduces the maximum distance between the water bath wall and the sound-generating membrane, and thus will limit the maximum imaging depth.

Ultimately, optical and acoustical scattering within the nano-composite membrane will limit the minimum lateral extent of the acoustic sources.

In a 2D all-optical ultrasound imaging paradigm, the lateral field of view was limited by the lateral extent of the acoustical aperture (15.5mm), which in turn was limited by the exit pupil of the optics. Thus, through a change in optics a wider source aperture could be achieved. However, to fully exploit a wider aperture, the optical alignment needs to be improved to avoid elevational offset of the sources. In addition, the fibre-optic acoustic receiver was positioned within the image plane and placed in front of the sound-generating membrane. As a result, ultrasound reflected off the generator membrane resulted in additional ghost images. These spurious reflections could be limited by positioning the receiver in the plane of the sound-generating membrane, at the expense of a reduced acoustical aperture due to optical shadowing. Alternatively, the ringing could be removed through source deconvolution.

The galvo mirror used in this work actually comprised two orthogonal angle-adjustable mirrors, of which one was kept fixed. However, in principle this galvo mirror allows arbitrary scanning of excitation light in 2D. Using the presented centimetre-scale nano-composite membrane, a 2D acoustic

source aperture is hence readily generated that could be used for 3D imaging. If the cylindrical lens were replaced with a spherical lens, an isotropic resolution of approximately $100\mu\text{m}$ could be achieved using the same imaging paradigm, at a frame rate of up to 1Hz. However, as the resulting optical focus is much smaller, the pulse energy of the excitation light would need to be reduced to avoid optical damage to the ultrasound-generating membrane.

For future configurations

In future, water surrounding the probe could therefore be replaced with acoustic coupling gel applied to only the surface of the imaging target, as is customary in routine clinical practice. Alternatively, a bundle of optical waveguides could be used to obtain a flexible imaging probe allowing free-hand operation similar to current clinical ultrasound probes, or miniaturised for applications.

As the electrical and metal components can be spatially separated from the acoustic sources and receiver, an all-optical ultrasound probe can be made insensitive to electromagnetic interference. This will enable the application of 2D or 3D ultrasound imaging in electromagnetically harsh or sensitive contexts, such as real-time monitoring of radio frequency ablation, electrophysiology and neuromodulation.

In addition, the application of all-optical ultrasound imaging within an MRI scanner will provide clinicians with concurrent, multiscale imaging yielding supplementary information during MRI-guided interventional procedures, such as high-precision instrument localisation, video-rate real-time monitoring of MRI-guided high-intensity focussed ultrasound (HIFU) treatment and visualising microbubble mediated drug delivery.

Finally, the adaptability of the frequency, bandwidth and geometry of optical ultrasound sources will allow seamless tailoring of an imaging system to the imaging target to optimise the image quality, frame rate and resolution. ■

PC-based ultrasound scanners and OEM components

In an industry in which ultrasound is not solely used for its initial intended purpose, **Teled** is producing custom solutions for an increasingly broad range of treatments.

Today, ultrasound imaging is not only a diagnostic tool. Ultrasound scanners are now also being used with other imaging, surgical and therapeutic devices to improve diagnosis and treatment. Teled offers a range of ultrasound solutions, from ready-to-market to custom-designed options.

Teled hardware includes various beamformers, customisable ultrasound keyboards and various ultrasound transducers. Ultrasound beamformers are capable of controlling linear, convex and phased array transducers. Each beamformer module includes front-end transmit/receive circuitry, power supply and a signal processing module. It is possible to interface with PCs using a USB 2.0 controller. Imaging modes include B, M, 4B (standard and colour), power, pulse wave and continuous wave (probe and system-dependent).



Teled offers a range of standard and custom ultrasound solutions for applications in diagnosis and treatment.

Teled's software development kit (SDK), provided with the system, offers an easy and fast way to develop a customised user interface for stand-alone imaging systems or application-specific devices, or to add ultrasound capabilities to existing equipment. The SDK is a set of C++ libraries providing user access to most system parameters.

Headquartered in Vilnius, Lithuania, Teled has been designing and manufacturing ultrasound components and complete scanners since 1992. Production quality is confirmed by an ISO/EN 13485

quality system and US FDA 510k-cleared products. ■

Further information

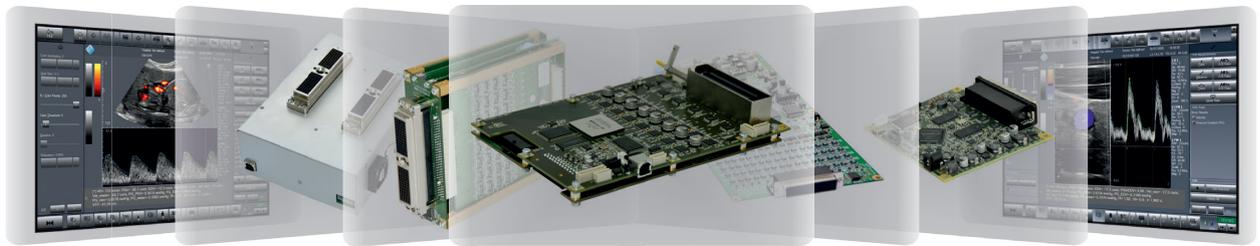
Teled
www.pcultrasound.com



TELEMED



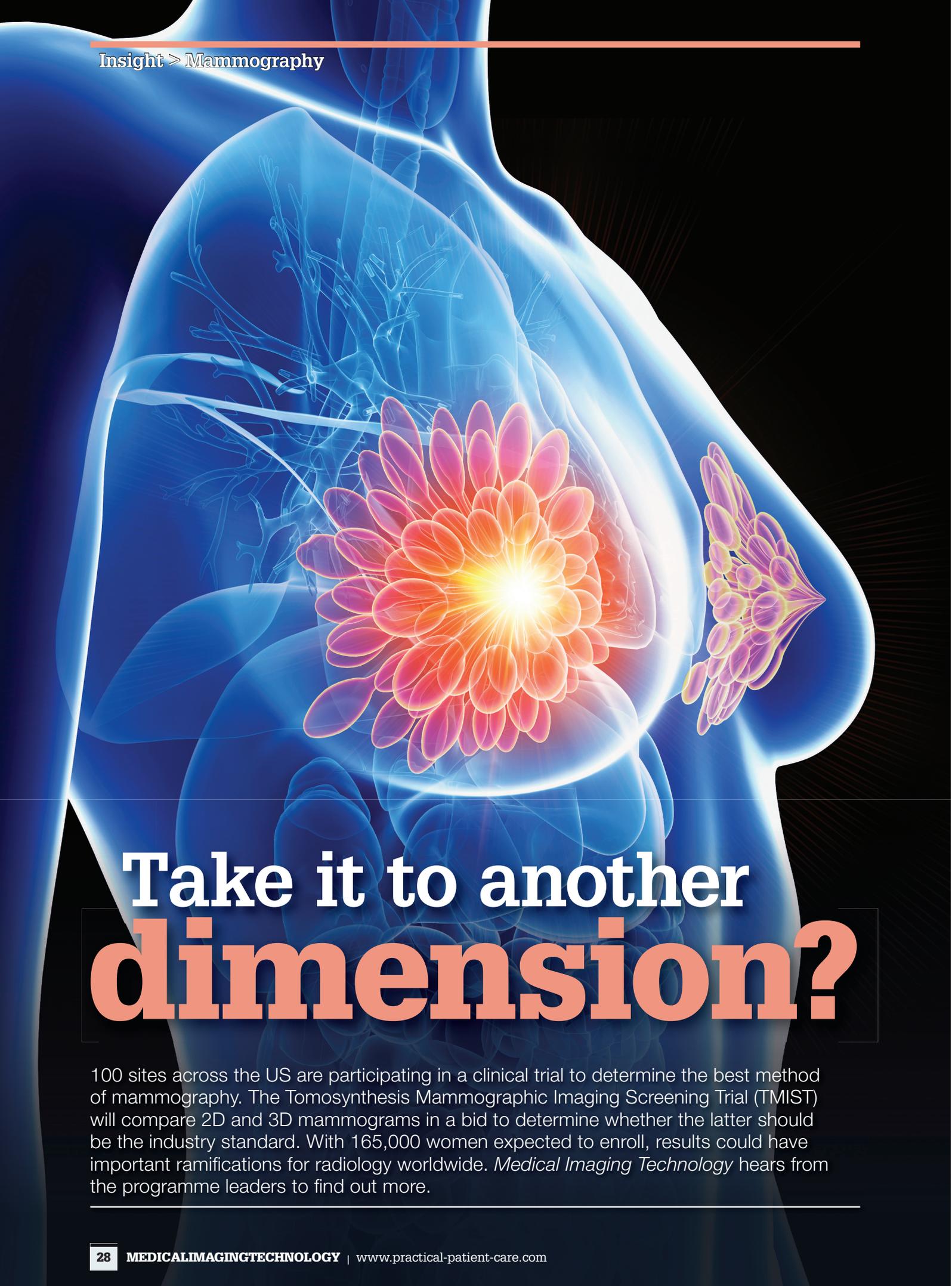
OEM components and solutions



for Ultrasound Medical Systems

October 29-November 1, **CMEF 2018** (Shenzhen, China).
November 12-15, **Medica 2018** (Dusseldorf, Germany), 9. D58
January 28-31, **Arab Health 2019** (Dubai, UAE), R. A01

<http://www.pcultrasound.com>
e-mail: info@teled.it



Take it to another dimension?

100 sites across the US are participating in a clinical trial to determine the best method of mammography. The Tomosynthesis Mammographic Imaging Screening Trial (TMIST) will compare 2D and 3D mammograms in a bid to determine whether the latter should be the industry standard. With 165,000 women expected to enroll, results could have important ramifications for radiology worldwide. *Medical Imaging Technology* hears from the programme leaders to find out more.

A large US-wide clinical trial has been launched to try to answer some important questions about the technologies used to screen for breast cancer.

The Tomosynthesis Mammographic Imaging Screening Trial (TMIST), an NCI-funded trial, is comparing two techniques used for mammograms. Namely, these two methods are tomosynthesis, often called 3D mammography, as well as standardised 2D digital mammography.

In late 2017, the first participating centres began enrolling women in the trial. Eventually, approximately 100 sites in the US and Canada are expected to participate, with a plan to enrol approximately 165,000 women of the ages 45–74 – peak age for risk.

The trial is designed to resolve an important unknown – whether tomosynthesis has a meaningful impact on the detection of potentially life-threatening breast cancers. So explains the study's principal investigator, Etta Pisano, of Beth Israel Deaconess Medical Center in Boston and chief science officer of the American College of Radiology.

The best-laid plans: a quest for efficiency and the allure of new technology

A key goal of TMIST is to help clinicians better understand the role of tomosynthesis in breast cancer screening.

"We know that we need to screen, period," says Pisano. "The question is, are the newer tools really benefitting women as much as we hope they are."

Led by the ECOG-ACRIN Cancer Research Group, TMIST is the first large randomised clinical trial of screening mammography in decades. It is the first to directly compare the current standard technology for breast cancer screening, 2D digital mammography, against tomosynthesis.

The trials from the 1980s and 1990s showed that regular screening with mammography could reduce the number of women who die from breast cancer. These trials used film mammography.



The trial is set to decide whether 3D mammography can become the new industry standard.

Digital mammography – meaning that the X-ray images are captured digitally and can be viewed more clearly on high-resolution computer screens – has largely overtaken film mammography over the past decade, explains Dr Martin Yaffe, of Sunnybrook Health Sciences Centre and the lead investigator for a TMIST lead-in trial, ongoing in Canada for nearly four years.

Although digital has advantages over film mammography, it still only produces flat two-dimensional images, akin to the moon's flat appearance in the sky.

With tomosynthesis, on the other hand, images are captured all around the breast and are then assembled by a computer into a 3D-like image. Tomosynthesis is "not truly 3D, but close to it", Yaffe explains.

The first tomosynthesis device for breast cancer screening was cleared by the Food and Drug Administration (FDA) in 2011. Of the machines currently used in the US, 28% are tomosynthesis machines, a number that, according to FDA data, has remained flat for at least the past year.

"The 3D technology has caught women's interest," says Jennifer Simas, a clinical trials coordinator at Carson Tahoe Cancer Center in Nevada, in the US. "TMIST is the first screening trial in which the centre has actively participated."

Carson Tahoe – which screens about 150–200 women a day for breast cancer – started offering

screening with tomosynthesis last year, and with that has come demand.

"A lot of women do want to be screened with the 3D machine," says Simas.

Pisano says she understands the allure of the newer technology. But, she continued, tomosynthesis does have some disadvantages compared with standard digital mammograms. The radiation dose with tomosynthesis, for example, can be more than two times what is received during standard digital mammography.

Yaffe explains that the higher radiation is due, in part, to the fact that tomosynthesis machines can perform standard 2D scans as well, and radiologists often conduct two types of scan. Because tomosynthesis is still relatively new, he says, radiologists do this "partly out of caution".

Tomosynthesis devices are more expensive than standard digital mammography machines. And more time is required for the screening procedure and analysis, meaning that "it's more expensive for patients and insurers", Pisano says.

Simas confirmed that cost, for the moment at least, has been an issue for some women. "Many women who ask to be screened using tomosynthesis do not receive it," she explains. "Their insurance would not cover it."

Nevertheless, with the two technologies in regular use, a direct comparison was needed. >>

Annual checks: the differentiation in regard to general health and age

Once enrolled in TMIST, women are randomly assigned to screening with either tomosynthesis or 2D digital mammography. Most women in the study are being screened once a year for five years.

“The trial should help to identify whether screening with tomosynthesis increases the overdiagnosis of breast cancer and to what degree.”

– Dr Bruce Rapkin, Montefiore Einstein Center for Cancer Care

However, women who are past menopause and who have none of the primary breast cancer risk factors (such as a family history of breast cancer or dense breasts) are screened every other year for five years – meaning they will only undergo three rounds of screening, rather than five.

Studies have shown that these women have a generally lower risk for developing aggressive breast cancer, so the panel of experts who helped design TMIST concluded that these women could safely undergo less frequent screening, Pisano explains.

The trial’s primary end point – the key question the study leaders hope to answer – is not how many women in each group die. Rather, the trial is designed to see whether tomosynthesis reduces the incidence of life-threatening breast cancers.

“In many ways, the end point is a matter of practicality,” Pisano explains. “We can’t do a mortality end point study, as it would take too long, ten to 20 years.”

So, reduction in the rate of advanced cancers – which are the most likely to be fatal – is, in effect, a surrogate for mortality.

“If one is a better screening tool than the other, there should be fewer advanced cancers in that group over five years of screening,” she says. “Any breast tumours likely to cause harm should have been found earlier, when they were smaller and more easily treatable.”

Thus, the trial design should help to answer the converse of this question, she added. Instead of detecting invasive cancers that could prove to be fatal, “are we finding too many issues that will not progress or that will not kill women because they are very slow-growing cancers?”

TMIST has several important informational goals beyond its primary end point. These secondary end points include whether women screened with tomosynthesis have fewer call backs, or recalls, and biopsies for suspicious findings that eventually turn out not to be cancer – so-called false positives.

A new hope: predictions for the employment of tomosynthesis as an industry standard

“One hope with tomosynthesis is that the more complete view of the breast will reduce the rate of false-positive results compared with standard digital mammography,” Pisano says. “But data on whether that’s the case has so far been mixed.”

“The trial should help to identify whether screening with tomosynthesis increases the overdiagnosis of breast cancer and to what degree,” says Dr Barry Kramer, director of NCI’s Division of Cancer Prevention. Overdiagnosis, which refers to the cancers diagnosed that likely would never have caused any harm because they were too slow growing.

Other secondary end points include the rate of interval cancers – that is, breast cancers diagnosed in the interval between a prior negative mammogram and the next scheduled mammogram.

The TMIST findings, Yaffe believes, will hopefully provide important information about how best to use these different screening technologies.

“For some women, we may find that a 2D digital mammogram is perfectly adequate,” he continues. “It may be that some women should continue to get 2D digital mammograms while others should get tomosynthesis, depending on the characteristics of their breasts.”

“The trial may very well help to answer other questions about the underlying biology of different forms of breast cancer,” Pisano hopes.” As part of the trial, a biorepository is being established to store tissue and blood samples from participants.”

The biorepository, she continues, should produce a bona fide treasure trove for cancer researchers, and will be a great resource for future studies.

TMIST investigators, for example, already have undertaken ancillary studies to look at biomarkers in tissue and blood samples that correlate not only with breast cancer but other cancer types as well.

The fresh approach: translating the results to inform future decisions in the field

The size and scope of the trial should have other tangible benefits, says Dr Bruce Rapkin of the Montefiore Einstein Center for Cancer Care in New York, one of many centres expected to participate in the trial that are part of the NCI Community Oncology Research Program (NCORP).

Montefiore is an NCORP minority underserved site, meaning it serves a large population of racial/ethnic minorities or rural residents.

“So it’s a great place for answering questions about things like the impact of cost, health literacy and all sorts of screening implementation issues,” says Rapkin, an NCORP investigator with the Montefiore programme, whose research focuses on the delivery of cancer care.

“One thing that’s going to be really important about the results of his trial is translating the results in a way that can help people make informed decisions about screening.” ■

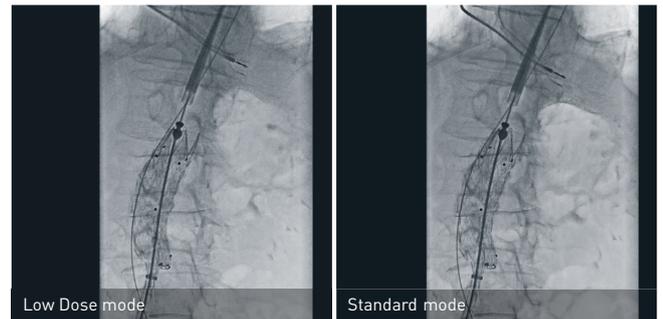


Supporting your patient care

Minimizing dose while maintaining image quality is an important goal worldwide for surgeons, their staff and patients. Ziehm Imaging supports this through further improvements to SmartDose¹ for different applications.

Comprehensive SmartDose concept

- **Low Dose mode in all anatomical programs** for particularly dose-sensitive procedures, e.g. in pediatrics
- **Beam Filtration² for reduced skin entrance dose** without compromising on image quality
- **ZAIP algorithm and filters** to display fast-moving objects like guide wires and even the smallest vessels in razor-sharp image quality



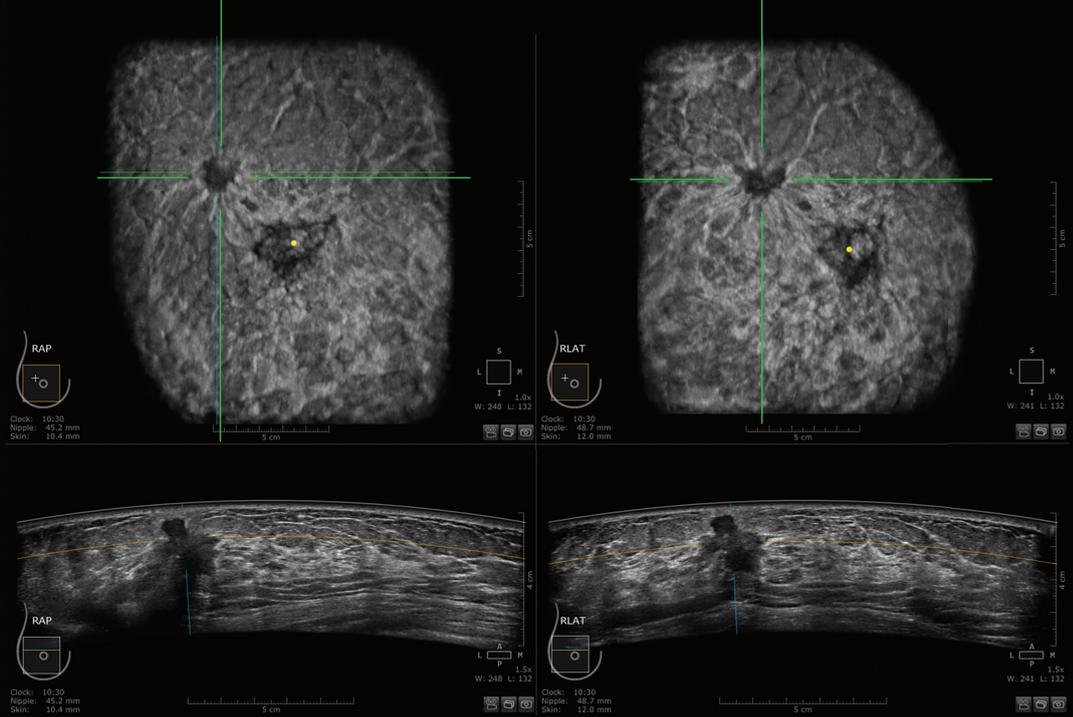
AAA, Ziehm Vision RFD Hybrid Edition CMOSline

www.ziehm.com/SmartDose

¹The SmartDose concept consists of a broad variety of different features. Due to regulatory reasons, the availability of each feature may vary. Please contact your local Ziehm Imaging partner for detailed information. ²The technology Beam Filtration reduces dose exposure for all CMOSline systems in comparison with conventional filtration techniques (status before September 2017). Data on file. Results may vary.

ALWAYS
AHEAD

 **ziehm imaging**



Top portion of the image displays the coronal view of a biopsy proven invasive ductal carcinoma with multiple satellite lesions. Bottom portion of the image displays the axial view of the selected lesion. Location, size and depth of the lesion can be identified in relationship to skin surface, nipple or satellite lesions.

Designed to help find more cancer in dense breast tissue over mammography alone, Invenia™ ABUS provides a global view of the breast.

3D ABUS volumes enable full evaluation of the breast and the unique ability to interpret exams utilizing the coronal view. The reproducible, wide field-of-view acquisition method also enhances prior exam comparisons – including correlation of multi-modality breast exams.

Learn more about how Invenia ABUS is used to improve breast care for patients with dense breast tissue for screening, diagnostic and surgical applications.



GE Healthcare Call for Prospective Research Proposals

Four \$100,000 (USD) awards.
Deadline to apply is October 26, 2018

Visit <https://gex.brightidea.com/ABUSResearch>

Learn more



Contact your GE Healthcare Representative if you would like to arrange a demonstration. Contact us at www.gehealthcare.co.uk/contact_us.

Invenia ABUS is part of the GE Healthcare suite of personalized breast care solutions.

Reliable adjunct screening

A recent study has bolstered research demonstrating the inimitable value of **GE Healthcare**'s Invenia ABUS in supplementing mammography in the detection of breast cancer. Here, the benefits are outlaid and the future of breast screening defined.

Automated breast ultrasound (ABUS) can be successfully used in the visualisation and characterisation of breast lesions, and can supplement mammography in the detection of non-calcified carcinomas in women with dense breasts. This is the conclusion of the study 'The performance of 3D ABUS versus hand-held ultrasound in the visualisation and BI-RADS characterisation of breast lesions in a large cohort of 1,886 women', originally published in *European Radiology*.

The study aimed to evaluate ABUS compared with HHUS in the visualisation and BI-RADS characterisation of breast lesions. The study involved 1,886 women with breast density category C or D – aged 48.6 ± 10.8 years. All participants underwent ABUS and HHUS examination and a subcohort of 1,665 women also underwent a mammography exam.

“We reported a high overall agreement (99.8%) in BI-RADS assessment between ABUS and HHUS.”

– **Athina Vourtsis, Diagnostic Mammography**

“We reported a high overall agreement (99.8%) in BI-RADS assessment between ABUS and HHUS,” says Athina Vourtsis, director and radiologist at Diagnostic Mammography in Greece. “More importantly, our results highlighted the value of ABUS and its integration in supplementing mammography by identifying non-calcified carcinomas that were obscured by dense breast tissue. Our results are in concordance with other studies that have found that multiplanar reconstruction data increases radiologists' diagnostic approach. The reported interpretation time was approximately three minutes per examination, allowing an efficient integration of ABUS into clinical workflow.”

The results are in

These results are consistent with a study recently conducted at the University Hospital Quirónsalud, Madrid, comparing the performance of ABUS and HHUS. In the study, which involved 155 patients following mammography, participants underwent an ABUS exam (performed by a technician trained and informed by a radiologist) and a HHUS exam performed by a different radiologist.

“Our study showed the same reliability between the ABUS and HHUS studies, however, ABUS provides the advantage that the radiologist is able to analyse the images without

having to perform the ABUS exam personally,” explains Dr Isaac Daimiel Naranjo of the Diagnostic Imaging Service at the university. “Additionally, ABUS provides the ability to store the result of the test in the patient's digital medical history, which allows comparison of ABUS results over time, since the exam is reproducible.”

According to Professor László Tabár, a professor emeritus of radiology at Uppsala University, Sweden, “Breast ultrasound has been recognised as an invaluable tool in supplementing mammography in women with intermediate risk. However, known limitations of HHUS, including subjectivity and operator dependence, have restricted its applicability for population-based screening. Shown to increase detection of 26–30% more invasive cancers when used in conjunction with mammography, ABUS is patient friendly, can be performed by a trained technologist or nurse, is reproducible and not subjective – it is specifically designed for screening large numbers of asymptomatic women with dense breasts.”

Earlier detection for better outcomes

“Several studies have reported the added value of the coronal plane on radiologist performance by demonstrating a retraction phenomenon sign; defined as merging of straight spicules that radiate perpendicularly in the periphery of the surface of a solid mass,” Vourtsis adds. “This sign corresponds to an architectural distortion and has high sensitivity and specificity for malignancy.”

Our study showed that an architectural distortion visualised on the coronal plane was the only sign of an invasive lobular carcinoma; while two radial scars were detected also on the coronal plane but not recognised in mammography or HHUS. Therefore, ABUS seemed to confer an added value on the coronal plane by displaying the architectural distortions.”

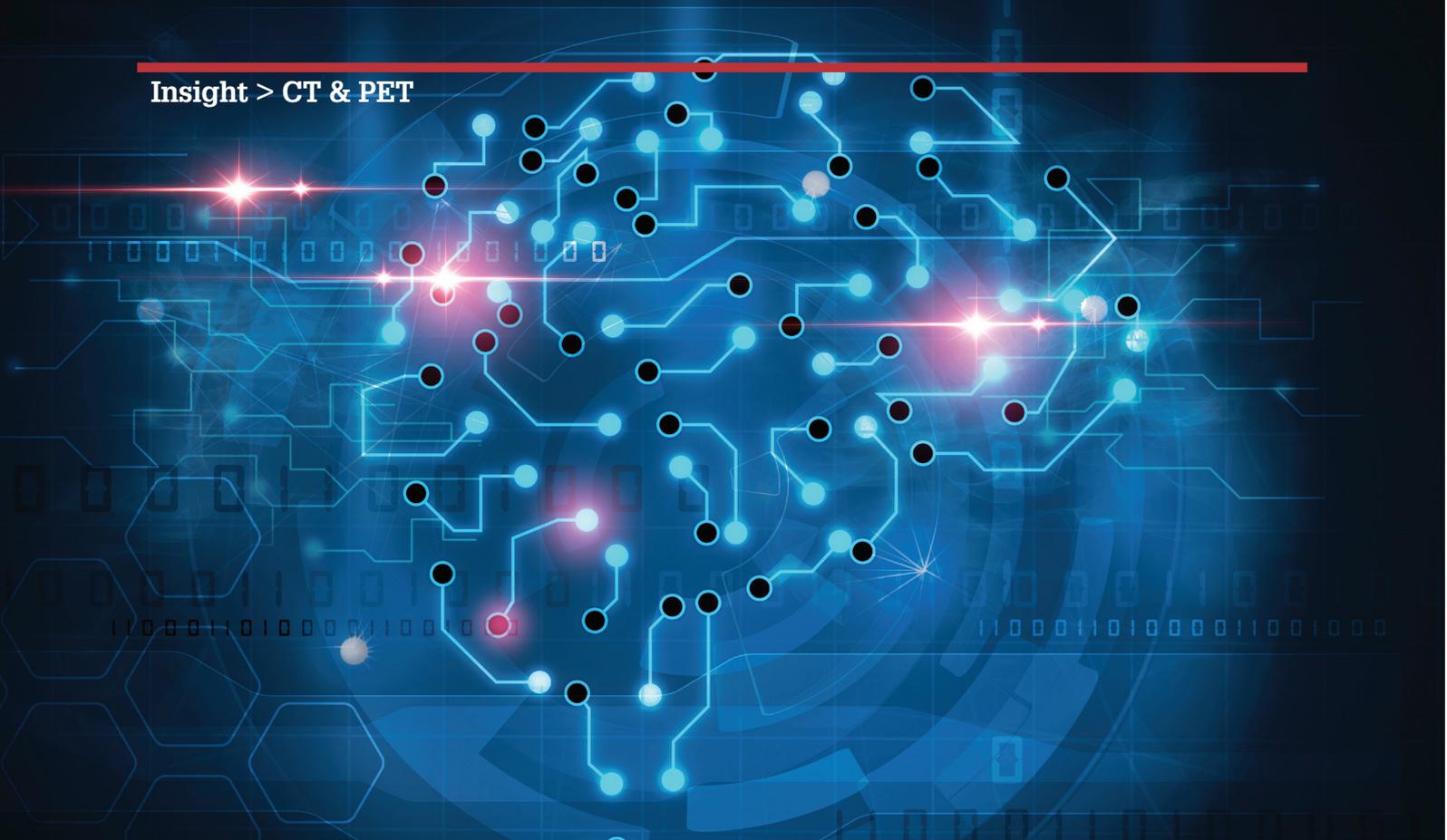
According to Vourtsis, well-trained technologists, adequate compression of the breast, and meticulous application of coupling lotion are key to produce an efficient ABUS examination and to improve performance.

“The ability of ABUS to separate the image acquisition from interpretation and to provide standardised images would substantially accelerate the application of 3D ABUS in high-volume screenings, with the goal of earlier detection and better outcomes,” Vourtsis concluded. ■

Further information

GE Healthcare
www.abusclub.net/emea/home





The future of the discipline

Artificial intelligence is rapidly moving from an experimental phase to implementation in many fields, including medicine. It is anticipated that the use of AI in the field over the next decade will significantly improve the quality, value and depth of radiology's contribution to patient care and population health, as well as revolutionise radiologists' workflows. Here, the Canadian Association of Radiologists ask how best we can handle the transition to new working practices and standards.

Radiologists are primarily known for their image interpretation skills. As a result, recent breakthroughs in image recognition introduced by deep-learning techniques have been equated in the media with the imminent demise of radiologists. This misconception has been amplified by bold statements made by prominent researchers in AI. These statements are best understood from the perspective of advances in a subset of tasks

accomplished by radiologists that require specialised intelligence, mainly detection of anomalies, segmentation and image classification.

However, the complex work performed by radiologists includes many other tasks that require common sense and general intelligence for problem solving – tasks that cannot yet be achieved through AI. Understanding a case may require integration of medical concepts from different scientific fields, such as

anatomy, physiology, medical physics and clinical specialties, to provide plausible explanations for imaging findings. Such tasks accomplished by radiologists on a daily basis include consultation, protocoling, review of prior examinations, quality control, identification and dismissal of imaging artefacts, cancer staging, disease monitoring, interventional procedures for diagnostic or therapeutic purpose, reporting, management guidance,

expertise in multidisciplinary discussions and patient reassurance. Additional tasks include education and the development of departmental policy.

Practice makes perfect

With technological advances in computer science, it is anticipated that an increasing number of repetitive tasks will be automated over time. The picture archiving and communication system (PACS) of all hospitals contain large imaging data sets with matching descriptions within radiology reports that can be used to perform multivariate machine learning (ML). The interactions between radiology images and their reports have been used to train ML for automated detection of disease in images. A review revealed that recent applications in medical image analysis focus on 2D convolutional neural networks that do not directly leverage 3D information. While 3D convolutional neural networks are emerging for analysis of multiplanar imaging such as CT, further research will require multiparametric imaging examinations.

“ With technological advances in computer science, it is anticipated that an increasing number of repetitive tasks will be automated over time. ”

Historically, residency programmes have successfully integrated basic sciences, such as biomedical physics and radiation protection, in their teaching curriculum. Because it is anticipated that the nature of the work accomplished by radiologists will evolve in the future, it follows that the radiology programmes should begin to integrate health, computer science and statistics courses in their curriculum.

AI research and development requires skill in statistics, coding, data structures and domain-specific data mining, in addition to new frameworks for data plumbing and computation. Building a medical image analysis tool may be as easy as learning the Python programming language and relying on existing software libraries. However,



Despite misgivings from some corners of the industry, AI in medicine is set to steadily increase.

understanding the underlying maths, statistics, data structures and algorithms is significantly more challenging.

Being able to generalise an algorithm to work on disparate input data, from multiple different imaging machines using myriad protocols, can prove to be terribly difficult.

On the other side, data scientists without experience in day-to-day radiology practice need to be aware of the depth and idiosyncrasies of radiology workflows. It is common at conferences to see scientific presentations and posters of AI projects that on the surface may appear to address a clinical setting, but miss critical parts that render the algorithm useless in practice. For example, fully automated segmentation of liver tumours may appear spectacular, but does not provide information – such as type of tumour, distribution of tumours, and relationship to vessels and staging – required by surgeons and oncologists for clinical management. In addition, how things are described in medical textbooks may differ from how they are implemented in practice.

Algorithms are amoral and, at their core, are built to optimise some function. As such, they are prone to bias, and potentially produce significant ethical issues. We have the responsibility to research and educate all stakeholders and the public on what types of ethical and bias issues may arise, and how to detect and manage them.

For example, a machine-learning model for stratifying the risk of cancer in pulmonary nodules detected on a CT scan achieved high performance on the training data set that included patients from the US National Lung Screening Trial, but much lower performance once applied to patients at Oxford University Hospitals. This suggests that a machine-learning model incorporates implicit selection biases from the demographics of the population used for its training which may not be representative of the target population in which it will be applied. If this discrepancy in diagnostic performance is not recognised, there is a risk of misdiagnosis and potential harm to patients.

Practising radiologists need to understand the value and the pitfalls, weaknesses and potential errors that may occur when an AI product performs image analysis. While these algorithms are powerful, they are temperamental, and may give inappropriate answers when presented with images outside of their knowledge set. This includes images with technical artefacts such as

movement or beam hardening, or images obtained with inappropriate techniques. For example, an algorithm evaluating brain CTs may work perfectly for long stretches, but then a new software upgrade to the CT occurs, or a new CT machine comes online and the algorithm produces faulty results. To alleviate this concern, in many modalities, new protocols for standardised imaging should be adopted with AI in mind, similarly to guidelines that have been proposed for image acquisition to enable quantitative analysis.

The responsibilities involved

AI is used for more than image analysis. It is a powerful tool to identify patterns, predict behaviour or events, or categorise objects. In the near future, these non-image-analysis tools may dramatically affect radiology. For example, these tools have the potential to improve radiology departmental workflow through precision scheduling, identify patients most at risk of missing appointments and empower individually tailored exam protocols. Perhaps most anxiety-provoking for radiologists, AI may enable programmes that use radiologists and their work as data, identifying details of each radiologists' practice pattern, and even categorising them, enabling the creation of a sophisticated radiology report card.

“Algorithms are amoral and, at their core, are built to optimise some function. As such, they are prone to bias, and potentially produce significant ethical issues.”

Commercialising an AI image analysis product requires understanding the clinical need, or use case; the business case; and new methods of product regulation, verification and monitoring. The computer vision literature provides countless examples of automated segmentation and computer-aided detection (CAD) tools that are not used in clinical practice despite decades of refinement. To overcome barriers to

clinical adoption, AI image analysis products must be integrated seamlessly in the clinical workflow and be able to interface with PACS software, which may otherwise act as a gatekeeper in the value chain.

There is a responsibility to inform the AI community of the role played by radiologists as consultants, experts, diagnosticians, interventionalists, educators and policymakers involved in patient care.

In addition, the radiology community should be prepared for automation of image interpretation tasks that will transform the nature of their work, particularly in 2D modalities. Furthermore, residency programmes should integrate health informatics, computer science and statistics courses in AI in their curriculum.

AI is currently having an immense impact on the research landscape of radiology departments. The availability of parallel computing hardware and ease of the open-source software tools have helped spark a movement towards AI research in academic departments that has frequently involved leadership from residents, fellows and junior staff who are comfortable with the technology. AI research, which can be done on data exports or even open source data, is significantly less expensive than imaging research involving patient recruitment and research coordinators scanning.

Labour to stay current

In the next five years, radiologists will see more competent AI application incorporated into PACS workflows, especially for laborious tasks prone to human error such as detection of bone metastases on CT. Currently, there is no evidence in the literature that AI can replace radiologists in day-to-day clinical practice. However, there is evidence that AI can improve the performance of clinicians and that clinicians and AI

working together are better than either alone. For example, research has shown that a radiologist-augmented approach could improve the performance of two deep neural networks by resolving their disagreements.

Healthcare budgets will need to include funding and support for new AI tools that potentially improve disease detection. In Canada, where PACS upgrades and optimisations are budget limited, radiology leaders will need to strongly advocate for solutions that incorporate AI into image interpretation workflows to optimise patient care, reduce detection errors and increase hospital efficiencies. To remain current, radiologists will need to follow and contribute to healthcare AI research and development, embrace the changes in workflow that will be required to support the implementation of clinical AI and adapt to changes in their practice that will improve care of their patients.

Radiologists should partner with the computer science and engineering departments of their affiliated universities to ensure that the problems under examination have maximum clinical benefit. Canadian associates (CAR) must educate government policymakers on the complexities of radiology and the consequences of misses, including associated morbidity and litigation costs. Furthermore, the CAR should provide a pathway for the implementation of AI tools in PACS environments, establishing minimum performance metrics for critical abnormalities.

AI applications currently focus on anomaly detection, segmentation and classification of images. Familiarity with the terminology and key concepts in this field will allow the radiology community to critically analyse the opportunities, pitfalls and challenges associated with the introduction of these new tools. Radiologists should become actively involved in research and development in collaboration with key stakeholders, scientists, and industrial partners to ensure radiologist oversight in the definition of use cases and validation process, as well as in the clinical application for patient care. ■

INTRODUCING BUSINESS REVIEW WEBINARS

BRW provides a global audience and platform for sponsoring companies to present thought leadership content to their peers within a number of industry verticals. The 60 minute webinar sessions are presented by leading industry experts and are aimed at giving business insights, educational value and access to new techniques and products without the need to travel.

Webinars are free to register. Our webinars are hosted live and on demand giving you the opportunity to either view on the live date or anywhere up to 12 months thereafter.



TO SPONSOR A WEBINAR:

CONTACT: Mark Leach

EMAIL: mark.leach@brwebinars.com

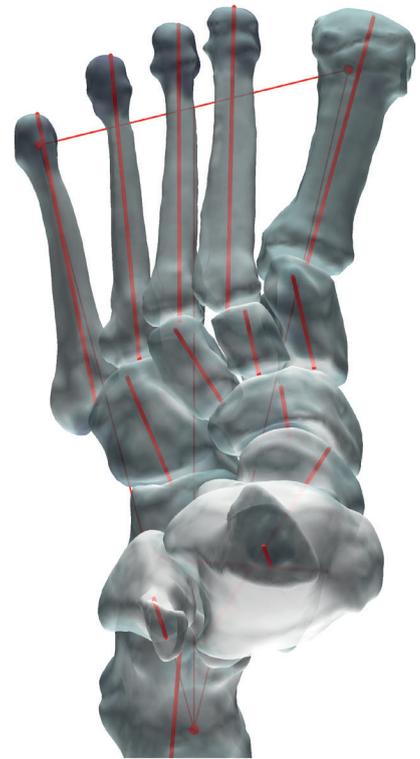
GENERAL ENQUIRIES:

enquiries@brwebinars.com



Unleash the full potential of your 3D imaging

with Planmed Verity® and Disior InGrid™



Planmed
www.planmed.com

Planmed Oy Sorvaajankatu 7, 00880 Helsinki, Finland, tel. +358 20 7795 300, sales@planmed.com

DISIOR
Analytics

www.disior.com

Haartmaninkatu 4, 00290 Helsinki, Finland, Tel. +358 50 483 6433

Innovation is afoot

Weight-bearing CT imaging has introduced new aspects to the diagnosis of foot and ankle diseases. Since its introduction in 2012, **Planmed's** Verity CBCT scanner has been used in challenging imaging cases of the upper and lower extremities.

Planmed has joined forces with Finnish start-up company Disior. The future now looks brighter than ever, as together the two companies promise to change the world of musculoskeletal 3D image analysis.

Cone beam computed tomography (CBCT) is a technology in which a series of low-intensity 2D X-rays are captured with a flat panel detector. The image series captured during a single or partial rotation is next reconstructed to a 3D volumetric image of the region of interest. This step is achieved using a combination of FDK and iterative algorithms.

CBCT is currently the only technology that is able to produce 3D volumetric imaging data of the foot and ankle under real, natural weight-bearing conditions. Combining the weight-bearing imaging with the fast image acquisition, low patient radiation dose and isotropic spatial resolution of 0.2mm allows the client to maintain complete confidence in their diagnostic diagnosis.

“The Disior InGrid algorithm effectively solves the problems related to 3D measurements of bones and joints.”

Taken to another dimension

Conventional 2D weight-bearing X-ray imaging has long been used as the standard of care to visualise skeletal diseases, and deformities of the foot and ankle. The measurement techniques are well described in the literature. However, 2D data is prone to projection differences and the superimpositions of the bones on one another can mask underlying issues.

3D weight-bearing imaging solves the challenges of projection differences and overlapping structures. The anatomy is shown in a naturally occurring position and can better reveal joint space narrowing and other conditions that may not be visible through conventional diagnostic means.

Adding the third dimension allows the anatomy to be visualised as 2D transversal slices. 2D transverse views enable the manual measurement of foot and ankle diseases and deformities. However, performing accurate and repeatable 3D measurements is not as easy as one might think.

Removing the chance of human error

The Disior InGrid algorithm solves the problems related to 3D measurements of bones and joints. It uses deformable shape models to segment bone tissue from imaging data.



The 3D image acquisition and reconstruction process, a 3D dicom image and an example of Disior InGrid processing analysis on the patient's foot.

Using the 3D image captured with Planmed Verity, the algorithm automatically extracts the landmarks and longitudinal axes needed for the measurements from the segmentation result using robust feature detection algorithms. This results in excellent measurement repeatability, without the steps prone to human error.

Transforming a DICOM image into a mathematical model of the anatomy serves as the basis for an analysis of the anatomy and kinematics. Based on this analysis, any 3D measurement can be taught and automatised in the software. As a result, the industry is no longer dependent on individual slices, but may use the whole data set for analysis. This way, transferring the measurement practices from weight-bearing 2D to 3D is easily achieved.

With the Planmed Verity and Disior InGrid algorithm, one can easily image and analyse common clinical cases in foot and ankle region.

For example, hallux valgus, flat foot and cavus foot are analysed in an unseen way by automatically measuring angle, such as the first and second intermetatarsal angle, or Meary's angle, from 3D weight-bearing data.

A step in the right direction

Additionally, more complex midfoot and hindfoot alignments and commonly use Saltzman view are easily available from the 3D weight-bearing data.

Combining automatic 3D measurements with quality 3D weight-bearing images has key implications for diagnosing foot and ankle anatomy. It carries great potential in clinical decision-making, surgical planning and post-operative analysis. In addition the outcome of the Disior InGrid processing has excellent quality for 3D printing of anatomic models. ■

Further information

Planmed
www.planmed.com
juhamatti.malm@planmed.com





Fresh

ideas

A new technique for quickly and affordably creating incredibly detailed 3D models of MRI, CT and other medical scans promises to add significant value to the medical community and empower patients. Leaders behind the development speak to Lindsay Brownell about the ramifications of their findings and the inspiration that drove them toward these discoveries.

What if you could hold a physical model of your own brain in your hands, accurate down to its every unique fold? That's just a normal part of life for Steven Keating, who had a tennis ball-sized tumour removed from his brain at age 26 while he was a graduate student in the MIT Media Lab's Mediated Matter group.

Curious to see what his brain actually looked like before the tumour was removed, and with the goal of better understanding his diagnosis and treatment options, Keating collected his medical data and began 3D printing his MRI and CT scans. However, he was frustrated that existing methods were prohibitively time-intensive, cumbersome and failed to accurately

reveal important features of interest. Keating reached out to some of his group's collaborators, including members of the Wyss Institute at Harvard University, who were exploring a new method for 3D printing biological samples.

"It never occurred to us to use this approach for human anatomy until Steve came to us and said, 'Guys,

here's my data, what can we do?'," says Ahmed Hosny, who was a research fellow at the Wyss Institute at the time, and is now a machine learning engineer at the Dana-Farber Cancer Institute.

The result of that impromptu collaboration – which grew to involve James Weaver, senior research scientist at the Wyss Institute; Neri Oxman, director of the MIT Media Lab's Mediated Matter group and associate professor of Media Arts and Sciences; and a team of researchers and physicians at several other academic and medical centres in the US and Germany – is a new technique that allows images from MRI, CT, and other medical scans to be easily and quickly converted into physical models with unprecedented detail.

“Our approach not only allows for high levels of detail to be preserved and printed into medical models, but it saves a tremendous amount of time and money, ”

– James Weaver, the Wyss Institute

"I nearly jumped out of my chair when I saw what this technology is able to do," says Beth Ripley, assistant professor of radiology, University of Washington, clinical radiologist at the Seattle VA, and co-author of the resulting paper. "It creates exquisitely detailed 3D-printed medical models with a fraction of the manual labour currently required, making 3D printing more accessible to the medical field as a tool for research and diagnosis."

The little details

Imaging technologies like CT scans produce high-resolution images as a series of 'slices' that reveal the details of structures inside the human body, making them an invaluable resource for evaluating and diagnosing medical conditions. Most 3D printers build physical models in a layer-by-layer process, so feeding them layers of medical images to create a solid structure is an obvious synergy between the two technologies.

However, there is a problem: MRI and CT scans produce images with so much detail that the object or objects of interest need to be isolated from surrounding tissue and converted into surface meshes in order to be printed. This is achieved via either 'segmentation': a very time-intensive process where a radiologist manually traces the desired object on every single image slice (sometimes hundreds of images for a single sample), or an automatic 'thresholding' process in which a computer program quickly converts areas that contain grayscale pixels into either solid black or solid white pixels, based on a shade of grey that is chosen to be the threshold between black and white. However, medical imaging data sets often contain objects that

are irregularly shaped and lack clear, well-defined borders; as a result, auto-thresholding (or even manual segmentation) often over or under-exaggerates the size of a feature of interest and washes out critical detail.

The new method described by the paper's authors provides medical professionals with a better solution, offering a fast and highly accurate method for converting complex images into a format that can be easily 3D printed. The key lies in printing with dithered bitmaps, a digital file format in which each pixel of a grayscale image is converted into a series of black and white pixels, and the density of the black pixels is what defines the different shades of grey rather than the pixels themselves varying in colour.

Similar to the way images in black-and-white newsprint use varying sizes of black ink dots to convey shading, the more black pixels that are present in a given area, the darker it appears. By simplifying all pixels from various

Better planning, smoother diagnostics

Three-dimensional (3D) printing technologies are increasingly used to convert medical imaging studies into tangible (physical) models of individual patient anatomy, allowing physicians, scientists and patients an unprecedented level of interaction with medical data.

To date, virtually all 3D-printable medical data sets are created using traditional image thresholding, subsequent isosurface extraction, and the generation of .stl surface mesh file formats.

These existing methods, however, are highly prone to segmentation artifacts that either over or under-exaggerate the features of interest, thus resulting in anatomically inaccurate 3D prints. In addition, they often omit finer detailed structures and require time-and-labour-intensive processes to visually verify their accuracy. To circumvent these problems, the authors of this paper present a bitmap-based multimaterial 3D printing workflow for the rapid and highly accurate generation of physical models directly from volumetric data stacks.

This workflow employs a thresholding-free approach that bypasses isosurface creation and traditional mesh slicing algorithms, hence significantly improving speed and accuracy of model creation.

In addition, using preprocessed binary bitmap slices as input to multimaterial 3D printers allows for the physical rendering of functional gradients native to volumetric data sets, such as stiffness and opacity, opening the door for the production of biomechanically accurate models.

Source: 'From Improved Diagnostics to Presurgical Planning: High-Resolution Functionally Graded Multimaterial 3D Printing of Biomedical Tomographic Data Sets'

shades of grey into a mixture of black or white pixels, dithered bitmaps allow a 3D printer to print complex medical images using two different materials that preserve all the subtle variations of the original data with much greater accuracy and speed.

In the entrenched elements

The team of researchers used bitmap-based 3D printing to create models of Keating's brain and tumour that



A 3D-printed foot model (left) and its cross section (right) clearly reveal the intricate internal architecture of the different bone types, as well as the surrounding soft tissue.

Steven Keating and Ahmed Hosny/Wyss Institute at Harvard University.

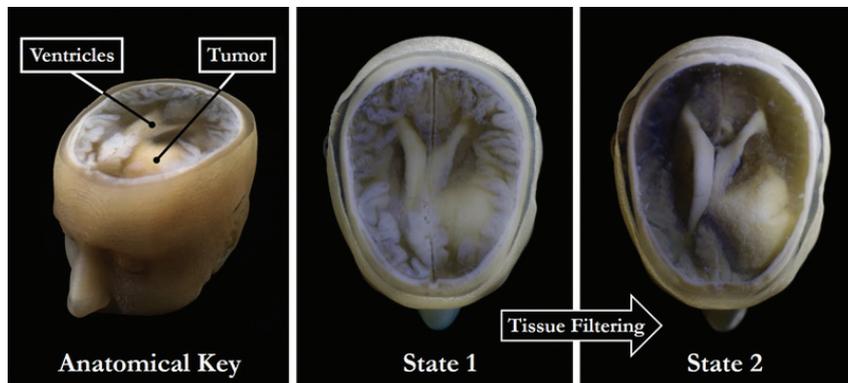


A 3D-printed multimaterial model of a calcified heart valve shows hard calcium deposits (white) with fine-scale gradients in mineral density that are impossible to fully capture using conventional biomedical 3D printing approaches.

James Weaver and Ahmed Hosny/Wyss Institute at Harvard University.

Three of the co-authors of the paper, left to right: Ahmed Hosny holding models of Steven Keating's tumor, Steven Keating holding a model of his own skull, and James Weaver holding models of Keating's MRI scan.

Wyss Institute at Harvard University.



High-throughput tissue filtering, a major feature of the approach developed by the authors of the study, can help quickly remove extraneous tissue to reveal the desired underlying structures (right) without sacrificing the resolution or intensity gradients present in the native imaging data (left and center).

James Weaver and Steven Keating/Wyss Institute at Harvard University.

muscles, soft tissue, and skin, for example, can take more than 30 hours, even by a trained professional – we were able to do it in less than an hour.”

High hopes

The researchers hope that their method will help make 3D printing a more viable tool for routine exams and diagnoses, patient education, and understanding the human body. “Right now, it’s just too expensive for hospitals to employ a team of specialists to go in and hand-segment image data sets for 3D printing, except in extremely high-risk or high-profile cases. We’re hoping to change that,” says Hosny.

In order for that to happen, some entrenched elements of the medical field need to change as well. Most patients’ data are compressed to save space on hospital servers, so it’s often difficult to get the raw MRI or CT scan files needed for high-resolution 3D printing. Additionally, the team’s research was facilitated through a joint collaboration with leading 3D printer manufacturer Stratasys, which allowed access to its 3D printer’s intrinsic bitmap printing capabilities. New software packages still need to be developed to better leverage these capabilities and make them more accessible to medical professionals.

Despite these hurdles, the researchers are confident that their achievements present a significant value to the medical community. “I imagine that, sometime within the next five years, the day could come when any patient that goes into a doctor’s office for a routine or non-routine CT or MRI scan will be able to get a 3D-printed model of their patient-specific data within a few days,” says Weaver.

Keating, who has become a passionate advocate of efforts to enable patients to access their own medical data, still 3D prints his scans to see how his skull is healing post-surgery and check on his brain to make sure his tumour isn’t coming back. “The ability to understand what’s happening inside of you, to actually hold it in your hands and see the effects of treatment, it is incredibly empowering,” he says. ■

faithfully preserved all of the gradations of detail present in the raw imaging data down to a resolution that is on par with what the human eye can distinguish from about 9-10in away. Using this same approach, they were able to print a variable stiffness model of a human heart valve using different materials for the valve tissue versus the mineral plaques that had formed within the valve, resulting in a model that exhibited mechanical

property gradients and provided new insights into the actual effects of the plaques on valve function.

“Our approach not only allows high levels of detail to be preserved and printed into medical models, but it saves a tremendous amount of time and money,” says Weaver, who is the corresponding author of the paper. “Manually segmenting a CT scan of a healthy human foot, with all its internal bone structure, bone marrow, tendons,

View our latest range of reports at www.globaldata.com/store

Decode the Future

View our latest market research in the medical industry

Our analysts produce quantitative and qualitative reports annually providing:

- Forecast and Historical Data Analysis
- Pricing, Revenue Trends and Sales Volume
- Competitor Analysis and Key Market Players
- Unmet Needs and Company Share Analysis

Contact GlobalData to find out more about our reports
or to find out how our intelligence solutions can help your business.

+44 161 359 5813 / reportstore@globaldata.com / www.globaldata.com/store

An air of distinction

Nanoscientists at Rice University have demonstrated a method for loading iron inside nanoparticles to create MRI contrast agents that outperform gadolinium chelates, the mainstay contrast agent that is facing increased scrutiny due to safety concerns. James Sanderson hears from members of the project team on the impact this discovery could have on future diagnoses and treatments.

MRI scanners image the body's interior by briefly aligning the nuclei of hydrogen atoms and measuring how long it takes the nuclei to relax to their resting state. Relaxation properties vary by tissue, and by repeatedly aligning nuclei and measuring relaxation times, an MRI

scanner builds a detailed image of the body's organs, tissues and structures.

Within this process, contrast agents improve scan resolution by increasing the relaxation rate of particles.

Radiologists can weigh the results of an MRI, making specific tissues appear either brighter or darker by varying the conditions of the test.

Two weighting techniques, named T1 and T2, are commonly used.

Gadolinium chelates revolutionised MRI testing when they were introduced in the late 1980s, and have been used more than 400 million times in the years since. Though gadolinium is a toxic metal, the chelating process covers each gadolinium ion with an organic wrap that reduces exposure and allows the drug to pass from the body via urination within a few hours.

In 2013, however, Japanese scientists made the discovery that gadolinium from contrast agents had accumulated in the brains of some patients, and subsequent studies found similar deposits in bones and other organs.

Experts previously believed gadolinium contrast material could not cross the blood-brain barrier, the semipermeable membrane that selectively filters materials from the bloodstream from entering extracellular fluid in the brain, as well as the central nervous system. Studies soon followed with attempts to gauge the risks the scenario posed.

Still, very little is known about the health effects of gadolinium that is retained in the brain. A major study, presented at the annual meeting of the Radiological Society of North America late last year, found no evidence that accumulation of gadolinium in the brain speeds cognitive decline. >>



Independent risk factors

For this study, lead author Dr Robert J McDonald, neuroradiologist at the Mayo Clinic, and his colleagues set out to identify the neurotoxic potential of intracranial gadolinium deposition following intravenous administration of gadolinium-based contrast agents during MRI.

The researchers used the Mayo Clinic Study of Aging (MCSA), the world's largest prospective population-based cohort on ageing, to study the effects of gadolinium exposure on neurologic and neurocognitive function.

All MCSA participants underwent extensive neurologic evaluation and neuropsychological testing at baseline and 15-month follow-up intervals.

Neurologic and neurocognitive scores were compared using standard methods between MCSA patients with no history of prior gadolinium exposure and those who underwent prior MRI with gadolinium-based contrast agents. Progression from normal cognitive status to mild cognitive impairment and dementia was assessed using multistate Markov model analysis.

The study included 4,261 cognitively normal men and women aged 50–90, with a mean age of 72. Mean length of study participation was three years and seven months. Of the 4,261 participants, 1,092 (25.6%) had received one or more doses of gadolinium-based contrast agents, with at least one participant receiving as many as 28 prior doses. Median time since first gadolinium exposure was five and a half years.

After adjusting for age, sex, education level, baseline neurocognitive performance and other mitigating factors, gadolinium exposure was not a significant predictor of cognitive decline, dementia, diminished neuropsychological performance or diminished motor performance. No dose-related effects were observed among these metrics. The conclusion was in – gadolinium exposure was not a risk factor in the rate of cognitive decline from normal cognitive status to dementia in this study group.



Gadolinium chelates have been used over 400 million times since the 1980s, but Rice University nanoscientists have now loaded iron inside nanoparticles to create superior MRI contrast agents.

“There is concern over the safety of gadolinium-based contrast agents, particularly relating to gadolinium retention in the brain and other tissues,” McDonald acknowledged upon publication. “This study provides useful data that at the reasonable doses 95% of the population is likely to receive in their lifetime, there is no evidence at this point that gadolinium retention in the brain is associated with adverse clinical outcomes.”

claim to have developed a method for loading iron inside nanoparticles to create MRI contrast agents that outperform gadolinium chelates.

“The possibility of eliminating gadolinium exposure and getting a two-fold improvement in T1 MRI contrast performance is going to intrigue radiologists,” says Rice’s Naomi Halas, the lead researcher on the project. “When they hear we have done this with iron, I expect they will be very surprised.”

“It’s widely believed [iron chelates] are wholly impractical for T1 contrast, but this study is a perfect illustration of how differently things can behave when you engineer at the nanoscale.”

– **Naomi Halas, lead researcher**

Despite these findings, the safety of gadolinium-based contrast agents used in magnetic resonance imaging remains a major source of debate in the medical and public spheres. Just one month after the report’s release, FDA launched a requirement for drug makers to add warnings to the medication guides for eight widely used gadolinium-based contrast agents.

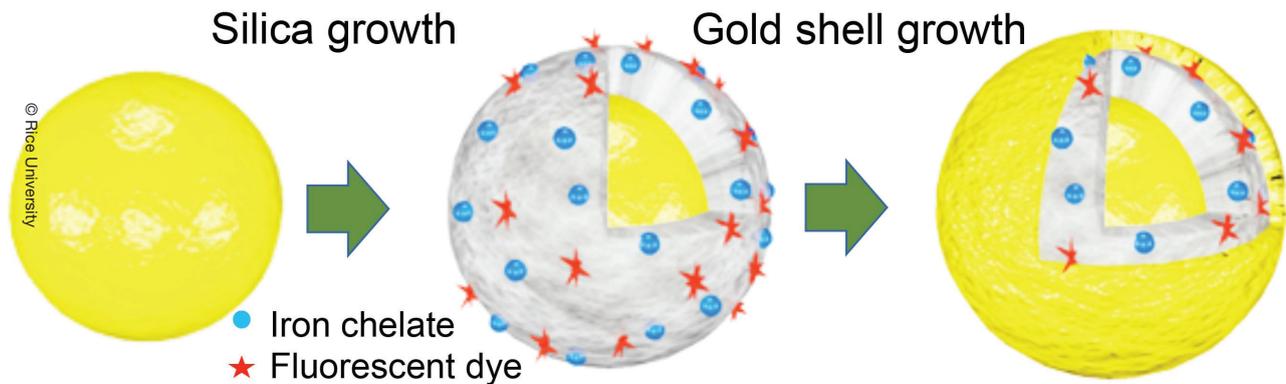
Chock-full of iron

Within this environment, research into alternative contrast agents has gathered pace, and Rice University nanoscientists

While iron-based contrast agents are frequently employed for T2 scans, there are few clinically available alternatives to gadolinium for T1 tests.

“Iron chelates aren’t new,” Halas acknowledges. “It’s widely believed they are wholly impractical for T1 contrast, but this study is a perfect illustration of how differently things can behave when you engineer at the nanoscale.”

Halas and colleagues from Rice, as well as the University of Texas Anderson Cancer Center, published their findings in a paper made available in the American Chemical Society



Scientists at Rice’s Laboratory for Nanophotonics added iron chelates (blue) and fluorescent dye (red) to multilayered gold nanomatryoshkas to create particles that can be used for disease therapy and diagnostics. The ‘theranostic’ nanoparticles have a core of gold (left) that is covered by silica containing the diagnostic iron and dye, which is covered by an outer shell of gold. The particles are about 20 times smaller than a red blood cell, and by varying the thickness of the layers, LANP scientists can tune the nanomatryoshkas to convert light into cancer-killing heat.

journal, *ACS Nano*. In the study, the collective created a modified version of nanomatryoshkas, concentric layered nanoparticles that draw their name from Russian nesting dolls.

Nanomatryoshkas and nanoshells, another layered nanoparticle Halas invented at Rice more than 20 years ago, are about 20 times smaller than a red blood cell and made up of layers of conductive metal and non-conductive silica. By varying the thickness of the layers, Halas’s team tuned the particles to interact with specific wavelengths of light. For instance, nanoshells and nanomatryoshkas can convert otherwise harmless near-infrared light to heat. This localised, intense heating has been used to destroy cancer in several trials of nanoshells, including an ongoing trial for the treatment of prostate cancer.

The new study is the latest chapter in Halas’s efforts to create light-activated nanoparticles with a combination of therapeutic and diagnostic features. These theranostic particles could allow clinicians to diagnose and treat cancer in the same office or hospital visit.

Luke Henderson, a Rice graduate student and lead author of the *ACS Nano* paper said, “If clinicians could visualise the particles through some sort of imaging, therapy could be faster and more effective. For example, imagine a scenario where a scan is performed to verify the size and placement of the tumour, heat is then generated to treat the tumour and

another scan follows to verify that the entire tumour was destroyed.”

When Henderson, a chemist, joined Halas’s Laboratory for Nanophotonics in 2016, Halas’s team had already shown it could add fluorescent dyes to nanomatryoshkas to make them visible in diagnostic scans. Work was under way on a study published in 2017 that showed gadolinium chelates could be embedded in the silica layer for MRI contrast.

“If clinicians could visualise the particles through some sort of imaging, therapy could be faster and more effective.”

– **Luke Henderson, lead author of *ACS Nano* paper**

“In the earlier work with gadolinium, we noticed that the nanomatryoshka design enhanced the relaxivities of the embedded gadolinium chelates,” Henderson said. “At the same time, we were hearing more calls from the medical community for alternatives to gadolinium, and we decided to try iron chelates and see if we got the same sort of enhancement.”

A nice surprise

The results surprised everyone. Not only was Henderson able to boost the relaxivities for iron, he was able to load about four times more iron into each nanomatryoshkas. That allowed the iron-laden nanomatryoshkas to perform twice as well as clinically available gadolinium chelates.

Henderson found a useful way to change the type of metal that was loaded. By adding unloaded chelate molecules to the silica first, he found he could load metal by soaking the particles in a bath of metal salts. By changing the metals in the bath, he found he could easily load different paramagnetic ions, including manganese, into the nanomatryoshkas.

After the metal ions were loaded into the silica, the final layer of the nanomatryoshka, the outer gold shell,

was added. The shell, which is vital or plasmonics, serves as a barrier to prevent ion leeching. Henderson said the gold barrier had a secondary benefit for the fluorescent dyes he added for dual-mode diagnostics.

“All fluorescent dyes are subject to photobleaching, which means they fade over time and eventually won’t give off a measureable signal,” Henderson said. “Even if you freeze them, which slows down bleaching, they typically don’t last more than a couple of weeks. I was looking at an old sample of nanomatryoshkas that had been in the fridge for months, and I found they were still fluorescing quite well. When we looked more closely at this we found the dyes were about 23 times more stable when they were inside the nanomatryoshkas.” ■



GREAT AND INNOVATIVE COMBINATIONS FOR MEDICAL IMAGING IN CT



ScanBag[®]
by XENETIX[®]

FlowSens[®]
DUAL SOFT BAG CT CONTRAST DELIVERY SYSTEM



OptiRAY[®]
Ioversol

OptiVantage[®]
DUAL-HEAD CT CONTRAST DELIVERY SYSTEM

OptiOne[®]
SINGLE-HEAD CT CONTRAST DELIVERY SYSTEM



Also available in vials
XENETIX[®] OptiRAY[®]



OptiVantage[®]
DUAL-HEAD CT CONTRAST DELIVERY SYSTEM

FlowSens[®]
DUAL SOFT BAG CT CONTRAST DELIVERY SYSTEM

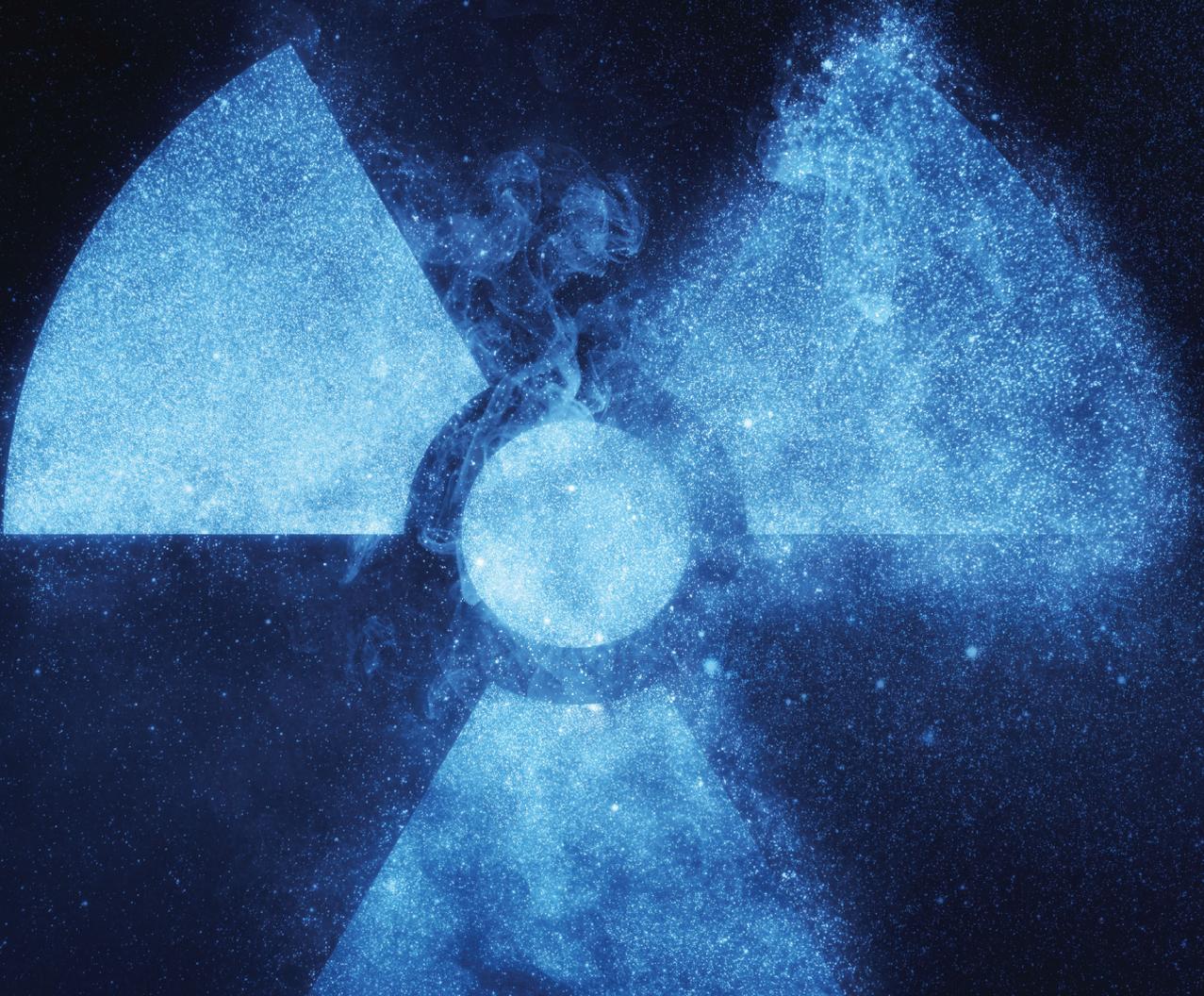
OptiOne[®]
SINGLE-HEAD CT CONTRAST DELIVERY SYSTEM

OptiRAY[®]: Please refer to the Summary of Product Characteristics before prescribing. **Composition:** OPTIRAY[®] 240 Ioversol, 509 mg/ml, which is equivalent to 240 mg/ml of elemental iodine. OPTIRAY[®] 300 Ioversol, 636 mg/ml, which is equivalent to 300 mg/ml of elemental iodine. OPTIRAY[®] Ioversol, 678 mg/ml, which is equivalent to 320 mg/ml of elemental iodine. OPTIRAY[®] Ioversol, 741 mg/ml, which is equivalent to 350 mg/ml of elemental iodine. **Indications:** OPTIRAY[®] non-ionic X-ray contrast medium for injection or infusion. Depending on the preparation, it is indicated for use in cerebral, coronary, peripheral, visceral and renal angiography, in aortography, left ventriculography, venography, intravenous excretory urography and computed tomography (CT) of the head and body. Except for OPTIRAY[®] 300, safety and effectiveness of OPTIRAY[®] in children has not yet been established. **Posology and Method of Administration:** The dosage may vary between 1 ml and 150 ml, maximum total dose 250 ml or less. Please refer to the Summary of Product Characteristics for the recommended dosage schedule. **Contraindications:** Proven hypersensitivity to iodine-containing contrast media. Manifest hyperthyroidism. **Special Warnings and Precautions:** OPTIRAY[®] may cause anaphylactic or other manifestations of pseudo-allergic reactions, e.g. nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. Pretesting cannot be relied upon to predict severe reactions. The thorough assessment of the medical history of the specific patient may be more accurate in predicting potential adverse reactions. A positive history of allergy is not a contraindication, but does require caution. Diagnostic procedures, which involve the use of iodinated intravascular contrast agents, should be performed under the direction of personnel skilled and experienced in the particular procedure to be performed. Serious or fatal reactions have been associated with the administration of iodinated X-ray contrast media. A fully equipped emergency cart, or equivalent supplies and equipment, and personnel competent in recognising and treating adverse reactions of all types should always be available for at least 30 to 60 minutes after administration. Patients with congestive heart failure should be observed for several hours following the procedure to detect delayed haemodynamic disturbances, which may be associated with a transitory increase in the circulating osmotic load. All other patients should be observed for at least one hour after the application, as it has been reported that most of the adverse events occur in this period. The patient should also be informed that allergic reactions may develop up to several days post administration; in such case, a physician should be consulted immediately. Caution must be exercised in patients with severely impaired renal function, combined renal and hepatic disease, anuria, diabetes mellitus, homozygotic sickle cell disease, or monoclonal gammopathy (multiple myeloma, Waldenström's macro-globulinemia), particularly when large doses are administered. Serious renal effects, including acute renal failure, may occur in these patients. Preparatory dehydration is dangerous and may contribute to acute renal failure. Iodine-containing contrast media may also be hazardous in patients with hyperthyroidism or with autonomous areas of the thyroid gland. In patients with phlebotomy a premedication with alpha-blockers is advisable when the contrast medium is administered intravascularly due to the risk of a hypertensive crisis. Serious neurologic events have been observed following direct injection into cerebral arteries or vessels supplying the spinal cord, or in angiocardiology due to inadvertent filling of the carotids. General anaesthesia may be indicated in selected patients. However, a higher incidence of adverse reactions has been reported in these patients, probably due to the hypotensive effect of the anaesthetic. In angiographic procedures, the possibility of dislodging plaque or damaging or perforating the vessel wall should be considered during catheter manipulation and contrast medium injection. In patients with advanced atherosclerosis, serious hypertension, cardiac decompensation, senility, preceding cerebral thrombosis or embolism, special caution should be exercised. Cardiovascular reactions such as bradycardia, rising or falling of blood pressure may occur more often. Angiography should be avoided whenever possible in patients with haemostaticia due to an increased risk of thrombosis and embolism. OptiRay[®] should be injected with caution to avoid perivascular application. However, significant extravasation of OptiRay[®] may occur especially during the use of power injectors. Generally, it is tolerated without substantial tissue injury applying conservative treatment. However, serious tissue damage (e.g. ulceration) has been reported in isolated cases requiring surgical treatment. **For interactions and specific warnings,** please refer to summary of product characteristics. **Summary of safety profile:** Adverse reactions following the use of OptiRay[®] formulations are generally independent of the dose administered. Usually, they are mild to moderate, of short duration and resolve spontaneously (without treatment). However, even mild adverse reactions may be the first indication of a serious, generalised reaction that can occur rarely after iodinated contrast media. Such serious reactions may be life-threatening and fatal, and usually affect the cardiovascular system. Most adverse drug reactions to OptiRay[®] formulations occur within minutes after administration, however contrast related hypersensitivity reactions may occur with a delay of some hours up to several days. **Adverse reactions may be classified as follows:** Hypersensitivity or anaphylactoid reactions are mostly mild to moderate with symptoms like rash, pruritus, urticaria and rhinitis. However, serious reactions may occur. Serious anaphylactoid reactions generally affect the cardiovascular and respiratory system. These may be life-threatening and include anaphylactic shock, cardiac and respiratory arrest, or pulmonary oedema. Fatal cases were reported. Patients with a history of allergic reactions are at increased risk of developing a hypersensitivity reaction. Other type 1 (immediate) reactions include symptoms like nausea and vomiting, skin rashes, dyspnoea, rhinitis, paraesthesia or hypotension. Vasovagal reactions (e.g. dizziness or syncope) which may be caused either by the contrast medium, or by the procedure. Cardiac side effects during cardiac catheterisation e.g. angina pectoris, ECG changes, cardiac arrhythmias, conductivity disorders, as well as coronary spasm and thrombosis. Such reactions are very rare and may be caused by the contrast medium or by the procedure. Nephrotoxic reactions in patients with pre-existing renal damage or renal vasopathy, e.g. decrease in renal function with creatinine elevation. These adverse effects are transient in the majority of cases. In single cases, acute renal failure has been observed. Neurotoxic reactions after intra-arterial injection of the contrast medium e.g. visual

disorders, disorientation, paralysis, convulsions, or fits. These symptoms are generally transient and abate spontaneously within several hours or days. Patients with pre-existing damage of the blood-brain barrier are at increased risk of developing neurotoxic reactions. Local reactions at the injection site may occur in very rare cases and include rashes, swelling, inflammation and oedema. Such reactions occur probably in most cases due to extravasation of the contrast agent. Extended paravasation may necessitate surgical treatment. Extravasation can cause serious tissue reactions including blistering and skin exfoliation, the extent of which is dependent on the amount and strength of the contrast solution in the tissues. **Marketing Authorization Information:** The marketing authorization holder, number and date of approval may differ one country to another. Volume, presentation and indication may also differ. For your specific information, please contact your local Guerbet Office or representative. Date of (partial) revision of the text: February 2016.

Xenetic[®]: Xenetic[®] 350 solution for injection (350 mg/ml) ; Xenetic[®] 300 solution for injection (300 mg/ml) ; Xenetic[®] 250 solution for injection (250 mg/ml) — Composition per 100 ml : Xenetic[®] 350 : 76.78 g of iohibitridol (corresponding to 35 g of iodine), Xenetic[®] 300 : 65.81 g of iohibitridol (corresponding to 30 g of iodine), Xenetic[®] 250 : 54.84 g of iohibitridol (corresponding to 25 g of iodine) — **Indications(**):** this product is for diagnostic use only. **Contrast agent for use in:** Xenetic[®] 350 intravenous urography, computed tomography, intravenous digital subtraction angiography, arteriography, angiocardiology — Xenetic[®] 300: intravenous urography, computed tomography, intravenous digital subtraction angiography, arteriography, angiocardiology, endoscopic retrograde cholangiopancreatography, arthrography, hysterosalpingography — Xenetic[®] 250: phlebography, computed tomography, intra-arterial digital subtraction angiography, endoscopic retrograde cholangiopancreatography — **Posology and method of administration(*):** the doses should be adapted to the examination and the territories intended to be opacified, as well as to the weight and renal function of the subject, particularly in children — **Contraindications(*):** hypersensitivity to iohibitridol or any of the excipients, history of major immediate or delayed skin reaction (see undesirable effects) to Xenetic[®], manifest thyrotoxicosis, hysterosalpingography during pregnancy. — **General comments for all iodinated contrast agents (**):** in the absence of specific studies, myelography is not an indication for Xenetic[®]. All iodinated contrast media can cause minor or major reactions that can be life-threatening. They may occur immediately (within 60 minutes) or be delayed (within 7 days) and are often unpredictable. Because of the risk of major reactions, emergency resuscitation equipment should be available for immediate use. — **Precautions for use(*):** intolerance to iodinated contrast agents, renal insufficiency, hepatic insufficiency, asthma, dysthyroidism, cardiovascular diseases, central nervous system disorders, phlebotomy, myasthenia; **Interaction with other medicinal products and other forms of interaction (**):** beta-blocker substances, diuretics, mefloquine, radiopharmaceuticals, interleukin II — **Fertility, pregnancy and lactation (**):** Undesirable effects(*): hypersensitivity, anaphylactoid reaction, anaphylactoid shock, angioedema, urticaria, erythema, pruritus, exzema, acute generalized exanthematous pustulosis, Stevens-Johnson syndrome, Lyell's syndrome, maculopapular exanthema, bronchospasm, laryngospasm, laryngeal oedema, dyspnoea, sneezing, cough, tightness in throat, nausea, vomiting, abdominal pain, agitation, headache, vertigo, hearing impaired, presyncope, tremor, paraesthesia, somnolence, convulsions, confusion, visual disorders, amnesia, photophobia, transient blindness, coma, feeling hot, facial oedema, malaise, chills, tachycardia, arrhythmia, ventricular fibrillation, hypotension, circulatory collapse, hypertension, angina pectoris, myocardial infarction, cardiac arrest, torsades de pointes, coronary arteriospasm, respiratory arrest, pulmonary oedema, thyroid disorder, acute renal failure, anuria, blood creatinine increased, injection site pain, inflammation, oedema, necrosis following extravasation. — **Overdose (**):** Pharmacodynamic properties (**): Pharmacotherapeutic group: Water-soluble, contrast medium with low osmolality; ATC code: V08AB11. **Presentation (**):** Xenetic[®] 250: 50 ml, 100 ml, 200 ml or 500 ml polypropylene bags; Xenetic[®] 300/350: 20 ml, 50 ml, 60 ml, 75 ml, 100 ml, 150 ml, 200 ml or 500 ml glass vials and 100 ml, 150 ml, 200 ml or 500 ml polypropylene bags. **Marketing authorisation holder (*):** Guerbet - BP 57400 - F-95943 Roissy CDG cedex - FRANCE. **Information:** tel: 33 (0) 1 45 91 50 00. **Revision:** September 2015.

(*): For complete information please refer to the local Summary of Product Characteristics. (**): Indications, volumes and presentations may differ from country to country. **Reporting of suspected adverse reactions is important as it helps to continuously assess the benefit-risk balance. Therefore, Guerbet encourages you to report any adverse reactions to your health authorities or to your local Guerbet representative.** **Injectors:** FlowSens[®]: Class IIb — CE0459 — Manufacturer: MEDEX - 240 Allée Jacques Monod, 69800 Saint-Priest, France. OptiOne[®], OptiVantage[®]: Class IIb — CE0123 — Manufacturer: Liebel-Flarsheim Company LLC - 2111 East Galbraith Road, Cincinnati, OH 45237, USA. These medical devices are intended for use by medical imaging and diagnostic healthcare professionals. For complete information about precautions and optimal usage conditions we recommend consulting the instructions for use/user's manuals. Please ask your local contact person for availability in your country, depending on local registration. OptiOne[®], OptiVantage[®] & FlowSens[®] are trademarks of Guerbet & Liebel Flarsheim. Issued and pending patents.



Bit by bit

In ongoing efforts to reduce radiation exposure to patients and healthcare professionals alike, how big a role might a new generation of radiation dose monitoring software have to play? The UK's National Institute for Health and Care Excellence (NICE) has developed a Medtech innovation briefing, inviting input from industry specialists on existing and incoming measurement techniques.

The use of radiation dose-monitoring software may improve the collection, analysis and reporting of radiation dose data compared with current manual or semi-automated methods. The detailed information provided by dose-monitoring software allows the best image quality possible, while minimising radiation exposure to the patient.

Dose-monitoring software can be used to alert healthcare professionals to radiation exposure when diagnostic reference levels (DRLs) are consistently exceeded. Some of the technologies may help facilitate management of protocols, contrast media and staff dose as well as image quality.

The systematic monitoring and analysis of radiation dose data can potentially reduce radiation exposure for people having multiple imaging procedures. It can help hospitals meet legal and policy requirements. Based on 'Medical exposure directive 97/43', in some European countries (currently including the UK), radiation protection legislation mandates the recording of individual patient doses (or parameters from which dose can be calculated). Current UK legislation includes 'Ionising radiation (medical exposure) regulations 2000 (IRMER)' from the Department of Health, which details DRLs and what to do in cases of excessive radiation exposure. Systematic dose monitoring may help to support quality assurance in terms of meeting directives such as the 'EU Council Directive 2013/59/EURATOM'.

Current guidelines and arrangements

Public Health England currently gathers radiation dose data for common examinations from a sample of UK hospitals through manually compiled databases. The Department of Health's response to COMARE's 16th report on the increased use of CT scans in the UK recommended that more frequent UK dose surveys need to be done. These surveys will provide data to support regular updating of national DRLs, including those specifically for children.

Manual and semi-automatic recording of radiation dose data requires data entry

in the radiology information system, a spreadsheet or on paper. This is time-consuming and may result in an error rate of up to 6%, according to a 2016 research paper on the matter.

The 2011 review of the Public Health England report 'CRCE-013: Doses from CT examinations in the UK' specifies that for a national audit on radiation dose data, a healthcare professional (either a radiographer or a physicist) with access to PACS should acquire the data.

“ If adopted, the technologies would likely be used with the available ionising radiation imaging equipment. ”

It is the data manager, whether they be a radiographer or a physicist, that should verify the data before transferring it to a record.

The technologies could be used for retrospective analysis by healthcare professionals specialising in radiation protection and with appropriate training. These would most likely be medical physicists, radiographers and radiologists. The technologies would be used in secondary care in the NHS to record and analyse data in the trust. Radiation dose data can be collected from anyone undergoing medical imaging with ionising radiation.

Cost of standard care

The main cost associated with manual dose data recording is the clinical time it takes. The cost of a hospital radiographer's time is £35 per hour and a medical physicist's time is £56 per hour. This includes all remuneration, qualifications, department overheads and capital costs. The cost depends on whether data is recorded manually (by radiographers filling in forms) or downloaded from the radiology information system. Specialist commentators estimate that it takes 20 minutes of a radiographer's time for data collection per examination. The data is then transferred to a medical physicist for verification of data entry, review, analysis and report production.

This takes at least one hour per examination. Combining the radiographer's and medical physicist's time, the estimated average cost is £68 per examination.

If data is instead taken from the radiology information system, little or no radiographer time is needed. However, extra medical physicist input may be needed to understand the data, eliminate outliers, confirm the validity of results and remove zero values before the data can be analysed.

One specialist commentator estimated that this is at least 1.5 hours of a medical physicist's time is needed for each individual examination, with an estimated average cost of £84.

Resource consequences

If adopted, the technologies would likely be used with the available ionising radiation imaging equipment. A mid-sized hospital trust could have an average volume of 100,000 images per year, whereas a large trust may do 250,000 images per year.

These technologies are software packages to be used with current hardware and so no additional facilities or technologies are likely to be needed. However, the hospitals will need to reallocate staff to manage information governance and software compatibility arrangements such that the technologies can be properly installed and used. This may prove to be time-consuming. The technologies will need IT involvement to set up and staff to maintain them. No published evidence on the resource consequences of adopting the technologies was found, including either economic evaluations or costing studies.

Specialist opinion

Comments on monitoring technology currently available were invited from clinical and scientific experts working

in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view. All five specialist commentators were familiar with these technologies. One specialist used at least one of the technologies infrequently (approximately five times per year); another used them regularly (on a weekly or monthly basis).

Two specialists stated that the radiation dose-monitoring software technologies are a minor variation of current technology, automating an existing process by using modern IT standards to interconnect imaging devices with data collection devices. Four commentators thought that the technologies could potentially improve data collection and image quality, and minimise radiation doses. One of the specialists stated that the technologies are a significant development in allowing real-time evaluation of all systems in an organisation, helping to identify imaging systems in which problems may be developing.

All but one specialist commentator thought that some level of training would be needed to use the software.

Potential patient impact

Three specialists anticipated that the technologies would have little or no direct effect on patients. However, three other specialists felt that the software could reduce overall population radiation exposure by allowing regular reliable audits, which would improve patient safety and reduce risk. Two specialists stated that the technologies would particularly benefit young people, and one felt that they could help to identify people with chronic conditions who have repeated examinations and therefore radiation exposure.

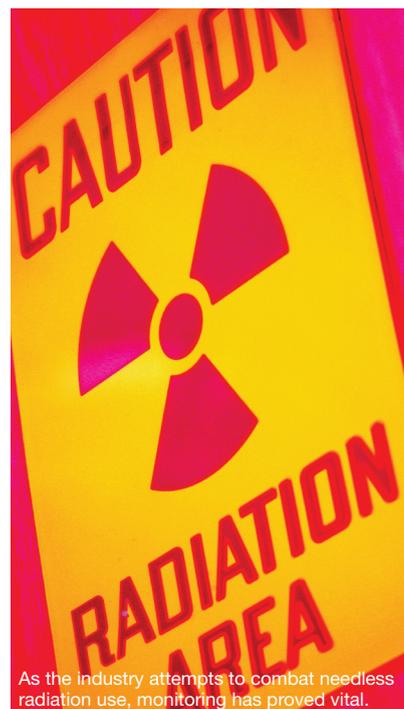
Three commentators thought that using the technologies could improve diagnostic accuracy and confidence, which would benefit patients. One stated that they may enable higher radiation doses to be used where appropriate to increase image quality. Another specialist stated that an alert system to identify relevant previous imaging might reduce a very small number of unnecessary examinations.

Potential system impact

The commentators agreed that the technologies would help to optimise images, which would be beneficial for the healthcare system. Three specialists felt that the automation would ease the burden of the current manual process of recording dose-monitoring data. One specialist stated that the technologies would help identify variation in techniques within or between institutions, highlighting the need for optimisation of radiation dose and image quality. Two commentators stated that using this software would lead to multidisciplinary teams optimising their work, possibly reducing the amount of time spent by the team on analysing patient dose data. However, another commentator expressed doubt that the additional information would reduce time spent by medical physicists on collection, analysis and reporting, stating that more time will be needed for analysis and interpretation. One of the commentators added that additional staff resources would be necessary for maximum benefit from the systems.

All the specialist commentators acknowledged that the database system would need to connect to existing IT infrastructure: some systems would be able to work with existing IT infrastructure with minimal changes and updates, whereas others may need a larger investment (for example, an increase in server capacity).

Four specialists thought that the potential for NHS cost savings was unclear, and one stated that a detailed cost analysis would be necessary to assess the cost implications. Another commentator stated that the financial savings would be minimal, because the technologies provide quality improvements rather than significant cost savings. One specialist stated that although dose-monitoring systems may make data recording faster, the process is likely to include more examinations than would have been included with manual data entry. Another explained that some people may choose to pursue legal action over WWexcess radiation exposures, so the technologies could reduce legal costs.



As the industry attempts to combat needless radiation use, monitoring has proved vital.

One specialist noted that the Public Health England report called for patient-size measurements to be taken from the images, because this information is rarely available and is a significant factor in terms of variation in radiation dose; the commentator did not feel that dose monitoring technologies would eliminate this manual step. Two specialists noted that dose monitoring systems are most useful if they are connected to multiple modalities, information systems and shared across organisations.

One commentator stated that regional or national dose collection would be needed for setting and optimising interventional DRLS; the potential for collection of large scale data offered by these technologies could transform the insight available. Another commentator expected the evidence to be generalisable across all technologies because the handling of data will have more of an effect than the technology itself.

According to another Public Health England report, 'Medical and dental X-rays: frequency and collective doses in the UK', 26% of medical imaging examinations with ionising radiation are for dental purposes and, the software will not be able to analyse most of these. ■

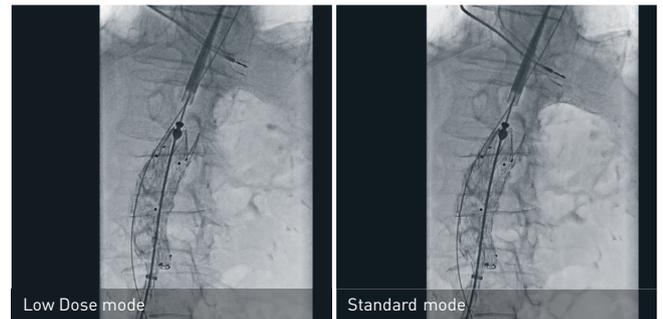


Supporting your patient care

Minimizing dose while maintaining image quality is an important goal worldwide for surgeons, their staff and patients. Ziehm Imaging supports this through further improvements to SmartDose¹ for different applications.

Comprehensive SmartDose concept

- **Low Dose mode in all anatomical programs** for particularly dose-sensitive procedures, e.g. in pediatrics
- **Beam Filtration² for reduced skin entrance dose** without compromising on image quality
- **ZAIP algorithm and filters** to display fast-moving objects like guide wires and even the smallest vessels in razor-sharp image quality



AAA, Ziehm Vision RFD Hybrid Edition CMOSline

www.ziehm.com/SmartDose

¹The SmartDose concept consists of a broad variety of different features. Due to regulatory reasons, the availability of each feature may vary. Please contact your local Ziehm Imaging partner for detailed information. ²The technology Beam Filtration reduces dose exposure for all CMOSline systems in comparison with conventional filtration techniques (status before September 2017). Data on file. Results may vary.

ALWAYS
AHEAD

 **ziehm imaging**



brainreader

Our vision is to revolutionize the diagnostic of neurodegenerative diseases

Introducing Neuroreader™

Neuroreader is a brain volume assessment software offering computerassisted analysis of brain MRI scans

Neuroreader performs a fully automated analysis of 45 visually identifiable brain structures in only 10 minutes

Neuroreader supplements subjective assessments of brain volume with quantifiable metrics

Neuroreader enables radiologists to increase productivity, optimize distribution of resources, reduce subjectivity and establish a new standard of radiological reading ensuring greater assessment confidence

"Neuroreader gives us easy, reliable, reproducible volume measurements, and takes the guess work out of analyzing structures in our patients' brains."

*Barton Branstetter,
MD - Professor,
University of Pittsburgh,
Medical Center, Pittsburgh*

"Neuroreader has established itself as an essential diagnostic aid in our memory disorders programme."

*John L. Ulmer,
MD - Professor of Radiology,
Froedtert & Medical College
of Wisconsin, Milwaukee*