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#### The 27th Annual Convention of the German Society for Senology

21-23 June 2007 Lübeck

Congress President Professor Juergen Dunst MD praises major advances and multidisciplinary efforts, and outlines future hopes for breast cancer patients

"Breast cancer plays a key role in oncology and health policy. It is the most common malignancy in women and an important cause of death and severe illness. Over the past 30 years, some major improvements have markedly changed the face of breast cancer. Major advances have been achieved in terms of early detection and screening programmes, improved pre-operative diagnostics, breast-preserving therapies, adjuvant systemic therapy and palliative treatment. In summary, these advances have markedly improved the long-term cure rate (from under 20% in the 1950s to over 50% in 2000), prolonged life, reduced treatment morbidity and increased quality of life.

Currently, breast cancer is an exciting field of basic and clinical research. A broad spectrum of research will, hopefully in the near future, bring modern and advanced diagnostic and therapeutic concepts into the clinic. These technologies include detection of isolated tumour cells in bone marrow and blood, individualised local therapies, systemic treatment based on molecular diag-

nostic tools and a variety of new drugs. Breast cancer was one of the first diseases that could be effectively treated by molecular therapies (e.g. the Her-2-neu antibody trastuzumab).

A major challenge in the diagnosis and treatment of breast cancer is the fact that these involve a variety of medical disciplines. This has led to the formation of specialised breast centres that bring together a large number of specialists, improve the multidisciplinary approach and provide high quality standards in all fields of care. Thus the development of breast centres set an example for other fields of multidisciplinary oncology.

The Annual Meeting of the German Society for Senology, with about 2,000 national and international participants, is one of the largest multidisciplinary cancer meetings held in Germany. The scientific programme reflects the manifold aspects of research and care in breast cancer and gives an overview over upcoming technologies and concepts."

\* Congress details: www.senologie.org

#### State governments unite to lower mortality

Australia - The Australian Institute of ly intervals. Participation in the scheme in Health and Welfare has reported a 26% decrease in the breast cancer mortality rate in 1996-97 to 55.6% in 2003-04. In 2004 among women aged 50-69 years between 1990 and 2004. The BreastScreen Australia sive breast cancers - 2,733 of them in the Monitoring Report 2003-2004 indicates target age group. that the rate is down from 68.5 per 100,000 women in 1990 to 50.9 in 2004, an average indigenous Australian women aged 50-69 decrease of 2.1% per annum. Although the years (35.3%) was much lower than the occurrence of breast cancer has risen, the general non-Indigenous rate (55.4%). report also shows that the rate of mortality However, the rate for Indigenous Australian has fallen due to a combination of early women increased significantly, from 30.3% detection and improvements in treatment. in 1998-99 to 35.3% in 2003-04.

BreastScreen Australia provides free screening mammograms for women – and of all Australian governments. particularly aged 50-69 years - at two year- *Details: www.aihw.gov.au* 

the target age group increased from 51.4% BreastScreen Australia detected 3,851 inva-

In 2003-04 the participation rate for

BreastScreen Australia is a joint initiative

# **MAMMO-UPDATE** Screening: Patients respond well to web-based reminders

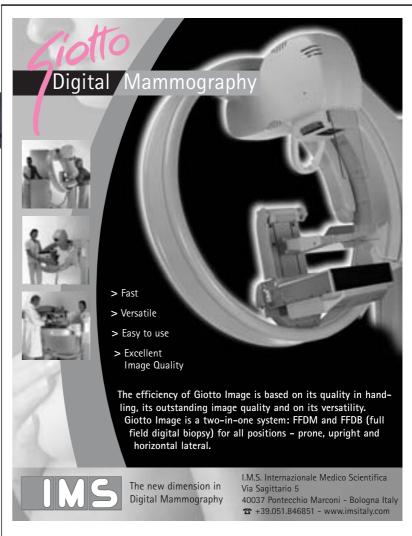
**USA** - Web-based mail and phone reminder software significantly increased the percentage of patients who received preventive health services, according to a study led by Rajeev Chaudhrythe Preventive Care ReminderMBBS, at the Mayo Clinic, publishedSystem (PRECARES), a web-based in May in *The Archives of Internal* Medicine.

Although the US national evidence-based guidelines advise that all women over aged 40 should have an annual mammogram, Dr Chaudhry said only about 65% of women had one in the last two years. 'The study showed we can increase that percentage through a team approach. With our new electronic tool and our related practice changes, one appointment secretary can now schedule mammography for over 10,000 women.' The tool he refers to is mail and phone reminder software designed by the Mayo team to help the Mayo secretaries arrange breast cancer screening appointments for eligible women

at the practice. Usually in the US, each woman is responsible for her own reminders to phone her physician's office and first obtain approval for an annual mammogram. She must then wait for an appointment. If the woman overlooks this, her test could be missed.

the woman is contacted by phone. During the study, the researchers focused on 6,675 women aged 40-75. Divided into two groups, the first received the mailings

and, when Dr Rajeev Chaudhry necessary, were phoned to remind them to book a mammogram. The control group did not receive reminders. Among the reminder



#### MAMMO-UPDATE

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As Dr Chaudhry points out, the reminder notice women receive via the software programme is preapproved, so mammography can be scheduled during her first phone call. Every month, the system produces a list of women over the age of 40 who are due for mammogram screening within the next three months, but who have not scheduled a screening. Each of these patients are sent a letter asking them to phone for an appointment. If a woman does not respond, a second letter is sent, and if this produces no response,

group, 64.3% had their annual mammogram, compared with 55.3% in the control group. Following the study, the programme expanded and compliance with annual mammograms grew to over 72%, with 86% of the Mayo Clinic patients have had one mammogram within the past two years.

Redesigning primary care so that appointment secretaries schedule preventive services was a key to the programme's success, Dr Chaudhry points out.

Robert Stroebel MD, chair of Primary Care Internal Medicine at Mayo Clinic, and the study's senior author, added: 'We already have expanded this reminder method to Pap smears and diabetes care, and will be adding other preventive services this year.'

ull-field digital mammography (FFDM) offers many advantages over film/screen mammography. Whereas most commercial FFDM systems have shown to have superior physical image quality over their analogue counterparts, large scale clinical trials have demonstrated that FFDM seems equivalent to screen/film mammography with statistically significant diagnostic advantages for certain populations, such as women under 50 years old, women with dense breasts, and pre- or perimenopausal women.

The main limitation of projection mammography is not quantum or

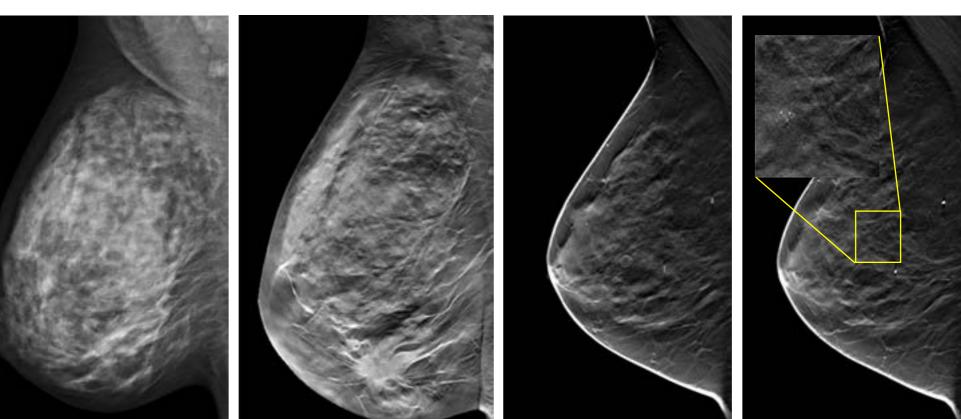
detector noise but the fact that the 3D anatomy is projected into a 2D image. Therefore, overlapping anatomical structures limit the radiologist's ability to detect certain lesions. Digital tomosynthesis promises to overcome this limitation of projection mammography by reconstructing slice images.

#### The principle of breast tomosynthesis

Breast tomosynthesis is a 3D imaging technology that acquires 2D projection images of a compressed breast at multiple angles during a sweep of the Xray tube. Objects at different heights in

# Digital breast tomosynthesis THE FUTURE OF MAMMOGRAPHY

By Thomas Mertelmeier, Principal Scientist at Siemens AG Medical Solutions



Digital mammogram of a R-MLO projection (Fig. 1a)

Reconstructed tomosynthesis slice of the same breast showing a tumour that is not visible on the mammogram (Fig. 1b) Reconstructed tomosynthesis slice of a breast in MLO position containing a well-marginated lesion (Fig. 2a) and a cluster of microcalifications (Fig. 2b). The insert is a magnified view of the area with the calcifications.

# **TESTING TIME FOR TOMOSYNTHESIS**

A pioneer of breast screening, **Dr Ingvar Andersson**, of Malmö University Hospital, Sweden, began the first randomised screening trial in 1976. These trials have continued ever since, and have confirmed that screening with mammography can reduce breast cancer mortality by between 25-30%.

Currently, Dr Andersson is vorking with the Siemens tomosynthesis prototype. 'Tomosynthesis,' he believes, 'will become a successful screening modality. We have done some studies that have shown that its sensitivity is superior to that of digital mammography. So we expect to find more cancers, and probably in an earlier stage. Moreover, in my opinion, tomosynthesis will be even more relevant in screening than in clinical use because, in a clinical setting, we always use ultrasound, which is a very good additional modality. In screening, we are basically limited to

What next? A combination of ultrasound and tomosynthesis?



mediolateral oblique) would be enough because it is a tomographic technique. However, there some data suggesting that, by adding the cranio-caudal projection, the cancer detection rate might increase.'

To know precisely how to proceed, such things need to be proven in a series of larger trials. Dr Andersson points out Although this has not been done at Malmö Hospital, so far, he has a concept for such a project. What is being done at Malmö is research on optimisation of the radiation dose to be delivered, the optimal angular range, number of projections and other technical factors. And what is the future of breast cancer screening? 'I would like to see a combination of tomosynthesis and ultrasound scanning in the same equipment. That would give us the best of both worlds.' But, he adds: 'Most likely it will take time before we are there.'

Dr Ingvar Andersson mammographic techniques. My impression is, that tomosynthesis will provide us with further also pla

will provide us with further information and that it will be a valuable technique that will be implemented into the market in a couple of years. However, before that, more investigations need to be done. We know that the sensitivity is better than in today's techniques but, for screening purposes, the specificity also plays a huge role. This means we have to do large trials under real screening conditions to see how tomosynthesis really works and how many women would be recalled for additional ovaminations. This figure must be

examinations. This figure must be low, because recalls cause anxiety

and cost time and money.' Dr Andersson adds that there is another problem to be investigated. 'When we carry out screening today – digital or film – we do two projections for the breast, one cranial-caudal and one mediolateral oblique. With tomosynthesis, the question that arises is whether one view (the

the breast are projected differently at different angles. The subsequent image reconstruction leads to a stack of slice images of the different depth layers parallel to the detector surface. The in-sliceresolution is predominantly determined by the detector resolution and usually much higher than the resolution between slices ('depth resolution') due to the incomplete sampling of the object within a relatively small angular scan range.

During the acquisition process the total dose is split among the single views. Because one voxel is probed by the same number of Xray quanta as in projection mammography, a tomosynthesis scan needs approximately the same dose as a projection mammogram under the assumption that the image detector does not excessively contribute to noise.

The objective of the Siemens tomosynthesis prototype device was to gain experience – together with our clinical partners – in how to provide a comprehensive solution for 3D mammography. The specific goals were to find the best acquisition mode for a tomosynthesis scan and to study reconstruction algorithms to optimise image quality. Another objective was to learn about the clinical performance and workflow of tomosynthesis.

The prototype is based on a Siemens MAMMOMAT NovationDR system modified for an X-ray tube motion over an arc of up to 50°. The detector used in this research system is a fast direct converting amorphous selenium detector, with an imaging area of 23.9 cm x 30.5 cm. The system is quantum noise limited, even for the lowest detector exposures used. A tungsten/rhodium anode/filter combination is used to keep the dose of one complete scan as low as that of one or two conventional 2D mammograms. The data of the examples presented here were acquired in a mode with 25 views and with scan time of 20 s.

#### **Clinical benefits**

Breast tomosynthesis has the potential to improve sensitivity in the detection of breast cancer due to reduced overlap of breast tissue, particularly in dense breasts. This may result in earlier cancer detection. Breast tomosynthesis may also lead to significant improvements in specificity as the 3D-analysis of the distribution of microcalcifications, and of shape and margin of lesions, might be easier. This could lead to a reduction in recall of patients and fewer biopsies. Finally, digital breast tomosynthesis might eliminate the need for multiple exposures of the same breast. Thus it might lead to dose reduction, if only one tomosynthesis view, such as in the MLO orientation, is needed.

ethics board. All human subjects also underwent standard digital mammography on a commercial FFDM unit.

One tomosynthesis example is shown in Figure 1. The 57-year-old woman with compressed breast thickness of 6 cm underwent tomosynthesis scans on each breast in MLO position. The mammogram of the right breast (Figure 1a) did not show the 2.8 cm palpable ductal cancer which is, however, clearly visible in the tomosynthesis data set, e.g. in the slice 2.5 cm above the patient table (Figure 1b).

A second example is shown in Figure 2. The breast of the 60-yearold human subject contains a wellmarginated lesion (Fig. 2a) about 2.3 cm above the table and a microcalcification cluster in a different plane (Fig. 2b). The magnified view (insert) nicely demonstrates the detailed microcalcifications. **Conclusion** - Currently, breast tomosynthesis is in research status, obtaining first clinical experience. The fundamental physical problems have been solved although many details need further investigation. One of the biggest challenges is related to data handling. For a tomosynthesis solution for routine clinical use, an efficient way of displaying, reading and archiving the huge amount of image data must be found.

Breast tomosynthesis has the potential to revolutionise mammography by significantly

reducing the tissue overlap problem, inherent in projection mammography. This might lead to improved sensitivity and specificity, fewer recalls, fewer biopsies, less dose and less painful compressions. It can be expected that breast tomosynthesis will be used as a diagnostic tool in the beginning. However, after a learning curve and the diagnostic benefit have been proven, breast tomosynthesis would most likely be applied in the screening setting.

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#### Image examples

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n 2002, Germany implemented an early detection programme for breast cancer. The digital Reference Centre For Mammography at the University Hospital Münster is one of five such centres in the country - and it's one of the most modern, providing digital systems for imaging and results evaluation as well as a mammo-PACS.

During a recent visit to Münster, **Professor Andreas Pinkwart**, Minister for Innovation, Science, Research and Technology of North Rhine-Westphalia, was updated on the screening programme by **Professor Walter Heindel** MD, who heads the Centre. They also discussed future diagnostic possibilities involving innovative programme at all times along with providing regular training to keep them up-to-date with the latest technological developments. *Currently you are also looking at new mammography technology photon-counting tomosynthesis. Is this an inferior form of CT diagnosis?* 

'Individual manufacturers are experimenting with a breast-CT. In terms of tomosynthesis, what we don't need and want is for women to be examined by yet another machine. In fact, the idea is to use tomosynthesis only to further investigate suspicious results. We are currently co-operating with the Radiology Department at the Charité in Berlin in an EU-funded project looking at the kind of medical questions where tomosynthesis will be



# Germany's early detection programme and research

imaging procedures. Present at the briefing, we asked Prof. Heindel about the programme's success and particularly the research project focused on tomosynthesis

In North Rhine-Westphalia the screening programme has been comprehensively implemented according to European guidelines, Prof. Heindel told us: 'New digital systems have been installed in many surgeries and hospitals, which shows how seriously radiologists take this subject. The feedback is also positive among women entitled to be screened. In the first year more than 50% of women that the programme targeted (aged between 50-69 years) took up the offer of being screened. This great response initially surprised us, and now we can present first scientific data showing that we have been able to detect small, and therefore curable, breast cancer with the help of early screening. Our objective is to lower mortality from breast cancer through early diagnosis.

'Being responsible for the mammography screening programme for North Rhine-Westphalia – Germany's biggest federal state – the Centre is responsible for technical and medical quality assurance, training of screening teams. Our scientific focus is the evaluation of digital mammography technologies and of the programme. We work in multidisciplinary teams comprising radiologists, medical physicists, medical documentation assistants and radiology technicians, so that we assist the doctors participating in the

helpful, with the objective of comparing those results systematically with MR mammography. So far, MR mammography has been a problem solver for many women, such as those affected by lobular carcinoma, which is hard to detect with X-ray mammography. Its spread is hard to determine, because it often does not differ from the density of the normal glandular tissue. MR mammography is the gold standard here, prior to resorting to surgery. The question is whether we will be able to better detect this lobular carcinoma with the help of tomosynthesis. This is where the photon-counting system supplied by Sectra\*, which significantly lowers the levels of scattered radiation, comes into the equation (see box). We have already

confirmed this with our own measurements. However, the most important question - as always in imaging – is to what levels we can lower doses whilst maintaining the quality of diagnosis. That's the decisive issue.'

#### Particularly because radiologists must resist the impulse to increase the dose to achieve brilliant images where a lot can be seen very precisely?

'Yes, this is a well-known problem - a problem with digital technology such as this type of technology "evens out", unlike conventional X-ray technology. Here you get over-exposed images when the dose is too high. This is the danger with digital mammography or generally with digital technologies. Theoretically the manufacturer or user can say: I want images of particularly



brilliance and quality, i.e. I will increase the dose a little. But even if you still stay below the legal exposure limits when doing so, the interest of the women patients must be at the centre of things. The objective is to make that important diagnosis whilst adhering to the principle of protection from radiation, which is accepted the world over: *as low as reasonably achievable* (ALARA). This is a fundamental issue, which our working group is also looking into.

How do you know whether you just can't see anything or whether you cannot see anything because the dose was too low? 'This is a problem, which is why we currently work with so-called reference values, i.e. you state what dose should be used for an average examination. However, in digital mammography we have maximum limits that have been specified across Europe. I am convinced that, with the help of these new technologies, we can lower the doses and that's why I have lobbied for this technology for our reference centre. Between brilliant images achieved with doses that are too high, and a situation where the doses are lowered to the extent that there is no diagnostic value left in the images taken, is where we need to define the right maximum and minimum values.

'This includes the comparison of different digital technologies by collating relevant data. This is also the background for a request from the State Ministry to our reference centre to collate data on the doses administered, and to correlate them with the diagnoses, which will help to make realisable and scientifically wellfounded conclusions. This is also of high interest from a political point of view, for instance in dealing with selfhelp groups for women.'

\* **Sectra** manufactures diagnostic imaging equipment, including digital

mammography systems. The firm reports that MicroDose Mammography is the only system that guarantees very low radiation doses for patients, and that the development of photon-counting tomosynthesis, with even lower radiation doses, is therefore a logical further development for the firm. Sectra adds that the system is currently only used for research purposes. The company is currently undertaking research in co-operation with, among others, Prof. Heindel within the EU research project '*High* Resolution X-Ray Imaging for Improved Detection and Diagnosis of Breast Cancer'.

#### The University of Münster

In Germany, Münster's Medical Faculty is one of the top faculties of its kind for teaching and research. The secret of this success lies in the organ-centred and interdisciplinary orientation of the study courses. During any one semester students are lectured on a certain topic in all relevant medical fields, for example radiology, pathology, laboratory medicine or surgery, so they learn their subjects relating to certain indications. The results achieved by the students in their first state examinations - held according to the new, stricter guidelines - appear to justify our methods, the Faculty points out. 'Münster students have done very well by comparison.'

A further strength in Münster is that innovative imaging, together with medical physics, constitute a defined platform at the Medical Faculty, and this will be further expanded. In this way, issues going beyond pure medicine, such as exposure to radiation, radiation measurements and safety issues can be swiftly evaluated.

# **TOMORROW'S IMAGING ON TODAY'S HORIZON**

**Professor Mats Danielsson**, at the Royal Institute of Technology and Sectra, in Sweden, explains what tomosynthesis means to his company today, and soon, to mammography for the future

'Tomosynthesis is a hot topic in all the companies involved in mammography', Professor Danielsson pointed out. 'But whereas they are developing more or less the same thing, Sectra has a totally different concept - photon-counting - a unique technology that, for the first time, processes X-rays one by one. So we have less noise and radiation compared with common systems that unselectively merge many and different kinds of photons with noise. Along with the electronic noise reduction we also receive more information from each X-ray. This data is acquired with a slit-imaging

detector (it has only thin slits to let the radiation through), which moves from left to right to collect the data. So we are talking about a very sophisticated system, which only Sectra is developing.

'Photon-counting tomosynthesis is a result of research in high-end physics. When researchers at Fermilab found the long missing sixth quark, the so-called top quark and a fundamental constituent of matter, that was only possible because of a new, very sensitive detector. This sensor uses similar technology to the sensor we now use for photoncounting mammography. So, I have shifted my experience from CERN into mammography development. Obviously, my advantage is that I work part-time, and independently for Sectra, and part-time at the Royal Institute of Technology in Stockholm, so I can match my experiences from both sides – as is the case for the tomosynthesis project.

'There are currently prototypes of the photon-counting tomosynthesis system for research purposes. Our focus is for example on the comparison of MR and tomosynthesis. At this stage, we are convinced that tomosynthesis can definitely compete with MR, because MR is expensive, and the resolution of tomosynthesis is far better. Even considering the radiation, which you don't have with MR, tomosynthesis has advantages, because the radiation is low and the images excellent. It's the same with CT - I think it cannot keep up with the resolution of tomosynthesis.'

Professor Mats Danielsson

# **REVEALING THE BREAST'S ARCHITECTURE**

2D imaging - whether analogue or digital - is thought to miss detection of 20-30% of breast cancers. Early clinical results from studies using the new technology *tomosynthesis* indicate its potential to lower those percentages.

During a tomosynthesis examination, an X-ray tube moves in an arc around the breast, producing image slices that are virtually free of overlapping parenchyma, so manufacturers say this system can provide more accurate 3D views of the breast than the 2D views currently produced by mammograms. Tomosynthesis also delivers a lower radiation dose.

During the recent German Radiology Congress in Berlin, **Roberta Agnes Jong** MD FRCPC, head of the Breast Imaging Unit in the Medical Imaging Department of Sunnybrook Health Science Centre, Toronto, Canada, and **José Abellan-Martinez**, Marketing Manager for mammography in the Global Diagnostic Imaging division of GE Healthcare, discussed this firm's tomosynthesis technology with *Meike Lerner* of European Hospital

'Compared with today's mammography, which provides us with a summation of images, where subtle abnormalities often



José Abellan-Martinez and Roberta Agnes Jong, with Meike Lerner of EH

get obscured by the images of other tissue, tomosynthesis will show us thin slices of the tissue of the whole breast,' explained Dr Jong. 'This will make it easier for the radiologist to look at the margins of masses, at architectural distortions and other signs of malignancy. So we hope that tomosynthesis will improve the early detection rate of breast cancer and will provide us with more accurate images that will reduce recall rates and the number of biopsies. This is a very important advantage for women, because a recall is always connected with fears and means great physiological and psychological stress. Furthermore, the new method the breast must only be compressed one time and maybe with slightly less compression, but this is not proven at the moment. As a study has shown, the radiation dose during a tomosynthesisexamination is less or equal to that of a two-view mammogram. 'For the radiologist, tomosynthesis will be a great help, for the analysis of the images will be much easier, because of their accuracy, and the danger of missing a detail will be minimised.' Asked what advantages GE's tomosynthesis equipment might have, compared with other similar technology in the works at other companies, José Abellan-Martinez said: 'GE's advantage is that we do have huge experience in the reconstruction of organs via CT, MR or RAD and we profit from our own technologies now regarding tomosynthesis. The technology we designed had all the features necessary for tomosynthesis, whereas other companies have to change their current technology used for digital mammography. So GE is one step ahead. A second point is, that our system is very efficient in terms of the radiation dose and image quality. But actually, we do not bother that much about other companies doing similar things; we have the right system and tomosynthesis is just another step to GE's aim of early health. What is important in the end is that our work will result in a good, proven instrument that will support us in the fight against cancer. 'Currently we are doing extended clinical trials that hopefully will prove our hopes. The first results will be available in the near future. Afterwards we need FDA approval. So, from my point of view, the first tomosynthesis systems will not be implemented before 2009 or 2010. But, as far as we know from other new innovations, it will be a long way before tomosynthesis

will be the common method for breast cancer examinations. Just look at digital mammography: GE Healthcare started with its digital system in 1999. In 2006, only around 20% of all US hospitals were equipped with a digital mammography system. So today we cannot predict when women will benefit from this new technology. Hopefully it will be as soon as possible.'

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ombining a scientific research laboratory with specialised clinic, the Netherlands Cancer Institute, in the Antoni van Leeuwenhoek Hospital (NKI-AVL), in Amsterdam, aims for a unique interaction of scientific research and clinical application. Along with this, the organisation disseminates knowledge and education for physicians to collaborate with academic teaching hospitals, universities and scientific research institutes in the Netherlands and abroad.

Patients are referred to the Institute either after breast screening through a local screening site or by the recommendation of their general practitioners (GP). Others come for a second opinion, because NKI-AVL is a dedicated cancer hospital.

Radiologist H J Teertstra and a team at the NKI-AVL are presently studying the clinical use of a new 3D method of imaging that can reduce or eliminate the tissue overlap effect called breast tomosynthesis. The system being tested was developed by Hologic, a leading developer of premium diagnostic and medical imaging systems for women. 'We've been working on breast tomosynthesis for a year,' Dr.

Teertstra said, during a recent European Hospital interview. 'We asked 1,200 patients who came to our out-patient breast clinic to participate in the study, about 500 agreed to participate. Analysing the results from 500 cases is a lot of research.'

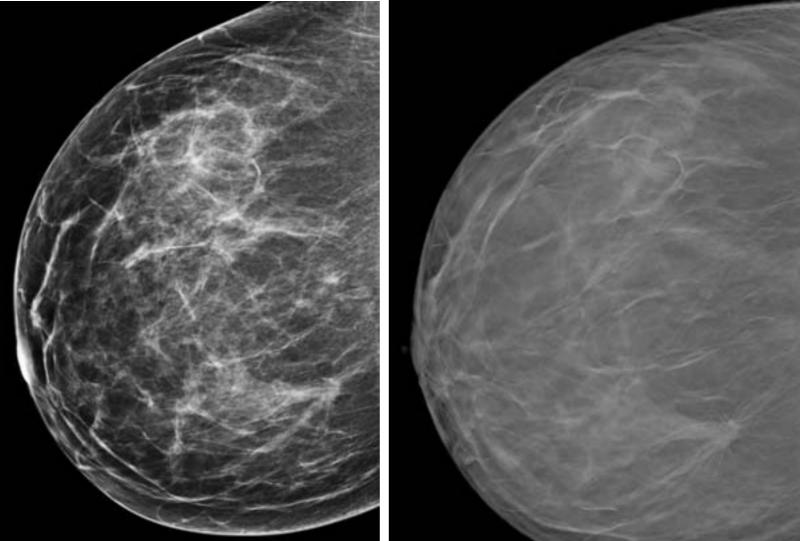
At present, breast cancer detection is done from mammography, ultrasound, MRI, and CT, Dr Teertstra said. 'Breast cancer screening programmes use conventional analogue or digital mammography, a two-dimensional imaging modality. In conventional mammography, pathologies of interest are sometimes difficult to visualise because of the clutter of signals from objects above and below. This is because the signal detected at a location on the film cassette or digital detector is dependent upon the total attenuation of all the tissues above the location.

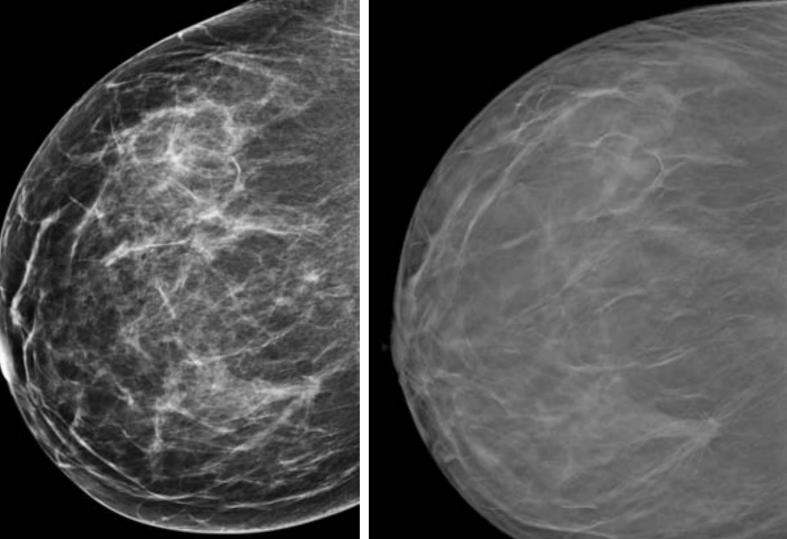
'Our research involved looking at the 3D or tomosynthesis patient's image in addition to her conventional 2D mammogram. To date we've read about 300 of the 500 cases that we have gathered. In the first 300 cases we found two cancers that were not seen on conventional mammography. In a lot of the other cases tomosynthesis didn't real help by giving us new or better information. Sometimes you can see a cancer easily, so you don't need it. You already know it's there. It's there on



'We've completed 300 cases to date using breast tomosynthesis. In two of the 300 cases, tomosynthesis was clearly better. In one case the patient had mammography, ultrasound and a biopsy in another hospital, but came here for a second opinion. We did not see the cancer on her conventional mammogram. But with tomosynthesis it's very easy to see the speculated and

# **Evaluating breast tomosynthesis for the Netherlands**





ill-defined lesion.

In the second case, we found a tumour with breast tomosynthesis that wasn't seen in her conventional mammogram. We had sent the patient back to her GP, but after reading the study we called her back for a biopsy. So we saved her with tomosynthesis. We don't yet know if we'll recommend doing tomosynthesis on all screening patients. We do know that it's definitely beneficial in certain cases.

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MAMMO-UPDATE 6



Demonstrating aspects of imaging for Daniela Zimmermann of EH (right)

mammography, and on ultrasound; it's there when you put a needle in it, so the diagnosis is clear.'

Hologic has five sites in America that are looking at the use of breast tomosynthesis with patients from a screening population. In the first phase of the AVL research, Dr Teertstra and his colleagues are investigating another population – patients already known to have cancer. 'We wanted to examine a lot of cancers. We want to see whether tomosynthesis can cut down on unnecessary patient recalls and breast biopsies. The problem with mammography is that you sometimes see things that are not there. Is it the composition and superposition of the tissue? Is it really a lesion? So patients must return for analysis of that with compression mammography or ultrasound. We think that tomosynthesis will help to reduce the recall rate. We hope that we can see more during screening.



'At AVL,' he continued, 'we are investigating the lesions that are recalls in our own population. In a year, we do about 10,000 mammographies and the recall rate is about 300-400. Using tomosynthesis, we want to examine them all to investigate, by a process of elimination, whether if we had done it initially, they would not have been recalled.

'In a later study we hope to look

#### Hologic's selenium-based breast tomosynthesis system

Although the principles of tomosynthesis technologies are the same, the prototypes of the several companies developing tomosynthesis machines have differences. Hologic, for example, is the only one to use a detector that moves with the tube. The advantage of a moving detector is that it can manage to keep the entire breast tissue imaged at all angles compared to a fixed detector that will have a smaller field of view, Andy Smith PhD, a physicist with Hologic pointed out. In addition, he added, the company's tomosynthesis system uses a selenium based, direct capture detector: 'Because images are acquired rapidly with

tomosynthesis, a fast imaging technique is needed. Selenium-based image receptors with their high Detective Quantum Efficiency (DQE), greater than 95 % x-ray absorption at mammographic energies, and rapid readout capabilities are ideal for that purpose.

'Tomosynthesis offers the possibility of revolutionising mammography. Clinical sites like AVL in the Netherlands are helping to determine if tomosynthesis can eliminate the problem of overlapping tissues. Other areas under investigation include whether the dose can be lower with breast tomosynthesis and if compression can be made less painful.'



Jack Cumming, Hologic's CEO: 'We expect tomosynthesis to be a major new advance in breast care, with the potential to improve cancer detection rates and reduce patient recall. This summer we expect to finish our clinical trials and file for necessary approvals to sell breast tomosynthesis systems in Europe, the U.S. and other major women's imaging markets.'

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at contrast-enhanced tomosynthesis. 'We want to find out if it's as good as MRI, for instance. Our ethical committee has not yet decided if it's ok for us to proceed with this study.' **Does he think the system will be used for screening in the Netherlands?** 

'Yes, that will be the way to go. In America a lot of research has been done on screening the population. But the problem with that kind of research is that, to evaluate it, you need so many patients. We're simply trying to find out if it's also suitable for our population. As yet, we don't know if it can really help us. You certainly can see the lineation of a tumour better. So it's adjunctive to mammography. And we have found cancers that were not seen during mammography.'



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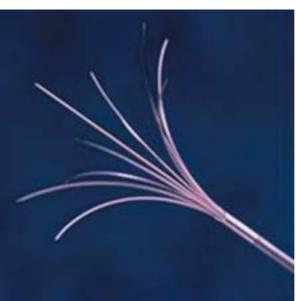


# **Radiofrequency ablation in**

By Beate M Stoeckelhuber MD, Associate Professor and Radiology (Interim) Director at the Department of Radiology, Luebeck University, Germany, with Smaragda Kapsimalakou MD, also at Luebeck

The past 20 years have seen marked changes in the surgical management of breast malignancies. Mastectomy has been largely replaced by breast conservation surgery. The latter has become more widely accepted by both patients and physicians because similar survival rates between patients who underwent mastectomy alone, and those who underwent lumpectomy with radiation therapy,

have been documented in large randomised studies. There is a major trend towards less invasive local treatment of breast cancer, which has the potential to destroy malignant tissue with little effect on the surrounding environment. These encouraging results have led researchers to investigate the next step towards minimally invasive procedures for the treatment of breast



tumours under visual control. One possible method for local tumour treatment is the local application of heat.

#### Radiofrequency ablation: the technique

Radiofrequency (RF) ablation has been demonstrated to be effective in the treatment of non-resectable hepatic malignancies, and promising results



Figs 1 & 2. RFA probes deployed

have been observed in the treatment of kidney, lung, brain, prostate and bone tumours. The experience of RF ablation in patients with breast cancer is far more limited. A few pilot studies have been published to date.

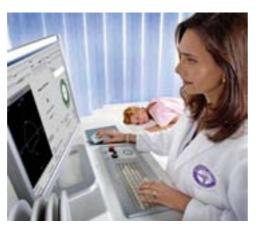
During RF ablation, high frequency 100–500 kHz alternating current emitted from the non-insulated tip of the needle electrode (Figs 1, 2) propagates into the adjacent tissues,

where it causes ionic vibration as the ions attempt to follow the rapidly changing direction of the alternating current. The tissue heats resistively in the area that is in contact with the needle electrode tip, and the heat then transfers conductively to more distant tissue.

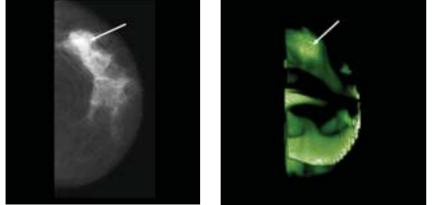
The objective of RF ablation is to generate local temperatures that will result in tissue destruction. In general,

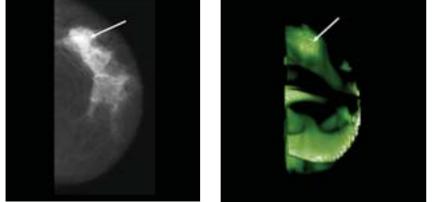


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# Greater bonding of radiation oncologists and diagnostic radiologists sought by RSNA

Radiation oncologists and diagnostic radiologists will be encouraged to forge partnerships at the Radiological Society of North America (RSNA) congress in Chicago this November helped by a new programme, called Bolstering Oncoradiologic and Oncoradio-therapeutic Skills for Tomorrow (BOOST)

'Radiation oncologists today have to work closely with diagnostic radiologists because if we know where the cancer is located, we know better where to treat. This new synergy of precision imaging for use in precision therapy has just unfolded. It's a wonderful way to get both disciplines working hand in hand,' explains Professor Sarah S Donaldson MD, RSNA Board Liaison for Publications and Communications and board representative to the RSNA Oncologic Imaging and Therapies Task Force, which devised the four-day programme. This will be unique in such meetings, she points out.

Co-chairs on the task force - Steven Leibel MD, medical director of the Stanford Cancer Centre and professor of radiation oncology at Stanford University, and David Panicek MD, vicechair for clinical affairs and director of educational programmes in radiology at Memorial Sloan-Kettering Cancer Centre, and professor of radiology at Cornell University Medical College in New York worked on the programme with Prof. Donaldson. The courses will be run from 8.30 a.m. to 6 p.m. between 26-29 November inclusive, and one type of cancer will be the focus each day (head and neck, prostate, lung or gastrointestinal) and feature experts from radiation oncology, diagnostic radiology, biology and physics. The first part of the day is akin to a refresher course, focusing on the oncologic principles of the disease site, the biology and pathophysiology and the anatomy using

Sarah Donaldson MD is associate chair of the Department of Radiation Oncology, deputy clinic chief and residency programme director for radiation oncology at Stanford University Medical Centre, California.



She is also the Catharine and Howard Avery Professor of Radiation Oncology at Stanford University School of Medicine

state-of-the-art imaging. Practical aspects will follow on radiation oncology or contouring, i.e. identifying the area to be treated as defined by the radiation oncology and diagnostic imaging experts.

'We're looking at radiation target volumes, the proper volume to treat, and the best imaging modality to identify what to treat,' explains Dr Leibel. 'We really want to focus on a disease site and emphasise all the issues around its imaging and treatment, but also present papers and special lectures on radiation biology and the role of interventional radiology and offer some panel discussions,' he adds. The latest developments will also be discussed: '...what the different imaging approaches are and what's on the horizon for radiation oncologists and diagnostic radiologists to use in a specific disease site to improve diagnosis and treatment." The design of BOOST has developed in response to what RSNA attendees have asked for, he points out. 'The real impact is to have diagnostic radiology onsite, with multimodality presentations. For example, the radiologists are going to tell us, "Here's how it spreads, this is how we image it, this is the role of PET *imaging.*" It's a unique way to allow the two disciplines to play off each other.' \* Registration for all RSNA 2007 courses begins on 18 June. Details: RSNA2007.RSNA.org



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# breast cancer would be more useful for treatment of tumours smaller than 3 cm in diameter.

the higher the target temperature, the less exposure time is needed for cellular destruction. It has been shown that, in the treatment of liver tumours, thermal coagulation begins at 70° C and tissue desiccation begins at 100° C, with resulting coagulation necrosis of the tumour tissue and surrounding hepatic parenchyma.

#### Literature review

The use of RF ablation to treat breast tumours was initially demonstrated by Jeffrey et al., who treated five women with locally advanced invasive breast cancer (range, 4 to 7 cm in size). By



Fig 3. Excision followed by radiofrequency ablation (from Klimberg VS, et al. Ann Surg Onc 2006), 13 (11): 1422-1433

# Steep drop in breast cancer rates Less hormone therapy plus less screening

**USA** – A steep drop in breast cancer rates between 2002 and 2003 correlates with the decline in hormone therapy use, according to research froma the American Cancer Society (ACS). However, the researchers also point out that the decline might indicate that fewer instances were detected because mammogram screenings had levelled off. (Between 1980-98, when mammograms became more common, breast cancer rates rose fast and by almost 40%).

The greatest decline in rates was among women 50-69 years old

their study design, only portions of the tumours were treated, so that the zone of ablation and margin separating the ablated and nonablated tissue could be assessed. All patients underwent either mastectomy or lumpectomy after the RF ablation procedure. On the basis of these initial results, the authors conclude that RF ablation was effective in causing invasive breast cancer cell death, but

Izzo et al. performed US-guided RF ablation followed by immediate resection in 26 patients with T1 and T2 breast cancers (range, 0.7 – 3.0 cm in size). They observed complete coagulation necrosis of the tumour in 25-96% of the patients. One patient had a microscopic focus of viable tissue adjacent to the needle shaft site.

Noguchi et al. studied 10 patients with breast cancer less than 2 cm in diameter. After RF ablation, wide

excision was performed in seven cases and total mastectomy in three cases. The surgical margin of the tumour was negative in all of the seven patients who underwent wide excision.

Fornage et al. had treated 20 patients with 21 malignant breast tumours </= 2 cm. All underwent primary RF ablation. In all cases histology showed complete loss of cell viability.

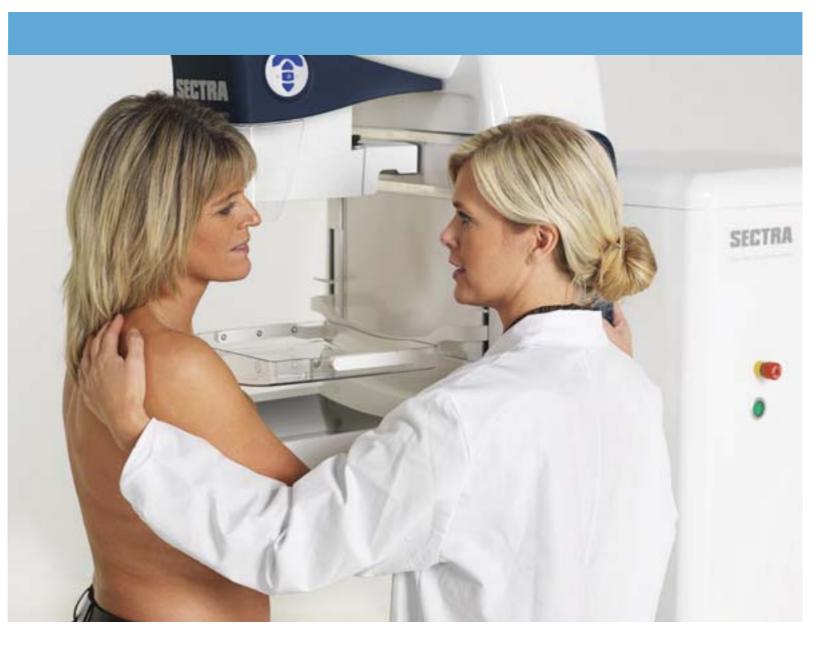
In another study, Klimberg et al. reported 41 patients who underwent mastectomy (group I 22 patients) or lumpectomy (group II 19 patients) followed by RF ablation of the

operation cavity as a means to achieve negative margins at the first operation (Fig 3). The cavity, with surrounding tissue, was resected and underwent histopathologic examination. No in site local recurrences have occurred during a median follow up of 24 months.

#### Conclusion

RFA in breast tissue is feasible. There is potential that thermal ablation might replace lumpectomy in small breast cancer in the future; however, this has to be confirmed in further studies. For references contact: stoeckel.@medinf.mu-luebeck.de

#### Welcome to the future of digital mammography



those most likely to receive hormone therapy. However, the researchers say that stopping hormone therapy cannot explain their other major finding: breast cancer rates started to drop in 1999, for all women 45 and above, well before the link between hormone therapy and health problems was discovered. They reason that the most likely explanation for this earlier decline is, after almost 12 years of increase, mammography use levelled off during those years.

The ACS also believes that part of the decline in breast cancer cases might be temporary, which would mean there has been a delay in detection, rather than an actual decrease in incidence.

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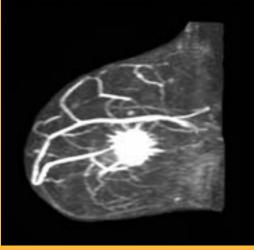
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# **CTLM for cancer detection in dense**



1a: MRI prior to neo-adjuvant chemotherapy in a 52-year-old patient with locally advanced breast cancer. A large volume of angiogenesis is present

Dense Breasts – In an earlier article in European Hospital (Milne ENC. 'CTLM, seeing through the dense breast'. EH Vol. 15 issue 2/06) Milne described the methodology of CTLM and the rationale for using it in the dense breast the low sensitivity of mammography but did not at that time quote the measured sensitivity and specificity of CTLM in clinical practice.

Methodology - In a study involving four different investigational sites in the USA (University of Virginia,

Elizabeth Wende Breast Clinic. Rochester and the Women's Imaging Centre, Orlando, Florida,) and Mexico (National Cancer Institute, Mexico City) CTLM was used as an adjunct to mammography in 705 breasts of 515 subjects. Biopsy results were available in 451 cases. 40% of these patients were characterised as having breasts of mammographic density 3, ACR categorv 'heterogeneously dense', and 43% as ACR category 4, extremely dense. 34% of the patients had a family history of

successful

breast cancer. 115 patients had nod-

1b: Post-treatment MRI shows no evidence of

angiogenesis, suggesting treatment has been

ules alone, 108 had calcifications alone, and 15 patients had both. **Results** – In these dense breast cases,

sensitivity, specificity, NPV, and PPV were as shown in the table on page 11. We believe the difference between

the two sets of results is due to the fact that the pathologically 'benign' form of DCIS shows angiogenesis in only 30% of cases, whereas comedocarcinoma shows angiogenesis in 75% of cases, an observation that might prove useful

for stratifying DCIS for treatment purposes.

1c: Post-treatment CTLM continues to show angiogenesis (red

arrows indicate normal venous drainage

arrows). Biopsy confirmed the presence of residual tumour. Blue

One of the more remarkable results specificity also improved along with sensitivity, reducing the negative biopsy rate. Using mammography alone, specificity invariably drops as sensitivity increases.

Using imaging to follow the success of neo-adjuvant therapy for breast cancer. Is CTLM more sensitive than MRI?

Paolo Belli MD, Carmen Malaspina MD and Professor Lorenzo Bonomo, of the Department of Radiology, UCSC, Policlinico A. Gemelli, Rome, discuss results from using computed tomographic laser mammography (CTLM) to detect cancers occult to mammography in of using CTLM as an adjunct was that dense breasts, and their comparison of CTLM with MRI to follow results of neo-adjunctive chemotherapy

# Buzz words: **digital mammography** Great! But is your hospital ready and able?



megabytes. Therefore, the manager of a breast screening centre that runs only 20 screenings a day needs to plan for the management of up to 4,000 megabytes (4 gigabytes) of new images daily. 'It may be possible to use lossless compression to reduce these file sizes to half or a third of their original size, but the file sizes still remain very large,' advises Christopher Varian, Director of Worldwide **Business Development Mammo**graphy Solutions, at Carestream Health Inc. 'A digital review of prior screening examinations doubles the volume of data that will need to be handled on a daily basis.'

There are, he says, some key factors hospitals should consider before they adopt a new digital



The PACS viewing tools can be customised for screening and diagnosis

**Viewing images** – Five megapixel monitors are needed for mammography, but most general radiology PACS do not have them. For this reason, screening units should consider buying new or updated orkstations to display the large file sizes of mammograms at full resolution. However, even that flat panel size does not show some image matrix sizes at full resolution – an automatic zoom and pan tool is essential if large volumes of mammograms are to be read. Rather than install dedicated workstations, centres for screening as well as diagnosis should opt for multi-modality breast imaging workstations, which enable reviews of all digital mammograms, as well as MR, ultrasound and other general radiography examinations. The bandwidth - Computer networks must be able to transmit the very large size of digital mammograms. Internal IT staff, or a network specialist supplied by a contracted vendor, can evaluate an existing network infrastructure and environment and work out what might be needed to produce acceptable image distribution speeds. 'This is an often-neglected part of an implementation,' Christopher Varian emphasises. 'In a screening facility the ability to display a full study, with priors, in a couple of seconds, will test the fastest network. If not addressed up front this aspect alone will greatly reduce the acceptance of the entire system.' Archiving – Depending on its capture device, in a year a small clinical centre, which carries out 20 screenings daily, generates around one terabyte of mammography images. Even with no increase in screenings, that means 25 terabytes of the legally stipulated 25-year image storage. 'An obvious issue here is the obsolescence of storage medium and files,' says Christopher Varian. 'A plan must be in place to migrate data on to current platforms or a major cost issue will be encountered in five to seven years

Christopher Varian

after the first images enter the system.' He points to the real advantage of using off-line data centres to manage this type of back-up and migration service. 'Most centre managers will want to factor in an appropriate percentage of growth when coming up with their anticipated storage needs for the immediate future,' he adds, advising that facilities conducting diagnostic breast examinations should also organise storage for these files.

Implementing digital mammography systems might prompt centres to expand storage devices earlier than planned. However, he suggests that a decision to outsource image storage to an image management vendor, with retrieval on demand, makes that third party responsible for maintaining, backing-up and retrieving archived examinations - beneficially freeing up radiographers' time. As said, legally examinations must be stored for years, and offsite storage and back-up in case of disasters must also be planned. Providers with existing business continuity/disaster recovery plans simply add mammographic images, but, without a plan, a mammography unit must develop and implement one, and might work with a hosted data management vendor to help develop and implement a business continuity strategy.

management options

Full field digital mammography (FFDM) and computed radiography (CR) based mammography systems may bring hospitals and breast imaging services closer to gaining digital mammography, but, according to a leading systems vendor, simply buying imaging equipment does not automatically lead to a more efficient workflow. To reap the biggest harvest from a digital system, every aspect of digital image capture, from viewing, distribution, storage and management, must be assessed before any purchase is made.

Depending on the mammoscreening equipment, the average file size of one screening procedure with a high resolution CR system could be as high as 200 the capture device, he points out.

system.

Patient and image data management and storage - For this, it is essential to fully integrate the radiology information system (RIS) and picture archive computer system (PACS). Along with the patient's identification (ID) and examination data, it is now generally understood that a RIS can automate mammography-specific activities, such as blind double reading, sending reminder letters for annual screening, producing customised patient letters for screening and diagnostic examinations and other functions.

**RIS and PACS should be installed** before installation of digital mammography or it should be part of a digital conversion. This is a far more complex task than installing

**Printing** – To share images with referring physicians, surgeons or patients, mammography units would need a high-resolution,

# breasts

MRI is being used increasingly to determine whether a particular treatment for breast cancer is succeeding and, for this purpose, has been considered the 'imaging gold standard'. However, false negatives occur and residual tumour may be present, even when the MRI study has reverted to apparent normality (Yeh E, Slanetz P, Kopans DB, Rafferty E et al. ,Prospective Comparison of Mammography, Sonography and MRI in Patients Undergoing Neo-adjuvant Chemotherapy for Palpable Breast Cancer'. Am. J Roentgenol. 2005; 184:868-8773).

Like MRI, CTLM images tumour angiogenesis in the intact breast, but it does not require ionising radiation or contrast medium. CTLM performs computed tomography with the same engineering approach, gantry and rotate/translate, as conventional X-ray CT, but replaces the X-ray tube with a laser diode tuned to 808nM, at which frequency the laser beam is selectively absorbed by both oxyhaemoglobin and deoxyhaemoglobin. CTLM utilises the body's own haemoglobin as a natural contrast medium and therefore visualises both normal blood-containing structures in the breast, veins and lobes, and abnormal vascular structures, particularly angiogenesis. CTLM, therefore, provides both morphologic and functional information. (Helbich T. 'Computed Tomography Laser

mammography-capable laser printer. They should check whether existing printers can be upgraded to that level.

Designing a system - 'Implementing a digital mammography workflow is a demanding task that can exceed the IT resources of even large facilities,' he points out. In this case, managers might decide to work on the design and implementation of an infrastructure with a vendor, or independent mammography consultant. The latter often recommends appointing a project manager with expertise in purchasing and/or integration of all necessary networking, data and management systems. To prevent outdated tasks and routines hampering the new digital system, and to optimise processes, the consultant might suggest a complete revision of scheduling, examinations and reporting. These advisors, he says, can not only help to maximise digital workflow but also help to evaluate the implementation of digital mammography technology, and to decide on

When DCIS was classified as malignant

|   | Sensitivity | Specificity | NPV   | PPV   |
|---|-------------|-------------|-------|-------|
| Mammography alone   | 50.0%       | 75.5%       | 90.9% | 23.5% |
| Mammography + CTLM  | 58.3%       | 86.8%       | 93.2% | 40.0% |
| If DCIS was classified as 'pre-malignant' the results changed slightly, as follows: |             |             |       |       |
|   | Sensitivity | Specificity | NPV   | PPV   |
| Mammography alone   | 43.8%       | 73.6%       | 93.2% | 13.7% |
| Mammography + CTLM  | 56.2%       | 84.4%       | 95.3% | 25.7% |
|   |             |             |       |       |

Mammography'. European Hospital Vol. 13. issue 3/2004; 4-5.4)

Because of its ability to visualise angiogenesis, CTLM is being tested as an imaging method for following the success, or otherwise, of neo-adjuvant chemotherapy for breast cancer.

#### Comparison between CTLM and MRI

Figure 1a and b demonstrate, using MRI, what appears to be complete resolution of a cancer of the breast following neoadjuvant treatment. However, a CTLM study made at the same time after treatment reveals definite residual angiogenesis (Fig 1c). Biopsy confirmed that

residual tumour was present. These studies are in their initial phase but, from the preliminary data, it appears that CTLM may be better able to detect residual tumour following treatment than MRI. This might be because gadolinium preferentially images areas supplied by abnormally permeable vessels, whereas CTLM, by its mode of action, images every vessel supplying the tumour, whether normally or abnormally permeable.

Other advantages of using CTLM to follow changes in angiogenesis include the speed, comfort, and low cost of an examination, the ease and speed of interpretation, and the fact that CTLM is noninterventional.

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#### [FACT]

According to a recent mammography screening study, detection rates of invasive cancer of 1.0 cm or less increased 164% and the mean age of patients was 5.3 years younger at time of detection when radiologists used R2 CAD to assist in reading mammograms.\*

either CR or DR.

Your own system – Whilst many mammography providers are evaluating digital mammography systems technical specifications and calculating a return on this investment, the managers equally should work to develop an environment and infrastructure that can support these systems.

Christopher Varian adds: 'As with general radiography, installing a CR-to-print or FFDMto-print solution offers very limited benefits, since it does not address the need to integrate these images into a digital workflow that includes automated input of patient and examination information, as well as fully featured soft copy viewing, and efficient image storage, distribution and back-up.' Combine the power of Selenia, the SecurView<sub>DX</sub><sup>ru</sup> diagnostic workstation, and ImageChecker<sup>ru</sup> computer aided detection, and you'll have a combination that can't be beat.

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> \*T. Cupples, J. Cunningham and J. Reynolds, "Impact of Computer Aided Detection in a Regional Screening Mammography Program," AJR: October 2005, 185:944-950



During the recent American Society of Clinical Oncology (ASCO) congress, the paper of **Professor Christiane K Kuhl** and her colleagues has been selected as 'Best of ASCO', for they had discovered that, to detect pre-invasive breast cancer (DCIS), the addition of high-resolution MRI and state-of-the-art mammography offered a significantly higher sensitivity compared with state-of-the-art mammography. **Dr Kuhl** is Professor of Radiology and Vice Chair at the Department of Radiology, and Director of the Division of Oncologic Imaging and Interventional Therapy at the University of Bonn.

# Why MRI should not be a health-political decision

hen European Hospital asked Prof. Kuhl why the University of Bonn was cited by her Discussant at ASCO to carry out the most breast MRI examinations in, perhaps, the entire world, she said it was possibly true, explaining: 'We have a very good team here and we have reserved one MR system more or less for breast examinations. Bonn also has a large, supra-regional catchment area. Many women - some who might have a known risk of breast cancer in the family. - come to us of their own

family - come to us of their own accord – for example, if they have had MRI examinations elsewhere and the results are not clear. 'I'm often asked what radiologists

should do to achieve results on a par with those we have in Bonn. The answer is quite simple: Radiologists should carry out more breast MRIs. Unfortunately this procedures is not utilised enough as the medical insurers quite often refuse to cover it, because they say it's too expensive! Magnetic resonance tomography did not arrive yesterday. It is an examination procedure that many areas of modern medicine can no longer do without. Think about orthopaedics or neurosurgery, for instance. MRI is of great importance in those fields. It has also been known for some time that MRI is the most sensitive examination procedure for the diagnosis of invasive breast cancer.

'With MRI you play in an entirely different league compared with conventional mammography or ultrasound. This has been known for years. However, as the procedure is expensive, so far MRI has mainly been used in a "targeted" way, i.e. when a patient has already suffered breast cancer and then later receives results from an X-ray mammography or ultrasound scan that are not quite clear. Then, and only, then, is the breast MRI covered by Germany's statuary medical insurers - apart from a few other, still rare indications. 'However, the medically meaningful, or possibly even more important, potential areas of use, such as preoperative staging or early detection are not covered. Staging means that if a type of breast cancer is detected by mammography or ultrasound, which is to be treated by breast conserving surgery (bearing in mind that over 80% of women are treated with breast-preserving procedures) then an MRI should be carried out prior to the operation to map the actual spread of

Professor Christiane Kuhl is no stranger at Bonn University, for it was there that she studied medicine and became a doctor. (In 1991, her thesis 'Magnetic Resonance spectroscopy in mitochondrial encephalomyopathies' was judged summa cum laude.) Indeed, her radiology residency was in the same department where she is now professor.

Before becoming Full Professor of Radiology and Vice Chairman of the Department, Prof. Kuhl also worked in the Neurosurgery Department, and she undertook neuro-interventional training in the Department of Neuroradiology in Duisburg, for certification as a neuroradiologist, and a Fellowship in Neuroradiology.

Her numerous awards include one for technical innovation from the German Federal Ministry of Science and Education; others from the Radiological Society of Germany and, beyond there, the American College of Radiology Imaging Network (ACRIN) award for 'Outstanding Contributions', and the European Magnetic Resonance Award 2006. In the United Kingdom, the Royal College of Radiologists Breast Group made her an Honorary Member.

the tumour. This use of breast MRI – staging – is not yet covered by medical insurers in Germany as standard, which I consider scandalous.

'The consistent use of MRI prior to surgery for breast cancer would have a significant impact on the treatment management for around 25% of patients. Breast cancer is a type of oncological disease where the surgical approach is curative, which is quite rare in oncology. And, of all things, it is just this situation where MRI cannot be used. However, it is used regularly in almost all other areas of oncology, such as, for instance, in patients with pancreatic carcinoma, which are rarely approached in a curative manner. This is a contradiction!'

Why? 'Cost is one factor. Breast cancer occurs much more often than c cancer. Secondly, the breast MRI only helps us in this situation when we can verify the MR diagnoses histologically for the surgeon and mark the area for surgery. Radiologists have quickly internalised and started to use the biopsy procedure for X-ray mammography, or ultrasound, and also the vacuum biopsy. But people still seem to shy from MRI-controlled biopsies - although they are no more complex than mammotome biopsies (particularly with the modern VAB systems, such as the Suros system). The problem again is that MRI can be used only infrequently, which essentially makes systems for MR guided procedures less profitable. The chronic under-usage of this examination procedure is therefore both the result and the cause of the current situation. Medical insurers

don't pay for it because the procedure allegedly produces too many wrong, positive results, therefore radiologists cannot use it - and then, if the procedure is actually used once in a while, results are insufficient and nobody is able to confirm these additional results adequately and in a minimally-invasive manner, which, quite rightly, leads to irritation and uncertainty among surgeons. In turn, this damages the reputation of this procedure and strengthens the insurers' perception that it is expensive and unsuitable – which is why it is not covered. That's how the cycle closes - and has done for years.

'There is a further issue: Radiologists specialising in breast examinations use mammography and ultrasound almost exclusively and therefore have great expertise in this area - they specialised in this at a very early stage. They have few or no points of contact with MRI. To them, MRI is like an "exotic animal". This unsettles them. Whenever I say: "MRI should be carried out as standard as part of any breast-preserving therapy," all I hear from the mammographers is "But who is going to pay for this?" And this is despite the fact that we are looking at one of the - if not the most extensively researched area of application for MRI in terms of clinical relevance. If these mammographers were to spend just one day in an MRI department they would be amazed at what is being examined with MRI these days, without "costs" being raised - for example, MRI of the spinal lumbar region, for which we know there is

little clinical relevance and which has little impact on therapy management for these patients.'

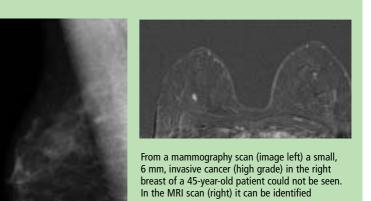
This is changing increasingly in the USA, she pointed out, there breast MRI is seeing enormous growth rates. Guidelines from the American Cancer Society stipulate that all women with a lifetime-risk of only 20% are to receive a breast MRI for early detection. 'This goes even further than the data currently available would call for,' said Prof. Kuhl. 'These data, a not insignificant proportion of which was collected in Bonn, state that women who are at higher risk due to the disease having familial history, should receive an annual MRI for early detection. And a risk of 20% is reached guite guickly.

'In future, all those women in the US will be examined with MRI for considered, even though this procedure is more or less a German product, and despite the fact that the data on which the recommendations are based originated mainly here and Europe. At the same time we know from new data from the DMIST study, carried out by Etta D Pisano, that the medium sensitivity of mammography is between 40-50%, i.e. out of 10 women suffering from breast cancer only 4 or 5 are actually detected, the rest are sent home as healthy, because mammography cannot visualise these cancers.

'For women who are at average risk, we don't know what the comparative sensitivity rate with screening MRI is, as yet. But the sensitivity of MRI for screening women at increased familial risk has been twice as high or, in some cases, more, up to three times as high as mammography, in all published studies. Breast MRI has a sensitivity of over 90%, mammography of 33-40%, combined with ultrasound this increases to 45-50%. By the way, this corresponds with data from the DMIST study - the only mammography study that has actually validated its data. Since our first publication in 2000, over 10,000 women have been examined, and more studies have been published in high-quality journals (NEJM, JAMA, The Lancet etc.). The results are surprisingly concordant: MRI is far more efficient than mammography and ultrasound - also for women who are only at moderate risk of developing breast cancer.'

Asked whether these convictions could mean the end for an entire industry, Prof. Kuhl replied: 'I wouldn't put it quite that way! Mammography definitely has its place, and we should also not say we want to carry out only MRI. But what we want to be able to do is to also carry out MRI. It cannot

early detection. But, in Germany, MRI for early detection is not being



be right that, in 2007, a

mammography screening project in Germany - for many millions - is based on technology delivering this level of sensitivity – using technology with well-known limitations. About 40 years ago, when screening projects began in Scandinavia, there was no other technology available. Today, we know all the mammography figures, they are on the table. Mammography cannot visualise many carcinomas due to limitations inherent in this procedure, not bad technology or because a radiologist lacks training. Even with the best technology and highest radiological expertise, certain carcinomas cannot be detected for purely physical reasons, because they are embedded in dense glandular tissue. We have known for some time that ultrasound can counterbalance some of mammography's shortcomings, but we should assume that MRI can do this even better. Therefore we must invest in this procedure - in order to make it ready for use in screening.

'We have known for quite a while that MRI, compared with mammography and ultrasound, is better for diagnosis of invasive breast cancer. However, people have said for years that MRI cannot visualise prebreast cancer stages - intraductal carcinoma or ductal carcinoma in-situ (DCIS). It was thought this was the sole domain of mammography. To explain this in more detail: Most breast cancers - 80-90% - develop in cells that build the inner lining of the milk ducts. There is a phase in almost all cancers where real tumour cells are already present, but where they remain in the milk ducts for a certain period of time. Therefore the term ductal carcinoma in-situ is used.

'At this point we are formally talking about cancer cells. Biologically though, for the patient the situation is still benign, because the cells are surrounded by the walls of the milk ducts and have no connection to blood or lymph vessels. At this stage breast cancer is therefore always curable.

'If you find breast cancer at this insitu stage this can be considered the "Holy Grail" of early detection. Prior to mammography, DCIS was not diagnosed prospectively, but was virtually always an incidental finding made at pathology. Since the introduction of mammography, around a fifth, i.e. 20% of carcinomas at the in-situ stage have been diagnosed, which is a reason why early detection with mammography works. As microcalcifications cannot be visualised via ultrasound or MRI, it was assumed that the diagnosis of insitu carcinoma is possible only with mammography. In fact, in-situ carcinoma can be visualised very well with MRI, they just look different to invasive carcinoma.

'We know that in-situ carcinoma can be divided into two categories:

mammography was 51%, MRI was 92% - figures that are clearly in favour of MRI. Mammography was particularly insufficient to diagnose high-grade in-situ carcinomas: it could not detect over half of the high-grade DCIS – because they had not developed any calcifications!

'It appears that a relevantly high proportion of the in-situ carcinoma does not calcify, so mammography cannot detect it. I said earlier that 20% of all diagnosed carcinoma are in-situ carcinomas. But we know that almost all carcinomas go through this stage – so what happens with the rest? We must assume that MRI will enable us to detect more carcinomas at this early stage, particularly the high-grade carcinoma.

'Basically, unlike what was previously believed, MRI is superior to mammography also for the preinvasive stages, the in-situ carcinoma. For the non high-grade in-situ carcinoma both procedures are complementary. For the high-grade insitu carcinoma they are not complementary – MRI is clearly superior.

'One of my favourite assumptions (but which cannot be proved) is that the perhaps 10% of DCIS that cannot be detected by MRI are not biologically relevant – because they are not preparing to invade and might never become invasive. For invasive growth, the DCIS requires vessels that deliver nutrients and oxygen. When those vessels are present MRI can detect the DCIS, so quite possibly we can see all those carcinomas that are preparing to invade. If we want to detect breast cancer at an early stage then, quite clearly, we want to detect it at the in-situ and early invasive stages. And we certainly want to find the high-grade carcinomas. If we know that the examination we currently use for early detection mammography - can only find half of

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the invasive and intra-ductal carcinomas, then the logical consequence is obvious.

'Logically, the next question would be whether we will use MRI for screening. Currently we cannot do this, because we still have to gather more data, because we must define exam standards and must establish a quality assurance analogue like that used in mammography, along with training radiologists etc. And even if all this will be settled - using MRI for screening will be expensive. Whether or not we, as a society, want to make this investment is a political, not a medical question.

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High-grade and non-high-grade. Nonhigh-grade means that carcinomas are dormant for years and possibly never turn invasive. Of the high-grade ones we know essentially that they always become invasive and that the intraductal phase is very short. The high-grade, i.e. G3 invasive carcinoma are very dangerous indeed. Therefore, it's essential to detect them at the insitu stage – once they grow invasively, the race is on.

'The interesting feature of our data is that, very unexpectedly, MRI has proved not only on a level with mammography in the detection of insitu carcinomas but, in fact, significantly superior – particularly in the diagnosis of high-grade in-situ carcinoma. In the detection of 167 insitu carcinomas the sensitivity of

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MAMMO-UPDATE 13

Italy – One of the biggest RIS/PACS implementations in Europe is being co-ordinated the Area Vasta Centro (AVC) group, which runs 12 hospitals in central Tuscany. Among these, CPA Pistoia hospital (one of three in the ASL 3 Pistoia group, a sub-\_\_ division of AVC) is streamlining its mammography workflow with a CR Mammography system supplied by Agfa HealthCare. 'We needed a mammography solution that provided superior image quality, was easy to learn and use, and due to the Tuscan Medical Technology (TMT)



# Hospital group streamlines screening

project, integration with other hospital systems and hospitals is also important. The Agfa HealthCare system met all of these criteria with ease. At the end of this year, we will integrate with other screening centres in our region,' said Dr Patrizio Pacini, Head of Senology at Pistoia hospital

CPA Pistoia conducts about 10,000 breast screenings annually. An additional 5,000 exams are performed at the Ospedale del Ceppo - also within the ASL 3 Pistoia hospital group. The mammography team at CPA Pistoia includes two doctors and three technologists.

The CR Mammography system was developed so that radiologists can use CR systems in mixed environments, for general radiology and mammography applications. According to Agfa, the solution, comprised of the CR 85-X digitiser, the NX 2.0 Workstation for Mammography and the Drystar 4500M, has proved itself ...a perfect fit for this busy mammo-screening unit'. The NX 2.0 Workstation for Mammography

includes image identification and quality control software tools, and has a touch screen. 'The intuitive interface of the NX workstation simplifies the standard tasks of our technologists,' Dr Pacini pointed out. 'It streamlines . both the exam and image processing procedures."



# **3D USCT nears reality**

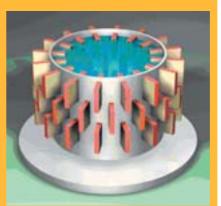


Hartmut Gemmeke

Back in the 70s, when scientists first speculated on the development of 3-D ultrasound computed tomography (3-D USCT) the available technology could not equal their dreams. Now, before the end of 2007, a prototype at Germany's Karlsruhe Research Centre will be used for the first in-vivo tests. EH reporter *Meike Lerner* asked **Professor Hartmut** Gemmeke, Head of the Institute for Data Processing and Electronics, at the Centre, and one of the developers of 3-D USCT, why such a prototype has taken so long to create, and what it might achieve

"Our prototype currently works with 1,600 ultrasound sensors implementation with that many sensors, using conventional sensor technology, would have been too expensive. So, first we had to develop effective but cheap sensor technology. Then again, the amount of data generated by a 3D ultrasound CT image is a problem. In mammography, the amount of data we receive, per image per breast, if left uncompressed would fill 32 CDs. Reconstructing this image from the measured data would take an average PC about a month. That's where we were dependent on the development of appropriate algorithms and hardware. Around five years ago we finally realised that technology had advanced to a stage where it was feasible to contemplate the idea of 3D USCT again.

Now we are at the stage where we have carried out the first tests with nylon threads of



During a 3-D USCT scan, the patient lies face down on a couch. The breasts hang through a cutout space in the couch. The USCT cylinder, filled with body-temperature water is directly below, so the breast can be comfortably positioned inside it. Thus the painful squashing experienced in traditional breast scanners is eliminated. Another advantage to USCT: no radiation exposure.

The surface of the cylinder has sensors (currently 1,600 in the prototype, but the hope is to increase this to 1,900). Each sensor in turn sends a signal, which the other sensors receive, so a view is obtained from every direction and then assembled into a 3D image.

Medicor

0.15mm, which were very successful. By the end of the year we will be able to test the sensitivity of this method for mammography in the first in-vivo tests.

The conditions are promising: On the one hand we'll be able to screen the breast from all sides, so therefore avoid shadowing effects. On the other hand the breast is not squashed, so that we will be able to locate growths and tissue changes in the 3D image as well. We expect to be able to detect tumours of less than 5mm. Moreover, this method will deliver reproducible images, which will also facilitate functional diagnostics. Compared with conventional ultrasound, 3D USCT not only measures reflections and reductions but also the speed of sound and frequency shifts. Because of the many sensors that are directed towards one picture element, the speckle noise typically produced with ultrasound scanning is extremely reduced, which is a further advantage.

Therefore, 3D ultrasound CT offers possibilities to show all modalities together in one image and this means we'll probably be able to obtain information about the disease pattern of breast cancer at a molecular level. We've carried out first examinations with tracers, which can then be seen in 3D via ultrasound; however, this method is still in its infancy and we cannot yet say much about the sensitivity. However, if our expectations are confirmed, this would mean we'll be able to detect and quantify breast cancer in its verv early stages.

Therapeutic use via hyperthermia is a further vision we have for 3D



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MAMMO-UPDATE 14

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# **Ireland** Pulling into Europe's fast lane for digital screening **Scotland** Under-funding, and clinical standards in breast cancer services are 'under review' By Brenda Marsh

In 2004, Ireland's health service recognised the need to serve the entire country through the Irish government-funded National Breast Screening Programme, BreastCheck. To provide a breast screening service at the highest possible level the usual procedures were necessary - funds had to be gained; equipment analysed; requests for tenders issued; evaluations made and finally contracts would be awarded then confirmed. Six companies tendered quotes. And now, 29 state-of-the-art mammography machines manufactured by GE, Hologic and Sectra - are about to make Ireland one of the first European countries to provide a fully digital, state-of-the-art breast screening service.

GE Healthcare is to supply thirteen Senographe Essential fullfield digital mammography (FFDM) machines, six of them for mobile units. (Within the total, two of the mobile units are from a previously awarded contract).

Ireland's rural roads are certainly a consideration for mobile units. Machine robustness is essential. Following 8,000 km vibration impact tests across the country, '... radiographers concluded positively on the digital equipment and workflow in the new mobile environment,' commented Niall Phelan, Chief Physicist of BreastCheck.

#### In Ireland, breast cancer is particularly virulent: 18.5% of all cancer related deaths among the women are due to breast cancer

Hologic has been contracted to supply nine of the 29 FFDM systems ordered by BreastCheck. Six will be the firm's Selenia FFDM mobile system, one a Selenia base system, and the order includes two MultiCare Platinum breast biopsy tables. 'We expect more new orders to follow,' says Hologic.

Outside of the new award from BreastCheck, Hologic already has at least one Selenia system installed and running within the Irish service, the company reports.

Sectra has been contracted to supply seven units to BreastCheck. In 2005, this screening programme began to evaluate the firm's MicroDose Mammography system, '...which is based on a unique photon-counting technology - a technique that an increasing number of experts point to as the radiology technology of the future,' Sectra reports, adding that they system also delivers the lowest radiation dose on the market.

Along with other manufacturers' equipment, it will be linked to the existing PACS, and the comprehensive digital infrastructure is expected to go into operation by the end of 2007. 'We've been pleased with the reliability and image quality of the Sectra systems and expect them to perform just as well in the more demanding environment of mobile screening trailers in which a number of the new systems will by used,' Niall Phelan said.

Following all the processing necessary in procurement, Niall Phelan confirmed that BreastCheck will be 'one of the most advanced screening services'. Wouldn't it have been easier and perhaps quicker, I wondered, to obtain equipment from just one company? Would this be like putting all one's eggs in one basket? 'All systems have their advantages and disadvantages,' Niall Phelan explained. There is also the question of ensuring that if one machine goes down for any reason, and must await servicing, the rest keep operating; after service will be critical to keep such a large and comprehensive service out and about on Ireland's roads.

BreastCheck - Working with a multi-disciplinary team of specialist clinicians, radiographers and breast care nurses, and including mammography, diagnosis and primary treatment, BreastCheck provides a free breast screening service to eligible women by personal invitation every two years. The programme screens systematically on an area-by-area basis - each service area reflecting electoral divisions.

Currently the service provides screening to women in the northeast, east, midlands and parts of the south east of the country through two static units (the Eccles Screening Unit, near Mater Misericordiae University Hospital and Merrion Screening Unit near St.Vincent's University Hospital) and a fleet of mobile units. In 2005, BreastCheck invited 78,945 women for screening; 59,443 women attended appointments, the service reports. Now, BreastCheck is expanding nationally to cover women in Ireland's south and west. The screening programme will be extended nationwide and the target date for commencement of expansion programme is by the end of autumn, this vear.

A Southern screening unit is being built in Cork, on the campus of South Infirmary Victoria Hospital and a Western screening unit will be located at University College Hospital, Galway. These units, plus a fleet of mobile units, will provide screening to the rest of the country.

Following this national expansion of the screening programme the upper age limit will be extended to women aged 69, in accordance with the European Council's recommendation.

#### Scottish woes

Last September news broke that, despite advice from its Breast and Cervical Screening National Advisory Group, Scotland's National Health Service (NHS) would not fund a £20 breast-screening test, which, according to oncologists, could have detected around 430 more tumours annually and saved dozens of lives. The result for other women was mastectomies that would have been avoidable if the breast cancer had been detected earlier.

By imaging women from just one angle, rather than two, the Service saved £20 per patient. The Advisory Group had recommended the introduction of a 'two-view' mammography programme, and even advised it would be cost-effective.

In 2004, the amount spent on the country's breast screening programme was £10 million. A further £2 million would have been needed to provide dual X-rays to the 121,000 women, aged 50-70 years, invited for screening each year.

It was said that although the NHS recognised the benefits of twoview mammograms, funds were being stretched to introduce colorectal cancer screening. The result was that, during a first screening, Xrays were taken of the woman's breast from above and the side; but in subsequent screenings the image was taken only from the side.

Many oncologists expressed concern that Scotland did not do what is being done just south of the border in England.

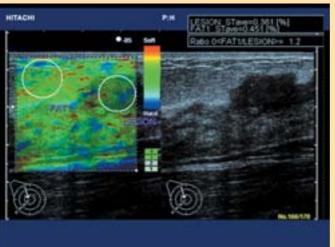
In Scotland breast cancer kills over 1,000 women annually. Although 2003 figures indicate that around 1,800 breast cancers were detected there during screening, more recent figures show that only 78.5% of cancer patients were treated within two months of an urgent referral by their general practitioner (GP) - well below a 95% target.

#### Scotland upgrades to two-view

In February this year, the Scottish Executive announced that the breast screening programme would be upgraded, to use two-view mammography.

# **Tissue elasticity reveals tumours**

When equally compressed, the tissue and structure of tumours and inflammations are harder than normal HITACH LESION STANSTO MIL INI tissue. Hitachi explains that, taking advantage of these alterations, the sono-elastography technique conducts real-time measurements of elasticity ratios during minor pressure to the breast, using conventional ultrasound transducers. The results are colour-coded and overlaid on the conventional breast image for evaluation through various logarithms. No additional equipment or particular transducers are necessary; only a software add-on module - Hitachi SonoElastography for the Hitachi EUB-8500, the company adds - to evaluate the shifts between the individual images in consecutive ultrasound recordings and indicate, via colour-coding, the alterations in expansion and determine the site. 'This enables differentiation of tumour tissue from healthy tissue, and of malign tumour tissue from benign tumour tissue.' Hitachi adds. 'Unlike conventional ultrasound procedures, sono-elastography measures larger scale shifts only in one compression phase without pseudo artifacts." This additional information about the visco-elasticity of breast tissue significantly increases the rate of breast cancer detection, Hitachi continues. 'Clinical studies conducted so far have shown that, with sono-elastography, lesions can be visualised safer and faster than with conventional 2D procedures; visualisation is even possible with the lesions that are undetectable with conventional breast image sonography." Full details: http://www.hitachi-eu.com

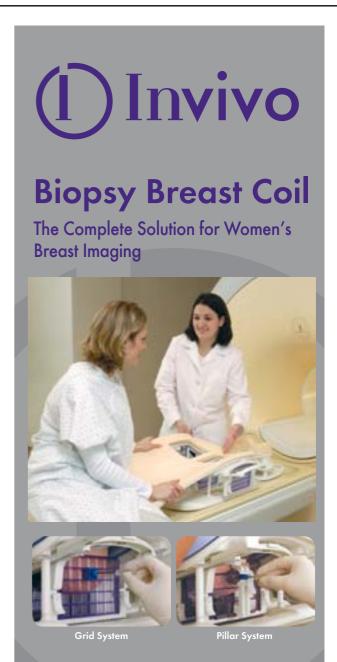


Recalled patients - After examining medical records of 1,600 patients over a previous 18-month period, 198 women being treated for suspected breast cancer at Inverclyde Royal Hospital, in Greenock, are being recalled by the health board to be re-examined because they had not received the required mammography or ultrasound and biopsy in addition to the standard clinical breast examination.

A full review of breast services at the hospital has been ordered by the NHS Greater Glasgow and Clyde, whose CEO, Tom Divers, said the differences in standards between Inverclyde and other breast clinics in the area first emerged during an audit of breast cancer care. 'This highlighted that, when compared to other centres, a lower percentage of patients seen at Inverclyde had diagnosis confirmed before surgical intervention. Further interrogation of these results has now identified that some patients did not receive the full range of appropriate tests when being assessed for suspected breast cancer. This has prompted us to launch a full review of practices at those clinics.

No other clinics within the Greater Glasgow and Clyde area are affected.

Health Secretary Nicola Sturgeon said she would carefully monitor the board's actions. 'All the lessons learned will be shared with NHS boards across Scotland,' she added. 'I am also asking NHS Quality Improvement Scotland to accelerate completion of the current review of clinical standards for breast cancer services, which are already in process of being updated in the light of advances in clinical knowledge and techniques.'



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MAMMO-UPDATE 15

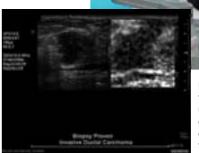
# New technology to reduce biopsies

Although about 75% of biopsies are negative, the side effects of that invasive procedure, plus the length of time to results, disturbs patients. Now, however, a new technology might be able to differentiate benign and malignant tissue due to an adjunct of a normal breast ultrasound examination.

eSie Touch Elasticity Imaging, a new software from Siemens Medical Solutions, has become available with the firm's 5.0 release of the Acuson Antares ultrasound system. Using this application, physicians can generate an 'elastogram' to obtain additional information about mechanical properties, such as the stiffness of breast lesions. (Generally, just a patient's heartbeat and respiration provide sufficient movement to generate an elastogram).

Several studies involving this method are showing 'promising success', Siemens reports. 'In a recently published American study, 80 patients with a total of 123 suspicious lesions were examined using the elasticity measurement. 18 lesions were classified as malignant, which was confirmed in 17 cases by a biopsy. Of the 105 lesions predicted as benign, all were also proven so by biopsy. Results are now being validated in comprehensive studies in Europe.'

Of course, the ability to visualise tissue elasticity could not replace biopsies in general, Siemens agrees. However, the firm adds, there is reason for hope that this method might reduce the number of unnecessary breast biopsies.



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#### gathering of cancer specialists told: Mammography is still key to survival Rapid diagnosis and treatment are the keys to breast cancer survival

the keys to breast cancer survival – and an elastogram mammography continues to play a central role in breast cancer detection according to research presented recently in Chicago, at the 43rd Annual Meeting of the American Society of Clinical Oncology (ASCO), writes lan Mason.

In abstract number 6589, chillingly titled 'Killing time: Treatment delay and breast cancer survival' Dr Sheinfeld Gorin and Colleagues (Columbia University, New York) tracked 43,359 females, aged 65 and older, who had been diagnosed with breast cancer between 1992 and 1999. Women who had over a threemonth delay in receiving treatment had a 34% increased risk of breast cancer death, compared with women with delays under three months.

The continuing importance of mammography was underscored by data from a study of over 1,000 women [abstract 17033] showing that those diagnosed via mammography/ultrasound had higher survival rates compared with women diagnosed via breast selfexamination and clinical breast examination, irrespective of disease stage at diagnosis.

Dr C. Kuhl, and colleagues, University of Bonn, Germany [abstract 1504] found that the addition of high-resolution MRI and of state-of-the-art mammography offered a significantly higher sensitivity (compared with state-of-the-art mammography) for detecting high risk pre-invasive breast cancer (ductal carcinoma in situ [DCIS]).

Another large study of more



than 15,000 older women, aged 80 and older, who had been diagnosed with breast cancer between 1996-2002 [abstract 9039] found that even in this age group, regular mammography was associated with earlier stage at presentation and smaller tumour size compared with mammography non-users. 'Health care providers should consider discussing potential benefits of screening mammography with their older patients,' the authors concluded.

Other presentations showed that mammography can be used successfully to target groups who fall through the screening net, such as ethnic minority women [abstract 17020] via the targeted use of bilingual community breast liaison nurses.

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