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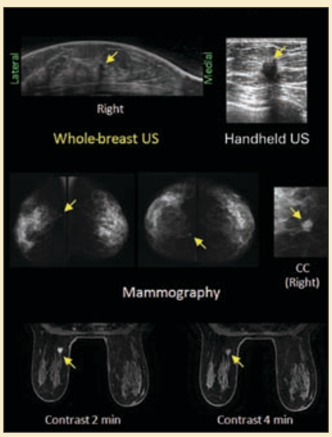
WINTER 2010

DIAGNOSTIC IMAGING ASIA-PACIFIC

The Newsmagazine of Imaging Innovation & Economics

A special region-specific publication from the editors of *Diagnostic Imaging*



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MODALITY COULD HELP AVOID LIFE-SUPPORT ERRORS BY DETERMINING COGNITIVE STATUS AFTER BRAIN INJURY

fMRI indicates cognition in unconscious patients

Using functional magnetic resonance imaging, researchers in the U.K. have gained a better understanding of what goes on in the minds of patients who have sustained severe neurological damage.

According to investigators, fMRI could yield evidence that patients might be fully aware even when the clinical assessment suggests they are comatose.

Clinicians typically infer whether patients with brain injury are conscious based on their behavior. However, recent studies indicate that 40% of patients who seem behaviorally unresponsive are, in fact, in a minimally conscious state and are erroneously diagnosed as being vegetative.

Such mistakes could have huge medical, ethical, and even legal consequences if they lead to termination of life-supporting therapies, said principal investigator Martin M. Monti, Ph.D., a research scientist for the U.K. Medical Research Council and Brain Sciences Unit, a University of Cambridge research partner institution.

Monti and colleagues enrolled 20 healthy volunteers and one minimally conscious patient diagnosed with anoxic brain injury in 2007. Subjects underwent imaging while instructed to listen to a sequence of words first and then count the number of times a key word was heard. All showed activation of neural areas governing target detection and working memory while performing the

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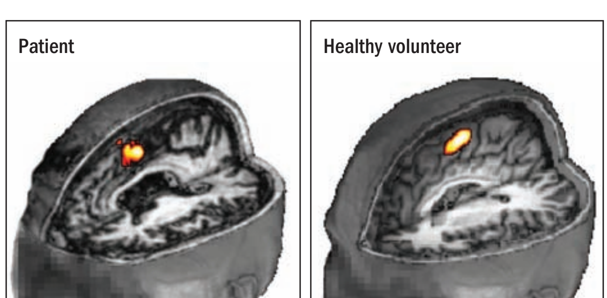

Superimposed fMRI data reveals activation pattern in minimally conscious patient nearly matches the pattern from a fully conscious, healthy volunteer. (Provided by M. Monti)

Disaster survivors show early signs of traumatic stress

An international research team has established the Wenchuan earthquake on May 12, 2008, exacted a toll beyond the nearly 70,000 deaths and 374,000 casualties from the magnitude 8.0 temblor.

Brain scans uncovered stress-related changes in the brains of survivors that suggest the alterations of cerebral function associated with post-traumatic behavioral disorders not only emerge progressively over years, but are also evident within days of the traumatizing event.

Dr. Qiyong Gong of the Huaxi MR Research Center and University of Liverpool led imaging scientists from China, the U.K., and the U.S. to perform whole-brain, resting-state fMRI on 44 adult quake survivors. The studies were performed within 25 days of the disaster.

Compared with control subjects, the survivors showed significant hyperactivity in the prefrontal and striatal systems and the presupplementary motor area (pre-SMA).

The prefrontal-limbic and striatal systems are important for emotional processing and play a critical role in anxiety disorders, including post-traumatic stress disorder, because of their importance for the recollection of traumatic memories and the processing of fear and pain, according to first author Dr. Su Lui. The striatum and pre-SMA are activated when decisions are made under time pressure.

The study was published in the *Proceedings of the National Academy of Science* (2009;106[36]:15412-15417).

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BY GOBERT N. LEE, PH.D., DAISUKE FUKUOKA, PH.D., TAKAKO MORITA, M.D., PH.D., AND HIROSHI FUJITA, PH.D.

Whole-breast ultrasound brings significant screening benefits

The high incidence of breast cancer in younger Japanese women poses problems for mammography-based early-detection programs

Breast cancer is one of the leading causes of cancer death among women. The risk of breast cancer typically increases with age in most countries. The chief exception is Japan, where the incidence of breast cancer increases in women aged 30 to 50 years old, peaks at the age of 50, and then declines.[1]

Early detection can improve cancer survival and simplify patients' treatment. This has led to the introduction of screening programs in many countries so that signs of breast cancer can be detected at an early stage.

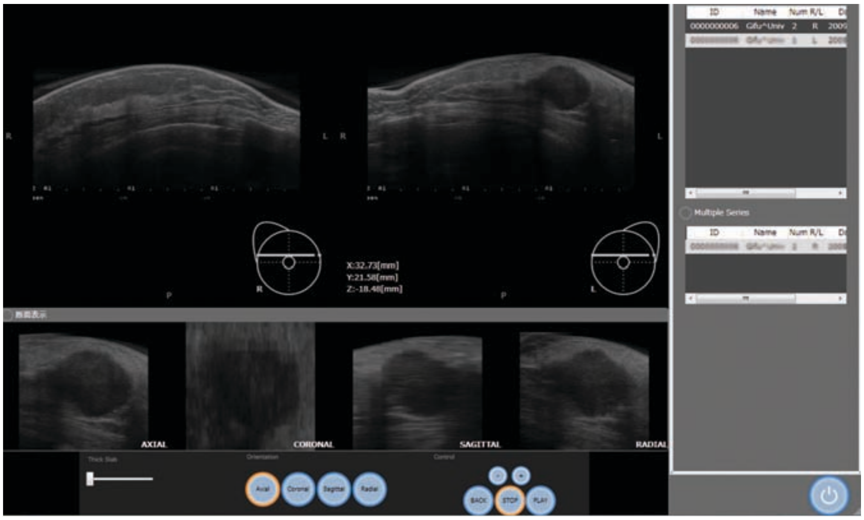

FIGURE 1. Whole breast ultrasound viewer showing bilateral axial views. Breast anatomical structures are easily identified, making bilateral analysis feasible.

Mammography is currently used routinely in population-based screening programs to check for signs of breast cancer in women aged 50 years and older. The technique is relatively simple, cost-effective, and has been shown to reduce mortality by more than 20%. Some studies show a reduction in mortality of up to 30% or even 40%.[2-5]

The sensitivity of mammography is, however, lower in younger women and in Asian women. Women in these groups tend to have dense breasts, but inherent limitations in mammography limit its ability to depict masses in dense breast tissue. This poses a significant problem to breast screening programs in Japan. Not only do Japanese women tend to have dense breast tissue, but the incidence of breast cancer is also higher in younger Japanese women, particularly those in the 40- to 49-year-old age group. This has prompted manufacturers and government authorities to seek out a more suitable imaging modality, or combination of modalities, to deliver breast care in Japan.

Interest in breast ultrasound has increased steadily and it is now considered a valuable adjunct to mammography. Ultrasound is effective at imaging soft tissues in the body, using the transmission and reflection of sound waves. The modality does not rely on x-ray absorption differences to generate detail in images and so its ability to depict masses is not limited by dense breast tissue.

Ultrasound imaging has suffered in the past from poor image quality, limited detail recognition, and low spatial resolution. Advances in ultrasound technology have allowed remarkable improvements in image quality and the modality has been greatly enhanced. High-resolution ultrasound can now provide an excellent, real-time depiction of anatomic details in the breast.

The use of ultrasound in characterizing breast masses was traditionally limited to differentiating fluid-filled cysts from solid masses, an important but limited role in breast cancer detection and diagnosis. Additional roles for

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Assisting in the preparation of this manuscript were Dr. Chisako Muramatsu, Dr. Yuji Ikedo, and Dr. Takeshi Hara, all from Gifu University; Prof. Etsuo Takada from Dokkyo Medical University School of Medicine in Tochigi, Japan; and Dr. Tokiko Endo from the National Hospital Organization at Nagoya Medical Center in Nagoya, Japan.

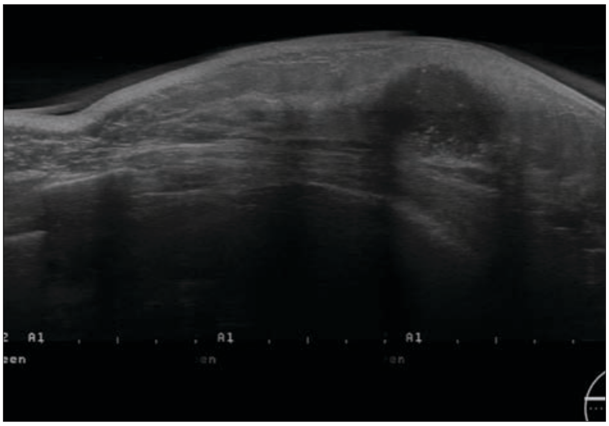

FIGURE 2. MIP breast ultrasound image, constructed from a 25-mm-thick slab, containing a 3-cm malignant lesion. Calcifications in the cancer are seen clearly.

the modality are now being developed, thanks to improvements in breast ultrasound technology. These roles include breast assessments for younger women, women who have less fatty breasts, women who are undergoing hormone replacement therapy, women who have breast implants, and Asian women.

This expansion in the role of ultrasound has prompted the development of whole-breast ultrasound systems. Such systems generate images that depict the entire breast, unlike conventional images that show only small regions.

Breast ultrasound examinations are typically performed by clinicians or sonographers using a small handheld probe (typically 4 cm across). Examination times vary significantly according to the size of the breast and its fat composition. An examination will typically take 15 to 20 minutes in Japan, and up to 45 minutes in Western countries. Most of the time, both breasts are examined in Japan; this examination time assumes bilateral examination.

Although freehand breast ultrasound is a valuable tool for breast cancer detection and diagnosis in the hands of experienced clinicians, results are highly operator-dependent. Some regions of the breast may be missed from the scan altogether, raising the risk that a cancer could go undetected. The reproducibility of freehand ultrasound images is also poor. Images acquired have a limited field-of-view (typically 5 x 5 cm) and do not provide full-field images of the breast. This suggests that freehand ultrasound is not sufficient for whole-breast ultrasound imaging.

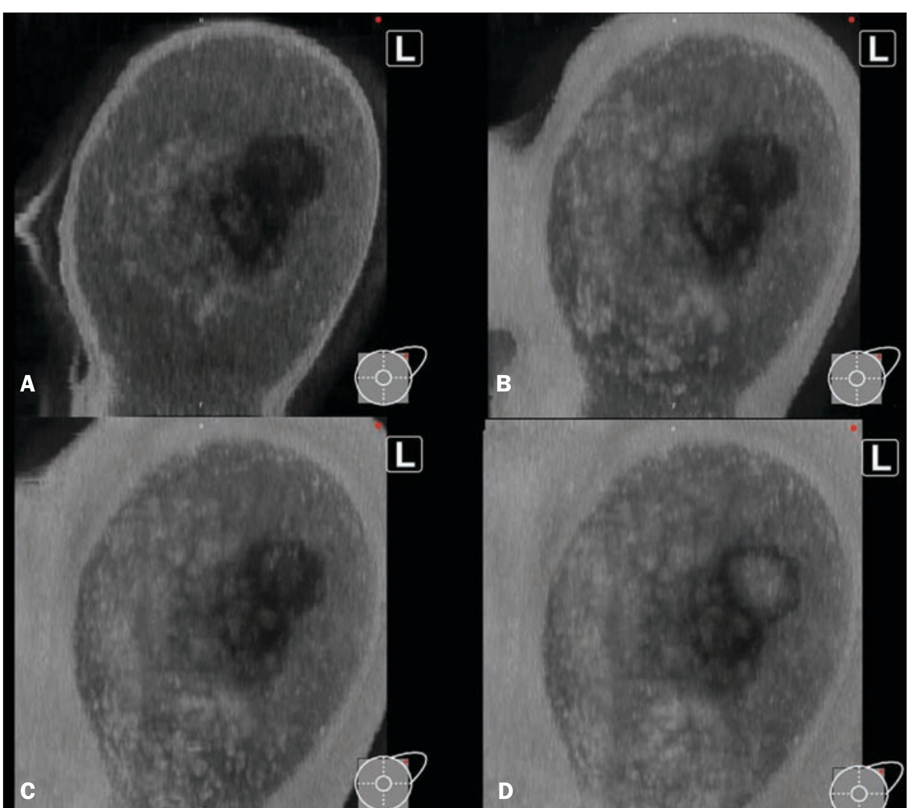

FIGURE 3. Volumetric data reslicing can help to characterize and assess extent of cancerous lesions. A: Coronal view, single slice. B: MIP of a 5-mm-thick slab. C: MIP of a 10-mm-thick slab. D: MIP of a 20-mm-thick slab.

WHOLE-BREAST IMAGING

One example of a dedicated whole-breast ultrasound scanner is the Automated Whole Breast Ultrasound Scanner ASU-1004 by Aloka. The device was developed specifically for breast cancer screening in Japan to address the issues outlined above.[6]

The device comprises a water tank and a 7.5-MHz, 6-cm linear transducer submerged in the water. The breast is positioned on top of a membrane stretching over the water tank and enclosing the water, and a scan is taken from below by the underwater probe. Original scans are acquired in the axial plane, with the probe running in three overlapping sweeps and covering a scan field of 16 x 16 cm.

Patients undergoing conventional breast ultrasound imaging are often positioned while lying on an examination bed. This patient preparation procedure can be a factor in the throughput rate in a screening environment. The positioning procedure used with the ASU-1004 scanner is quite different. The patient stands up and bends forward, as if she were taking a Japanese bow. She then lowers one of her breasts onto the scanner, adopting a modified prone position.[7]

Data from the three sweeps are "stitched" together using software developed at Gifu University in Gifu, Japan. Any breast cancers can then be detected and evaluated from the resulting volumetric data (Figure 1). This whole-breast imaging data can be displayed in axial, sagittal, and coronal form, though the original (axial) scanning plane will have the highest resolution.

The size of images generated (axial view) is 694 x 400 pixels with a resolution of 0.23 mm/pixel and 256 gray-scale levels. A unilateral breast study with a

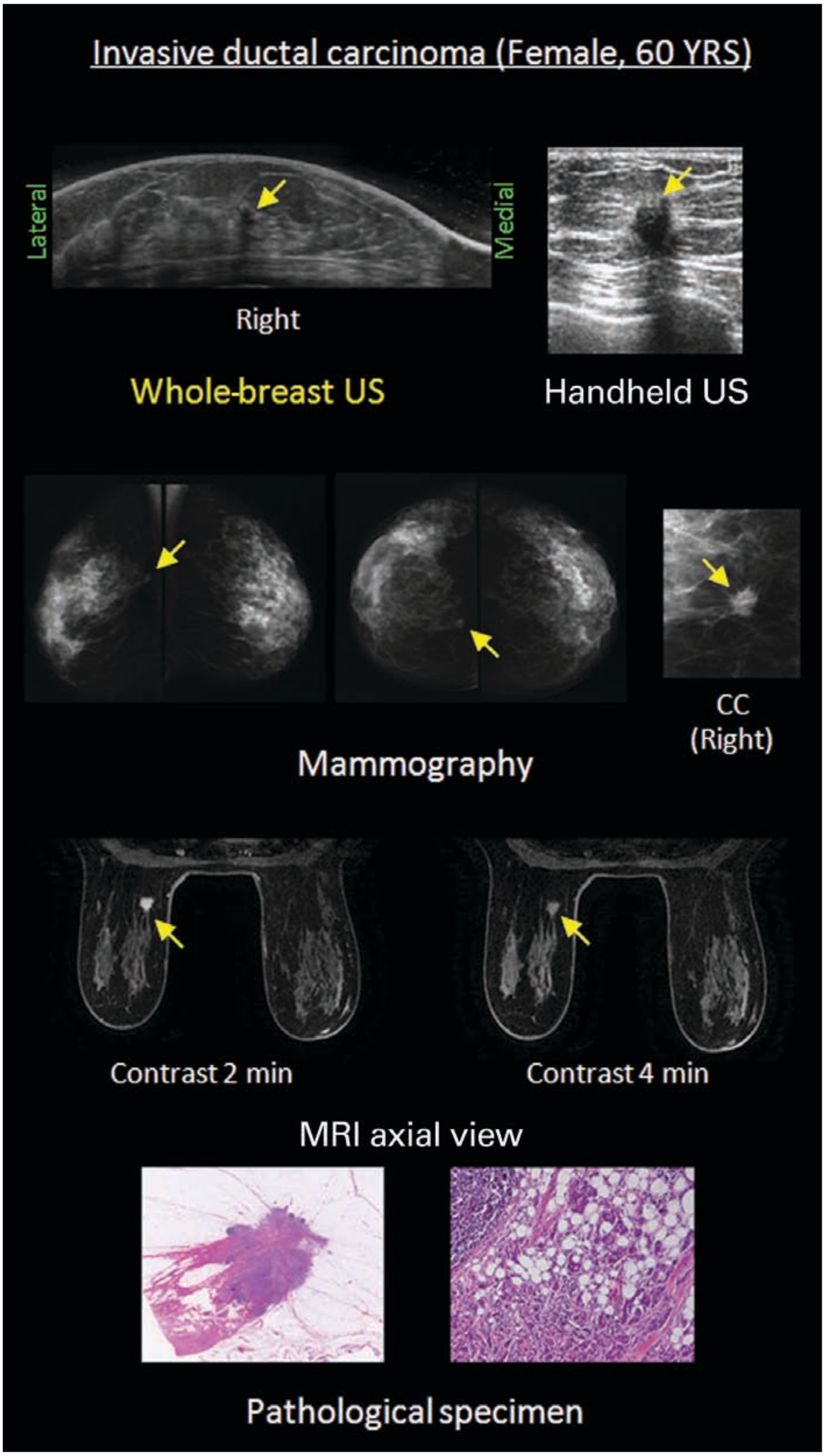

FIGURE 4. Whole-breast ultrasound data can be compared with MRI and mammography. Images from handheld ultrasound and histopathology are also shown. Images show invasive ductal carcinoma in a 60-year-old woman.

slice-to-slice interval of 2 mm will contain 84 (axial) images. Image acquisition time is 20 seconds. On decreasing the slice interval to 1 mm, 0.5 mm, or 0.25 mm, the number of images will increase to 168, 336, and 672, respectively, and the acquisition time to 40 sec, 80 sec, and 160 sec, respectively.

VOLUMETRIC ANALYSIS

The depiction of calcifications has widely been considered a challenge for breast ultrasound. The volumetric data produced by whole-breast ultrasound imaging is helping to redress this (Figure 2).

The identification of anatomical structures means that corresponding breast regions can be registered, leading to the feasibility of bilateral and/or temporal analysis. This is important if the breasts are to be analyzed systematically. Clinicians' assessments of abnormalities and estimations of their extent are greatly assisted by the manipulation and presentation of data in three orthogonal views and reslicing of the volumetric data (Figure 3).

Clinical imaging diagnoses are moving steadily toward multiplane and multimodality protocols. Visual comparisons of images from different modalities must consequently be performed. Whole-breast ultrasound makes it possible to identify a lesion's location relative to surrounding breast tissue. Ultrasound images can also be compared (and registered) with images from other modalities, such as mammography and MRI (Figure 4).[8]

The ability of whole-breast ultrasound to distinguish between benign and malignant lesions has been reported. Preliminary studies based on the ASU-1004 volumetric whole-breast ultrasound data show that the diagnostic value of the data is not lower than that of conventional handheld ultrasound. Specifically, the sensitivity in discriminating benign and malignant masses is over 92%.[9,10]

The vast amount of data generated by volumetric imaging and the high throughput rate in mass screening programs suggest that computer-aided detection (CAD) could be of use. Cancers could otherwise be missed by radiologists who are fatigued after viewing large numbers of disease-free cases. CAD systems can also act as a second opinion or second pair of eyes.

Although most breast CAD systems are designed to work with mammography, some have also been developed

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lesions that also have invasive elements, and when diagnosing subtle lesions.

The quality and resolution of whole-breast ultrasound images will continue to improve as the technology develops. For instance, the elimination of artifacts, such as lateral shadowing and shadowing behind the nipple, will improve the accuracy of ultrasound for diagnosing cancer.

It is hoped that whole-breast ultrasound will bring benefits to breast cancer screening programs for Asian women. ■

Dr. Harald Østensen (second right) was a regular visitor to the Asia Pacific region during his spell at the WHO.

purchase and installation costs can sometimes be financed by savings in film and chemicals, allowing sites to break even after two or three years.

The solution to the lack of medical specialists may be to send images electronically to another institution where radiologists are available. Sites using digital radiography systems should be able to do this easily, given that most have access to e-mail. Compressed x-ray images saved as jpg files and sent as attachments are sufficient for urgent diagnostic evaluation in most cases. Broadband is desirable but not essential. Such a system will require formal collaboration with the receiving site and some sort of remuneration for the doctor reading the images, but it is doable.

Upgrades to small and midsized hospitals in remote locations do not attract media attention. Politicians thinking about headlines and reelection may choose to support the purchase of an extremely expensive item of high-tech medical equipment that may appear to benefit a population. In reality, it will not be utilized properly. Guidelines from international organizations stating that "Every district hospital should at least have one CT machine" may also lead to inappropriate donations. Too many hospitals in poor countries have unused CT scanners that may not even have been installed.

No healthcare system can function properly without the necessary bits and pieces in place. An adequate and appropriate diagnostic imaging service is one of these bits. ■

BREAST

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specifically for whole-breast ultrasound data. Research in this area is focusing on the automated detection and classification of breast masses, and the identification of different mammary gland patterns.[9-13]

LOOKING AHEAD

Breast ultrasound will take on a more substantial role in breast cancer detection and diagnosis as ultrasound technology continues to develop. The availability of information on the whole breast, similar to that available from mammography, is an important step in this direction. Whole-breast images can be essential when interpreting complex cases, such as patients presenting with benign

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