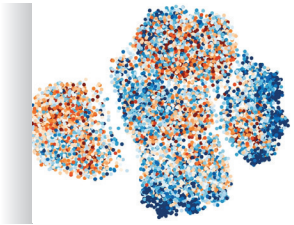
DI EUROPE

DIAGNOSIS · TECHNOLOGY · THERAPY · INTERVENTIONAL

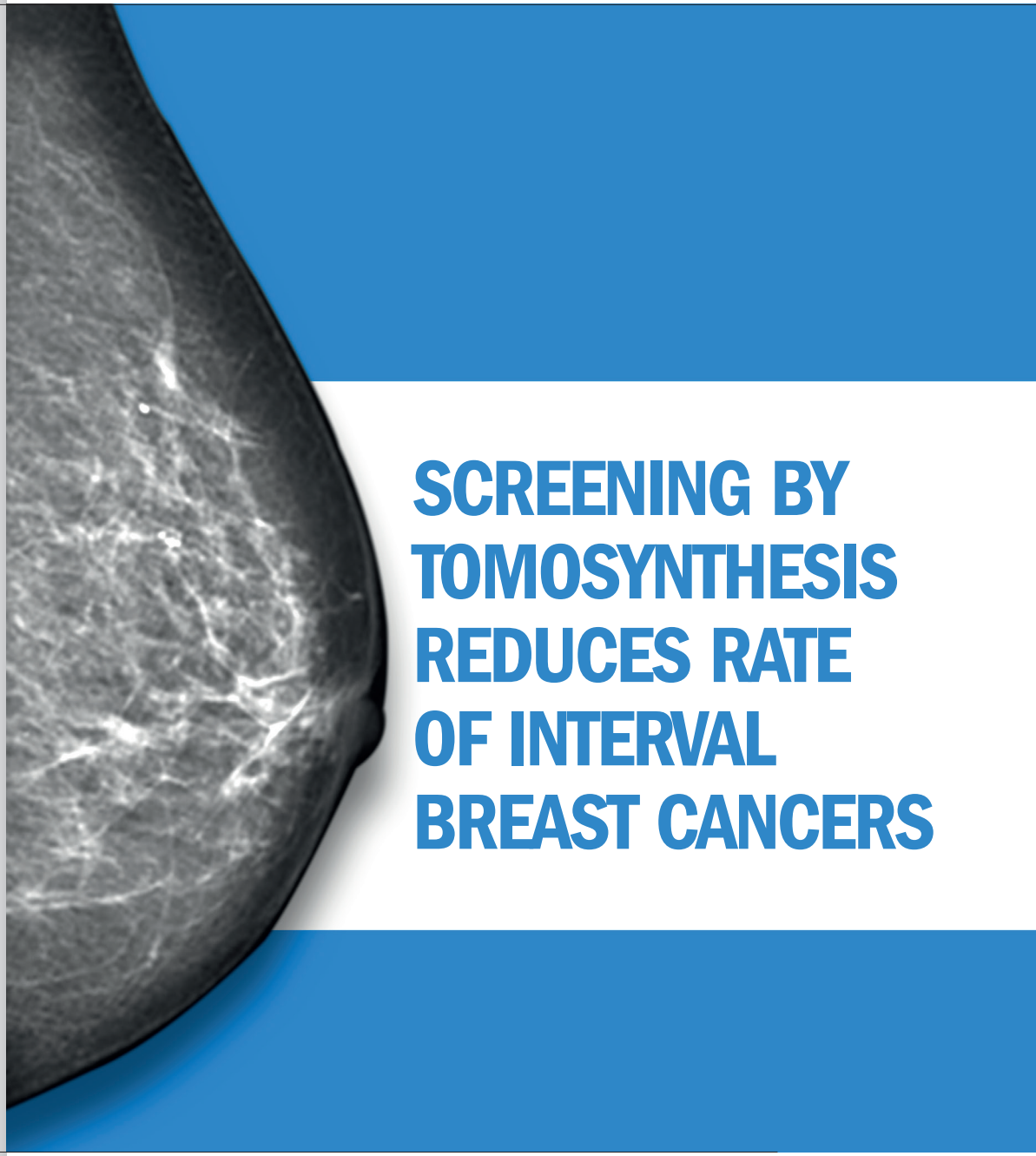
JUNE 2021

DIAGNOSTIC IMAGING EUROPE

Coronary artery disease



Using machine learning to standardize diagnostic testing pathways in suspected CAD

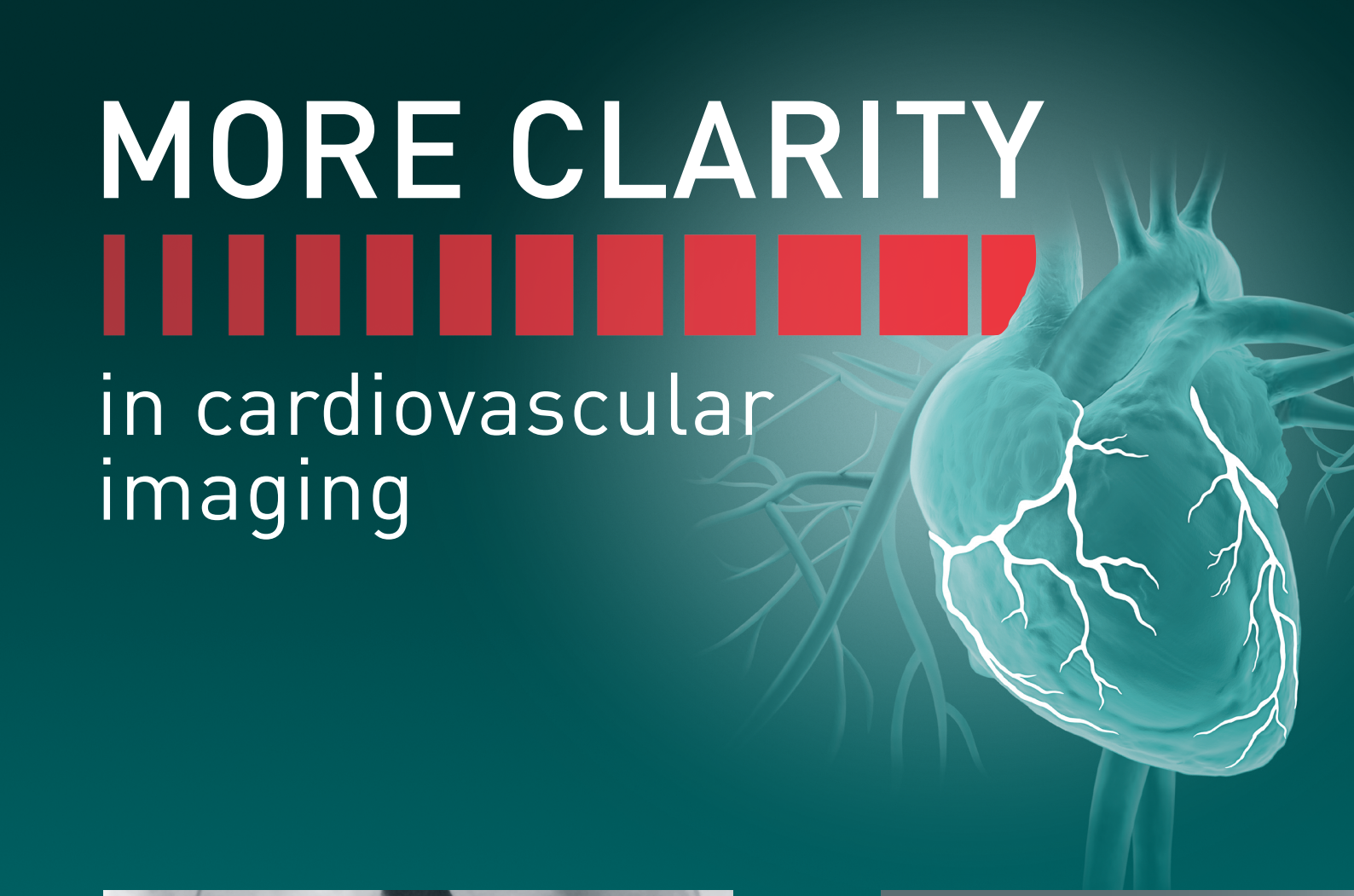


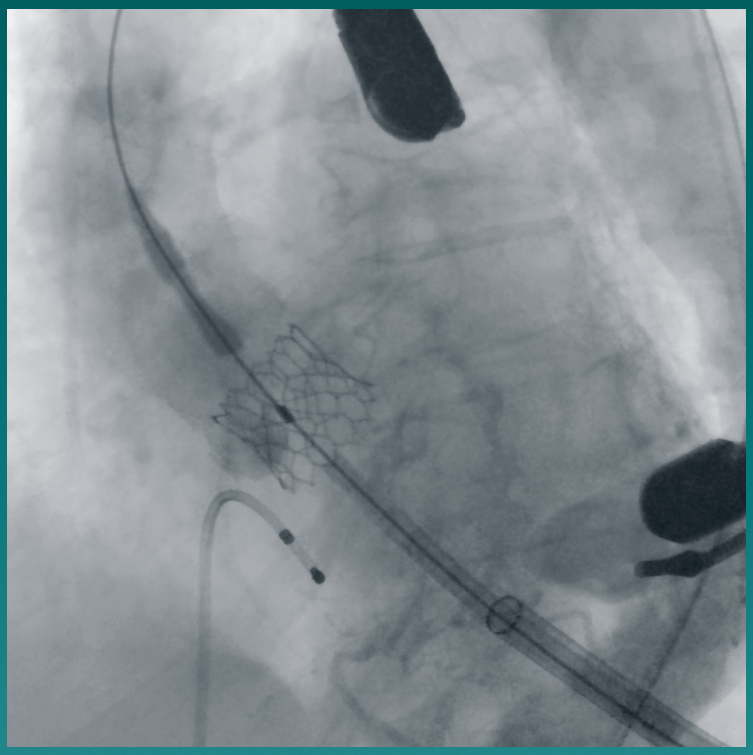
SCREENING BY TOMOSYNTHESIS REDUCES RATE OF INTERVAL BREAST CANCERS

DIEUROPE.COM

MORE CLARITY

in cardiovascular imaging





Visit us at
ebooth.ziehm.com

Due to an aging population, we are seeing a rising burden of cardiovascular diseases. Therefore we have developed sophisticated intraoperative imaging solutions that bring more clarity into cardiovascular interventions.

ALWAYS AHEAD

ziehm imaging

DI EUROPE®

VOLUME 37, NUMBER 2

SUBSCRIBER SERVICES
Telephone: +44 1442 877777

SUBSCRIPTION AND ARTICLE REPRINTS:
E: info@dieurope.com

SUBSCRIPTION RATES PER ANNUM:
Within Europe €70.00
ROW €130.00

INTERNATIONAL SALES OFFICES

Europe, North America & Japan
DI Europe Ltd
Tel: + 44 (0)1442 877777
Marika Cooper
E-mail: m.cooper@dieurope.com

China
Adept Marketing
E-mail: adonism@adeptmkg.com.hk
Telephone: +852 2891 7117
Contact: Adonis Mak

Korea
Young Media Inc
E-mail: ymedia@chol.com
Telephone: +82 2 2273 4819
Contact: Keon Chang

DIAGNOSTIC IMAGING EUROPE is published six times a year by DI Europe Ltd Printed by Manson, St-Albans, UK. Annual subscriptions are available for €60 within Europe where it is also sent free of charge to physicians and radiology department heads. Outside of Europe, there is an annual subscription charge of €130 for air mail. Single copy price is €15. Editorial Advisory Board members suggest topics for coverage and answer questions for the editors. They do not conduct a formal peer-review of all manuscripts submitted to DI Europe.

DI Europe Ltd
2 Claridge Court
Lower Kings Road
Berkhamsted, Herts HP4 2AF
UK
Telephone: +44 1442 877777

DIEUROPE.COM

BY ALAN BARCLAY, Ph.D.

Learning the lessons

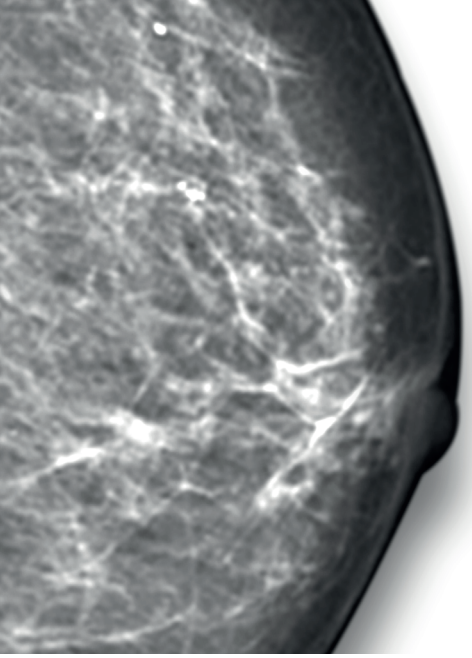
Apart from continuing and worrisome COVID-19 hot-spots and the as yet unquantified likely impact of new viral variants on the effectiveness of vaccines, the feeling in most of Europe is that the worst of the COVID-19 pandemic is over — for the time being at least. It is tempting to think that as COVID-19 vaccinations increase and infections decrease, patients will be willing to return to hospitals and clinics. With almost everyone recognising that things will never return to exactly what they were before the pandemic, there is a wide-spread awareness that the lessons of the pandemic must be learned and all appropriate actions implemented.

The starting point for the process of learning lessons is an objective analysis of hard facts — data on the impact of the virus on health are now beginning to appear. The provisional 2020 mortality data for the United States have just been published and give the first insight of the overall impact of COVID -19, with the figures showing a significant increase in the total number of deaths compared to 2019 (*Farida B et al. Provisional Mortality Data - United States, 2020 MMWR Morb Mortal Wkly Rep. 2021; 70: 519. doi:10.15585/mmwr.mm7014e1*). Unsurprisingly, the data show that most of the increase in deaths from 2019 to 2020 was directly attributed to COVID-19. However, increases were also noted for several other leading causes of death. These increases may indicate, to some extent, underreporting of COVID-19, e.g. limited testing at the beginning of the pandemic may have resulted in underestimation of COVID-19 mortality. Increases in other leading causes, especially heart disease, Alzheimer disease, and diabetes, may also reflect disruptions in health care that hampered early detection and disease management. At a more granular level of the data, there are ominous signs that the real impact of COVID -19 may only be appreciated much further in the future. According to a new survey from the American Society for Radiation Oncology (ASTRO), cancer clinics in the US report that new patients are arriving for treatment with more advanced disease than before the COVID-19 pandemic. As Dr. T Eichler, Chair of the ASTRO board of directors put it, *"One year into the COVID-19 pandemic, we already see the consequences of pandemic-driven drops in cancer screening and diagnostics"*. Two-thirds of the radiation oncologists surveyed said new patients are presenting with more advanced-stage cancers. Nearly three-quarters of the radiation oncologists said physicians in their practice are noticing that patients are not receiving cancer screenings, and many also said existing patients experienced an interruption in their radiation treatment due to the pandemic.

From the purely radiology point of view, there have been some encouraging signs that the pandemic hasn't completely affected the services expected of the sector. Thus, a study in the UK (*J K Seehra et al. Impact of COVID-19 on access and availability of radiological imaging and surgical intervention at the East Midlands Major Trauma Centre: An ICON Trauma Study. Br J Surg . 2021 Apr 30; 108: doi: 10.1093/bjs/znab014*) showed that the UK recommendations for the optimal handling of trauma cases which stipulate that CT must be available within 15 minutes of a hospital admission of a major trauma case were actually met just as completely during the pandemic as in pre-pandemic times. However this apparently encouraging statistic has to be considered in the light of the fact that, overall there was an absolute reduction of more than 40% in the total number of trauma admissions during the COVID-19 period.

Sooner or later all these national and regional observations will be melded into a consensus view of the effect of COVID-19 in radiology. However even now, one important message is beginning to appear, namely the increased level of stress and consequent decrease in morale experienced by many health care providers, particularly radiographers. (*Yasin* ***et al.*** *The impact of the Covid-19 pandemic on the mental health and work morale of radiographers within a conventional X-ray department. Radiography (Lond). 2021; S1078-8174(21)00047-X. doi: 10.1016/j.radi.2021.04.008.*).

Due recognition of this effect of COVID-19 must be made, and corrective action taken. ■



Interval cancer rates with DBT and digital mammography were 1.6 per 1,000 screened, compared to 2.8 per 1000 with digital mammography only.

Image adapted from Johnson K et al Interval Breast Cancer Rates and Tumor Characteristics in the Prospective Population-based Malmö Breast Tomosynthesis Screening Trial. Radiology. 2021; 000:1–10 Image credit RSNA

DIAGNOSTIC IMAGING EUROPE

JUNE 2021

Front Cover Story

STUDY SHOWS BREAST SCREENING BY TOMOSYNTHESIS REDUCES RATE OF INTERVAL CANCERS

A recently published study from a Swedish group reports that breast screening with digital breast tomosynthesis (DBT) reduces the rate of interval breast cancers compared to screening with digital mammography.. The study adds to a growing body of evidence supporting DBT as a breast cancer screening tool with important advantages over mammography. 23

Breast Imaging

REPORTS

First experiences with a wide-bore small footprint MRI system operating at 0.55 Tesla, the Magnetom Free.Max from Siemens Healthineers.

Page 26

The Business Interview. Franco Fontana, the CEO of Esaote talks about the impact of the COVID pandemic and describeds the potential of Esaote going forward.

Page 36

Mobile C-arms meet the challenge of making surgical interventions more efficient, while maintiaing maximum safety.

Page 39

CARDIOVASCULAR IMAGING

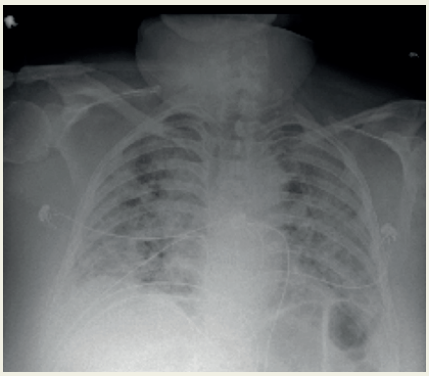
IMAGING NEWS

DI EUROPE

COMING IN THE NEXT ISSUE:
Ultrasound
MRI
Breast imaging

VISIT US AT
DIEUROPE.COM

AI tool uses chest X-ray to identify worst COVID-19 prognoses



Chest X-ray from patient severely ill from COVID-19, showing (in white patches) infected tissue spread across the lungs. Image credit npj Digital Medicine

The results of a new study show that software trained to recognize patterns by analyzing thousands of chest X-rays, can predict with up to 80 percent accuracy which COVID-19 patients would develop life-threatening complications within four days (*Shamout FE et al. An artificial intelligence system for predicting the deterioration of COVID-19 patients in the emergency department NPJ Digit Med. 2021; 12;4(1):80. doi: 10.1038/s41746-021-00453-0)*.

Developed by researchers at NYU Grossman School of Medicine, the program used several hundred gigabytes of data gleaned from 5,224 chest X-rays taken from 2,943 seriously ill patients infected with SARS-CoV-2.

For reasons not yet fully understood, the health of some COVID-19 patients suddenly worsens increasing their chances of dying, and requiring intensive care.

The authors cite the "pressing need" to be able to quickly predict which COVID-19 patients are likely to have lethal complications so that treatment resources can best be matched to those at increased risk. In a bid to address this need, the NYU Langone team fed not only X-ray image information into their computer analysis, but also patients' age, race, and gender, along with several vital signs and laboratory test results, including weight, body temperature, and blood immune cell levels. Also factored into their mathematical models, were the need for a mechanical ventilator and whether each patient went on to survive (2,405) or die (538) from their infections. Researchers then tested the predictive value of the software tool on 770 chest X-rays from 718 other patients admitted for COVID-19 through the emergency room at NYU Langone hospitals from March 3 to June 28, 2020. The computer program accurately predicted four out of five infected patients who required intensive care and mechanical ventilation and/or died within four days of admission.

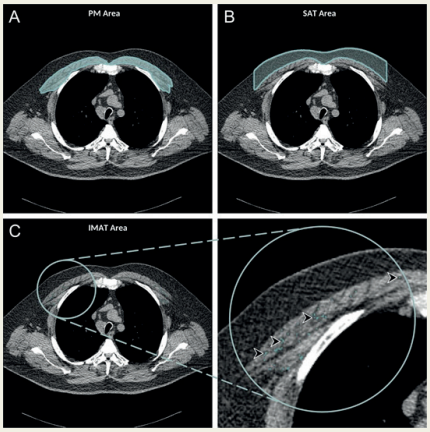
"*Emergency room physicians and radiologists need effective tools like our program to quickly identify those COVID-19 patients whose condition is most likely to deteriorate rapidly so that health care providers can monitor them more closely and intervene earlier*," said study co-lead investigator Dr Farah Shamout. Study senior investigator Dr. Krzysztof Geras, said that "*a major advantage of machine-intelligence programs such as ours is that its accuracy can be tracked, updated and improved with more data. The team is evaluating what additional clinical test results could be used to improve our test model*".

doi: 10.1038/s41746-021-00453-0.

Chest CT can give mortality risk in patients with COPD

Body composition information derived from routine chest CTs can provide important information on the overall health of people with chronic obstructive pulmonary disease (COPD), including their risk of all-cause mortality, according to a recent study (*Pishgar F et al. Quantitative Analysis of Adipose Depots by Using Chest CT and Associations with All-Cause Mortality in Chronic Obstructive Pulmonary Disease: Longitudinal Analysis from MESArthritis Ancillary Study. Radiology. 2021 Jun;299(3):703-711. doi: 10.1148/radiol.2021203959*).

COPD is a group of chronic, progressive lung diseases such as emphysema and chronic bronchitis. It is frequently associated with obesity and sarcopenia. Obesity is associated with lower mortality in patients with COPD. The longer survival rates of obese patients compared to leaner counterparts, a phenomenon known as the "obesity paradox," has been



Axial chest CT examination in a 54-year-old participant. A, On the axial noncontrast chest CT image, the pectoralis muscle (PM) area was segmented and measured in the section above the aortic arch. B, The subcutaneous adipose tissue (SAT) area as the area between the PM and the skin surface on the same section was also measured and the attenuation of pixels in the SAT area was used to determine the individualized threshold for the intermuscular adipose tissue (IMAT). C, The IMAT within the PM was segmented as the areas with Hounsfield units below this threshold for the IMAT (arrowheads).
Image credit RSNA

suggested in several chronic illnesses. Chest CT is often used to characterize COPD or screen for lung cancer. Beyond lung assessment, these exams offer an opportunity to assess obesity and sarcopenia through soft-tissue biomarkers.

"*Chest CT scans have long focused on the lungs or heart*," said study coauthor Dr. DA Bluemke. "*Few prior investigators have evaluated muscle quality, bone density, or degeneration of the spine as an index of overall health. Yet these are readily available and quantifiable in these CT examinations.*"

For the new study, the team used chest CT exams to study the associations between imaging-derived soft tissue markers and all-cause mortality in COPD. The study group was made up of 2,994 participants drawn from the Multi-Ethnic Study of Atherosclerosis (MESA), the large trial investigating the

roles of imaging-derived soft-tissue and bone markers for predicting outcomes relevant to cardiopulmonary diseases. Of the 265 patients in the study group with COPD, 49 (18%) died over the follow-up period.

A greater amount of intermuscular fat was associated with higher mortality rates. Existing research has linked higher levels of intermuscular fat with diabetes and insulin resistance. Higher subcutaneous adipose tissue, in contrast, was linked to lower risks of all-cause mortality. The authors convincingly showed that fat in the muscle was much more predictive of bad outcomes than a simple distribution of subcutaneous fat.

The findings point to a role for body composition assessment in people with COPD who undergo chest CT. Such assessments are readily obtainable in clinical practice. In theory, CT-derived body composition assessments would provide an opportunity for earlier interventions in patients who face a higher risk of adverse health events.

Body composition assessments taken from chest CT also present an opportunity for artificial intelligence-derived algorithms that could quickly and automatically add risk assessment to the imaging report.

"*I expect that more studies in the future will begin looking at all information on the CT, rather than just one organ at a time*," Dr. Bluemke said. "*Clinicians will need thresholds when to intervene when fat or bone abnormalities become severe.*"

doi: 10.1148/radiol.2021203959

Lung cancer screening predicts risk of death from heart disease

A recent study from a Dutch group of researchers shows that a deep learning algorithm accurately predicts the risk of death from cardiovascular disease using information from low-dose CT exams carried out for lung cancer screening (*de Vos BD et al. Deep Learning-Quantified Calcium Scores for Automatic Cardiovascular Mortality Prediction at Lung Screening Low-Dose CT. Radiol Cardiothorac Imaging. 2021;3(2):e190219. doi: 10.1148/ryct.2021190219).*

Cardiovascular disease is the leading cause of mortality worldwide, even outpacing lung cancer as the leading cause of death in heavy smokers. Low-dose CT lung scans are used to screen for lung cancer in high-risk people (such as heavy smokers). These CT scans also provide an opportunity to screen for cardiovascular disease by extracting information about calcification in the heart and aorta. The presence of calcium in these areas is linked with the buildup of plaque and is a strong predictor for cardiovascular disease mortality, heart attacks and strokes.

For the new study, researchers tested a faster, automated method created using the power of deep learning, that can predict five-year cardiovascular disease mortality with only minimal extra workload. Using data from 4,451 participants, median age 61 years, who underwent low-dose CT over a two-year period in the National Lung Screening Trial, the researchers trained the method to quantify six types of vascular calcification. They then tested the method on data from 1,113 participants.

The prediction model using calcium scores outperformed the baseline model that used only self-reported participant characteristics, such as age, history of smoking, and history of illness.

The method works in two stages, according to study lead author Dr. Bob D. de Vos from Amsterdam University Medical Center in Amsterdam, the Netherlands. The first stage determines the amount and location of arterial calcification in the coronary arteries and the aorta using deep learning. The second stage uses a more conventional statistical approach for mortality prediction. The second stage also indicates which features are most predictive for five-year mortality.

"*The analysis shows we found predictors that are typically not described in the literature, possibly because we performed analysis in lung cancer screening participants who are already at high risk of cardiovascular disease from a history of heavy smoking and the presence of extensive arterial calcification,*" Dr. de Vos said.

The method could easily be integrated into lung cancer screening, Dr. de Vos said. It does not require any special equipment and would not add time to the exam.

Projections of all aligned chest CT scans show feasibility of slab-based quantification of calcium, resulting in an average image. For alignment, only translation, rotation, and scaling were allowed, resulting in a blurry image, because not all anatomy is exactly the same across participants. From left to right, the center axial, sagittal, and coronal sections are shown. Note that field of view is similar to cardiac CT, which is a consequence of image alignment by the used automatic calcium scoring method. Image alignment allowed the determination of calcification distributions into slabs as a proxy measure for proximal and distal calcifications, of which the borders are indicated by the horizontal lines. Image credit RSNA.

"*The method uses only image information, it is fully automatic, and it is fast*," Dr. de Vos said. "*The method obtains calcium scores in a complete chest CT in less than half a second. This means that the method should be easy to implement in routine patient work ups and screening.*"

Most importantly, the method could help identify people in a population of heavy smokers who might be at increased risk of death from cardiovascular disease-related causes.

"Lung screening studies show that heavy smokers die from cardiovascular disease as much as from lung cancer," Dr. de Vos said. "But we also see that some people with very high calcium scores survive, while others with low scores do suffer from major cardiac events. The work offers a direction for future research to precisely pinpoint which calcifications are dangerous."

The researchers have developed a number of methods for automatic calcium scoring that can be applied to a wide variety of data. They are now working toward a calcium scoring method that accurately detects arterial calcification in low-quality data, like data affected by cardiac motion, low image resolution or high noise levels.

"*We developed a method, for example, that can detect coronary calcifications even when the lesions are below the clinically used threshold,*" Dr. de Vos said. "*This way, we hope to increase the reproducibility of calcium scoring and enable more accurate prediction.*"

doi: 10.1148/ryct.2021190219

AB-CT Advanced Breast-CT

Discover the Next Generation of **BREAST IMAGING**

nu:view

Empowering Radiologists

- REAL 3D images (360°)
- High isotropic resolution – voxel size: (150 µm)³
- Superimposition-free volumetric imaging
- Low dose and high dose efficiency

Respecting Patients

- Excellent patient comfort without compression
- No squeeze, no touch
- High intimacy
- Displays the breast in its natural shape

Designed for Clinical Excellence

- Short scan and examination times
- Easy to use
- Flexible support of clinical workflows

DISCOVER MORE

www.ab-ct.com

ARM 2021 | ANNUAL™ RADIOLOGY MEETING IN UAE

10 – 12 October 2021

Dubai World Trade Centre

In-person Event
Radiology Dedicated
Middle-East Focused

DON'T MISS IT OUT!

1,000+ Participants

60+ Leading Brands

3-Day Focused Radiologist Conference

2-Day Dedicated Radiographer Sessions

1-Day Special Ultrasound Seminar

CME Accredited

They Trust Us

UNITED IMAGING · AGFA HealthCare · AMICO x-ray technologies · Canon · PHILIPS · EIZO · FUJIFILM · HITACHI Inspire the Next · INFINITT · SIEMENS Healthineers

APPLY NOW

Exhibition inquiries:
exhibit@radiologyuae.com

Conference inquiries:
info@radiologyuae.com

Radiology_UAE

radiologyuae.com

INDEX® Conferences & Exhibitions Organization Est.
INDEX Holding Headquarters, Road D-62, Opposite to Nad Al Hamar | P.O. Box 13636, Dubai, UAE
Tel: +971 4 5208888 | Fax: +971 4 3384193 | e-mail: info@radiologyuae.com | index.ae

Organized by

In collaboration with

The implications of swollen lymph nodes following COVID-19 vaccination

Experts offer guidance to reduce false positive tests and avoid unnecessary biopsies

Lymph nodes in the armpit area can become swollen after a COVID-19 vaccination, and this is a normal reaction that typically goes away with time. Radiologists at Massachusetts General Hospital (MGH) who recently published an approach to managing this situation in women who receive mammograms for breast cancer screening have now expanded their recommendations to include care for patients who undergo other imaging tests for diverse medical reasons [1]. "*Our practical management plan extends the impact of our recommendations to the full spectrum of patients having imaging tests after vaccination*," says lead author Dr. Constance Lehman chief of Breast Imaging, co-director of the Avon Comprehensive Breast Evaluation Center at MGH, and professor at Harvard Medical School.

Lehman and her colleagues — from multiple subspecialties in radiology — note that as COVID-19 vaccination programs ramp up, radiologists should expect to see increasing numbers of patients who show swollen lymph nodes on imaging exams. They recommend that imaging centers document COVID-19 vaccination information — including the date(s) of vaccination, the location of the injection site, and the type of vaccine — on all patient forms and ensure that this information is easily available to radiologists at the time the image is interpreted.

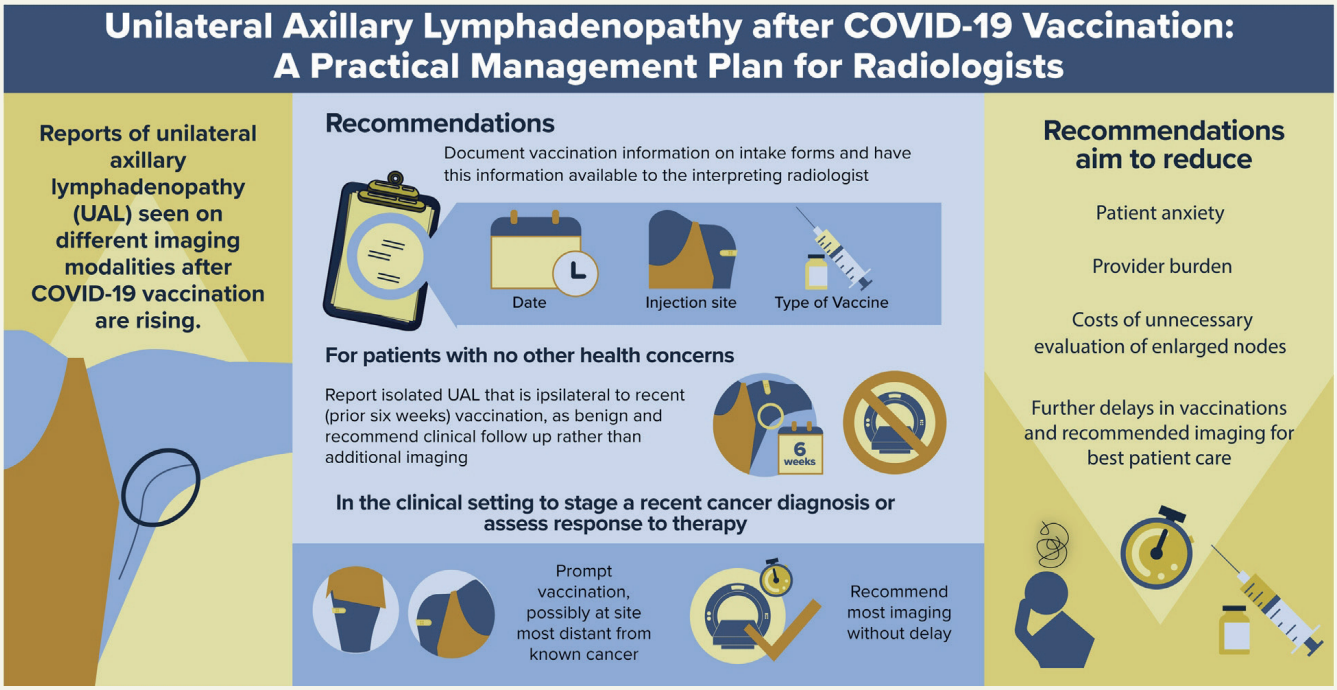
In most cases, no additional imaging tests are needed for swollen lymph nodes after recent vaccinations unless the swelling persists or if the patient has other health issues. Additional tests may be warranted in cases where there was a heightened concern for cancer in the lymph nodes before the imaging test was performed. "*In a patient with a recent cancer diagnosis, the patient's full care team and the radiologist can work together to determine how best to manage nodes that appear abnormal on imaging after a recent vaccination. That way, they can tailor care to the individual patient,*" says Dr. L Lamb breast imaging specialist at MGH and co-author of the study.

Radiologists' communication with clinicians and patients should stress the importance of avoiding delays in either vaccinations or recommended imaging tests to ensure their optimal care throughout the pandemic. "*Advanced planning can support our patients to feel confident and safe to receive their vaccinations as well as undergo recommended imaging in their usual care,*" says Lehman.

The team's management recommendations will continue to be updated as more data are available to guide best practice.

REFERENCE

1. Lehman CD *et al.* Unilateral Lymphadenopathy After COVID-19 Vaccination: A Practical Management Plan for Radiologists Across Specialties J Am Coll Radiol . 2021 Jun;18(6):843-852. doi: 10.1016/j.jacr.2021.03.001.



JACR Visual abstract. Image reproduced with permission from Ref 1. J Am Coll Radiol.

Pressure-based compression in breast tomosynthesis

The Christine E. Lynn Women's Health & Wellness Institute in Boca Raton, FL, USA is renowned for providing a broad continuum of care addressing women's medical needs in South Florida and has a range of the most advanced imaging systems to support its mission. In keeping with its policy of offering the most-up-to-date equipment, the Institute has recently evaluated a pressure-based breast compression system from the Dutch company Sigmascreening, for use in mammography and breast tomosynthesis examinations.

We wanted to find out more about the Institute in general and the new pressure-based compression system in particular, so we spoke to Dr. Kathy Schilling, radiologist and medical director of the Institute.

Dr Kathy Schilling is Medical Director of the Christine E. Lynn Women's Health & Wellness Institute at the Boca Raton Regional Hospital in Boca Raton, FL, USA
Email: KSchilling@baptisthealth.net

Q *Before we get on to the new pressure-based breast compression system, please give us a brief description of your institute*

We have been established here in South Florida for some time now — we celebrated our 30-year anniversary in Boca Raton last year. Currently our Institute comprises a main building but we also have two satellite centers and a mobile mammography van.

The breast imaging procedures that we carry out currently include 2D and 3D screening and diagnostic mammography, screening and diagnostic ultrasound, Contrast Enhanced 2D mammography, Molecular Breast Imaging, Diagnostic breast MRI and Abbreviated MRI protocols. All told, in 2019 we performed 23,600 3D screening exams, 8428 3D diagnostic exams, 2188 2D diagnostic exams, 13,654 breast ultrasound exams, 1533 breast MRI, 30 CESM and 22 Molecular Breast Imaging procedures, giving a grand total of 49,455 procedures. From these data you can see that the breakdown of the exams we carry out is 70% screening and 30% diagnostic.

To carry out all this workload we have 11 GE Pristina mammography units providing 2D and 3D exams (with two of them able to carry out Contrast Enhanced Mammography and CEM-guided biopsies). We also have 9 Hologic SuperSonic Imaging ultrasound systems, a 3T GE MRI system and a GE Molecular breast imaging unit.

Our center is staffed with 3 radiologists per day - we provide real time reads on all our procedures except MRI. We have 14 mammography technologists, 8 US technologists, 2 MRI technologists and 4 Special procedure/NM technologists. The majority of our patients come from the surrounding area.

We endorse annual mammography screening in all women beginning at age 40 so long as they remain healthy and prepared to act on any findings. Patients can self-refer and there is no out-of-pocket cost for a screening procedure. Across the U.S.A, it is estimated that about 66% women have had a screening mammogram within the last 2 years. Digital Breast Tomosynthesis (DBT) is our screening method of choice including for women imaged on the mobile mammography van.

Q *What about breast density?*

For every mammogram we acquire, breast density is determined by Volpara Density software and reported according to the BIRADS 5th edition recommendations. Florida is one of the states in the U.S.A. where legally we are now required to report breast density to the woman concerned — in fact we had already been doing this for years before this law was enacted. The issue of breast density is important so we spend a lot of time and effort to educate our patients and referring physicians about the significance of breast density. Currently we give each patient a form, "Know Before You Go" which informs the patient of her personal breast density as well as her NCI Lifetime Risk of developing breast cancer. Recently we also began reporting the presence of breast artery calcifications and, because of the association of such calcifications with coronary artery calcification and cardiovascular risk will, if appropriate, recommend a cardiology consultation. We also recommend smokers to consider low dose CT lung cancer screening. Navigators assist patients in seeking out supplemental screening exams.

To get back to breast density, we most commonly recommend bilateral ultrasound supplemental screening for patients with high density breasts. Alternatives include contrast mammography and, less often, MRI. These modalities are also used for patients at high risk of breast cancer.

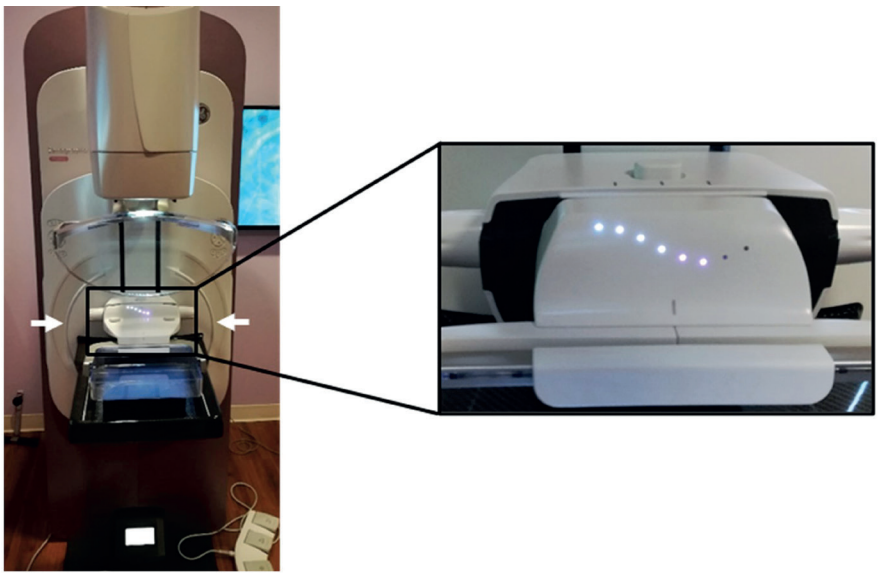


Figure 1. The flexible pressure-based compression paddle from Sigmascreening. fitted to a GE Senographe Pristina mammography system. The compression system is based on pressure measurements as opposed to the usual force. As seen in the Right Panel above, eight light emitting diode (LED) lights indicate the pressure level to the technologist and the participant. LED lights #5–7 (pink) indicate the target pressure range (8–13.9 kPa). Once the target range is reached, the indicator lights, present on the patient handles (arrows in Left Panel), automatically switch off. In the above Left Panel image, the handle lights are off. Image reproduced with permission from Reference 1.

We do not double-read exams but for about a year now we have been using an artificial intelligence-derived algorithm (the ProFound AI system from iCAD) to assist in DBT interpretation. A recent reader study of Profound AI found that it decreased interpretation time by 52%, increased the cancer detection rate by 7% and reduced recall rates by a similar amount. Currently the recall rates for our eight radiologists range from 5-13% (the recommended rate is <10%). We are currently carrying out research to determine any change in our interval cancer rates brought about through the use of the AI-derived software.

Q *And now let's get on to the question of breast compression*

The discomfort related to mammography breast compression is one of the main reasons patients fail to comply with screening guidelines. We were fortunate to participate in a research protocol utilizing the pressure-based compression device developed by Sigmascreening. The details and the results of this research work have now been published [1].

The paddle system itself was easily integrated into our Pristina mammography unit [Figure 1]. Our technologists quickly realized the benefit of standardized, consistent compression afforded by the device and easily adapted to it, so there was no learning curve involved. Importantly also, the patients readily understood the importance of the paddle.

We have only utilized the Sigmasceening compression-based paddle in the context of the research project as it is not (yet) currently commercially available for use in the US.

The results of our study showed that there was reduced variability in compression force — in particular there was less over-compression of smaller breasts and less under-compression of the larger breasts. This is important since the pain experienced by women with smaller breasts may in particular contribute to their lack of compliance with screening guidelines. With optimization and standardization of the compression, we should see improved image quality due to better compression of women with larger breasts, as well as reduced radiation dose.

We offer patient-assisted compression to our patients in general as we did to the 50 patients who participated in the Sigma paddle project. I believe that overall these patients feel they have better control over the procedure as compared to technologist compression. However, the attitude to patient-assisted compression is a personal one — many women prefer not to participate in the patient-controlled compression process.

The main outcomes of the research project evaluating the Sigma Paddle pressure-based system included:

1. An improvement in the experience for both the technologist and patient when the pressure based compression system was used. This may increase compliance with screening guidelines but will require future study.

2. Mean breast thickness and glandular dose were significantly reduced, so improving standardization of the image acquisition.

Q *How do you see future developments regarding the pressure-based compression system and screening mammography in general?*

I would anticipate utilizing pressure-based compression throughout our practice for standardization and optimization of outcomes when the system becomes available for routine clinical use in the USA.

As regards screening in general, I definitely believe that we will be moving from age-based screening to risk-based screening in the future and I think artificial intelligence together with personal genomics will become the standard method of determining risk. Algorithms will ultimately be developed which should optimize cancer detection and minimize interval cancers. As recommended by the American College of Radiology, the Society of Breast Imaging and the American Society of Breast Surgeons, every woman should undergo a personal risk assessment by the age of 30 so as to identify women for whom screening should be initiated before the age of 40.

REFERENCE.

1. van Lier MGJTB, de Groot JE, Muller S, den Heeten GJ & Schilling KJ Pressure-based Compression Guidance of the Breast in Digital Breast Tomosynthesis Using Flexible Paddles Compared to Conventional Compression Journal of Breast Imaging, 2020; 2,: 541. https://doi.org/10.1093/jbi/wbaa070

AI-derived software in screening for breast cancer

The Breast Imaging Group in the Department of Medical Imaging at the Radboud University Medical Center in the Netherlands is widely renowned for its work in the improvement and evaluation of radiological techniques for the detection and monitoring of breast cancer. Recently the group has been evaluating an AI-generated software package from the Dutch company Screenpoint for the detection of cancerous lesions in the breast. We wanted to find out more about the department in general and their experience of Screenpoint's Transpara algorithm in particular, so we spoke to Dr. Ritse Mann, breast radiologist and head of the Breast Imaging Group.

Dr. Ritse Mann is head of the Breast Imaging Group in the Radboud University Medical center in Nijmegen, The Netherlands.
Email: Ritse.Mann@radboudumc.nl

Q *Before we get onto discussing your experience with the AI-derived software please tell us about your center in general.*

In fact our breast imaging group is spread between two quite distinct hospitals: the Radboud University Medical Center (Radboudumc) and the Netherlands Cancer Institute.

Radboudumc has a local/regional role in breast cancer diagnostics and treatment similar to what's provided in many other community hospitals, with perhaps the difference that we have a very large screening program for women at increased risk. Thus, in Radboudumc, each year we treat about 200 women with breast cancer.

On the other hand, the Netherlands Cancer Institute has a nation-wide tertiary referral function and therefore sees a very large number — about 700 annually — of patients with (often large, developed) breast cancers.

From a scientific point of view, within the Radboudumc we carry out extensive pre-clinical research and development in the field of imaging and in the evaluation of AI tools for screening. In the NCI, research is predominantly focussed on the clinical assessment of patients with lesions and on image-guided de-escalation of therapy. As for equipment, both centers have Digital Breast Tomosynthesis (DBT) systems. In Radboudumc we have Siemens whereas in NCI it's Hologic. For ultrasound we have Siemens and Philips systems respectively and for MRI Siemens and Philips. Automated Breast Ultrasound (ABUS) is only available in Radboudumc. We don't use CESM; for screening purposes we routinely run abbreviated breast MRI protocols with ultrafast acquisitions.

So, all-in-all, between the two institutions, we have a broad experience with many of the currently commercially available breast imaging systems.

Q *Regarding screening, what is the usual programme for screening women in The Netherlands?*

As in most European countries, women in the Netherlands are invited for screening every two years in the age range of 50 to 75. The take-up rate can vary — there is generally a higher participation in rural areas than in the cities — but overall, about 75% of invited women accept screening, a rate which is higher than in most European countries. Of course there are some women who drop out of the screening programs. There is no precise up-to-date information on the reasons for this but previous studies have shown that drop-outs are partly the result of women having had a negative experience with mammography and/or being relatively more anxious. Other so-called drop-outs are simply the result of women who choose to undergo their mammograms at a different centre.

Currently women at high risk of breast cancer, e.g. those with BRCA mutations, undergo annual screening from age 25 with abbreviated protocol MRI. Women at familial risk undergo breast MRI at a lower frequency.

Regarding another risk factor, namely breast density, we determine this by automated analysis of the images, although our radiologists always have the possibility to overrule the software-generated values. In the clinic, women with dense breasts currently undergo supplemental automated ultrasound. On the basis of the results of the recent DENSE trial, the Dutch parliamentary authorities have recommended that, in screening, women with extremely dense breasts be offered MRI once every 4 years, but we are awaiting practical implementation of this policy decision.

Q *What about the performance statistics regarding screening?*

It's important to be able to monitor the overall performance of screening services, but in practice this is quite difficult for us since the Dutch national breast screening program is fully extramural, i.e. it's organized totally outside of the hospitals, with hospital radiologists being hired by the screening organizations to carry out the reading of the screening images. This means that breast screening actually carried out within hospitals is restricted to women at increased risk. All this makes it difficult to rapidly generate statistics regarding the performance of the screening programs as a whole or to assess personal performance.

Having said that, our ***cancer detection rates*** are around 6/1000 with screening mammography; these detection rates vary by breast density category (around 3/1000 in category a; 6.8/1000 in category d) In a screening context, it's difficult to say if the imaging modality, e.g. DBT or mammography, has an effect on the detection rates. However if we consider women presenting with symptoms, the yield of tomosynthesis for cancers elsewhere in the breast is about 8/1000, so approximately 25% higher than for mammography.

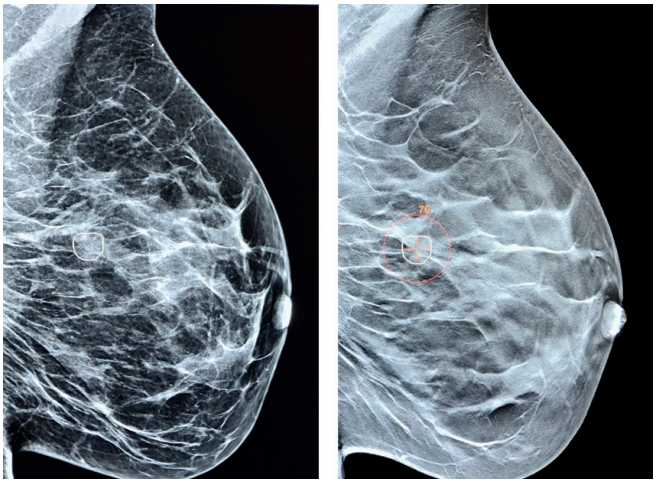
In the Dutch screening programs it is recommended that the ***recall rates*** should be below 2.3%. In practice we are slightly above this target but obviously this depends on the risk the women has of developing breast cancer. On average, about 1 in 4 recalled women actually has breast cancer, regardless of the imaging modality used for screening. These rates are low and are similar to those observed in the Nordic countries.

As for the rates of ***interval cancers***, in population screening these are about 2-3/1000 and are higher in women with dense breasts (up to 5/1000 in category d). The DENSE trial that I mentioned earlier clearly showed that we could effectively overcome the issue of interval cancers almost entirely by shifting the screening of women with dense breasts to MRI.

Regarding ***biopsies***, Positive Predictive Values (PPV) of over 40% have been reported for screen-recalled masses visible under ultrasound. Stereotactic biopsy tends to have a much lower PPV of around 20%. MRI guided biopsy is similarly positive in one in four to one in five patients.

Q *And now let's turn to the Transpara software from Screenpoint*

Our experience with the software actually goes back a long time, since for as long as I have been working at Radboudumc we have carried out research projects on the software and have been beta testing it. The software is now fully up and running and is used in routine, in tomosynthesis mode (we don't carry out normal mammograms within the Radboudumc any more, except for a few very specific situations such as women who have also been screened with MRI).



A spiculated mass identified at DBT by the Transpara software (and missed by the radiologist).

Left panel. As a detection aid, the software can act as a second pair of eyes to support radiologists. AI markers immediately highlight suspicious calcifications and soft tissue lesions on the sytnthetic mammogram.

Right Panel. When clicking on the mark, the software takes you directly to the most suspicious slice in the tomostack, also providing a lesion score. This helps by providing objective information equivalent to that of a radiologist on the areas of suspicion. Transpara findings are graded between 1-100

Personally I always use the software for any images in the so-called "grey area", i.e. images where I may have some doubt and would appreciate a second look. What is really interesting is that often, even before I get to see the images, our technicians will spontaneously check the mammograms with Transpara.

The software itself is fairly straightforward, so any issue is not about actually using the system but getting to trust it. The importance of trust in the software is shown by the fact that, any time there has been a stupid mistake made by the software — and this can happen, although rarely — there is a subsequent, small dip in its use until trust is regained.

In practice, the system works both as a standard CAD tool pointing at specific abnormalities, and also as a decision aid. In other words the radiologist can ask the system for an opinion on a particular area that might be suspected of being abnormal. I really like this aspect, since it basically provides me with an extra pair of eyes in a setting where, most of the time I tend to work alone.

Theoretically there is a danger that the radiologist could be distracted by software-generated marks and not give full attention to other parts of the images. (However, even if you only read what the system points out, you still wouldn't be doing too badly at all). I have to say that overall, the system is as good as I am — however, when we're together, we're better, especially in a clinical context. Thus the radiologists should always continue to keep their eyes open.

As I mentioned earlier we carried out clinical studies in-house, so right from the start I was quite confident that it would work well in routine. The challenge was more in training my colleagues than in anything else. For example, the scores given by Transpara do not directly correspond to a specific likelihood of cancer, so this can be a bit confusing if you are not used to it. Basically what you need to learn is simply that a score of 40 means that the lesion is probably benign and can be safely ignored. Otherwise specificity is ruined, together with trust in the system.

Q *Published data from the clinical trials have shown that the performance of the software is non-inferior to that of radiologists. How do your radiologists react to this — do they perceive the software as a threat or are they grateful for help?*

In fact it's a bit of both. Screening *per se* can be tedious, and it's easy to make preventable errors. This is where eventually I'd guess we will leave it to the computers. But, if this is where the radiologist earns most, it definitely is a sort of a threat. However, in a clinical setting, where the mammogram is reported directly after it is obtained and the results also communicated right away to the patient, the situation is different — it's much easier to embrace the help of a system.

In practice, the case-based scores generated by the system help the radiologist to assess whether or not an extra few seconds should be spent on a mammogram, and in this context I think the scores are really valuable. Thus, if you don't see anything at first glance and the Level of Suspicion (LOS) score is very low, it is easy, safe and reassuring to just move on.

The performance of the software can vary slightly depending on which vendor's mammography system is being used. Since currently the largest datasets used for training the software are from Hologic, the best results are with Hologic mammograms. However I use it mainly in the Radboudumc where we have Siemens mammography machines, i.e. I trust it for the other vendors too.

Similarly the software's efficiency in detecting lesions varies a little depending on the type of lesion. For example there may be slightly more false-positives with calcifications, but that is easy to deal with. In fact the software is deliberately set up to do just this — radiologists will not easily miss a mass, but they might just overlook a small group of microcalcifications.

Theoretically neural-network-based software could "learn by itself" as it handles more and more images, but in practice the Transpara software doesn't work like this. Currently the algorithms are fixed when they are brought to market, so the performance won't change until a new upgrade is installed. It would be really nice in the future to have a local self-learning system that could continuously try to improve itself. This would mean that on a daily basis a benchmark would have to be carried out on a very large independent and validated dataset to check that the performance doesn't actually become poorer. Of course, it should be realized that such a system would also need access to the ground truths, i.e. pathology and follow-up data. In addition, we would need clear and formal regulation to make sure that any such self-learning system works — for example that the validation set is truly independent.

For the moment the Transpara software is thus not optimized specifically for a local situation, but rather is the same everywhere. This has obvious drawbacks, but does have the advantage that if we see an individual patient who happens to come from a population that is not usually seen in our hospital, the software will still work satisfactorily. In that sense it guarantees a sort of equality that I, as radiologist, cannot offer.

Q *So overall, what is your impression of the software? What are the most significant pros and cons?*

The software is very easy to use. Currently, we use a form of the software that is integrated in our workstations. This is easier than as a stand-aside tool on a tablet computer, which is how we started out. We mainly use its decision support feature, i.e. I hardly look at it in clearly normal or abnormal cases, whereas in more difficult cases it simply provides me with some additional confidence.

There have been several instances where I, or one of my colleagues have detected a cancer only because the system pointed it out so it's possible that the software increases the sensitivity but by exactly how much is difficult to say. I would guess by a few percent at best.

What we appreciate is that in practice when we're dealing with somewhat more irregular mammograms and DBT examinations, with the software it is much easier to move on to the next case without any lingering doubts. This certainly speeds up the overall evaluation rate, because it is these cases that typically hold the radiologist up.

However to be honest, I think that the impact of the system will remain only minor so long as the system is used concurrently. We might become a little better and a little faster in our everyday practice, but it won't be a game-changer.

"… The system can be configured so that performance parameters such as sensitivity and/or recall rates can be set. These thus become medico-political choices…."

Only when we are willing to step aside and use the system for a form of independent reading (either as first, second or third reader), will it make a huge difference in workload and costs of screening. Even then, it won't necessarily make screening a lot better, since we are bound by the technology limits of mammography and/or DBT to show early cancers. However the software could bring about a homogeneity in the performance of screening across the world. This in turn could enable an adequate selection of women at higher risk for supplemental screening tests.

The system can be configured so that performance parameters such as sensitivity and/or recall rates can be set. These thus become medico-political choices. It shouldn't be forgotten that even with human reading we don't aim for maximum sensitivity, but rather for an acceptable balance between sensitivity and recall.

There is a different version of the software for mammography and DBT, but in essence it works similarly in each case. For DBT the software first analyses the individual tomoslices, and when any significant findings are identified, these are projected on to the synthetic 2D mammogram. When these are clicked the software goes to the relevant slice in the tomostack.

Currently, I still always scroll once through each of the tomostacks, but I must admit that if the software hasn't signalled anything I don't scrutinize each slice in as much detail. Looking at each slice has the advantage of preventing reportable findings from being overlooked (e.g. large cysts are often automatically ignored by the system, but sometimes it is good to devote a line or two to cysts in the report).

Although the system can be set up in various ways, in our experience it is easiest to just choose one way of working and get used to that.

DBT systems from different vendors have different characteristics, e.g. angle of sweep. Personally, I have only experience with the Transpara software in Siemens DBT, which has a relatively wide sweep angle. However, recently results were published on its use on Hologic DBT (with a small angle) with equally good results. We have contacts with many other centers, who use different DBT machines, as well as different thresholds for recall. Overall, the results have been consistent, which implies that the software is robust and trustworthy, — and, unlike many other AI applications, is satisfactory no matter the particular setting in which it operates.

Q *Do you think that sooner or later, the current European practice of double reading will evolve to a system of a single human reader plus AI software as a second reader?*

Personally, I don't think we can ignore for much longer the use of computers in this field. As humans we simply make too many silly errors, typically because we are distracted for a moment, or because we accidently hit the next button. Such errors would easily be solved by implementing an AI system as a third reader.

However if you ask me, the second reader approach is more difficult. Studies we have conducted so far in consecutive screening series show that humans and AI have similar detection performances but there is a huge difference in the cases actually recalled. Hence, the findings of the AI and humans need to be integrated and arbitrated to keep the recall rate under control. Theoretically it is possible to do this by

group arbitration, but it remains to be seen what the relevant contribution would be of the AI and human detected cancers in such a situation. For example it could be possible that the humans overrule all additional cancers detected by AI, which would render its value zero.

If the legal requirements can be satisfied and appropriate QC programs set up, I would be more in favor of using AI as a first reader. This would involve simply selecting the subset of cases for which human reading might be useful (i.e. preselection) — all other cases would then be excluded from human intervention. This would dramatically reduce the workload and might actually boost both sensitivity and specificity of the screening programs.

Q What about DBT being eventually favoured over mammography in Europe as the preferred screening modality?

I think that this will happen. Whether we will actually read all the DBT images is another matter. Good AI software may be embedded in the image reconstruction and simply highlight all potential findings in the synthetic mammogram. There is, after all, little reason why a synthetic mammogram should look exactly like a normal mammogram (if so we would actually be deliberately masking tumors again, which is ridiculous when put that way).

Such approaches would inevitably mean changes in the role of the radiologist. I like to compare such a future role with that of a hematologist; no-one expects the hematologist to do a manual cell-count on every blood sample. Instead hematologists should be capable of explaining what it means when the computer reports something abnormal, and be able to implement a logical follow-up. That doesn't free the hematologists from the responsibility for the diagnosis, though. To get back to radiology, it is very likely that in the near future a mammography machine will no longer just yield only an image, but will accompany the image with a full report on the characteristics of the breast including density and any abnormalities observed.

In such a scenario, it is clear that rules will need to be re-defined. Currently radiologists are officially obligated to look at every image that is stored in the PACS system. It isn't generally realized that *de facto* such a rule has already been obsolete for some time — in CT and MRI this usually doesn't happen. Radiologists shouldn't be freed of responsibility, but rather they need to ensure that they check that what the computer produces is logical, and that the results are incorporated in the patient-care pathway in such a way that is beneficial to the patient.

Coming back to legal responsibility, in essence AI mammography is a piece of machinery, like a CT or MRI scanner. If the radiologist uses it on a patient, he/she is responsible, not the manufacturer. This means that there will have to be certain standards and benchmarks against which the program can be checked. It would be for the radiological community as a whole to organize this.

"... If the legal requirements can be satisfied and appropriate QC programs set up, I would be more in favor of using AI as a first reader ..."

Q How would radiologists react to the prospect of only dealing with positive or difficult cases and never seeing "normal cases"?

Some re-adjustment will obviously be needed. Also radiologists would probably become less confident in reporting normal cases as normal. However, this will mainly just mean another change in our profession — there are very few radiologists I know that started to read mammograms because most of them are normal.

We shouldn't forget that any new ways of working will have to be explained to the women involved. This should be done simply and clearly, always stressing the safety brought about by the changes. In general people adapt really quickly to technological advancements, and I see no reason why AI-assisted radiology couldn't be acceptable (patients don't complain about tests from the hematologists and clinical chemists either).

Q What about the replacement of the current general population screening strategy by one based on personalized risk assessment to reduce radiologists' workload ?

I doubt that personalized screening will lead to a reduction in workload. Screening is the one thing that reduces mortality and enables de-escalation of therapy. Personalized screening mainly tackles the underdiagnosis that is currently abundant in screening, by offering more or better screening to women for whom standard mammography is insufficient. In these women, we might only observe a shift from one screening modality to another, but this will not reduce the overall amount of work. Only the subgroup for which we could safely do less screening would enable us to truly lower the workload for radiologists. Instead I see the implementation of computer-based image interpretation as more useful in this respect.

However this doesn't mean that screening strategies should be frozen in their current form — indeed, some adaptation of screening is imminent. For example, we should soon get supplemental or replacement screening in women with very dense breasts, because mammography in this population really underperforms.

Q Is the debate on the over-diagnosis/over-treatment aspects of screening finally becoming less heated? If so why?

A little. Overdiagnosis is still a major issue, prticularly among those physicians who actually have to carry out the treatment and follow-up. However, virtually no one doubts any more that early detection does decrease mortality. For some lesions that were formerly treated as cancer, watchful waiting has now become acceptable, so this makes the effect of overdiagnosis less dramatic. Likewise, image-guided de-escalation of therapy in small breast cancers also reduces the negative impact of overdiagnosis. Despite this, overdiagnosis is still a problem, and we should continue to pay attention to it. But if we use imaging not just to find the cancers early, but also to minimize the impact of treatment for any cancers detected, we could largely overcome the problems underlying this debate.

Q what about likely future trends in the incidence of breast cancer?

There seems to be a real increase in the number of women that will get breast cancer at some point in their life. The statistics in the Netherlands have been increasing gradually over time. Our current estimates are that 1 in 6.6 women will have breast cancer, which is about the highest incidence in the world. Probably there are dietary, lifestyle and hormonal factors that play a major role here, along with the fact that life expectancy is still increasing. However there is no single behavioral practice which could be implemented to reduce the increase in the incidence of breast cancer, like stopping smoking decreases the risk of lung cancer.

So, all we can do right now is alleviate its harms. In that sense, the importance of screening can only increase.

Breast CT in women with breast implants

The Institute of Diagnostic and Interventional Radiology in the University Hospital Zurich, Switzerland has been the longest-standing user of a dedicated new breast CT system equipped with a photon-counting detector. The team have just published a paper on the use of the new system in patients with breast implants [1]. We spoke to Prof. Andreas Boss, Senior Consultant responsible for breast imaging.

Prof Andreas Boss is Senior Consultant responsible for breast imaging at the Institute of Diagnostic and Inter-ventional Radiology.
Andreas.Boss@usz.ch

Q Before we get to the use of the new breast CT system in detail, please describe the breast imaging unit at the University Hospital Zurich and the Swiss breast screening system in general.

OK. Let's start with our imaging equipment: this includes a mammography/tomosynthesis unit from Siemens Healthineers; a handheld US device and an automated 3D breast ultrasound (ABUS) both from GE; and two 3T MRI from Siemens Healthineers. In addition we have an AI-derived software system from the company b-rayZ for the analysis of breast density and mammography image quality. And as you mentioned we also have the new spiral breast-CT system from AB-CT.

All this equipment is put to a lot of use, since we see a lot of patients. Each year we carry out 2,500-3,000 mammographies and approximately 700 breast-CT examinations.

In Switzerland, the practical implementation of organized QC mammography breast cancer screening programs is the responsibility of the canton. Overall, approximately 60% of Swiss women in the age range 50-70 have access to such screening programs. However, many cantons — particularly in the German speaking part of Switzerland, including the canton of Zurich — have not yet implemented systematic organized screening programs. In these areas women who want to be screened typically have to resort to "opportunistic" screening examinations in a radiology institution (which is not necessarily covered by public health insurance). Depending on the particular risk profile and the risk awareness of the individual patient, opportunistic mammography breast cancer screening starts at the age of 40 years, typically with examinations every two years. One advantage of opportunistic breast cancer screening mammography compared to the organized screening program is that additional breast ultrasound can be carried out in patients with dense breasts. It is well known that the sensitivity of conventional mammography drops substantially in patients with dense breasts. In such cases adjunct ultrasound examinations significantly increase the detection rate for breast cancer. In our institution, a "lean" workflow is implemented. Thus, immediately after the screening mammography examination, the images are analyzed with the "b-box" AI medical device from the Swiss company b-rayZ to assess the breast density according to the ACR BI-RADS system. For women with the highest breast density categories, i.e. categories c-d, an additional ABUS examination is carried out by the technician.

We hear a lot about AI in radiology these days but an excellent example of its usefulness is in the determination of mammographic breast density. The BI-RADS breast density system doesn't use a quantitative score scale but instead uses both the amount and the distribution of breast tissue to attribute density to one of four categories (a, b, c, d). The result is that software tools relying on quantitative measurements of the amount of breast density are miscalibrated to a ACR BI-RADS score. Artificial Intelligence algorithms such as those in the b-box system can significantly improve classification,

Women at highest risk, e.g. with known BRCA mutations, are recommended to follow a more intense screening schedule, according to the guidelines of the Swiss Cancer League, which suggest that such women should undergo yearly breast MRI examinations.

All the above is a simplified description of our standard screening procedures, but a problem is that a large number of women in Switzerland are unwilling to undergo the often painful breast compression required for mammography or tomosynthesis. For such patients, we now offer breast cancer screening examination using the nu:view breast-CT system from AB-CT. [Figure 1]

Figure 1. The nu:view Mamma-CT system was developed and is produced by the German company AB-CT - Advanced Breast CT. The design of the new scanner allows compression-free imaging of one breast at a time. To do this, the breast CT system uses a rotating gantry on which the X-ray tube and photon-counting detector are mounted. During the image acquisition process, the gantry rotates around the breast in a downwards-oriented spiral trajectory. In the course of a single scan up to 12,000 projection images are acquired. A full spiral scan takes as little as 7 – 12 seconds. The radiation dose is similar to that of conventional mammography.

The breast-CT image quality is high with microcalcifications being clearly visualized. In addition, if the breast-CT examination is carried out with contrast enhancement, both soft tissue enhancement of the breast cancer and associated microcalcifications can be visualized at the same time, which cannot be done with any other imaging modality.

Q Now let's turn to women with implants.

Approximately 10-20% of the patients referred for breast-CT imaging have silicone implants, either for cosmetic purposes or for reconstruction after breast cancer treatment. Overall the number of women with silicone implants seems to be slowly but steadily increasing. Implants for cosmetic reasons are seen mostly in younger women, whereas silicone implants used in breast reconstruction are mostly seen in patients of higher age.

There are typically two complications associated with silicone implants, namely rupture and capsule fibrosis. Both show typical patterns in breast-CT. In case of rupture, the so-called "linguine signs" which are caused by the broken elastomeric casing of the implant can be clearly seen. [Figure 2]. Capsule fibrosis is the other common problem of silicone implants, and is caused by a foreign body reaction of the surrounding tissue. Often, capsule fibroses show calcifications, which can only be visualized using breast-CT [Figure 3]. A common chronic complication is pain caused by capsule fibrosis, but it should be remembered that breast pain can also be caused by hormone-stimulated glandular tissue.

At the moment, there are no guidelines recommending specific imaging modalities for women with breast implants. Because of the potential risk of iatrogenic rupture of silicone implants caused by breast compression, conventional mammography is not performed at our institute in patients with breast implants.

Breast-CT is particularly well suited for screening patients with silicone implants not only because there is no compression involved, but also because the system can detect not just breast cancer but also precursor lesions associated with microcalcifications. Ultrasound could also be used for the examination of patients with silicone implants, however the diagnostic accuracy

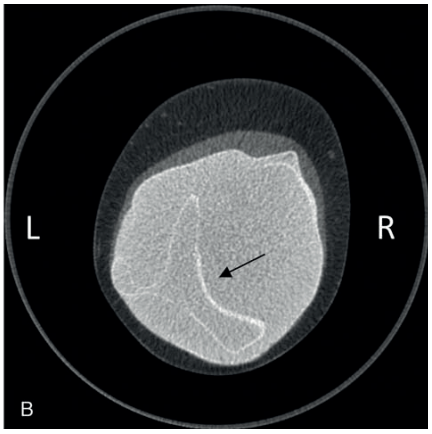


Figure 2. A 35-year old woman presenting with a family history of breast cancer and bilateral gel implants for six yrs. Breast CT clearly showed a positive Linguine sign (arrow) in the right breast indicative of an intracapsular rupture. Image adapted with permission from Ref 1.

of ultrasound alone in such cases is lower than that of breast-CT.

Q What are the particular radiological challenges in conventional mammography that women with implants present?

There are several. For example, the use of conventional mammography in such patients has the disadvantage that there can be superimposition of tissue by the implant, with the potential risk of masking lesions. As mentioned above, other dangers are that the implant may burst under the breast compression used in mammography In addition, the mammography examination itself can be more painful due to capsule fibrosis. Finally the combination of a lower compression used to minimize the risks of

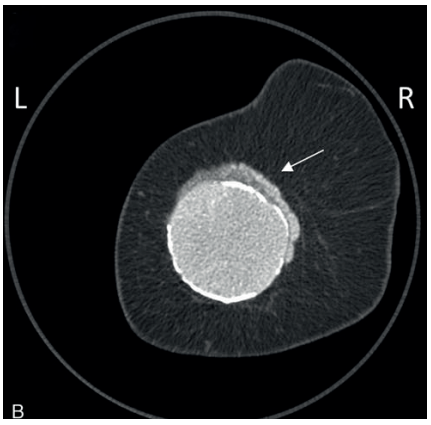


Figure 3. A 62-yr old woman who has had bilateral breast implants for 46 yrs presented to our clinic with bilateral breast induration. Severe calcifications surrounding the implant can be seen in the coronal breast CT image. Image adapted with permission from Ref 1.

rupture together with the absorbance by the silicone means that radiation dose could be higher in the mammography of patients with implants.

However, it has been shown that silicone implants do not affect the overall risk of developing breast cancer, so the recommended screening schedules remain identical for women with or without breast implants.

Usually, no specific radiology checks are required directly after the initial insertion of the breast implant. However, if there is any suspicion of acute or chronic complications, breast imaging becomes important.

Breast-MRI is an alternative for the investigation of implant rupture and capsule fibrosis since silicone implants can be visualized clearly in MRI using silicone-sensitive sequences, However MRI has significant drawbacks compared to breast-CT, principally the much longer examination time and the higher costs of MRI compared to breast-CT. The issue of cost is all the more relevant nowadays in that health insurance organizations are increasingly unwilling to cover the costs of purely cosmetic operations. An additional, performance-related drawback of breast MRI (which it shouldn't be forgotten, frequently involves the use of gadolinium-based contrast agents) compared to breast-CT is that neither microcalcifications nor calcifications associated with capsular fibrosis can be seen in MRI.

Thus all-in-all, breast-CT is an attractive procedure for women with silicone implants.

Q Since when have you had the nu:view breast CT system from AB-CT?

We actually purchased and installed the breast-CT at the University Hospital Zurich as far back as spring 2018, with approval for its use with patients being granted in August 2018, so now we have acquired a broad body of experience with it. At the time it was the first installation of the system in the world.

Since the nu:view system is a completely new approach to breast imaging, there was a steep learning curve at the beginning, both for technicians and radiologists. However now breast-CT examinations are no more challenging nor time-consuming for our technicians than conventional mammographies.

Our radiologists also quickly adapted

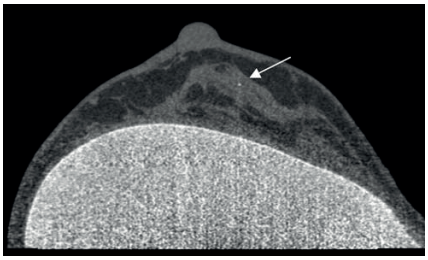


Figure 4. Single microcalcification seen in the axial plane in a 65-yr old woman with bilateral gel implants. Image adapted with permission from Ref 1.

to the reading of the datasets. Initially, detecting microcalcifications in the 3D datasets was a challenge, as they appear less prominent than in mammography because of the high isotropic spatial resolution. In practice we adapted to this by creating maximum-intensity-projections with our PACS viewing system with slice thicknesses of the order of 2-3 mm, which allows microcalcifications to be detected with an accuracy similar to that of mammography [Figure 4]. The reading time for an individual breast-CT examination for all four data sets (standard and highly resolved datasets on each breast) is in the order of 2-3 minutes.

Q What did your study of the performance of the system in women with implants entail?

In our retrospective observational study [Ref 1, Ruby *et al*], we described our experience in the first 21 women with implants who underwent breast-CT. The majority of these women had bilateral breast implants for cosmetic reasons, with one patient having a single breast implant after breast resection for cancer. Regarding dense breasts, we used the same procedure as in mammography and in breast-CT examinations of women without implants, namely we carried out additional ultrasound examinations.

Both the silicone inside the breast implant and the elastomeric capsule/shell enclosing the silicone have high radiation absorption and can therefore easily be seen in the breast-CT datasets. Implant folds, which are a common finding in intact implants, are clearly visualized in breast-CT, as are the Linguine signs which indicate implant rupture. [Figure 2] Extensive capsule fibrosis was detected in 3 out of the 21 patients. In one patient extensive calcifications were found in the capsule fibrosis, and was best detected in breast-CT. In the surrounding glandular breast tissue, we were able to show that both microcalcifications and soft tissue lesions can be detected, which justifies the use of breast-CT in patients with breast implants not just for diagnostic and screening purposes, but also for follow-up examinations after breast cancer.

One shortcoming of breast-CT in many cases is the absence in the datasets of the part of the breast that is close to the thoracic wall, which is also common in mammography examinations of patients with breast implants. From this point of view, breast MRI with its complete coverage of the breast could have an advantage. While we're on the subject of MRI, I currently still see breast-MRI as the preferred modality for patients with a high risk of breast-cancer (family history of breast cancer, known BRCA mutations), due to its broadly accepted high sensitivity for the detection of breast cancer. However, as mentioned before, MRI has its own significant disadvantages.

Q How is the new system integrated into the work-flow of your breast imaging service ?

The large majority of patients undergoing breast-CT at our institution are referred to us specifically for breast cancer screening because they are unwilling to repeat the painful breast compression experience they had in a previous mammography/tomosynthesis examination. We receive excellent feedback from those patients, with more than 90% expressing positive acceptance of the new technique. Because of this we have a growing number of women referred to us for breast-CT.

However if women for whom mammography is indicated have no problem with breast compression, we still go for conventional mammography.

We find that the diagnostic accuracy of breast-CT is comparable to mammography. As the absorption of breast glandular tissue and soft tissue lesions is very similar, an additional ultrasound examination is required in patients with dense breasts, which is also the case for mammography.

Q Any future developments you would like to see?

At the moment, one short-coming of our breast-CT system is the relatively long reconstruction time of 20-25 minutes per exam. Since the radiologist's decision on any additional ultrasound exams can only be taken after the images are available, the overall examination time can be relatively long for patients who may need supplemental ultrasound exams. Shortening the reconstruction time would clearly be helpful.

The vast majority of breast CT examinations we carry out are without contrast-medium. Because of the additional efforts required for contrast media administration, e.g. the placing of a peripheral venous access and preparation of the contrast itself, we restrict our use of contrast medium in practice to only a very small number of patients with highly suspicious findings. Given this, plus the fact that the breast-CT can only carry out a dynamic examination on one breast at a time, an interesting new technological development would be to use the spectral information from the photon-counting detector to calculate a virtual non-enhanced dataset. Then, contrast-media injection would be more applicable in patients since each breast could be examined with a virtual dynamic examination.

Q And the overall conclusion on the potential of the technology?

To summarize our experience with breast-CT in patients with silicone implants and its role in a regimen using supplemental ultrasound in patients with dense breasts we found that it is a breast imaging modality of high accuracy and with a radiation dose similar to mammography. With its many advantages over alternative imaging modalities, breast-CT has the potential to become the modality of choice for both breast cancer screening and diagnostic imaging.

REFERENCE.

1. Ruby L *et al*. Diagnostic value of a spiral breast computed tomography system equipped with photon counting detector technology in patients with implants. Medicine (Baltimore). 2020; 99(30): e20797. doi: 10.1097/MD.0000000000020797

FURTHER READING:

• Berger N, Marcon M, Saltybaeva N, Kalender WA, Alkadhi H, Frauenfelder T, Boss A. Dedicated Breast Computed Tomography With a Photon-Counting Detector: Initial Results of Clinical In Vivo Imaging. Invest Radiol. 2019; 54:409-. doi: 10.1097/RLI.0000000000000552.

• Berger N, Marcon M, Frauenfelder T, Boss A. Dedicated Spiral Breast Computed Tomography With a Single Photon-Counting Detector: Initial Results of the First 300 Women. Invest Radiol. 2020; 55: 68. doi: 10.1097/RLI.0000000000000609.

• Shim S, Saltybaeva N, Berger N, Marcon M, Alkadhi H, Boss A Lesion Detectability and Radiation Dose in Spiral Breast CT With Photon-Counting Detector Technology: A Phantom Study. Invest Radiol. 2020; 55: 515. doi: 10.1097/RLI.0000000000000662.

• Wieler J, Berger N, Frauenfelder T, Marcon M, Boss A. Breast density in dedicated breast computed tomography: Proposal of a classification system and interreader reliability. Medicine (Baltimore). 2021; 100: e25844. doi: 10.1097/MD.0000000000025844.

Medical imaging with monochromatic X-rays

By Dr E Silver

This article summarizes the results of a recently published report on the successful development of a monochromatic X-ray tube for routine imaging in the clinic

It is well-known that X-ray imaging with monochromatic X-rays reduces the radiation dose and increases the signal-to-noise-ratio (SNR) of image features [1-6]. It may also help to spectroscopically determine *in vivo* the chemical composition of tumors and surrounding tissue. A recent publication in Medical Physics reported the development of a monochromatic X-ray tube suitable for routine use in the clinic [7]. The new tube can be fitted in all current X-ray and CT imaging systems and can potentially replace the ubiquitous century-old broadband X-ray technology.

While previous research studies using Bragg crystal monochromators coupled to either large synchrotron light sources or traditional broadband X-ray tubes [8-12] demonstrated the advantages of monochromatic X-ray imaging, neither technology is suitable for general clinical applications. The viability and performance of the new concept described in the Med Phys article [7] stems from its ability to produce a selectable monoenergetic X-ray energy spectrum with sufficient intensity over a wide field-of-view, enabling high quality images at low dose, all within the footprint of existing conventional mammography systems.

In its first application, the patented tube technology was installed into a laboratory prototype of a monochromatic X-ray mammography system. Image quality was evaluated as a function of radiation dose using the signal-to-noise ratio (SNR) measured for high and low contrast masses and microcalcifications in standard breast phantoms with a variety of thicknesses. Spatial imaging properties were assessed from these images as well as from modulation transfer analysis (MTF). Measurements using an iodine contrast agent were also performed.

The Author

Eric Silver, PhD

CEO

Imagine Scientific, Inc.

Norwalk, MA USA

Email: eric.silver@imaginescientific.com

The results were compared to those obtained using a commercially available, conventional X-ray mammography system. The prototype system reduced radiation dose by factors of 5 to 10 times for the same SNRs as obtained from a conventional system. The high SNRs for very thick breast phantoms provide strong evidence that screening with lower breast compression is possible while maintaining image quality. In addition, Contrast Enhanced Digital Mammography (CEDM) with monochromatic X-rays was shown to provide a simpler and more effective technique at substantially lower radiation dose.

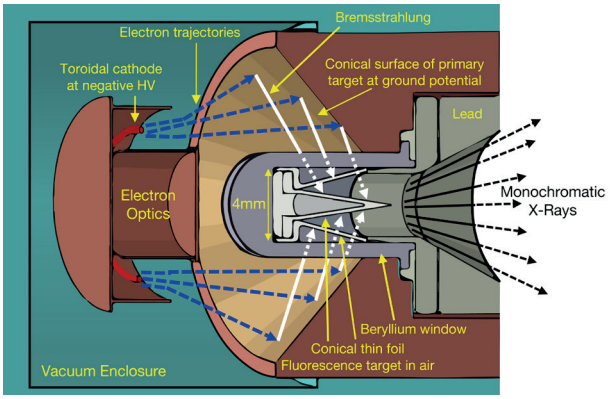


Figure 1. A 3D section of the prototype monochromatic X-ray tube. A toroidal cathode at negative HV emits electrons that follow trajectories, shown schematically in dark blue, that end on the inside surface of the conical metal target. Broadband X-rays from the conical target, shown schematically in white, pass through a beryllium window that seals the vacuum enclosure from atmospheric pressure. These X-rays interact with the conical thin foil metal to produce monochromatic X-rays via fluorescence

THE MONOCHROMATIC PROTOTYPE

The IP-protected technology combines two X-ray emission processes to generate monochromatic X-ray beams. As shown in Figure 1, the inside surface of a conically-shaped annular metal ring is bombarded with high energy electrons to emit broadband X-ray energies. These X-rays are concentrated onto a compact, thin-foil, metallic target placed at the center of the annular ring. The foil subsequently emits monochromatic X-rays via fluorescence with an energy that uniquely identifies its elemental composition.

An example of the fluorescence spectrum emitted by a foil target of tin (Sn) is shown in Figure 2. It consists of two monochromatic emission lines, one very strong Kα line at 25.27 keV and a much weaker Kβ line at 28.49 keV. The emission from the tin target is 96% monochromatic

which means that only a small amount (~4%) of the broadband spectrum from the first stage reaches the detector as displayed in the inset at the top right of Figure 2.

The monochromatic energy can be selected by changing the material of the fluorescence target. Molybdenum, palladium, silver, and antimony generate similar monochromatic fluxes and all are potentially useful in mammography. Three of these are displayed in Figure 3. Higher energy monochromatic fluxes can be generated with target materials such as neodymium, samarium, dysprosium, tungsten and gold. The spectrum from a neodymium target is also included in Figure 3. The tube allows for easy manual exchange of the fluorescence target to select the monochromatic energy because the target is located outside the vacuum of the X-ray tube. Automated target replacement is under development. The tube technology has received a number of international patents [13-22].

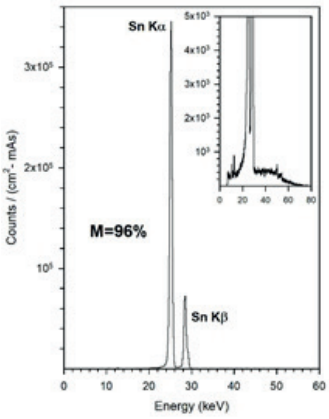


Figure 2. The fluorescence spectrum from a target of tin (Sn) emitted by the prototype is 96% monochromatic.

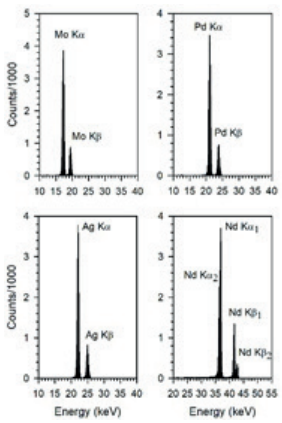


Figure 3. Additional examples of monoenergetic fluorescent X-ray lines used for imaging. Top left: molybdenum (Mo); top right: palladium (Pd); bottom left: silver (Ag); bottom right: neodymium (Nd).

IMAGING PERFORMANCE

A brief review of the imaging measurements of 4 breast phantoms with thicknesses of 4.1; 4.5; 7.1 and 9 cm reveals the image quality produced by the monochromatic system. Figure 4 shows side-by-side images from a conventional broadband mammography system (left) and the monochromatic prototype (right) of a 4.5 cm thick phantom with a 50% glandular-50% adipose equivalent tissue composition. For equal SNR (403) of the high contrast 100% glandular step wedge measured within the 5mm x 5mm black square, shown in Figure 4, the dose of the monochromatic image (0.18 mGy) is 7 times lower than that of the conventional image (1.26 mGy).

The advantage of monochromatic X-rays is even clearer for the 9 cm compressed breast phantom. The monochromatic SNR (418) was 2.6 times higher and the dose (0.65 mGy) 4.2 times lower than the respective values (158 and 2.75 mGy) obtained with the conventional system within the same 5mm x 5mm square area of the 100% glandular step wedge. For the conventional broadband system to equal the SNR of the monochromatic system, it would require a dose of 19 mGy, 29 times higher than the dose delivered by the monochromatic system.

Similar superiority in SNR and low dose are also characteristic for measurements of low contrast masses and microcalcifications. Again, comparing monochromatic and broadband imaging for equal SNRs, the conventional system requires 5 – 8 times the dose of the monochromatic system to image low contrast lesions in 4.1 cm and 7.1 cm thick phantoms. When imaging microcalcifications ranging in diameters from 400 microns to 170 microns, the dose delivered by the monochromatic system is 6.6 times lower and Figure 5 shows the comparison between the images of both technologies. It was also noted that the microcalcifications are 6 cm above the detector image plane.

.

Contrast Enhanced Digital Mammography

CEDM is receiving increased attention in the screening of women at high risk of developing breast cancer and as a diagnostic tool when suspicious lesions are seen in routine screening mammograms. In addition to implementing the conventional two-image, dual energy subtraction technique commonly used with broadband systems, the recent study [7] showed how CEDM using monochromatic X-rays can be performed simply and effectively with a single image using monochromatic X-ray energies either below or above the iodine K absorption edge. The single and dual energy method used with monochromatic X-rays each has its advantages and both reduce the radiation dose compared to conventional procedures while providing high contrast and SNR. Notably, a single image acquisition typically has less statistical noise and requires less dose.

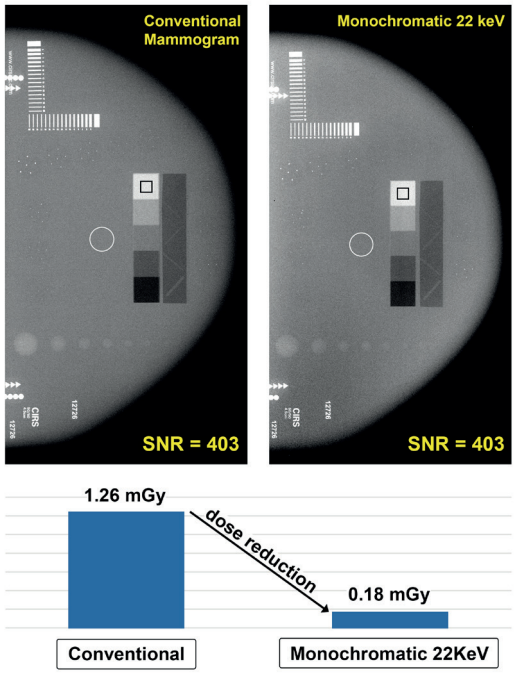


Figure 4. A 4.5cm thick breast phantom imaged with a conventional mammography unit (left) and with 22keV monochromatic X-rays from the prototype (right). The SNR for the 100% glandular step wedge is calculated for the 5mm x 5mm square outlined in black.

Using a dose of only 0.057 mGy in a single measurement, a contrast of 10% with high SNR (40) can be obtained for an iodine column density of 4.5 mg/cm^2. This means that a column

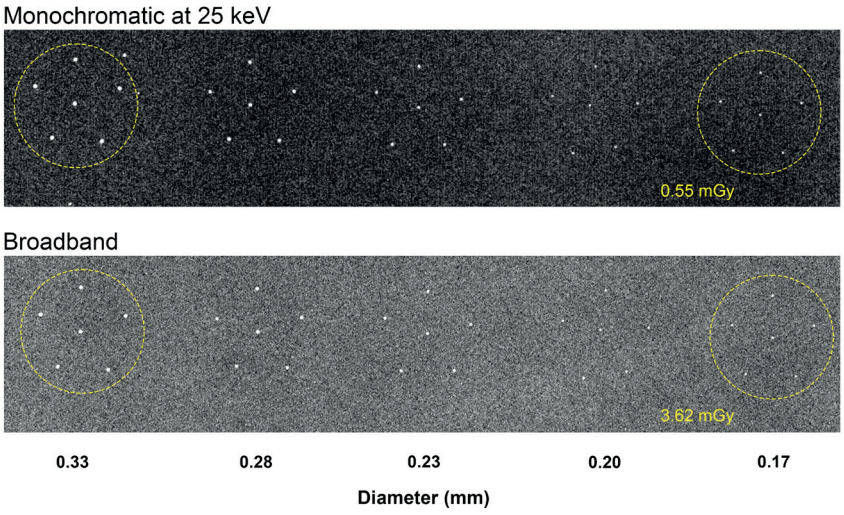


Figure 5. Images of simulated microcalcifications with diameters of 330, 280, 230, 200 and 170 microns in a 4/1 cm thick phantom for both instruments. The SNR values are equal but the dose of the monochromatic image is 6.6 time lower. The microcalcifications are 6 cm above the image plane.

density of ~0.1 mg/cm^2 could be detected with a SNR = 3 by increasing the dose to 0.65 mGy. Dual Energy subtraction using monochromatic X-rays can increase the contrast by a factor of 5 times by using a monochromatic energy below and above the iodine K-edge. This assumes that the imaging detector has a quantum efficiency of at least 85% at energies immediately above the iodine K edge. These results indicate that monochromatic X-rays enhance the potential for widespread use of CEDM while substantially reducing radiation exposure. Furthermore, single images with monochromatic X-rays could enable dynamic studies of the rate of contrast uptake by the lesion and surrounding tissue since several images can be taken in succession while still keeping the total dose at acceptable levels.

WHAT THE FUTURE HOLDS

Presently, the exposure times for the monochromatic imaging studies are relatively long, especially for imaging thick breast tissue (9 sec for 4.5 cm and 50 sec for 9 cm thick phantoms). They however serve as benchmarks for ongoing work to increase the monochromatic flux by at least 10 times, thereby reducing image acquisition time to below 5 sec on average. It is noted that current broadband mammography systems require about 17 sec to match the SNR achieved by the monochromatic prototype for the 9 cm phantom. The enhanced sensitivity adds substantial benefits and new options for screening dense and thick breasts. Screening with significantly less compression while preserving detection sensitivity is possible, thus improving patient comfort and hopefully lead to improved compliance with annual screening guidelines. When follow-up diagnostics are necessary to image small tumors or other unresolved features detected during screening, monochromatic X-rays can be used at doses approaching those currently used in breast screening by broadband mammography systems but with significantly more sensitivity. CEDM with monochromatic X-rays may be another alternative for superior diagnostic follow-up.

"...The enhanced sensitivity adds substantial benefits and new options for screening dense and thick breasts....."

The factor of 5 to 10 times reduction in radiation dose per mammogram made possible by monochromatic X-rays will lead to a major reduction in total exposure from breast cancer screening and a dramatically lower risk of radiation-induced cancers in at-risk women. It is planned to carry out an initial pilot study of the technology on women by the end of this year.

REFERENCES

1. Clark GL. Medical, biological and industrial applications of monochromatic radiography and microradiography. Radiology 1947; 49 (4): 483-495. doi: 10.1148/49.4.483.

2. Ter-Pogossian M. Monochromatic roentgen rays in contrast media roentgenography. Acta Radiol 1956; 45 (4): 313-322.

3. Oosterkamp IW. Monochromatic X-rays for medical fluoroscopy and radiography, Medicamundi. 1961; 7: 68-77 .

4. Carroll F. Use of Monochromatic X Rays in Medical Diagnosis and Therapy What Is It Going to Take? Journal of X-ray Science And Technology 1994; 4: 323-333. doi: 10.3233/XST-1994-4407.

5. Hoheisel M, Lawaczeck R, Pietsch H, Arkadiev V. Advantages of Monochromatic X-rays for Imaging, Medical Imaging: Physics of Medical Imaging, edited by Michael J. Flynn, Proceedings 2005.

6. Sugiro FR, Li D, MacDonald CA. Beam Collimation with polycapillary X-ray optics for high contrast high resolution monochromatic Imaging, Medical Physics 2004; 31(12):3288-397 doi: 10.1118/1.1809779.

7. Silver E, Shulman S, Rehani, Madan M, Innovative Monochromatic X-ray Source for High Quality and Low Dose Medical Imaging, Medical Physics, Volume 48, Issue 3, JUNE 2021, Pages 1064-1078, https://doi-org.ezp-prod1.hul.harvard.edu/10.1002/mp.14677

8. Rubenstein E, Brown GS, Harrison DC, Hofstadter R, Hughes EB, Kernoff RS, Otis JN, Thompson AC, Zeman HD. *et al*. Synchrotron radiation for transvenous coronary angiography. Trans Am Clin Climatol Assoc 1986;97:27-31.

9. Tokumori K, Toyofuku F, Kanda S, Baba S, Mito Y, Hyodo K, Ando M, Uyama C, Monochromatic X-ray CT using fluorescent X-rays excited by synchrotron radiation, Engineering in Medicine and Biology Society, Proceedings of the 22nd Annual International Conference of the IEEE 2000;, 4: 2987 – 2989.

10. Burattini E, Cossu E, Di Maggio C, *et al*. Mammography with synchrotron radiation. Radiology 1995;195(1):239-244. doi:10.1148/radiology.195.1.7892478

11. Arfelli F, Bonvicini V, Bravin A, *et al*. Mammography of a phantom and breast tissue with synchrotron radiation and a linear-array silicon detector. Radiology 1998;208(3):709-715. doi:10.1148/radiology.208.3.9722850.

12. Kulpe S, Dierolf M, Braig E, et al. K-edge subtraction imaging for coronary angiography with a compact synchrotron X-ray source. PLoS One. 2018;13(12):e0208446. Published 2018 Dec 10. doi:10.1371/journal.pone.0208446.

13. Silver EH. Monochromatic X-ray Methods and Apparatus, U.S. Patent 8331354 (2012).

14. Silver EH. Monochromatic X-ray Methods and Apparatus, U.S. Patent, 9066702 (2015).

15. Silver EH. Monochromatic X-ray Methods and Apparatus, U.S. Patent 9326744 (2016).

16. Silver EH. Monochromatic X-ray Methods and Apparatus, U.S. Patent, 10299743 (2019).

17. Silver EH. Monochromatic X-ray Systems and Methods, U.S. Patent 10398909 (2019).

18. Silver EH. Monochromatic X-ray Imaging Systems And Methods, US Patent 10398910 (2019)

19. Silver EH. Monochromatic X-ray Imaging Systems And Methods, US Patent 10532223 (2020)

20. Silver EH. Monochromatic X-ray Systems And Methods, US Patent 10806946 (2020)

21. Silver EH. Monochromatic X-ray Systems And Methods, US Patent 10857383 (2020)

22. Silver EH. Methods and Apparatus for Determining Information Regarding Chemical Composition Using X-radiation, U.S. Patent Application Pub. No.: US 2018/0284036 A1 (2018).

23. Lewis TC, Patel BK, Pizzitola VJ. Navigating Contrast-enhanced Digital Mammography, Appl Radiol. 2017; 46 (3). https://appliedradiology.com/articles/navigating-contrast-enhanced-digital-mammography. Accessed on Aug 18,2020.

24. Phillips J, Miller MM, Mehta TS, *et al*. Contrast-enhanced spectral mammography (CESM) versus MRI in the high-risk screening setting: patient preferences and attitudes. Clin Imaging 2017;42:193-197. doi:10.1016/j.clinimag.2016.12.011

ICIS
International Cancer Imaging Society

International Cancer Imaging Society
20th Annual Teaching Course

Concepts in Cancer Imaging

Virtual Meeting
19–22 September 2021

President 2021: Dr Aslam Sohaib, London, UK

Learning objectives

To improve your knowledge of

- Cancer diagnosis and staging
- Response assessment
- State of the Art oncological imaging techniques
- Role of imaging in treatment planning
- Cancer genetics
- Interventional radiology for cancer
- Mimics of malignancy

This course is designed for all radiologists, radiation oncologists, medical oncologists and other specialists interested in the diagnosis and management of cancer patients.

Call for Abstracts
Deadline 1 July 2021
submit online at: icimagingsociety.org.uk

Submission of abstracts for scientific papers and posters are invited; those selected for presentation will also be published online in the Proceedings of the ICIS 20th Annual Teaching Course.

Programme Planning Committee:
Khaled Elsayes (USA), Dow-Mu Koh (UK), Kieran McHugh (UK), Giovanni Morana (IT), Anwar Padhani (UK), Aslam Sohaib (UK), Harriet Thoeny (CH) and Annick Van Den Abbeele (USA)

Study shows tomosynthesis reduces rate of interval cancers

A recently published study from a Swedish group reports that breast screening with digital breast tomosynthesis (DBT) reduces the rate of interval breast cancers compared to screening with digital mammography.

The study adds to a growing body of evidence supporting DBT as a breast cancer screening tool with important advantages over mammography. DBT operates by acquiring a series of X-ray images of the breast from different angles. Previous research has shown that DBT has a higher sensitivity for breast cancer detection than digital mammography. However, the impact of these additional DBT-detected cancers is not fully understood. While they may constitute a screening benefit, they could also contribute to overdiagnosis, that is the diagnosis of early-stage, slow-growing cancers that would not have caused harm to the patient in their lifetime.

The rate of interval cancers — cancers that arise between routine screenings — offers one way to better elucidate screening benefits. Interval cancers are considered more aggressive than cancers detected during a screening exam.

"*Interval cancers have, in general, a more aggressive biological profile than screen-detected cancers,*" said study lead author Dr. Kristin Johnson "*This means that the prognosis is less favorable for interval cancers compared to screen-detected cancers.*"

Interval cancer detection rate reporting is required in many screening programs as an indicator of effectiveness. A reduction in the interval cancer rate when using DBT might be attributed to improved detection of rapidly growing cancers with poorer prognosis, possibly contributing to lower breast cancer mortality.

For the new study, Dr. Johnson and colleagues compared interval cancer rates in Sweden's population-based Malmö Breast Tomosynthesis Screening Trial with those from an age-matched control group of patients who underwent digital mammography at the same center.

The study group included almost 15,000 women who were screened with DBT and digital mammography between 2010 and 2015. Those women were matched with a control group of more than 26,000 women who had only digital mammography screening during the same time period.

The interval cancer rate in the patients screened with DBT and digital mammography was 1.6 per 1,000 screened, significantly lower than 2.8 per 1000 in the group screened with digital mammography only. The interval cancers in the trial generally had non-favorable characteristics.

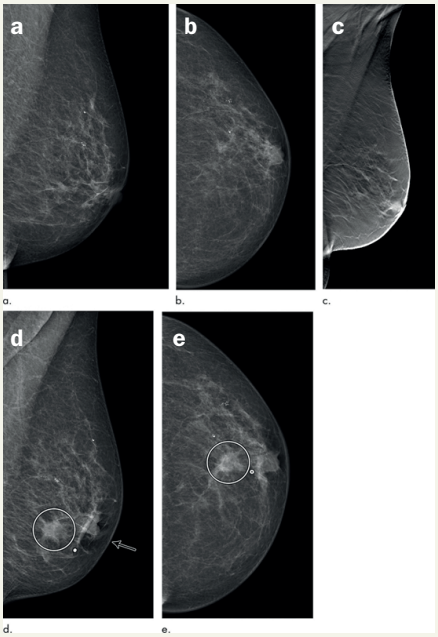
The reduced interval cancer rate after screening with DBT could translate into screening benefits, according to Dr. Johnson.

"*One could speculate that some of the additional cancers detected in DBT screening would have been diagnosed as interval cancers if not detected by DBT,*" she said.

At a glance

- DBT reduces the rate of interval breast cancers (cancers that are diagnosed between screenings) compared to screening with only digital mammography.
- Interval cancer rates with DBT and digital mammography were 1.6 per 1,000 screened, compared to 2.8 per 1000 with digital mammography only.
- Interval cancers are generally more aggressive than cancers detected during a screening exam.

The results support the growing evidence of DBT as a screening modality with potential to replace digital mammography in future breast cancer screening. However, Dr. Johnson cautioned that other trials have not shown significantly reduced interval cancer rates in DBT screening compared to digital mammography screening. And interval cancer rates, while important, are not the only measure when evaluating the potential benefits from DBT in screening.



Images in a 72-year-old woman who was diagnosed with a 13-mm lymph node-negative invasive lobular carcinoma luminal B-like human epidermal growth factor receptor 2 breast cancer 18 months after a screening negative for cancer in the Malmö Breast Tomosynthesis Screening Trial. (a) Mediolateral oblique and (b) craniocaudal digital mammography (DM) images at screening. The slight retraction of the nipple was unchanged compared with previous DM screening images. c) Digital breast tomosynthesis at screening. DM images of (d) mediolateral oblique and (e) craniocaudal views at diagnosis, small marker at lump location. Increased nipple retraction (arrow) and central mass (circle on d and e).
Image credit RSNA

"*Other factors, such as cancer types detected and cost-benefit, have to be taken into account,*" Dr. Johnson said.

Toward that end, the researchers are working on a cost-benefit analysis of the Malmö Breast Tomosynthesis Screening Trial. They are also analyzing the trial for false positive recalls, i.e. those instances when patients are called back for additional screening for suspicious findings that end up being benign.

REFERENCE

1. Johnson K et al Interval Breast Cancer Rates and Tumor Characteristics in the Prospective Population-based Malmö Breast Tomosynthesis Screening Trial. Radiology. 2021; 000:1–10 https://doi.org/10.1148/radiol.2021204106.

Abbreviated breast MRI for breast cancer screening: introduction and review of the literature

By Dr. L Heacock

Screening mammography decreases breast cancer mortality and increases the detection of early stage, more easily treated breast cancer [1]. While mammography is the mainstay of breast cancer screening [2,3], it has known limitations in evaluating patients with dense fibroglandular breast tissue [4] and has been shown to preferentially detect slower-growing, low-grade cancers or ductal carcinoma *in situ* [5,6]. More biologically relevant, fast growing cancers are often masked by benign breast tissue on mammography [5,6].

BREAST MRI ADVANTAGES

The limitations of screening mammography are easily overcome by the use of breast MRI, which has been shown to demonstrate high sensitivity compared to other screening modalities [7-10] with increased detection of high-grade invasive cancers compared to mammography and ultrasound [6]. This is due to the superior tissue contrast offered by MRI and the physiologic uptake of gadolinium contrast, which exploits the rapid wash-in and wash-out of contrast observed due to angiogenesis in breast cancer. However, widespread use of breast MRI has been limited to those patients considered at high (>20%) lifetime risk of breast cancer [1], despite its cancer detection rate of 14.6-16.0 cancers per 1000 women in this high risk group compared to 7.7 per 1000 women when compared to mammography and ultrasound screening alone [2]. Further studies have shown that women at intermediate lifetime risk (15-20%) of breast cancer can similarly benefit from breast MRI [1, 3], with recent studies even suggesting average risk women may benefit from a screening MRI every 2-3 years [14]. Despite these benefits, even 42.1% of high risk women offered a free screening breast MRI as part of the American College of Radiology Imaging Network (ACRIN) 6666 study declined to participate [4]. A subsequent analysis of breast MRI utilization demonstrated only 1.5% of women with high lifetime risk have ever had a breast MRI [5].

DRAWBACKS OF BREAST MRI

Despite the clear benefits of breast MRI in cancer screening, the cost, patient tolerance of the exam, and accessibility remain key issues. An growing number of women at increased risk of breast cancer who might benefit from breast MRI have high deductible insurance plans [6] for which an MRI co-pay may be a prohibitive expense. The prone positioning traditionally used for breast MRI is difficult for many women to tolerate, leading to motion degradation and patient reluctance to undergo future breast MRI. Finally, socioeconomic disparities have been observed in screening breast MRI, with nonurban residents traveling further to obtain it [7].

RATIONALE FOR ABBREVIATED MRI AND BASIC PRINCIPLES

Abbreviated breast MRI (AB-MRI), in which only a selected number of sequences and post-contrast imaging is acquired, exploits the high sensitivity of breast MRI while reducing table time and reading time to maximize availability, improve patient tolerance and accessibility of breast MRI. First described in 2014 by Kuhl *et al,* [8], AB-MRI has rapidly become integrated into many practices and academic institutions.

Kuhl *et al* introduced the first clinical study of an abbreviated MRI protocol for breast cancer screening, which included a non-contrast T1 weighted and first post-contrast T1 weighted sequence, subtraction images and a single maximum intensity projection (MIP) image [8]. This abbreviated protocol was performed in 606 screening MRI in 443 women at mildly to moderately increased risk of breast cancer. All 11 breast cancers were identified on both abbreviated and full protocols with equivalent diagnostic accuracy, while the interpretation of MIP images alone missed one cancer. Kuhl et al demonstrated the specificity (94.3% v 93.9%) and positive predictive value (PPV) of abbreviated versus full diagnostic protocol (24.4% v 23.4%) were equivalent, with both reduced image acquisition time (17 minutes vs. 3 minutes) and radiologist interpretation time. Average interpretation time of the abbreviated protocol was 28 seconds for first post-contrast images and 2.8 seconds for the MIP image alone.

Kuhl's proposed abbreviated protocol is in contrast to the American College of Radiology (ACR) accreditation requirements for breast MRI, which include a scout localizer, a T2-weighted sequence and pre-contrast, early post-contrast and delayed post-contrast T1-weighted images. Many breast imaging centers acquire at least three post-contrast sequences to generate time signal intensity curves [3, 9]. In contrast, the essential sequences for abbreviated breast MRI

The Author
Dr. Laura Heacock
Department of Radiology,
New York University Grossman School of Medicine, New York, NY USA.
Email: Laura.Heacock@nyulangone.org

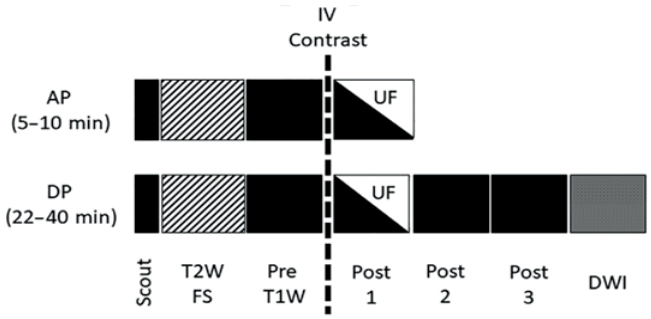


Figure 1. Comparison of a typical abbreviated breast MRI protocol (AP) to a typical diagnostic breast MRI protocol (DP). At a minimum, the AP should include pre- and first post-contrast T1-weighted images, with generated subtraction images and maximum intensity projection (MIP) image if desired. T2-weighted images are required for American College of Radiology (ACR) MRI accreditation requirements. Ultrafast imaging and diffusion weighted imaging can be included in either AP or DP as part of a multiparametric protocol. Abbreviations: DWI = Diffusion weighted imaging, FS = Fat saturated, Post 1 = first post-contrast T1-weighted, Pre T1W = Pre-contrast T1-weighted, T2W = T2 weighted, UF = ultrafast. [37]
Above figure adapted from Figure 6, Reference 37 Heacock et al. Radiol Clin North Am

include at a minimum only a single series of T1-weighted pre- and post-contrast imaging, which does not meet current ACR accreditation standards. Both abbreviated and full protocols often include subtraction and maximum intensity projection (MIP) images [Figure 1].

SUMMARY OF LITERATURE TO DATE

Multiple variations on Kuhl's basic protocol have been tested in the literature. Subsequent early studies on known biopsy-proven cancer and cancer-enriched populations demonstrated the similar high sensitivity of first post-contrast (FAST) images for the detection of breast cancer, with mean sensitivities ranging from 86-99.6% [10-13]. Although Kuhl's original study reported a fast interpretation time (3 seconds) for MIP images, the decreased sensitivity of MIP image interpretation alone in subsequent studies demonstrated that optimal interpretation includes evaluation of FAST images [10]. These early retrospective studies also reported substantially faster image acquisition and interpretation times for abbreviated protocols compared to prior full breast MRI protocols. Cancers proven to be difficult to visualize in abbreviated protocols were more likely to be low-grade invasive cancers, DCIS, or axillary lesions [10, 12]. Grimm *et al.* evaluated a second post-contrast acquisition did not significantly improve sensitivity or specificity [13].

As T2-weighted images are required for ACR breast MRI accreditation, the value of T2-weighted imaging in an abbreviated breast MRI remains a topic of interest. Heacock *et al.* [12] investigated the role of T2-weighted imaging in AB-MRI and found that it improved perceived lesion conspicuity in a known cancer cohort but did not change the cancer detection rate (CDR). Image acquisition time increased by 5 minutes but with increased interpretation times of 10-15 seconds [12]. Stahl *et al.* prospectively assessed the impact of each full breast MRI protocol sequence and concluded that T2-weighted imaging improves breast cancer screening [14]. Other studies [8, 10, 15] demonstrating comparable diagnostic accuracy between AB-MRI without T2-weighted images and full diagnostic MRI protocols suggest that T2-weighted sequences may not add significant benefit. However, as few of these studies were carried out in a pure screening population, it is possible that

Reference	Ultrafast	Standard temporal resolution						Sens	Spec	Max AUC
		Pre-T1W	FAST T1W	Second/ delayed post T1W	T2W	Sub	MIP			
Platel et al 2014 [38]	Y	Y	Y	N	N	Y	Y	NA	NA	0.87
Kuhl et al 2014 [8]	N	Y	Y	N	N	Y	Y	100%	94.3%	NA
Mann et al 2014 [36]	Y	N	N	N	N	N	N	90%	67%	0.812
Mango et al 2015 [10]	N	Y	Y	N	N	Y	Y	93-98%	NA	NA
Grimm et al 2015 [13]	N	Y	Y	Y	Y	Y	N	86-89%	45-52%	NA
Harvey et al 2016 [27]	N	Y	Y	N	N	Y	Y	100%	94%	NA
Heacock et al 2016 [12]	N	Y	Y	N	Y	Y	N	97.8-99.4%	NA	NA
Moschetta et al 2016 [22]	N	Y	Y	N	Y	Y	Y	89%	91%	NA
Abe et al 2016 [34]	Y	Y	Y	N	N	Y	N	85%	79%	0.89
Machida et al 2017 [23]	Y	Y	Y	N	N	N	N	87.1-93.5%	83.4-91.7%	NA
Chen et al 2017 [19]	N	Y	Y	N	N	Y	Y	92.9-93.8%	86.5-88.3%	NA
Petrillo et al 2017 [15]	N	Y	Y	N	N	Y	Y	99.5%	75.4%	NA
Panigrahi et al 2017 [25]	N	Y	Y	N	N	Y	Y	81.8%	97.2%	NA
Romeo et al 2017 [26]	N	Y	Y	N	Y	Y	N	99%	93%	NA
Oldrini et al 2017 [39]	Y	Y	Y	N	Y	Y	N	93.1%	70.8-83.3%	NA
Choi et al 2017 [40]	N	Y	Y	N	Y	Y	Y	100%	89.2%	NA
Oldrini et al 2018 [24]	N	Y	Y	N	N	Y	N	100%	95.1%	NA
Lee-Felker et al 2019[29]	N	Y	Y	N	N	Y	Y	99%	97%	NA

Table 1. Summary of sequences included in various abbreviated MRI protocols and the reported sensitivity, specificity and area under the curve (AUC) for that protocol. Studies that used an ultrafast sequence had a temporal resolution of less than 10 seconds and were run both before and after contrast injection. [37]
Abbreviations: AUC, Area under the curve; FAST, first post contrast; Max, Maximum, MIP, Maximum intensity projection; N, No; Pre-, Pre-contrast; Sens, Sensitivity; Spec, Specificity; Subs, Subtraction images; T1W, T1-weighted; T2W, T2-weighted; Y, Yes
Above Table adapted from Table 1 ref 37, Heacock et al. Radiol Clin North Am.

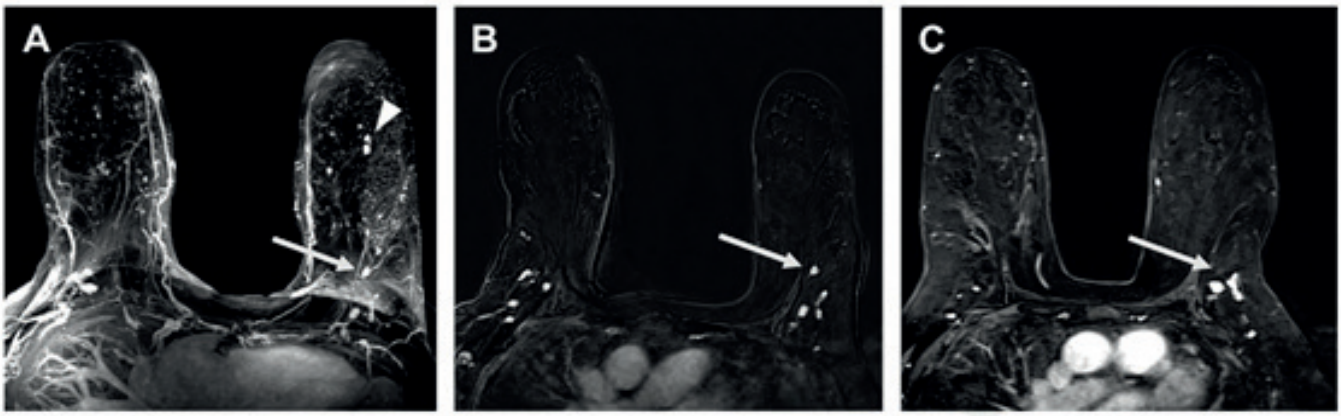


Figure 2. A 56-year-old woman with a personal history of atypia and a strong family history of breast cancer, presenting for high-risk screening. An oval, homogenously enhancing 0.8-cm mass in the left breast at 2:00 (arrow) seems to be a benign axillary lymph node on MIP image (A), but is slightly anterior to axillary lymph nodes on corresponding first postcontrast subtraction images (B). However, the mass is new compared with prior MR imaging (C). MR imaging-guided biopsy yielded metaplastic carcinoma. Arrowhead denotes a previously biopsied left breast benign masses. Axillary lesions are a known pitfall of MIP interpretation; this area should be reviewed carefully on first postcontrast images.
Above figures adapted from Figure 6, ref 37, Heacock et al. Radiol Clin North Am.

the added value of T2-weighted imaging may be most valuable in increasing specificity and biopsy positive predictive value.

Gadolinium-based intravenous contrast remains essential to abbreviated breast MRI. Studies evaluating noncontrast sequences alone, including diffusion weighted imaging (DWI) show sensitivities of 40-78% [16-18] in breast cancer enriched screening populations. These low sensitivities compared to those observed in contrast-enhanced studies demonstrate that DWI and similar noncontrast techniques remain inferior in breast cancer detection. However, adding DWI to a multiparametric contrast-enhanced abbreviated protocol has the potential to improve specificity and sensitivity [19].

The groundwork laid in these prior studies led to the landmark prospective ECOG-ACRIN trial EA1141, "*Comparison of abbreviated breast MRI and DBT in breast cancer screening in women with dense breasts*" [20]. This multicenter study compared digital breast tomosynthesis (DBT) with same day abbreviated breast MRI in asymptomatic, average-risk women with dense breasts, with an overall cancer detection rate of 15.2/1000 women compared to the DBT overall cancer rate of 6.2/1000 women. No invasive cancer was detected by DBT alone. AB-MRI increased short-term follow-up recommendations (BI-RADS 3) compared to DBT (7.5% vs. 1.2%); however, 10.1% of DBT exams required additional imaging (BI-RADS 0) compared to 0% of AB-MRI. Additional analysis is ongoing [21].

To summarize, abbreviated breast MRI has been performed in over 5,400 women in 8 different countries [Table 1] with similar accuracy in contrast-enhanced protocols despite these heterogeneous populations, imaging sequences and equipment [8, 10, 22-27]. The reproducibility of the high accuracy and sensitivity of worldwide protocols highlights the fact that AB-MRI is able to detect biologically aggressive and mammographically occult breast cancer similar to routine breast MRI but with the advantage of decreased imaging time.

LIMITATIONS

The limitations of abbreviated MRI appear similar to those of a full breast MRI protocol. Missed known cancers on AB-MRI are more likely to be DCIS or low-grade invasive cancers [10, 12]. Axillary lesions are a potential pitfall, particularly on review of MIP images (Figure 2) [10, 12]. The lack of delayed postcontrast images inherent to an AB-MRI protocol means that it is less suited to post-neoadjuvant chemotherapy follow up than a full protocol [3, 28], although AB-MRI has shown initial promise in the evaluation of known breast cancers [29].

IMPLEMENTATION CHALLENGES

The major implementation challenges to more widespread use of AB-MRI are those related to reimbursement and workflow optimization. There is still no United States Current Procedural Terminology (CPT) code for AB-MRI, although some breast imaging centers offer a self-pay exam that is not billed to insurance [30]. The cost of this examination varies due to geographic and technical considerations; the goal in self-pay pricing is to offer an examination price that is lower than that of the out-of-pocket deductible for a full breast MRI on high-deductible plans. This is similar to other common cross-sectional screening examinations such as noncontrast CTs for lung cancer screening and cardiac calcium scoring [31].

Clinical workflow optimization remains the other major obstacle to AB-MRI implementation. Early research noting the decrease in AB-MRI image acquisition time referred to what can be called "scan time," (the time it takes to acquire images) which from an operations standpoint is different from the true "table time," or the time from which the patient's intravenous line is placed to the time they are taken off the MRI table. This information is critical to estimating the price point for an abbreviated MR exam and for integrating it into an operations workflow. Borthakur *et al* [32] evaluated full protocol compared to AB-MRI studies in clinical practice and found that the realized gains in patient flow rate (38% for abbreviated MRI compared to a full protocol) were lower than expected based on scan time decrease (65%) because of increased technologist activity time for the AB-MR protocol [32]. This is unsurprising when room setup, patient inflow and exit, IV placement and other considerations are included

when increasing the number of scans performed in the clinical day. Practical considerations when adding AB-MRI to the workflow include keeping the breast coil on the table, duplicating key equipment, and embedding AB-MRI hours into the MRI schedule [31, 33].

FUTURE DIRECTIONS

Clinical research, including the recent EA1141 trial, have shown the promise of AB-MRI protocols in breast cancer screening, particular in increased risk women and women with dense breast tissue. However, further research is still needed and ongoing. An important upcoming study is the planned ECOG-ACRIN PRISM: PRImary Screening with MRI Prospective randomized trial, which will compare DBT and whole breast screening MRI to abbreviated MRI. Additional large-scale clinical trials are ongoing in evaluating AB-MRI in BRCA mutation carriers (Clinicaltrials.gov Identifier: NCT03475979) and in women post breast conservation therapy (NCT03664778). The use of AB-MRI in preoperative MRI staging, evaluating neoadjuvant chemotherapy response, or problem-solving remains unclear and under investigation.

Other novel research protocols include the incorporation of ultrafast imaging acquired immediately post-injection to evaluate wash-in kinetics as a substitute for traditional wash-out time signal intensity curves, which cannot be evaluated in AB-MRI [34-36], and the development of multiparametric protocols. Future directions will likely incorporate deep learning tools for lesion detection, background parenchymal enhancement analysis, and synthetic MRI reconstruction.

CONCLUSION

AB-MRI has the potential to increase patient tolerance and breast MRI screening accessibility to women with intermediate and high lifetime risk of breast cancer, while decreasing scan time and cost. Worldwide studies to date have shown high sensitivity and accuracy for breast cancer screening, including multicenter data demonstrating AB-MRI has improved cancer detection when compared to DBT. These and ongoing studies have proven the utility of AB-MRI in breast cancer detection; reimbursement and clinical implementation remain current challenges to be overcome. Although further research is needed and ongoing, AB-MRI has the potential to transform breast cancer screening in the future.

REFERENCES

1. Monticciolo DL *et al.* Breast Cancer Screening in Women at Higher-Than-Average Risk: Recommendations From the ACR. J Am Coll Radiol, 2018. 15(3 Pt A): p. 408-414.
2. Kuhl C *et al.* Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. J Clin Oncol. 2010; 28: 1450.
3. Mann RM, Cho N & Moy L. Breast MRI: State of the Art. Radiology. 2019; 292: 520.
4. Berg WA *et al.* Reasons women at elevated risk of breast cancer refuse breast MR imaging screening: ACRIN 6666. Radiology, 2010; 254: 79
5. Wernli KJ *et al.* Patterns of breast magnetic resonance imaging use in community practice. JAMA Intern Med, 2014; 174:125.
6. Cohen RA & Zammitti EP. High-deductible health plan enrollment among adults aged 18–64 with employment-based insurance coverage. NCHS Data Brief. 2018; 317: 1.
7. Onega T *et al.* Travel Burden to Breast MRI and Utilization: Are Risk and Sociodemographics Related? J Am Coll Radiol. 2016; 13: 611.
8. Kuhl CK *et al.* Abbreviated breast magnetic resonance imaging (MRI): first postcontrast subtracted images and maximum-intensity projection-a novel approach to breast cancer screening with MRI. J Clin Oncol. 2014; 32: 2304.
9. ACR. American College of Radiology website. Breast magnetic resonance imaging (MRI) accreditation program requirements. 2017 [cited 2019 October 17]; Available from: http://www.acraccreditation.org/~/media/ACRAccreditation/Documents/Breast-MRI/Requirements.pdf?la=en.
10. Mango VL *et al.* Abbreviated protocol for breast MRI: are multiple sequences needed for cancer detection? Eur J Radiol. 2015; 84: 65.
11. Partridge SC *et al.* Breast DCE-MRI: influence of postcontrast timing on automated lesion kinetics assessments and discrimination of benign and malignant lesions. Acad Radiol. 2014; 21: 1195.
12. Heacock L *et al.* Evaluation of a known breast cancer using an abbreviated breast MRI protocol: Correlation of imaging characteristics and pathology with lesion detection and conspicuity. Eur J Radiol. 2016; 85: 815.
13. Grimm LJ *et al.* Abbreviated screening protocol for breast MRI: a feasibility study. Acad Radiol. 2015; 22: 1157.
14. Strahle DA *et al.*, Systematic development of an abbreviated protocol for screening breast magnetic resonance imaging. Breast Cancer Res Treat. 2017; 162: 283.
15. PetrilloA *et al.* Abbreviated breast dynamic contrast-enhanced MR imaging for lesion detection and characterization: the experience of an Italian oncologic center. Breast Cancer Res Treat. 2017; 164: 401.
16. Yabuuchi H *et al.* Detection of non-palpable breast cancer in asymptomatic women by using unenhanced diffusion-weighted and T2-weighted MR imaging: comparison with mammography and dynamic contrast-enhanced MR imaging. Eur Radiol. 2011; 21: 11.
17. McDonald ES *et al.* Performance of DWI as a Rapid Unenhanced Technique for Detecting Mammographically Occult Breast Cancer in Elevated-Risk Women With Dense Breasts. AJR Am J Roentgenol. 2016; 207: 205.
18. Trimboli RM *et al.* Breast cancer detection using double reading of unenhanced MRI including T1-weighted, T2-weighted STIR, and diffusion-weighted imaging: a proof of concept study. AJR Am J Roentgenol. 2014; 203: 674.
19. Chen SQ *et al.* Abbreviated MRI Protocols for Detecting Breast Cancer in Women with Dense Breasts. Korean J Radiol. 2017; 18: 470.
20. Kuhl CK Abbreviated breast MRI for screening women with dense breast: the EA1141 trial. Br J Radiol. 2018; 91: 20170441.
21. Comstock CE *et al.* Comparison of Abbreviated Breast MRI vs Digital Breast Tomosynthesis for Breast Cancer Detection Among Women With Dense Breasts Undergoing Screening. JAMA, 2020. 323(8): p. 746-756.
22. Moschetta M *et al.* Abbreviated Combined MR Protocol: A New Faster Strategy for Characterizing Breast Lesions. Clin Breast Cancer. 2016; 16: 207.
23. Machida Y *et al.* Feasibility and potential limitations of abbreviated breast MRI: an observer study using an enriched cohort. Breast Cancer. 2017; 24: 411.
24. Oldrini G *et al.* Impact of an abbreviated protocol for breast MRI in diagnostic accuracy. Diagn Interv Radiol. 2018; 24: 12.
25. Panigrahi B *et al.* An Abbreviated Protocol for High-risk Screening Breast Magnetic Resonance Imaging: Impact on Performance Metrics and BI-RADS Assessment. Acad Radiol. 2017; 24: 1132.
26. Romeo V *et al.* Preliminary Results of a Simplified Breast MRI Protocol to Characterize Breast Lesions: Comparison with a Full Diagnostic Protocol and a Review of the Current Literature. Acad Radiol. 2017; 24: 1387.
27. Harvey SC *et al.* An Abbreviated Protocol for High-Risk Screening Breast MRI Saves Time and Resources. J Am Coll Radiol. 2016; 13: 374.
28. Kim SY *et al.* Dynamic Contrast-enhanced Breast MRI for Evaluating Residual Tumor Size after Neoadjuvant Chemotherapy. Radiology. 2018; 289: 327.
29. Lee-Felker S *et al.* Abbreviated Breast MRI for Estimating Extent of Disease in Newly Diagnosed Breast Cancer. 2019.
30. FAQs About Mammograms, Including 2D and 3D Mammograms, ABUS and Fast Breast MRI. 2018 05/25/21]; Available from: www.pennmedicine.org/cancer/about/focus-on-cancer/2018/october/faq-about-breast-cancer-screening-at-penn.
31. Marshall H *et al.* Implementing Abbreviated MRI Screening Into a Breast Imaging Practice. AJR Am J Roentgenol. 2019; 213: 234
32. Borthakur A *et al.* Comparison of Study Activity Times for "Full" versus "Fast MRI" for Breast Cancer Screening. J Am Coll Radiol. 2019; 16: 1046.
33. Recht MP *et al.* Optimization of MRI Turnaround Times Through the Use of Dockable Tables and Innovative Architectural Design Strategies. AJR Am J Roentgenol. 2019; 212: 855.
34. Abe H *et al.* Kinetic Analysis of Benign and Malignant Breast Lesions With Ultrafast Dynamic Contrast-Enhanced MRI: Comparison With Standard Kinetic Assessment. AJR Am J Roentgenol. 2016; 207: 1159.
35. Heacock L *et al.* Comparison of conventional DCE-MRI and a novel golden-angle radial multicoil compressed sensing method for the evaluation of breast lesion conspicuity. J Magn Reson Imaging. 2017; 45: 1746.
36. Mann RM *et al.* A novel approach to contrast-enhanced breast magnetic resonance imaging for screening: high-resolution ultrafast dynamic imaging. Invest Radiol. 2014; 49: 579.
37. Heacock L *et al.* Abbreviated MR imaging for breast cancer. Radiol Clin North Am, 2021; 59: 99.
38. Platel B *et al.*, Automated characterization of breast lesions imaged with an ultrafast DCE-MR protocol. IEEE Trans Med Imaging. 2014; 33: 225.
39. Oldrini G *et al.* Abbreviated breast magnetic resonance protocol: Value of high-resolution temporal dynamic sequence to improve lesion characterization. Eur J Radiol. 2017; 95: 177.
40. Choi BH *et al.* Usefulness of abbreviated breast MRI screening for women with a history of breast cancer surgery. Breast Cancer Res Treat. 2018;167: 495.

Figure 2 (adapted from Figure 6, Heacock et al Radiology Clinics NA)

iCAD signs global distribution agreement with Sectra

iCAD has announced that it has signed a worldwide distribution agreement with Sectra, the international medical imaging IT and cybersecurity company. Under this agreement, iCAD's ProFound AI and ProFound AI Risk packages will be offered through the Sectra Amplifier Marketplace, so expanding access to more facilities and imaging centers worldwide.

"*iCAD's technology offers unparalleled benefits to clinicians and patients alike. ProFound AI is clinically proven to enhance breast cancer screening by improving radiologists' accuracy and efficiency. ProFound AI Risk is the first and only commercially available clinical decision support tool that provides an accurate two-year breast cancer risk estimation that is personalized for each woman, based solely on a screening mammogram*," said Michael Klein, Chairman and CEO of iCAD. "

Sectra develops and sells imaging IT solutions. Nynke Breimer, Global Product Manager AI Radiology, Sectra said "*To help healthcare providers get on the AI adoption journey, we have created the Sectra Amplifier Marketplace. We aim to facilitate easier access and usage of AI applications in medical imaging. With iCAD's tools deeply embedded in the Sectra diagnostic workspace, we provide our radiologists with enhanced diagnostic confidence for breast imaging reading,*".

iCAD,
NASHUA, NH, USA
www.ICAD.com
SECTRA,
LINKÖPING, SWEDEN
www.Sectra.com

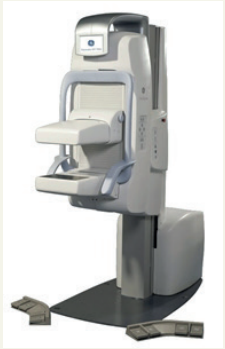
SmartBreast acquires GE's MBI system

SmartBreast Corporation has acquired the Discovery NM750b Molecular Breast Imaging (MBI) assets from GE Healthcare.

SmartBreast will manufacture, market and distribute the MBI scanner, rebranded as "EVE CLEAR SCAN e750."

MBI saves lives by detecting breast cancer earlier in women with dense breasts, who comprise about 40% of American, European and African women and 70% of Asian women.. In a clinical study [1] with one-year follow up of 1585 women with dense breasts, researchers at the Mayo Clinic reported that mammography found 3.2 cancers per 1,000. Adding low-dose MBI increased the number of cancers found to 12 per 1,000.

"*GE Healthcare's MBI system has developed a positive reputation for helping physicians with the detection of cancer lesions in dense breast tissue*," says Erez Levy, General Manager of Nuclear Medicine, GE Healthcare. "*We are proud of this system's legacy and will continue to support its mission with our world-class Cadmium Zinc Telluride (CZT) detectors for SmartBreast's use in the MBI system*"



According to Dr. James Hugg, CEO, SmartBreast, "*We will become the largest global player in secondary screening and diagnostics for women with dense breasts by providing the most effective tool for locating and diagnosing cancers occult on mammography. We have acquired Dilon's and also GE Healthcare's MBI product lines, consolidating clinically proven reliable products with 217 installations globally*".

1. DJ Rhodes, et al, American Journal of Roentgenology 2015, 204: 241

SMARTBREAST CORPORATION:
PITTSBURGH, PA, USA

Elekta and Philips deepen partnership in individualized oncology care

Philips and Elekta have recently signed agreements to deepen their existing strategic partnership aimed at advancing comprehensive and personalized cancer care through precision oncology solutions. The extended collaboration builds on the two companies' successful cooperation in the fast-emerging field of MR-guided adaptive radiation therapy.

The strengthened strategic partnership intends to further deliver a superior experience in diagnosis and adaptive, personalized treatments for clinicians, shorter treatment times and more precise therapy for patients, as well as lowered costs of care for healthcare providers.

"*I expect this extended partnership to unlock opportunities that will provide better outcomes for people with cancer,*" said Gustaf Salford, Elekta's President and CEO. "*Together, we'll combine advanced informatics and image-guided RT solutions to deliver greater precision in oncology. This means easier selection by clinicans of the optimal treatment strategy and more efficient and effective therapy delivery.*"

Kees Wesdorp, Chief Business Leader of Precision Diagnosis at Philips said "*By continuing our already-successful collaboration with Elekta, we will accelerate towards our goal of providing clear care pathways and predictable outcomes for every cancer patient. The announcement of our deepening partnership is an important next step in the implementation of our strategy in precision diagnosis.*"

PHILIPS
AMSTERDAM, THE NETHERLANDS
www.philips.com
ELEKTA
STOCKHOLM, SWEDEN
www.elekta.com

Italian design

EXPLORING THE INSIDE.

MyLab™ X9

Opening infinite horizons

www.mylabx9.com

MyLab™ X75

Enhancing the experience

www.mylabx75.com

Esaote S.p.A. - sole-shareholder company
Via Enrico Melen 77, 16152 Genova, ITALY, Tel. +39 010 6547 1, Fax +39 010 6547 275, info@esaote.com

esaote

The potential of low-field MRI

an initial experience with a small, wide-bore 0.55 T MRI in a real life clinical setting

Founded more than 700 years ago, the Basel University Hospital is one of the oldest hospitals in Switzerland. Despite its venerable age, the hospital has a deserved reputation for using the most up-to-date technology whenever clinically appropriate. An example of this is the recent acquisition of a small, 0.55 Tesla, wide-bore MRI scanner, the Magnetom Free.Max from Siemens Healthineers. We wanted to find out more about the clinical experience with the new system so far and the potential of low-field MRI in general, so we spoke to Prof. Elmar Merkle, head of the Department of Radiology, together with Dr. Hanns-Christian Breit and Dr. Michael Bach.

Prof. Elmar Merkle is head of Radiology at The Basel University Hospital
Elmar.Merkle@usb.ch

Hanns-Christian Breit, MD
Senior resident, radiology training
hanns-christian.breit@usb.ch

Michael Bach, Ph.D
Physicist, specialized in MR
michael.bach@usb.ch

Q *Before we get into discussing the new MRI system, please give us a brief background to your hospital itself and the central radiology department.*

In 2020 we performed a total of 145,315 imaging examinations of which 49,188 were CTs and 22,021 MRIs, Focussing on MRI, the principal indications were joints, prostate and brain imaging. To carry out this workload we have three 3T scanners (2 Siemens Healthineers Magnetom Skyra, & 1 Siemens Healthineers Magnetom Prisma) and two 1.5T systems (Siemens Healthineers Magnetom Avanto). The latest arrival and completing our current range of MRIs is the new Siemens Healthineers Magnetom Free.Max 0.55T whose installation here in Basel was one of the first in the world.

Q *So let's turn to the Magnetom Free.Max.*

The system was actually installed in March of this year, with the first patients being scanned at the beginning of May after the system received the CE mark.

As for the installation itself, that was greatly facilitated by the small dimensions and weight of the new 0.55 T system. For the first time with an MRI installation, we were able to physically deliver the machine simply through the standard hospital corridors. The contrast with the installation of our higher field systems was stark — for the 1.5T and 3.0T systems we were obliged to break down the external wall of our building, resulting in substantially higher costs of time and money. In addition the 0.55T machine uses only a small amount of helium, so there is no need for expensive helium quench evacuation piping. Overall, we calculated that the costs of preparing the site before installation were 30% lower for the Magnetom Free Max than for "conventional" MRI scanners.

Although the scanner has significantly smaller dimensions than the higher field models, we deliberately installed it in a generously spacy room, since we anticipate that ICU patients, with all the associated ancillary equipment, will also be imaged in the future. In terms of actual patient handling and operation, the low-field system behaves just like our higher field machines so we don't need a dedicated team of operators specialized on one system — our operators can be freely assigned to machines of any field strength.

The learning curve for the radiographers was straightforward — comparable to that after a major software update or installing a new "conventional" MRI and was made easier by our familiarity with other Siemens Healthineers MRI systems.

However, given that this is a new scanner with a "new" field strength, we had quite a lot of work to do on the initial set-up of the sequences, with a radiologist and a medical physicist devoting nearly a month full-time to set up the most important protocols. Other hospitals may not need to start from scratch like this, — perhaps that's the downside of being the one of the first installations in the world — but it is unavoidable that sequence optimization is a time-consuming process, albeit a necessary one for validation and to fulfil the maximum potential of the machine.

Q *How many patients have you seen so far in the new system and what are your first reactions?*

We have seen approximately 150 patients so far, including some volunteers scanned for test purposes. So far with the new system we have been focussing on patients with metal implants, as well as spine imaging, (experimental) lung imaging and for patients from the emergency department. For spine, stroke, hip, abdominal and joint imaging we use the same pulse sequences as on our other scanners (T1/T2/PD, TSE, EPI, SWI, TOF, HASTE, TRUFI, VIBE, DIXON, SPACE).

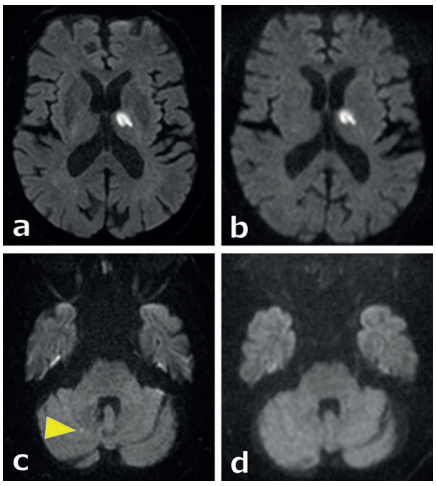


Figure 1. Stroke patient. DWI, b = 1000 s/mm², slice-thickness = 3 mm.
Top Panels. Image (a) acquired by Magnetom Avanto 1.5T, Time of acquisition (TA): 2:06 min compared with (b) Magnetom Free.Max, 055T, TA 4:35 min. The stroke area is clearly depicted on both systems. Bottom Panels. Image (c) acquired by Avanto I.5T compared with image (d) acquired by Free.Max. Small stroke lesion (less than 2 mm, yellow arrowhead) is missed occasionally at lower field strength. We are currently investigating these findings in more depth.

We'll talk about image quality, noise and performance later on, but one first, non-radiological impression was how useful and appreciated was the wide bore, especially when we're dealing with obese patients — the Free.Max has a bore diameter of 80 cm. Since acoustic noise varies with field strength, we expected our patients to positively comment on the low noise levels in the new system, but in fact the patients' messages about noise weren't clear-cut — some even thought the noise level was higher than with our 1.5T systems. We haven't yet carried out objective acoustic noise measurements.

Q *What about image quality and general system performance?*

Given that our experience so far has been with 1.5 and 3.0T systems, we had some initial scepticism about image quality at 0.55T, but we are confident that the new system can nicely complement our existing MRI scanner spectrum. As for spatial resolution, there are some cases, such as knee and brain, with their need for higher resolution, which are challenging and could even be borderline. However these cases can be handled using our existing policy of triaging specific examinations to appropriate scanners.

In general, the Signal to Noise ratio (SNR) is proportional to the magnetic field so, at a first cut this means that the signal at 0.55 T is roughly only 40 % of that at 1.5 T. However the use of lower field strength actually also has three characteristics that can have a significant favourable effect on SNR. First, a lower bandwidth can be used to achieve the same chemical shift. Secondly, the Specific Absorption Rate (SAR) is reduced by a factor of 7.5 / 30 in comparison to 1.5T / 3T scanners respectively so it is usually not necessary to use refocusing flip angles below 180°, which improves SNR. Finally, T1 is shorter at 0.55 T, which also helps to increase SNR. Taking all these effects into account together we are roughly in the range of 60 to 70 % SNR compared to a 1.5 T system.

In practice we can accept a lower SNR — as long of course as the image remains of diagnostic quality. We could improve image quality by going for a longer acquisiton time, depending on the indication, the sequence and the imaging region. However we use the AI-derived algorithms and simultaneous multi-slice imaging to keep the measurement time as short as possible. Currently, we are investigating the Deep Resolve postprocessing in detail and use it in most of our protocols. There are several parameters, for example the sequence type, body region, or original resolution that can influence the final result but we need to investigate this in more detail.

The Deep Resolve reconstruction process takes a bit more time, but even then there is only a small delay (less than one minute) compared to standard reconstructions.

Our first impressions of susceptibility related artifacts are that they are significantly reduced. Certainly, the imaging of metal implants seems to be very promising.. Finally, one other area where we were pleasantly surprised was in fat saturation, since generally, the lower the field strength, the more difficult is spectral fat saturation, as the frequencies of water and fat come closer. In fact we observed that spectral fat saturation worked better than expected.

Q *How do you assign patients to either the 0.55 T MRI or to higher field MRI?*

We always assign patients depending on the indication, For imaging of joints and brain, e.g. brain nerve protocols where higher resolution is required, we would prefer to go for scans at higher field strength, whereas in general we would prioritize scanning at 0.55T for patients with particular patient-related circumstances such as obesity or claustrophobia.

Q *So what is your impression so far of the Siemens Healthineers Magnetom Free.Max?*

Overall, it is a robust tool which completes our scanner-portfolio and is especially suitable for imaging of patients with metal implants. There are still some limitations as concerns resolution in joint imaging and in several other specialized imaging protocols, e.g. prostate imaging.

Of course as radiologists we are always looking forward for further improvements,

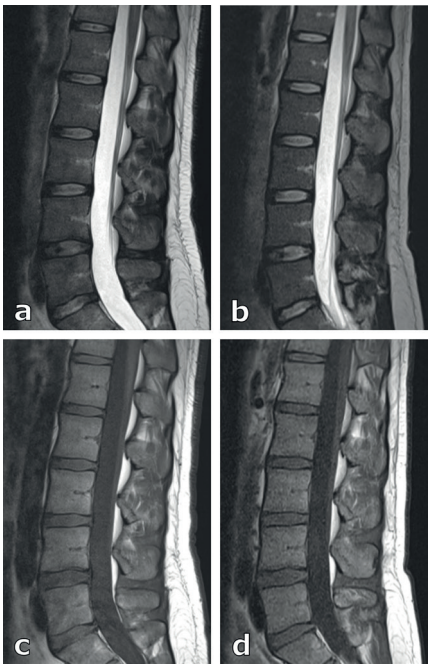


Figure 2. Standard spine examination. Magnetom Avanto 1.5T images (a) and (c) and Magnetom Free. Max 0.55T images (b) and (d).

Comparison of (a) vs. (b). Sagittal T2 TSE, slice-thickness: 4mm. (a) Avanto 1.5T, TA: 1:44 min. (b) Free. Max 0.55T, TA: 3:36 min.

Comparison of (c) vs (d) Sagittal T1 TSE, slice-thickness: 4 mm. (c) Avanto 1.5T, TA: 2:29 min. (d) Free.Max 0.55T TA: 2:28 min.

The image quality at the lower field strength is comparable to that of 1.5T and certainly of diagnostic quality.

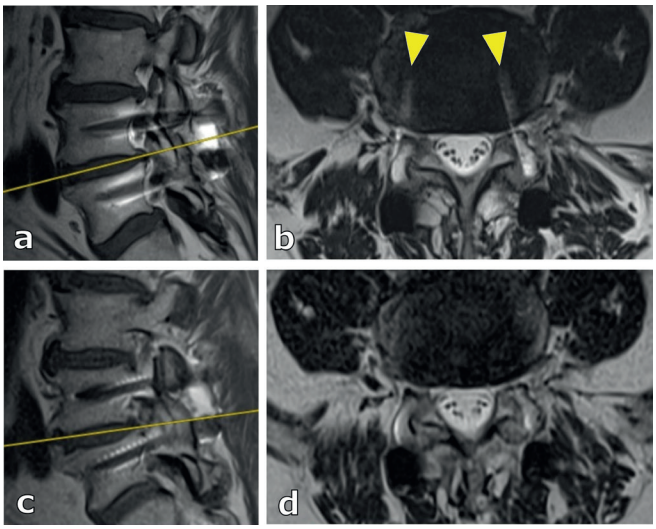


Figure 3. Spine implant examination, comparison between the Avanto 1.5T (top) and Free.Max 0.55T (bottom).
Artifacts are less pronounced on the Free.Max system
Metal artifacts in the oblique transversal plane (between the pedicle screws - yellow lines in (a) and (c)) are seen at 1.5T (b, yellow arrowheads) but not at lower field strength (d). Acquisition times for images (a),(b),(c),(d) are: 4:19 min, 3:37 min, 3:54 min, 4:07 min respectively

so on our personal wish-list we would like to see coil development, more powerful AI-solutions to improve SNR and resolution and acceleration techniques. Another positive development would be more powerful gradients.

Q Do you think that the small foot-print and easy installation of the Magnetom Free.Max could open up the use of MRI in places where MRI is not usually available, e.g. the ICU ?

Yes. A low-field MRI inside the ICU would provide rapid access to advanced imaging for patients who have a high demand for highly specialized medicine — including imaging — without the need for cumbersome transfer of the patient to a central radiology facility. There are indeed quite a number of indications e.g. stroke patients or infection cases, which may require further imaging but which cannot be adequately handled by the only imaging modality usually available in the ICU, namely ultrasound. Another advantage of the Magnetom Free.Max in such a context its low level of susceptibility artifacts, that can be caused by intracorporeal catheters and devices which are often placed in ICU patients. Of course if an ICU patient needs MRI, then it will be carried out if at all possible. Currently this means transfer of the patient to the radiology department; for these very sick patients this can be quite complicated logistically and uses up precious time of busy ICU personnel.

Ideally, we could envisage such an MRI imaging service in the ICU being operated 24/7 by ICU personal as well as by radiology staff. In any case the diagnostic evaluation would always be provided by highly specialized radiologists, so hopefully the service could be run successfully without any "turf wars" breaking out.

We have been talking so far only about a possible use of the low field MRI in the ICU, but since we are in a speculative mood, we could also envisage the use of a small footprint MRI system in other locations, such as the emergency department, where it would provide immediate access to imaging of acceptable diagnostic quality.

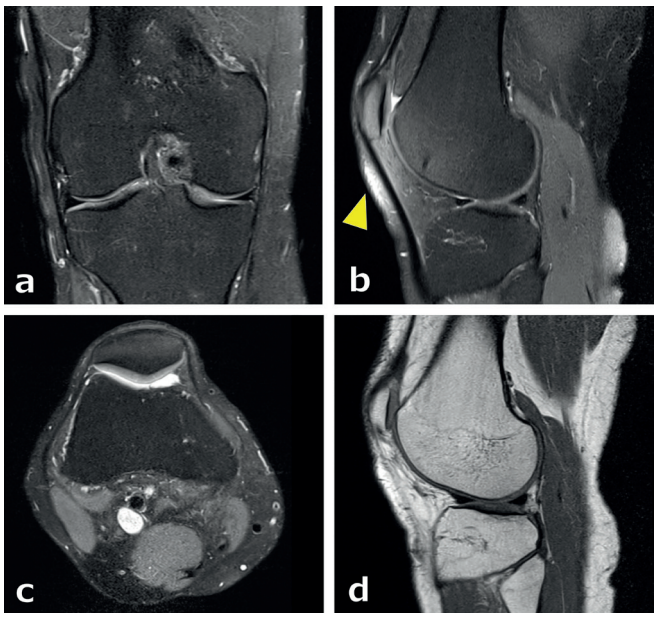


Figure 4. Standard knee examination at the Magnetom Free.Max.
(a) Coronal PD TSE with fat saturation, Acquisition time: 2:58 min.
(b) Sagittal PD TSE with fat saturation. Acquisition time: 3:43 min, Minor fat saturation problems occur in the area anterior to the Hoffa fat pad (yellow arrowhead).
(c) Transversal PD TSE with fat saturation. Acquisition time: 2:47 min.
(d) Sagittal T1 TSE. Acquisition time: 1:51 min.

Q Continuing the "blue sky thinking" could the new MRI play a role in post-COVID hospital environments where there is likely to be more emphasis on reducing the need for inter-department transfers of patients?

As in most hospitals we found here in Basel that during the COVID-19 pandemic the provision of vital imaging services to patients with COVID was really challenging logistically, so anything that could reduce the need for the inter-departmental traffic of transfer patients who are highly infectious and/or in critical condition would of course be welcome.
But more broadly what we're talking about here is the issue of access to MRI in general. In Switzerland we have one of the highest number of MRIs per million of population, with 215 scanners in the hospital sector alone (the population of Switzerland is approximately 8.5 million). Thus, waiting times for MRI in Switzerland are low, typically about one week, although that of course depends on the indication and examination. If necessary we at Basel provide immediate imaging for any patient 24/7. However the level of access to MRI that we have in Switzerland isn't the same as in other countries. Developing countries in particular could benefit from the lower costs and installation requirements, which are major advantages of the new low-field system. In this way, we think there is a great potential to improve diagnostic possibilities via MR imaging in many areas of the world.

Q Do you think that the era of domination in MRI by 1.5T/3.0 T systems is now definitively over or will they still remain a vital component in MRI for the foreseeable future?

We think 1.5T and 3T systems will still remain the mainstay of MRI imaging but they could be usefully complemented by new low-field scanners which can provide imaging of diagnostic quality in several particular examinations. We can even imagine specific areas where low-field MRIs could be better, e.g. the metal artifacts shown above.
Finally, given the incessant increase in the demand for MR imaging, the significant economic advantages of low-field MRI can't be ignored.

Discover **ProFound AI®**

Precise, Powerful, Proven AI Solutions for Breast Cancer Screening and Diagnosis

NEW: ProFound AI® Risk

The only clinical decision support tool that provides an accurate two-year breast cancer risk based only on a mammogram and age.

ProFound AI® for 2D and 3D Mammography

Clinically proven to support cancer detection.

PowerLook® Density Assessment

Learn more and request a demo at
www.icadmed.com/profoundai-risk.html

iCAD®

Trust the Proven Leader in Breast AI

Bucking the Trend

Ever since the outbreak of the COVID-19 pandemic, hospitals have increasingly had to focus almost exclusively on meeting the challenges of the viral infection and consequently have had to put on hold investments for capital equipment in fields not directly related to the emergency. This has created difficult market conditions for companies selling products into the diagnostic imaging business. Despite the current tough market situation, the Italian company Esaote has posted better than expected sales revenues. We wanted to find out more about Esaote's success in bucking the current market trend so we spoke to Franco Fontana, CEO of the Esaote Group.

Franco Fontana is CEO of the Esaote Group

Q *What exactly has been the effect of the pandemic on the diagnostic imaging market in general?*

2020 was a challenging year that saw the front line of the medical industry understandably focussed almost exclusively on meeting the demand for diagnosis and treatment of patients with COVID-19. The performance of the global diagnostic imaging market showed an overall contraction because of the pandemic, which negatively affected investments in areas not directly involved in dealing with the emergency (e.g. MRI, cath-labs, nuclear medicine, etc.). A similar contraction (10%) also occurred in the Healthcare Information Technology sector, again due to priorities shifting capital expenditures to face the emergency.

Q *One of your key sectors is ultrasound. How did this sector fare world-wide?*

According to the healthcare market research company Signify Research, in 2020 the total market for ultrasound, including portable and cart-based systems, showed a global decrease of about 9%, with the biggest decline being in premium and high-end cart-based systems. What demand there was for ultrasound was mainly driven by critical care and emergency medicine while there was a decline in areas like general radiology, cardiology and ob/gyn.

Q *Despite this overall market contraction, Esaote posted a growth in revenues in ultrasound sales. How do you explain this?*

We were able to react to the changing market needs by timely re-direction and re-organization of our production and activity in our compact models and mid-low cart-based systems. Thus our revenues in ultrasound as a whole grew by about 7% compared to 2019, with sales driven by portable systems, whose agility and versatility make them particularly suitable for the needs of intensive care units and emergency rooms. We also had excellent results with our latest X-line generation of cart-based ultrasound systems, especially in the mid-low range. While we're on the subject of ultrasound, it should be said that our latest generation ultrasound systems are highly appreciated in the market principally because they allow optimization of the workflow, that in turn means higher productivity and image quality. In addition, our wide range of probes and software applications result in high performances in shared service situations, so providing huge added value to end-users.

Q *In the other significant parts of your business, namely IT healthcare and MRI, did you succeed in limiting the effect of the global market contraction on your sales?*

Yes. In the MRI and healthcare IT business lines, we succeeded in limiting the contraction to that of the general market, despite both sectors suffering by the shift of priorities caused by the pandemic. In fact, considering the changing scenario both lines actually performed comparatively well — in some regions, like Western Europe for example, our dedicated MRIs even experienced single-digit growth compared to 2019. Our healthcare IT business was able to leverage our large installed base, diversified channels and long-term contracts, so allowing us to contain the contraction to that of the general market or slightly better.

Q *What effect have these results had on internal investment and head-count? Did you make use of any "safety net" plans that were put in place by many government authorities to mitigate the effects of the pandemic on companies and their employees?*

The Group did not make any use of social safety nets during the year. Instead we continued to pursue our growth strategy by maintaining and increasing our activities across the board, from production right through to technical assistance in the field. Against this background, we pursued a human resource policy which has led to an overall growth in the number of employees during 2020: the Esaote Group now counts about 1.200 employees, which is an 8% growth with respect to 2019.. New hires were especially directed to

R&D and the Sales & Marketing sectors, as we want to be ready as soon as possible as normal hospital functioning re-starts.

Q *Talking of increasing head-count, is it easy to hire new staff of the high quality you need?*

Esaote cooperates closely with Italian and European Universities to attract young talent. We are especially proud of our recently launched "*e-generation*" project, which is an Esaote Academy aimed at prioritizing the hiring of young graduates in the STEM (Science, Technology, Engineering and Mathematics) disciplines. These new recruits are typically employed in our R&D, application and marketing departments, through a structured and comprehensive focussed program of theoretical and practical studies.

Q *A couple of years ago, the share capital of Esaote was acquired by a consortium of Chinese investors. Who are these investors and how is the new situation working out?*

The relationship with our new shareholders is extremely positive. The consortium is composed of leading medical technology and healthcare companies: Yuwell and Wandong Medical, as well as financial investors, YF Capital, and Shanghai FTZ Fund, Tianji who have significant experience in the healthcare sector. We view this as a great opportunity for Esaote and the company's future development particularly since the consortium share the Esaote vision of excellence in our core businesses.

Close cooperation with our two new industrial partners was particularly useful during the COVID pandemic. For example, along with our own core portfolio, Esaote was able to deliver mobile DR imaging and respiratory units to meet the need of critical care units. We are also working together on new projects with the aim of expanding our portfolio and further developing our position in the diagnostic imaging industry. The whole management team and I are very happy to be working with the new investors — we have succeeded in combining Italian creativity with the Chinese pragmatic approach to put together an ambitious industrial plan that blends innovation — which is still the core of our competitiveness — and channeled creativity.

Q *Traditionally Esaote's markets have been Europe and North America. Should China now be added as a domestic market?*

Geographically speaking, Europe, China and North America will continue to be the reference markets for Esaote, but with Italy and China now in the role of "*double domestic market*". That this can work is thanks on the one hand to the truly Italian combination of research, design and marketing based in Genoa and Florence and on the other hand to synergies with our Chinese shareholders for expansion in a market with enormous potential.

"...we have succeeded in combining Italian creativity with the Chinese pragmatic approach to put together an ambitious industrial plan..."

Our global presence is shown by the fact that we have fourteen directly-owned subsidiaries and a wide distribution network so that in total Esaote is present in more than one hundred countries. In addition, we have our own R&D centers and production plants in Genoa and Florence in Italy and in Sittard in the Netherlands;

Q *You outlined 2021 as being a key year for the continued development of Esaote in general and in technological innovation. What are the company's objectives for the rest of this period?*

We wanted to build on the positive results of 2020 which confirmed the group's growth strategy, aimed at playing a leadership role in our three reference sectors. In 2021 we will measure ourselves on our ability to leverage our new products to drive a further growth step.

In particular we continue to focus on innovation as a key differentiator of our unique offer of non-invasive technology. We see a gradual return in 2021 to a more or less normal market which will nevertheless still be affected by some restrictions at least until the fourth quarter. However, key to this is facilitating the return of patients to hospitals and private clinics for routine, but important, examinations that may have been postponed during the pandemic. After more than a year in which COVID-19 completely dominated all diagnostic priorities, we believe that healthcare providers will be actively encouraging their personnel to get patients back into follow-up exams and preventive diagnostic processes.

Q *What technological developments can be expected in the rest of 2021?*

Contrary to what you might expect in the middle of a pandemic, in 2020 we actually intensified our plans to be ready to take-up the post-pandemic demand in all our three sectors. So, we will be launching new products and technology that are new advances on the state-of-the-art. In the ultrasound sector, we have just launched two new high-performance systems in the mid-high segment [See Inset] and a range of new ultrasound probes that complete and strengthen our product portfolio. In general, Esaote will continue to make available products that are increasingly aligned with our customers demands. We will integrate high-diagnostic solutions with artificial intelligence- derived algorithms to increase productivity in the actual carrying out of exams and to facilitate diagnosis.

Q *You mentioned AI. To what extent is Esaote involved in AI methodology?*

Esaote has a strong background in AI which principally comes from our Healthcare IT division. AI is making a lot of headlines these days and the reason is simple. The application of AI-derived algorithms makes it possible for health professionals not just to increase their diagnostic certainty but also to issue reports more quickly and in general to make the clinical decision-making process easier. We believe that the true success of AI in healthcare will happen when the time that humans spend on routine, tedious and repetitive tasks is taken over at least partly by AI, so that human intelligence can focus on other more important subjects. Thus, our AI research is always aimed at helping healthcare professionals — we recognize that they retain a central role and responsibility in analysis and the final decision-making processes.

Q *Some of Esaote's competitors in the diagnostic imaging field are much bigger than you. How does this affect your strategy?*

One of the great advantages of being a medium-sized company is the ability to

react quickly to the changing demand of the market and to provide swift solutions. This was clearly shown during the most critical period of the COVID pandemic, as our agility allowed us to adapt and act quickly both to the market and within our organization to ensure continuity of supply in a safe environment. In addition, our size means we can innovate more actively, which has historically always been our key success element.

Q *Most of our conversation so far has focussed on ultrasound but we mustn't forget your Healthcare IT and MRI business. What about them?*

I don't want to give the impression that we are only an ultrasound company. Healthcare IT is our second largest business in terms of revenues. Through our subsidiaries Ebit in Italy and PMI/3mensio in the Netherlands, we play a leadership role in accelerating digital transformation. Our Healthcare IT solutions in enterprise imaging and quantitative analysis software are present in almost 30% of Italian hospitals and in approximately 60% of the world's interventional cardiology centres. Our software enables processes ranging from the optimization of hospital workflows to the application of artificial intelligence to guide professionals during diagnostic and therapeutic processes. The pandemic has accelerated the global need for digital transformation of the healthcare system. Our healthcare IT systems are ready to drive those changes, which in turn will favor de-centralization and closer patient monitoring. We foresee that technologies such as telemedicine, second-opinion, remote monitoring leveraged by AI and interoperable systems will experience strong growth in the context of advanced IT infrastructures.

In MRI, Esaote has pioneered and is a leader in the worldwide market of dedicated MRI systems which allow high-quality imaging and shorter scanning time in reduced space. We believe these features will increasingly be recognized in the future. For MRI, 2021 is again a crucial year for us to re-affirm our leadership, with important innovations planned to strengthen our core portfolio. Similarly, we expect a new wave of strong demand in dedicated MRI systems pushed by hospital re-organization, increased post-pandemic requests and the aging population. This is confirmed by new arrivals in the field, testifying to the high interest in such technologies.

Q *Overall how do you see the future of the healthcare imaging market in general and in Esaote in particular?*

Before the pandemic, medical imaging was expected to grow constantly over the next five years and there is still active development in many fields. Analysts predict that in one or two years there will be a recovery and growth will return to previous rates but in any case there is no doubt that the industry will still be attractive. The healthcare imaging sector will be called on to provide further solutions not just to facilitate safe diagnoses but also to progressively shift to supporting prognoses and monitoring patient response to therapy.

Thus, as I hope I have got across in our conversation, Esaote has ambitious growth plans whose roots lie in the uniqueness of our portfolio. More and more the synergy between our three businesses is bringing competitive advantage. Image fusion, advanced clinical applications based on AI, IoT, image quality and post-processing, optimized workflow are just examples of areas of excellence which are spread across all our businesses and will undoubtedly strengthen our position in international markets.

A Powerful and Innovative Ultrasound System based on Advanced X ULTRA™ Technology

Esaote has just launched the new MyLab™X9 ultrasound system. Powerful and innovative, thanks to the premium 64-bit X ULTRA™ platform, MyLab™X9 guarantees the highest level of image quality and data processing capability, using the latest technological solutions to explore the new frontiers of ultrasound imaging.

"*The introduction of* MyLab™X9 *marks an important step in the current international market, where many companies have been forced to revise their development and investment plans, because of the pandemic*," says Guillaume Gauthier, Global Product Marketing Manager. "*Artificial intelligence, intuitiveness, connectivity, and multimodality combined with an Italian design improve the daily clinical experience by matching high-quality performance 3-year technical coverage, to reinforce the return on investment*".

MyLab™X9 offers a wide range of premium technologies and a multi-parameter approach to diagnosis in various applications, such as

- innovative packages for breast imaging with the exclusive BreastNav™ MRI for fusion imaging of ultrasound and MRI images;
- liver disease diagnosis and staging; monitoring and treatment guidance of focal lesions with a renewed and enhanced version of the Virtual Navigator fusion imaging function;
- urology, with UroFusion, real-time image fusion with transrectal or transperineal approach to support prostate biopsies and ultrasound-guided focal treatments;
- musculoskeletal imaging, sports medicine, and rheumatology, with probes up to 25MHz and advanced technologies such as QElaXto 2D for tissue elasticity assessment.

The new MyLab™X9 system incorporates many of the latest technological advances, including a high quality 24" Barco Eonis monitor, iQProbe probes using Single Crystal technology with high sensitivity and appleprobe ergonomics, and an eStreaming solution for sharing clinical images and camera stream in real-time on various devices, such as tablets, mobiles, and laptops.

ESAOTE
GENOA, ITALY,
www.esaote.com

New advances in interventional cardiology

The mobile Cath Lab from Ziehm

The worldwide aging population, the rise of chronic health conditions and of the incidence in cardiovascular diseases are leading to an increase in the demand for interventional procedures and Operating Room (OR) utilization. For all these reasons it is becoming ever more necessary for surgical operations to be as efficient as possible, while of course maintaining safety.

The intraoperative use of mobile C-arms meets this challenge. Increased surgical accuracy improves clinical outcomes, which, in turn, significantly reduce revision rates and thus overall healthcare spending. Mobile x-ray imaging devices also have lower acquisition and installation costs, which results in a faster return on investment in comparison to fixed installed systems.

COMPREHENSIVE MOBILE HYBRID SOLUTION

The Ziehm Vision RFD Hybrid Edition* mobile C-arm is designed to handle demanding interventional procedures. Additionally, for easy control, the new Hybrid Edition C-arm is the only system on the market to offer motorization of all four axes. For maximum dependability and to avoid any system failures due to overheating and to maintain a constant system temperature the new system is equipped with an Advanced Active Cooling system.

Meeting all the requirements to transform conventional ORs into hybrid rooms in no time, the system requires no changes to the OR and so is ready for use immediately – without any extensive construction work.

Connectivity to 3D vascular navigation systems and contrast injectors — together with versatile display options, ceiling-mounted monitors, wireless solutions and a unique Usability Concept — make the new system ideal for demanding hybrid procedures such as TAVI, angioplasties and EVAR.

Together with their French daughter company Therenva, Ziehm are investing in the future of intraoperative 3D vascular navigation. Therenva's mobile image fusion system EndoNaut enables physicians to achieve better accuracy during challenging hybrid surgeries. Combining preoperative CT data with intraoperative images from the mobile C-arm on the EndoNaut system reduces radiation exposure and contrast media usage and gives even more precise results.

Software features such as Enhanced Vessel Visualization with automatic color display of vessels help define precisely contours and side branches, facilitating communication in the OR.

POWERFUL CARDIOVASCULAR IMAGING IN A MOBILE CATHLAB

With the introduction of the most powerful generator on the market for mobile C-arms, the Ziehm Vision RFD Hybrid Edition with 30 kW(available in combination with dedicated cardio packages) provides increased clarity in cardiovascular imaging. The result of faster and sharper imaging, reduced motion artifacts and the use of dedicated parameters is that more details can be displayed. In addition, dedicated functions for coronary interventions and electrophysiology provide the best possible support during what are often very demanding procedures. Furthermore, special display and transmission options are available that are especially suitable for cath labs. Such options are well-known and have been established through many years of practice in hybrid rooms.

Together with their Dutch partner company, Fysicon, Ziehm Imaging are now going one step even further by offering a dedicated mobile hemodynamic measurement station to meet the needs of interventional cardiologists worldwide, The mobile CathLab solution provides more flexibility and freedom of movement and represents an alternative to conventional setups. "*The mobile concept has only advantages for me, my staff and my patients. I have not yet had a case that I could have solved better with a fixed system,*" said Dr. Rajaram Prasad about the Ziehm Vision RFD Hybrid Edition CMOSline in his mobile CathLab.

*Ziehm Vision RFD Hybrid Edition represents a group of optional hardware and software that creates an option package on the device named Ziehm Vision RFD.

ZIEHM IMAGING
NUREMBERG, GERMANY
www.ziehm.com

The role and added value of CT-FFR in the diagnosis of coronary artery disease

By Dr J Peper, Prof. Dr.T Leiner & Dr. M. J. Swaans

This article summarizes the results of a recently published study [1] which assessed the added value of CT-derived Fractional Flow Reserve (CT-FFR) in the diagnosis of coronary artery disease (CAD). It was found that the use of an on-site CT-FFR based approach in patients with angina pectoris and suspected CAD led to an increase in the area under the ROC curve compared to a basic model comprising pre-test likelihood and exercise electrocardiography.

INTRODUCTION

Invasive fractional flow reserve (FFR), the physiological test that serves as a proxy for myocardial blood flow, is the generally accepted reference standard for the assessment of stenosis-specific ischemia and for the diagnosis of coronary artery disease (CAD) [2,3]. Given the frequent mismatch between anatomical and hemodynamic estimation of the severity of coronary stenosis, FFR is recommended as a complement to invasive coronary angiography (ICA) in patients with coronary stenosis of between 50-90% or in cases of multi-vessel disease [4]. The European Society of Cardiology (ESC) guidelines for Chronic Coronary Syndromes recommend that, prior to invasive testing with ICA and FFR, non-invasive tests be carried out in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone. Non-invasive functional imaging for the detection of myocardial ischemia as well as coronary computed tomography angiography (CCTA) to evaluate the degree of coronary diameter reduction are recommended as initial tests in the diagnosis CAD [4]. Current non-invasive tests are, however, limited to either anatomical or functional assessments of the coronary blood flow, resulting in the need to use multiple tests in the diagnostic workflow. A balanced strategy needs to be identified in which clinical evaluation, non-invasive imaging and stress testing for risk stratification can be weighed gainst (invasive) diagnostic over-testing.

Risk stratification prior to ICA and FFR routinely includes electrocardiographic evaluation (ECG), echocardiography, X-Thorax and exercise ECG (X-ECG), but these methods are only helpful in a minority of patients. Other non-invasive imaging techniques such as CCTA, MRI, SPECT and PET-CT can improve the diagnostic process, but increase the risk of complications, exposure to radiation and contrast-agent, as well as negatively impacting the quality of life of patients and increasing costs.

The relatively recently introduced non-invasive imaging technique of CT-derived FFR (CT-FFR) combines both anatomical and functional information. CT-FFR is determined by the use of sophisticated hemodynamic flow algorithms which operate on CCTA data sets. Various algorithms have already been evaluated in multicenter studies and have shown that diagnostic accuracy is improved compared to CCTA alone, with a pooled sensitivity of 0.85 and a pooled specificity of 0.78 being reported [6]. Based on previous studies, it is reasonable to assume that complementing CCTA with CT-FFR will yield an enhanced diagnostic value, especially since no additional testing, radiation or contrast medium are required. However, to date, the diagnostic performance of CT-FFR has only been evaluated as a stand-alone, single test and not in the context of the overall clinical work-up of patients with (suspected) stable angina pectoris. To address this, we carried out a cross-sectional study evaluating the added value of CT-FFR beyond other currently used non-invasive tests in patients with angina pectoris and suspected CAD.

STUDY DESIGN AND METHODOLOGY

This single center study involved patients with a clinical suspicion of angina pectoris and an intermediate to high pre-test likelihood of CAD. To avoid referral bias, all patients underwent X-ECG, stress/rest SPECT, coronary calcium score (CCS), CCTA, CT-FFR and ICA independently of the results of the non-invasive imaging. Examples of CCTA, CT-FFR and invasive FFR images are shown in Figure 1. FFR measurements were

The Authors

Dr. Joyce Peper [1,2], Prof. Dr. Tim Leiner [2] & Dr. Martin J. Swaans [1]

1. Department of Cardiology,
St. Antonius Hospital, Koekoekslaan 1,
3435 CM Nieuwegein, The Netherlands.
2. Department of Radiology, University Medical Center Utrecht,
Utrecht University, Utrecht, The Netherlands

Corresponding Author:
Dr. J. Peper,
Department of Cardiology, St. Antonius Hospital, Nieuwegein,
The Netherlands.
Email: j.peper@antoniusziekenhuis.nl

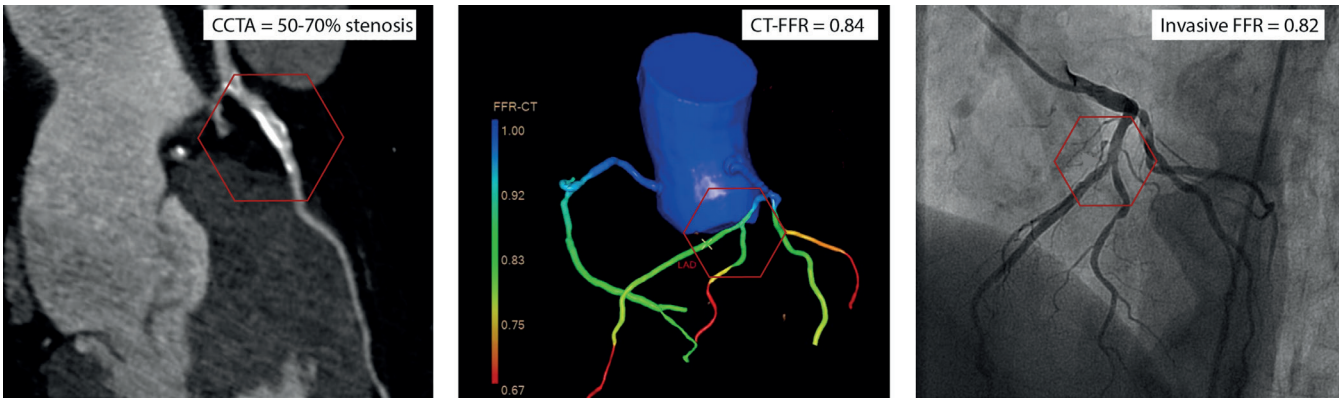


Figure 1. Examples of CCTA, CT-FFR and invasive FFR in a study patient. An Agatston CCS of 707 is observed. CCTA shows a significant stenosis of the mid LAD, whereas the CT-FFR indicates non-significant ischemia. SPECT perfusion imaging indicates mild to moderate ischemia proximal anterolateral and proximal inferoposterolateral. Invasive FFR measurements demonstrates obstructive stenosis and a FFR value of 0.82 indicating no vessel ischemia.

performed in cases of intermediate stenosis. Imaging acquisition was performed on a hybrid SPECT-CT system, consisting of a gamma camera using a weight-adjusted dose of 400-600 MBq ^{99m}Tc-sestamibi in combination with a 64-slice CT scanner (CardioMD and Brilliance 64, Philips Medical Systems, Best, The Netherlands). Prior to carrying out stress SPECT, X-ECG was performed. Rest SPECT was carried out in the case of an abnormal stress SPECT. CCS and CCTA imaging were obtained using a prospectively ECG gated scan acquisition protocol, whereas a non-enhanced acquisition was performed prior to the CCTA to calculate the Agatston CCS.

CT-FFR was calculated using an on-site CT-FFR prototype simulation algorithm (Philips Medical Systems, The Netherlands). ICA biplane views were acquired from all major coronary arteries using Allura catheterization equipment (Philips Medical Systems, The Netherlands) via femoral or radial artery access. Intermediate stenoses, defined as a diameter reduction between 50-70%, were subsequently assessed by FFR. The evaluation method and cut-off values of the various diagnostic tests are described in Table 1.

To assess the ability of the different models to distinguish between patients with and without CAD, the area under the ROC-curve and the area under the curve (AUC) were calculated.

The variables were added to the multivariable model in chronological order as in clinical practice, starting with the pre-test likelihood and X-ECG. The models tested include the single and combined results of SPECT, CCS, CCTA and CT-FFR.

The primary end-point of our trial was the comparison of the areas under the receiver operating characteristic curve (ROC-curve) between the diagnostic strategies.

RESULTS

A total of 202 patients with mean age 63.1 ± 9.8 years (61.4% male) were included in the study. Five multivariable logistic regression models were used to assess the combined diagnostic value of the non-invasive tests. The basic diagnostic model used the pre-test likelihood of CAD and the result of the X-ECG. Table 2 shows the effect of the addition of one or more methodsto the basic model. It can be seen from Table 2 that the addition of SPECT, CCS and CCTA data to

Test	Evaluation method	Definition abnormal Test
X-ECG	All X-ECG were reviewed in consensus by 2 experienced cardiologist	Abnormal: horizontal shift of the ST segment at 80ms after the J-point of =0.1 mV in 3 consecutive beats. Non-conclusive: decrease of >30 mm Hg in systolic blood pressure, typical angina pectoris during stress, unable to reach >85% of the predicted heart rate without (ECG) evidence of ischemia and/or uninterpretable ECG.
SPECT	Stress and rest SPECT imaging were interpret using the QGS/QPS software package.	The definition of normal, non-conclusive and abnormal myocardial perfusion on SPECT according to segmental scores is previous described by Abidov et al.[5] SPECT classified as non-conclusive was regarded as abnormal in the analysis
CCS	Agatston calcium score	The CCS result was used as continuous variable
CCTA	Obstructive stenosis were scored in a 16-segment model in five categories using the CADRADS™.	At least 1 stenosis on CCTA =50%. Segments affected by motion artefacts or blooming due to severe calcification were not assessable and classified as non-conclusive and regarded as abnormal in the analysis.
CT-FFR	Point estimates of the computed FFR were taken at the lesion of interest - the most severe stenosis at CCTA	CT-FFR =0.80 in at least one of the vessels
ICA	The coronary tree was fully examined for the presence of stenosis according to the 16-segment model as used for the assessment of CCTA.	At least 1 stenosis on ICA =70%
FFR	An intermediate stenosis on ICA, defined as a diameter reduction between 50-70%, was by FFR	At least 1 FFR measurement = 0.80

Table 1 Interpretation and cut-off values of the (non-invasive) imaging methods

	Variables	HL-statistic (p-value)	AUC (95% CI)	p-value
Model 1	LLH CAD + X-ECG	0.29	0.79 (0.73-0.85)	<0.001
Model 2	SPECT	0.25	0.90 (0.85-0.94)	0.008
Model 3	CCS+CCTA	0.47	0.88 (0.83-0.92)	<0.001
Model 4	CCS+CCTA + CT-FFR	0.57	0.93 (0.90-0.96)	0.398
Model 5	SPECT +CCS+CCTA	0.28	0.94 (0.92-0.97)	Ref.

Table 2: Discrimination and calibration of the diagnostic models of interest.
Abbreviations: AUC area under the curve, CAD coronary
artery disease, CCS coronary calcium score, CCTA coronary computed tomography angiography, CI
confdence interval, CT-FFR computed tomography fractional fow reserve, LLH pretest likelihood, SPECT single photon emission computed tomography, X-ECG exercise electrocardiography.
It can be seen that the basic multivariable model of LLH CAD and XECG has an AUC of 0.790 which increased to 0.897 with the addition of SPECT (Model 2) Addition of CCTA and CCS to the basic model increased the AUC to 0.876 (Model 3); the addition of CT-FFR gave an AUC of 0.929 (Model 4). The basic model with the addition of SPECT, CCS and CCTA yielded the highest AUC of 0.94.

those of the basic model yielded the highest AUC of 0.94. However there was no significant difference (p-value = 0.398) in terms of AUC between this SPECT, CCS and CCTA model and the model including CCS, CCTA and CT-FFR which had an AUC of 0.93. Figure 2 shows the ROC-curves of the diagnostic models. All diagnostic models were found to have good calibration i.e. all had p-values above the threshold of 0.05 using the Homer-Lemeshow test of overall goodness of fit.

CONCLUSIONS AND FUTURE PERSPECTIVES

The aim of this study was to determine the added value of CT-FFR over and above other non-invasive tests which are routinely performed in patients with a clinical suspicion of having (recurrent) angina pectoris.

We found that the addition of CT-FFR improved the diagnostic performance of both SPECT and CCTA. The performance of the CT-FFR approach was not significantly different from that of the CCTA-SPECT based strategy in terms of area under the ROC-curve, suggesting that SPECT could be replaced. Such a substitution of SPECT by CT-FFR would mean a saving of 10 mSv on the doses of ^{99m}Tc-sestamibi for the stress and rest SPECT. In addition, no extra scan time would be required [7].

The addition of CT-FFR to the existing pathway increases diagnostic value after a positive or inconclusive CCTA, and does not require additional testing procedure, radiation or contrast medium. Moreover, CT-FFR is easy to use, fast and reproducible. The technique can be cost-effective even though it does require additional operator time (approximately 20 minutes). This depends heavily on the scan quality and the amount of calcification present [8,9].

CT-FFR is considered as cost effective by the UK's National Institute for Health and Care Excellence in patients with stable, recent onset chest pain [10]. The use of CT-FFR in the UK has resulted in a substantial reduction in referrals to ICA. The PLATFORM study [11] also evaluated medical costs: the mean per-patient downstream costs (i.e. without cost of initial tests, including CT-FFR) were similar for CT-FFR and usual care ($2,755 vs. $2,260, respectively).

However, generalization of these results to other countries is difficult due to differences in outcome measures, healthcare cost levels, the epidemiology of disease, patient cohorts and local expertise [12].

We hypothesize that a CT-FFR guided strategy increases cost-effectiveness by reducing the percentage of patients referred for invasive pressure measurements. The adoption of the CT-FFR based approach will also increase patient comfort and should lead to a lower rate of complications, which in turn further improves its cost-effectiveness.

To definitively establish the cost benefits of CT-FFR, more head-to-head cost-effectiveness studies are needed in different healthcare systems in addition to further studies comparing CT-FFR with methods based on invasive pressure measurements.

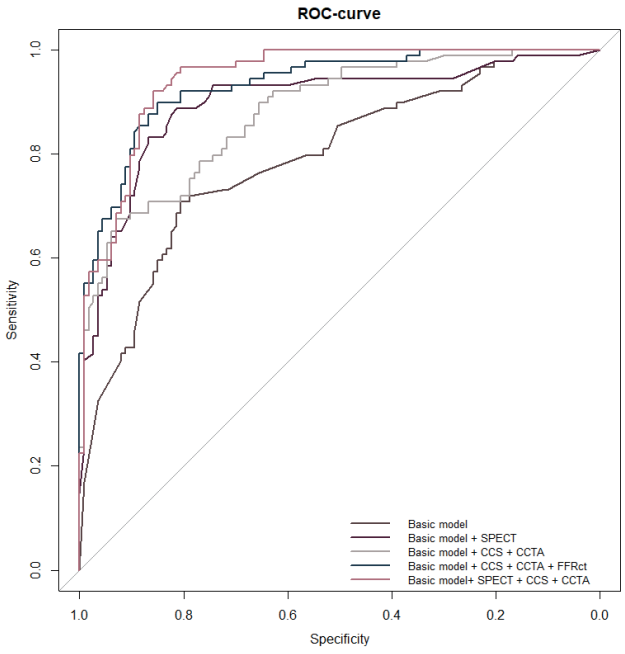


Figure 2. The Receiver Operator Characteristics curve for the five diagnostic models.

REFERENCES

1. Peper J *et al.* Added value of computed tomography fractional flow reserve in the diagnosis of coronary artery disease. Sci Rep. 2021; 11: 6748. doi: 10.1038/s41598-021-86245-8.

2. Pijls NHJ *et al.* Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. N. Engl. J. Med. 1996; 334: 1703

3. Tonino P A *et al.* Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009; 360: 213

4. Knuuti J *et al.* 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur. Heart J. 2020; 41: 407

5. Abidov A *et al.* Are shades of gray prognostically useful in reporting myocardial perfusion single-photon emission computed tomography? Circ. Cardiovasc. Imaging 2009; 2: 290.

6. Celeng C *et al.* Anatomical and Functional Computed Tomography for Diagnosing Hemodynamically Significant Coronary Artery Disease: A Meta-Analysis. JACC Cardiovasc. Imaging 2018;12: 1316.

7. Knuuti J *et al.* Risks and benefits of cardiac imaging: An analysis of risks related to imaging for coronary artery disease. Eur. Heart J. 2014: 35: 633.

8. Douglas PS *et al.* Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFR(CT): outcome and resource impacts st. Eur Heart J 2015; 36: 3359.

9. Hlatky MA *et al.* Quality-of-Life and Economic Outcomes of Assessing Fractional Flow Reserve with Computed Tomography Angiography: PLATFORM. J. Am. Coll. Cardiol. 2015; 66: 2315

10. Moss A J *et al.* The Updated NICE Guidelines: Cardiac CT as the First-Line Test for Coronary Artery Disease. Curr. Cardiovasc. Imaging Rep. 2017;10: 15.

11. Colleran R *et al.* An FFR CT diagnostic strategy versus usual care in patients with suspected coronary

12. Tragardh E. et al. Systematic review of cost-effectiveness of myocardial perfusion scintigraphy in patients with ischaemic heart disease A report from the cardiovascular committee of the European Association of Nuclear Medicine. Endorsed by the European Association of Cardiiovascular Imaging. European Heart Journal Cardiovascular Imaging 2017; 18, 825.

Using machine learning to standardize diagnostic testing pathways in suspected coronary artery disease

By Dr. EK Oikonomou & Dr. R Khera

INTRODUCTION

Coronary artery disease (CAD) affects nearly 200 million people in the world, with chest pain representing one of the major presenting symptoms [1, 2]. Significant advances in the field of cardiovascular diagnostics have led to the development of several imaging and testing modalities, which can be used as gatekeepers prior to consideration of invasive coronary angiography. Such tests differ in their speed, costs, sensitivity, and specificity and their use is often guided by clinical reasoning as well as local expertise and availability [3].

Two main groups of diagnostic imaging modalities that are deployed in the investigation of chest pain are currently used in clinical practice [4]. Anatomical testing, through coronary computed tomography angiography (CCTA), enables the description of coronary anatomy and detection of structural abnormalities including luminal stenoses. On the other hand, functional testing, including stress electrocardiography, stress echocardiography, stress magnetic resonance imaging, and the most commonly used nuclear testing through single positron-emission computed tomography (SPECT) or positron emission tomography (PET) rely on the detection of regional ischemia through a combination of exercise/pharmacologic stimulation and diagnostic imaging [5].

For years, these were used interchangeably in the absence of clinical trial data comparing their efficacy and safety. However, in 2014, PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) [5] and in 2018, SCOT-HEART (Scottish COmputed Tomography of the HEART Trial) [6, 7] demonstrated that anatomical imaging has similar cardiovascular outcomes when compared to stress testing and may even improve long-term outcomes when used in addition to standard of care, including stress testing. To date, PROMISE remains the largest randomized controlled trial to have compared CCTA to functional testing in low-risk symptomatic patients with stable chest pain [5].

Since the publication of the PROMISE and SCOT-HEART trials, CCTA has gained ground as an alternative to functional imaging [4, 8]. However, the clinical equipoise on which test to select for each patient remains, with the most recent European Society of Cardiology (ESC) guidelines assigning Class I recommendation to both CCTA and non-invasive functional testing as appropriate initial tests to diagnose CAD in symptomatic patients [9].

PERSONALIZING THE INTERPRETATION OF CLINICAL TRIALS

In general, randomized trials assess the efficacy and safety of an intervention across a population, but in their standard form do not enable inference on the personalized benefit that each individual patient derives from an intervention A versus a second intervention B. To identify patient populations that derive differential benefit from either approach, subgroup analyses in PROMISE demonstrate evidence of heterogeneity across broad subgroups, with women compared with men, and patients with diabetes compared with those without diabetes experiencing fewer adverse cardiovascular events with anatomical testing than with functional testing [10-12]. However, such analyses dichotomize the phenotypic variation seen in the study population across a single axis and fail to account for large variation in demographic and clinical features within such subgroups.

In our work [13], we developed and validated a novel machine learning-based methodology that projects a trial's baseline population into a multidimensional space, where each dimension represents a phenotypic variable recorded prior to randomization, thus enabling a topological representation of the phenotypic variation seen in the study. In simple words, each individual is projected to a space, where their closest neighbours are characterized by a combination of phenotypic features spanning the full breadth of information recorded prior to randomization that most closely resembles that of the index patient. With increasing distance from each patient, the phenotypic similarity decreases. This enables the description of phenotypic neighbourhoods around each patient which included the 5% most similar study participants, thus providing a way of extracting individualized risk estimates of major adverse cardiovascular events (MACE) with anatomical versus functional testing. In a series of *in silico* experiments, each patient's neighbourhood formed the population for a simulated mini-trial, with the process repeated for each of the participants in the trial..

The Authors

Dr. EK Oikonomou[1] & Dr. R Khera[2,3]

1. Department of Internal Medicine, Yale School of Medicine, New Haven, CT, USA

2. Section of Cardiovascular Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, CT, USA

3. Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, CT, USA

Corresponding author: Dr. Rohan Khera,

Email: rohan.khera@yale.edu; @rohan_khera

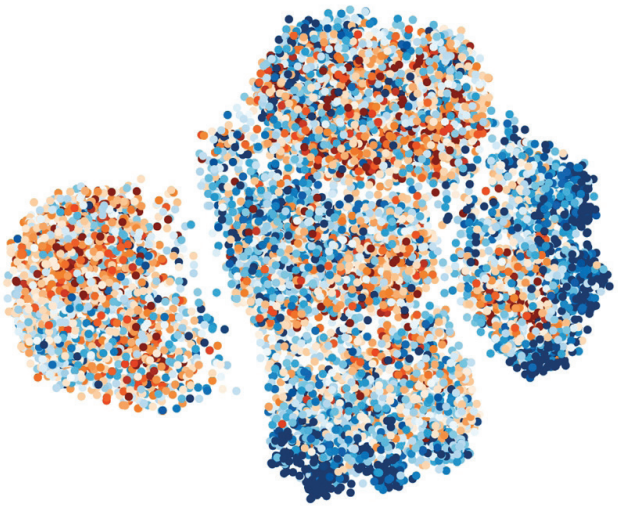


Figure 1. Risk phenomaps of the PROMISE trial. A manifold embedding of the baseline phenotypic variance seen in the PROMISE chest pain population based on 57 pre-randomization phenotypic traits. Labelling of the phenomaps with the neighbourhood-derived individualized risk estimates demonstrated distinct topological neighbourhoods favouring anatomical imaging or functional testing based on the observed risk in PROMISE. PROMISE: Prospective Multicenter Imaging Study for Evaluation of Chest Pain. (Reproduced with permission from Eur Heart J, ehab223, *https://doi.org/10.1093/eurheartj/ehab223*).

A MACHINE LEARNING METHOD TO PERSONALIZE THE INTERPRETATION OF CLINICAL TRIALS

Applying the method described above [13], we were able to uncover treatment effect heterogeneity across the PROMISE trial population, identifying phenotypic (topological) neighbourhoods where anatomical imaging was associated with a reduction in the risk of MACE compared to functional testing, and vice versa [Figure 1]. Whereas our analysis confirmed that across the study population, the two diagnostic strategies appear to be equivalent, it highlighted that at an individual level, certain patients benefit more from one strategy than the other.

GENERATION OF THE ASSIST TOOL

Having described the existence of treatment effect heterogeneity, we sought to identify which factors were most strongly associated with benefit from one strategy over the other, and built a parsimonious phenotypic signature that could be used prospectively to estimate the personalized benefit of anatomical versus functional testing. For that, we divided our PROMISE population randomly into an 80% subset, used for training and cross-validation, and 20% used for testing. We trained an extreme gradient boosting tree algorithm to predict the personalized relative hazard based on the topological analyses described above and used concepts from machine learning and game theory to assign relative feature importance values to each potential predictor. Using a combination of 15-features that most reliably and consistently correlated with personalized relative hazards favoring one strategy over another, we defined a decision support tool, named ASSIST©(Anatomical vs. Stress teSting decIsion Support Tool) [13]. To facilitate adoption of this tool for research purposes, we have made it available as part of an online browser-accessible online calculator (Cardiovascular Data Science (CarDS) Lab. ASSIST©: *https://www.cards-lab.org/assist*) [Figure 2] .

VALIDATION OF THE ASSIST TOOL

We validated ASSIST in the remaining 20% of PROMISE participants that were not included in its development as a part of an internal validation strategy. Furthermore, in a selected unmatched and propensity score-matched population of SCOT-HEART (external validation) we pursued external validation of ASSIST. Herein, we explictly accounted for the different design of SCOT-HEART compared to PROMISE. In SCOT-HEART, anatomical testing was added to standard of care, which in most patients also included stress electrocardiography, and therefore, we only included patients in the CCTA arm who underwent anatomical testing without antecedent stress test (anatomical-first arm), whereas in the standard care arm we included all individuals with an initial stress test (functional-first arm). We observed that in both the internal and external validation sets, agreement between the ASSIST recommendation and the actual test performed was associated with a significantly lower incidence of MACE, for both of PROMISE's and SCOT-HEART's primary endpoints [Figure 3]. Of note, a post hoc analysis of individual risk factors in the external validation cohort did not identify patients more likely to have favourable outcomes with anatomical vs. functional testing ($P_{interaction}$ = 0.79 for sex, 0.35 for hypertension, and 0.85 for diabetes mellitus), further highlighting the generalizability of our approach over broad subgroup assessments.

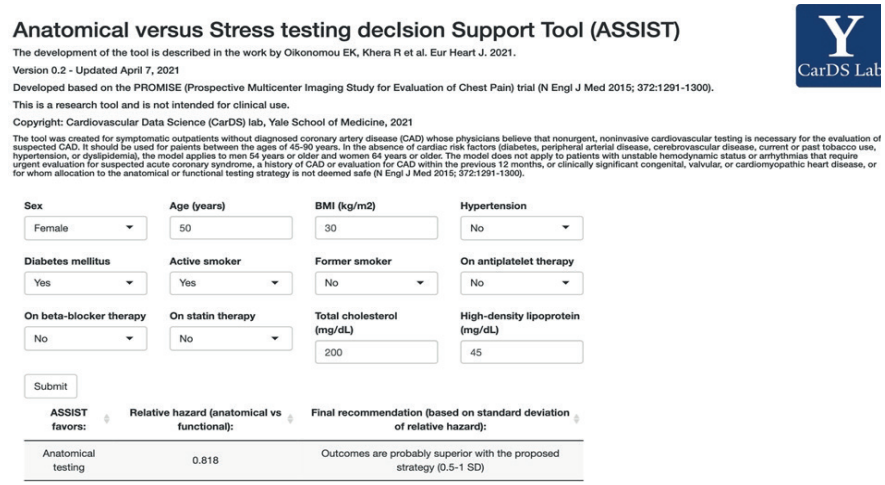


Figure 2. The ASSIST (Anatomical vs. Stress teSting decIsion Support Tool) tool. Available as part of an online browser-accessible online calculator (Cardiovascular Data Science (CarDS) Lab. ASSIST©: *https://www.cards-lab.org/assist (accessed* 11 June 2021)).

NEXT STEPS

In using the ASSIST calculator, one should be mindful of several considerations. First, this only applies to the patient population recruited as part of PROMISE, that means "*symptomatic outpatients without diagnosed CAD whose physicians believed that nonurgent, noninvasive cardiovascular testing was necessary for the evaluation of suspected CAD*". Notably, PROMISE investigators included participants with an age of more than 54 years (in men) or more than 64 years (in women) or an age of 45 to 54 years (in men) or 50 to 64 years (in women) with at least one cardiac risk factor (diabetes, peripheral arterial disease, cerebrovascular disease, current or past tobacco use, hypertension, or dyslipidemia).

Second, as described earlier, SCOT-HEART recruited a different population and instituted CCTA on top of standard care, which in most cases included stress testing. Our analysis in SCOT-HEART resulted in loss of randomization since we had to exclude patients whose management deviated from that of PROMISE, thus exposing these observations to potential confounding. However, the consistency of the internal and external validation was reassuring of our validity and generalizability.

Third, our analysis focused on cardiovascular endpoints, rather than diagnostic outcomes. Most of the literature has traditionally compared metrics of diagnostic accuracy and pre-, post-test probability using obstructive CAD on invasive coronary angiography as the gold standard [14]. Therefore, a discordance between diagnostic and hard clinical outcome measures should be accounted for when interpreting the results of our algorithm. Furthermore, since both PROMISE and SCOT-HEART were trials of diagnostic interventions, differences in outcomes are more likely to be explained by changes in therapeutic interventions and medications downstream of the diagnostic testing. Further research is needed to better understand these and explore to which extent they may be modifiable. Validation in prospective trials and real-world cohorts is needed and is currently underway.

CONCLUSIONS

In summary, we have recently developed an approach that defines an evidence-based strategy to pursue an anatomical versus functional evaluation of patients with suspected CAD.[13] In the first-ever application of a novel machine learning approach for personalized interpretation of clinical trial data, we were able to perform a series of local experiments to uncover and describe patterns of intervention effect heterogeneity in the PROMISE trial. A generalizable decision support tool derived from the PROMISE trial phenomap, named ASSIST [13], was validated in two geographically distinct large studies, and can be used to facilitate broader use of this information in shared decision-making in clinical practice.

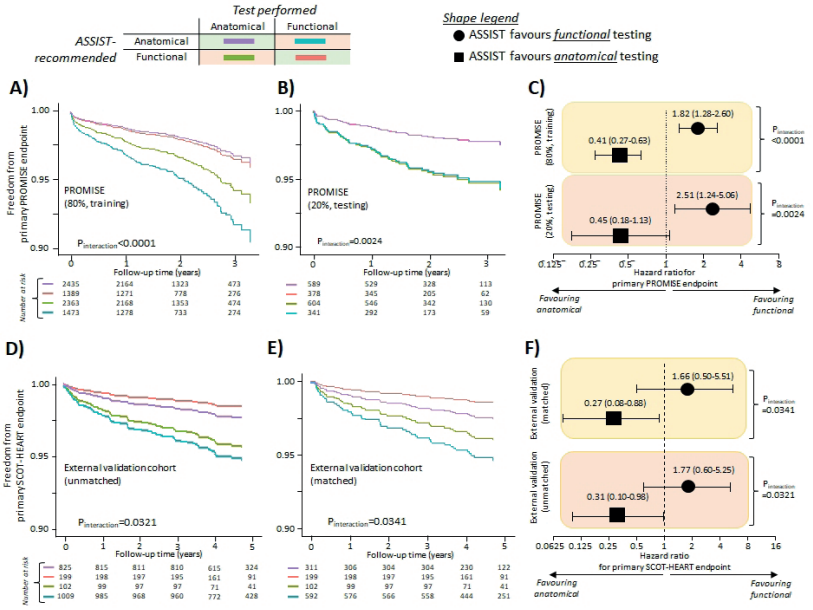


Figure 3. Internal and external validation of ASSIST. Application of the ASSIST tool in both the training and testing (internal validation) set of PROMISE demonstrated that concordance (vs. disagreement) between the ASSIST-proposed best initial diagnostic strategy and a patient random allocation to functional or anatomical testing was associated with an approximate two-fold reduction in the risk of the study primary composite endpoint (A-B: Adjusted survival curves; C: Forest Plot). These findings were replicated in the external validation cohort of SCOT-HEART for the primary composite endpoint of the study (D-E: Adjusted survival curves; F: Forest Plot). ASSIST, Anatomical vs. Stress teSting decIsion Support Tool; PROMISE, PROspective Multicenter Imaging Study for Evaluation of Chest Pain; SCOT-HEART, Scottish COmputed Tomography of the HEART Trial. (Reproduced and edited with permission from Eur Heart J, ehab223, https://doi.org/10.1093/eurheartj/ehab223).

REFERENCES

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020. 396: 1204.

2. Davies SW. Clinical presentation and diagnosis of coronary artery disease: stable angina. Br Med Bull. 2001; 59: 17.

3. Poon M *et al.* Current Evidence and Recommendations for Coronary CTA First in Evaluation of Stable Coronary Artery Disease. J Am Coll Cardiol. 2020; 76: 1358.

4. Foy AJ *et al.* Coronary Computed Tomography Angiography vs Functional Stress Testing for Patients With Suspected Coronary Artery Disease: A Systematic Review and Meta-analysis. JAMA Intern Med. 2017; 177: 1623.

5. Douglas PS *et al.* Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015; 372: 1291.

6. SCOT-HEART Investigators, CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. Lancet. 2015; 385: 2383.

7. Scot-Heart Investigators *et al.* Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. N Engl J Med. 2018; 379: 924.

8. Moss AJ *et al.* The Updated NICE Guidelines: Cardiac CT as the First-Line Test for Coronary Artery Disease. Curr Cardiovasc Imaging Rep. 2017; 10: 15.

9. Knuuti J *et al.* 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J, 2020; 41: 407.

10. PagidipatiNJ *et al.* Sex Differences in Functional and CT Angiography Testing in Patients With Suspected Coronary Artery Disease. J Am Coll Cardiol. 2016; 67: 2607.

11. Sharma A *et al.* Stress Testing Versus CT Angiography in Patients With Diabetes and Suspected Coronary Artery Disease. J Am Coll Cardiol. 2019; 73: 893.

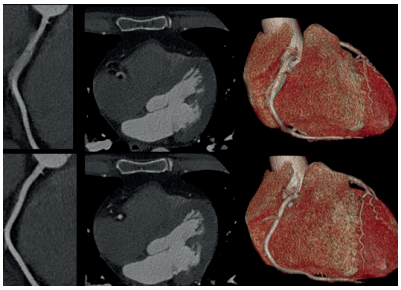
12. Hemal K *et al.* Sex Differences in Demographics, Risk Factors, Presentation, and Noninvasive Testing in Stable Outpatients With Suspected Coronary Artery Disease: Insights From the PROMISE Trial. JACC Cardiovasc Imaging. 2016; 9: 337.

13. Oikonomou EK *et al.* A phenomapping-derived tool to personalize the selection of anatomical vs. functional testing in evaluating chest pain (ASSIST). Eur Heart J. 2021 ehab223. doi: 10.1093/eurheartj/ehab223.

14. Montalescot G *et al.* 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013; 34: p. 2949.

New CT provides spectral data on every scan, every patient

Philips has introduced its newest solution for precision diagnosis with the global introduction of its spectral detector-based Spectral Computed Tomography (CT) 7500. This latest intelligent system delivers high quality spectral images for every patient on every scan 100% of the time so helping to improve disease characterization, and reduce rescans and follow-ups, all at the same dose levels as conventional scans. The time-saving spectral workflow is fully integrated, enabling the technologist to get the patient on and off the table quickly – spectral chest scans and head scans take less than one second, and a full upper body spectral scan can be completed in less than two seconds – while still delivering high quality imaging.



Advanced cardiac capabilities such as AI-enabled motion-free cardiac scanning make spectral imaging available to more types of patients and conditions.

Missed and delayed diagnoses contribute to roughly 10% of patient deaths annually, while an estimated 10-20% of all medical diagnoses are inaccurate. The financial costs resulting from unnecessary, suboptimal and repeat imaging costs as much as $12 Billion USD annually. To meet these challenges the new Spectral CT 7500 was designed for first-time-right diagnosis and has demonstrated a 34% reduction in time to diagnosis, a 25% reduction in repeat scans and a 30% reduction in follow-up scans.

Kees Wesdorp, Chief Business Leader of Precision Diagnosis at Philips said "*Our detector-based spectral technology ensures spectral data is always available and is seamlessly integrated into current workflows, meaning scans are fast.*"

Spectral CT has demonstrated a higher sensitivity in detecting malignant findings and has improved readings of incidental findings. With Philips spectral detector CT, photons add more value by helping salvage sub-optimal injection scans without the need to re-scan the patients, shortening the time to diagnosis.

"*Conventional CT scanners are limited and can only show us where things are located – like lesions, cysts, bleeds, fractures and more. Philips spectral detector-based systems help to characterize what the finding is, not just where it is, providing us greater confidence in diagnoses,*" said Dr. Finn Rasmussen, of Aarhus University, Denmark. "*We have seen significant reductions in rescans and follow-ups by adopting spectral into our workflow for faster and more accurate diagnosis.*"

The spectral insights are available for all patients, from pediatric to bariatric, and for any clinical indication, including challenging cardiac scans with high and irregular heart rates, without compromising image quality, dose or workflow.

PHILIPS
EINDHOVEN, THE NETHERLANDS
www.philips.com

Boosting radiographer productivity through hardware and AI-software

Agfa's new SmartXR portfolio uses a unique combination of hardware and AI-powered software to lighten radiographers' workloads and provide image acquisition support. This newest member of Agfa's DR portfolio offers key assistance during the radiology routine.The SmartXR portfolio brings intelligence to digital radiography (DR) equipment at the point of care. Integrated sensors and cameras combined with powerful AI software, 3D machine vision, deep learning and machine intelligence, support the radiographer with first-time-right image acquisition. By reducing retakes, this speeds up the radiology workflow, and optimizes utilization and equipment costs. In addition, the new system provides recommendations on dose tailored to the patient, but also ensures greater consistency in positioning, exposure and AEC settings. Reducing variability, this enables more confident comparison of current and prior images, even when different radiographers are making the images.

SmartXR includes a range of tools designed to support the radiographer intelligently:

- SmartAlign: uses sensors to ensure that the tube and panel are optimally aligned, and provides recommendations if necessary.
- SmartPositioning: augments a first-person LiveVision camera view of the patient with smart overlays to project the image area and exposure control onto the patient's body. Visual cues indicate when positioning can be further optimized.

- SmartDose: uses 3D machine vision to determine the thickness of the patient, and then tailors exposure parameters specifically for that patient's anatomy.
- SmartRotate: uses a Deep Neural Net to interpret the image contents and automatically rotates the image in the correct orientation, ready for viewing, saving time in post-processing.

AGFA HEALTHCARE
MORTSEL, BELGIUM
www.agfa.com

Latest generation AI software for Digital Breast Tomosynthesis gets CE Mark approval

third generation of artificial intelligence solution for 3D mammography offers considerable improvement in algorithm specificity performance and much faster processing

iCAD has just announced that the third generation (Version 3.0) of their ProFound AI software for Digital Breast Tomosynthesis (DBT) software has received CE Mark approval. Compared to previous software versions, the latest generation of ProFound AI offers up to a 10% improvement in specificity while maintaining an industry-leading high sensitivity level, as well as being approximately 40% faster in processing on the new PowerLook platform [1].

"*The CE Mark certification is another momentous achievement that positions iCAD in the vanguard of cancer detection and illustrates our commitment to offering leading-edge solutions that continue to be unmatched by other technologies*," said Michael Klein, Chairman and CEO of iCAD. "*This regulatory milestone will provide the opportunity for our recently installed customers to upgrade to the latest version of the technology, while also expanding the potential to bring this solution to more markets – and more women – worldwide.*"

The third generation of ProFound AI for DBT offers clinicians the ability to interpret the vast amount of data generated in DBT cases with greater precision and efficiency. A recent study involving the Version 2.0 of ProFound AI and presented at two major breast imaging conferences earlier this year found that when radiologists factored in breast density and age, ProFound AI helped radiologists identify up to 58.6 percent of normal cases, with no false negatives [2]. The ProFound AI Version 3.0 now offers additional specificity and performance improvements which stands to further improve these study results, and may also contribute to a reduction in the rate of false positives, without compromising cancer detection.

Built with the latest in deep-learning technology, Version 3.0 rapidly analyzes each tomosynthesis image, detecting malignant soft tissue densities and calcifications with high accuracy. Certainty of Finding and Case Scores are assigned to each detection and each case respectively. These are relative scores computed by the ProFound AI algorithm and represent the algorithm's confidence that a detection or case is malignant. This crucial information may help radiologists in clinical decision making.

"*The European launch of our third generation of ProFound AI for DBT demonstrates iCAD's unwavering dedication to improving breast cancer detection,*" said Michele Debain, Vice President, Europe, Middle East, Africa and APAC at iCAD. "*Since obtaining CE Mark certification with our first generation of this technology in July 2019, ProFound AI has been installed in a growing number of medical imaging centers across Europe. ProFound AI offers benefits not only to physicians, but also to women. It helps improve workflow for radiologists and enhances their ability to accurately detect suspicious lesions and ultimately find cancers at earlier stages, which can lead to better patient management, with less burdensome treatments and increased chances of survival. This CE Mark certification will help us to bring the latest generation of our advanced technology to more physicians and women across Europe.*"

ProFound AI Version 3.0 was developed using over five million images from 30,000 cases, including almost 8,000 biopsy-proven cancers, and validated on approximately one million images from 3,500 cases that included 1,200 biopsy-proven cancers. The technology was also recently cleared by the U.S. Food and Drug Administration (FDA) in JUNE 2021.

"*Breast cancer is the most common cancer among women; however, the chances of survival are constantly increasing, especially thanks to technological advances in medical imaging that are improving the performance of screening. ProFound AI is fully in line with the desire to constantly improve radiologists' abilities to detect breast cancer as early as possible. This is why I chose to install the new generation of the ProFound AI solution in my medical imaging center, which is dedicated to breast imaging, in order to offer my patients the best possible care,*" said Elena Cauzza, MD, a radiologist at Radiomedica and xDonna, a mammography and breast diagnosis center in Bellinzona, Switzerland.

In a reader study ProFound AI for DBT Version 2.0 was clinically proven to reduce radiologists' reading time by 52.7 percent, improve sensitivity by 8 percent, and reduce false positives and unnecessary patient recall rates by 7.2 percent [3].

iCAD's Breast Health Solutions suite also includes ProFound AI for 2D Mammography and ProFound AI Risk, a clinical decision support tool that provides an accurate two-year, breast cancer risk estimation that is truly personalized for each woman and is based only on a screening mammogram [4] and software to evaluate breast density.

REFERENCES

1. iCAD data on file. Stand-alone performance varies by vendor. FDA Cleared.

2. Conant E *et al.* Use of an artificial intelligence software to identify low-likelihood of cancer exams collected across four commercial digital tomosynthesis screening systems. Abstract presented at European Congress of Radiology (ECR) Virtual Meeting and the Society of Breast Imaging (SBI) Symposium, 2021.

3. Conant E *et al.* Improving Accuracy and Efficiency with Concurrent Use of Artificial Intelligence for Digital Breast Tomosynthesis. Radiology: Artificial Intelligence. 2019; 1: 1. doi/10.1148/ryai.2019180096

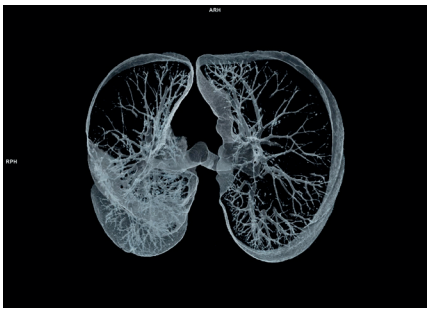
4. Eriksson M *et al.* Identification of Women at High Risk of Breast Cancer Who Need Supplemental Screening. Radiology. 2020; 297: 327. doi: 10.1148/radiol.2020201620.

CT scanner for rapid diagnosis in demanding clinical areas

Siemens Healthineers have introduced the Somatom X.ceed, a new high-resolution, high-speed CT scanner engineered specifically for the most challenging clinical areas where time and precision are of the essence. To support medical staff in their workflows during critical situations, two "companions" for automated user guidance are provided: myExam Companion guides users through diagnostic procedures; myNeedle Companion supports targeted needle path planning as well as laser-guided insertion across multiple modalities.

With its large bore of 82 centimeters and its user-friendly tablet operation, Somatom X.ceed is designed from the ground up to enhance user and patient experience, The system's power and fast rotation time is used to full potential thanks to the intelligent automation of myExam Companion, achieving high-speed and high spatial resolution, key for cardiac, emergency, and spectral imaging.

CT is one of the most used imaging modalities when cross-sectional image guidance is needed for percutaneous interventional procedures, like biopsies, ablations, or pain therapy. Almost 50% of sites perform at least 3 CT-guided interventions per day. The use of myNeedle Companion — a unique combination of hardware and software designed to greatly reduce the complexity in CT guided interventions means that the workflow is greatly simplified. Familiar user interfaces let the radiologist concentrate on what matters: accurate needle positioning with the help of the unique myNeedle Laser: a powerful, fully integrated option that projects the needle entry point and insertion angle directly on the body of the patient – even in advanced double-angulated procedures with multiple needle paths.



Visualization of structural changes in the lungs. HIgh resolution across the entire lung. Image courtesy of Kantonspital Baden, Baden, Switzerland

In the last 20 years the demand for CT-imaging in emergency departments has increased by 250%. In a busy emergency environment, inefficient workflow can slow down radiologists who need to triage patients and perform multiple, demanding tasks quickly. With the intelligent support of myExam Companion, staff members can easily unlock the full potential of Somatom X.ceed, speeding up procedures from patient preparation to image evaluation. Applications powered by artificial intelligence provide ready to read results aimed to facilitate diagnostic tasks.

The ability of cardiac CT to rapidly evaluate multiple cardiovascular conditions has allowed CT to become an important diagnostic instrument for steadily rising numbers in cardiovascular diseases (CVD). From 2011 to 2019, CT cardiac procedures more than doubled from 1.4 to 3.0 million. These procedures, some of the most complex in CT, are now performed routinely by staff of all skills levels. Here, as in emergency imaging, myExam Companion plays a major role in guiding the user towards more standardized results and low dose levels. "*As the number and complexity of radiological procedures increase, demands on staff are reaching heightened levels. This continues to cause unwarranted variation, in both diagnostic and interventional procedures. Somatom X.ceed, together with myNeedle Companion, is a true game changer for CT-guided interventions. After the introduction of myExam Companion last year, reducing the overall complexity of scanner operation in as many aspects as possible was our next logical step*," says Philipp Fischer, Head of CT at Siemens Healthineeres

SIEMENS HEALTHINEERS
ERLANGEN, GERMANY
www.siemens-healthineers.com

Point-of-Care Ultrasound

Driven by pandemic realities and clinical demand for portable and intelligent point-of-care ultrasound (POCUS), GE Healthcare has introduced Venue Fit, the smallest system in GE Healthcare's Venue Family, featuring an easy-to-clean touchscreen, intuitive scanning tools, and a small footprint designed to fit in tight spaces often found in point-of-care settings.

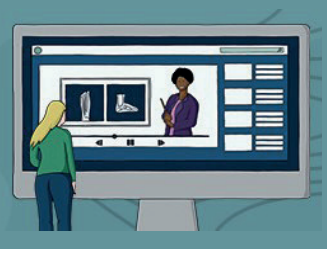
Offering portability, real-time images, cleanability and workflow efficiency, POCUS has become an essential tool enabling clinicians to quickly triage and monitor patients in and outside of COVID wards. Accordingly, GE Healthcare saw orders for its existing Venue Go system increase more than fivefold in 2020 compared to the year prior.

Dr. Joseph Minardi, Director of the Center for Point-of-Care Ultrasound at a West Virginia academic medical center said "*With the new Venue tools, I don't have to struggle with the interface to be efficient. I can bring the device in with me, scan the patient, and using the Lung Sweep and RealTime EF (ejection fraction), I have the information I need right away.*"

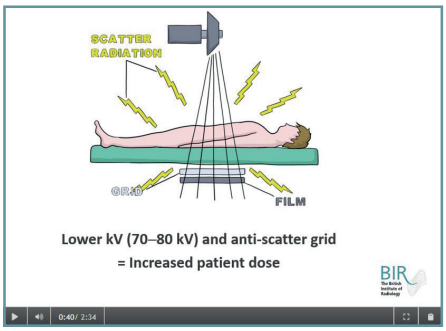
GE HEALTHCARE
CHICAGO, IL, USA
https://venue-pocus.gehealthcare.com/

BIR
The British Institute of Radiology

BIR video courses for busy imaging professionals



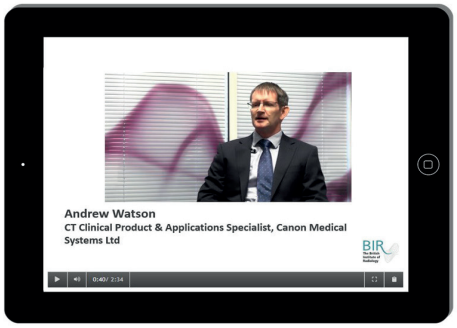
Out now: Radiation Safety 2021 and Dose 2021



- Online educational videos for radiologists, radiographers and physicists
- Short sessions, including illustrations, animation, live action, and recorded interviews
- Stop and start at any time to fit in with your schedule
- For you and your team
- CPD certificate with RCR and CoR accreditation

DI Europe reader discount price ~~£79.99~~ £65.99

Use the following codes at checkout: Radiation Safety 2021 - RS21DIEU, Dose 2021 - DS21DIEU



"One of the best radiation safety training courses I have seen"

"As a long established radiographer I found this course to be extremely beneficial"

Group licences available

Engaging | Memorable | Relevant

PET–CT Essentials, CT Essentials & MR Essentials coming soon

www.bir.org.uk/videocourses

video.sales@bir.org.uk

Registered charity number: 215869

MAGNETOM Free.Max

Breaking barriers

siemens-healthineers.com/magnetom-free-max

First 80 cm bore

MAGNETOM Free.Max[1] breaks barriers to expand the reach of MRI. Where patients have felt discomfort, the world's first 80 cm bore sets a new paradigm in patient comfort. Where infrastructure was an obstacle to MRI, MAGNETOM Free.Max slots into an existing helium-free infrastructure. Where access to MRI was not viable, MAGNETOM Free.Max makes access affordable. And where conventions have limited our thinking, MAGNETOM Free.Max breaks out of conventions to explore new clinical opportunities in MRI.

[1] *The product is pending 510(k) clearance, and is not yet commercially available in the United States. Its future availability cannot be guaranteed.*

SIEMENS Healthineers