Detecting early breast cancer by integrating full-field digital mammography and automated breast ultrasound

By Prof. Christopher L Vaughan

Screening for breast cancer using full-field digital mammography (FFDM) has benefited many women over the past two decades, despite the poor sensitivity of this imaging modality in dense breast tissue. This has led more recently to the development and application of automated breast ultrasound (ABUS) as an adjunctive modality to reduce the incidence of false negative findings.

In this article, we review the studies that have sought to integrate FFDM and ABUS in a single platform, and then summarise our own research findings obtained with our dual-modality Aceso system.

There is compelling evidence that screening with FFDM – digital X-ray images of cranio-caudal (CC) and medio-lateral oblique (MLO) views of both breasts – has been successful in diagnosing healthy women for the early detection of breast cancer [1], despite some recent reports to the contrary. Although FFDM has reduced mortality, the imaging modality performs poorly in women who have dense breast tissue — often the case for premenopausal women younger than age 50 — and sensitivity drops to less than 50% [2]. The problem is that dense fibro-glandular tissue often masks underlying tumours and the resulting false negative finding at screening can have devastating consequences for the woman concerned: a poorer prognosis and more costly treatment.

Despite its poor spatial resolution, ultrasound is able to distinguish very well tissues of different density and has therefore been employed as an adjunct to mammography. Because hand-held ultrasound suffers from repeatability problems and is time-consuming, automated breast ultrasound (ABUS) devices — where the patient lies supine on a bed and her breasts are naturally compressed under gravity — have been developed and introduced over the past decade [2]. With this approach, the radiographer locates the transducer assembly on the patient's breast and a B-mode ultrasound probe scans across the breast in the frontal plane, gathering multiple 2D images that may be combined to produce 3D volumetric data of the underlying tissue.

Strong evidence to support the use of FFDM followed by ABUS as a screening tool was reported by Giuliano and Giuliano [3]. They studied 3,418 women with mammographically dense breasts and reported that when ABUS was added, their detection rate was 12.3 breast cancers per 1,000 women screened compared to 4.6 per 1,000 by FFDM alone. Brem *et al.* [4] showed that FFDM plus ABUS produced an additional 1.9 detected cancers per 1,000 screened, although there was a concomitant increase in false positive findings. In a study of 185 asymptomatic women with dense breasts (BI-RADS c or d), Giger *et al.* [5] reported that when ABUS was added to FFDM, sensitivity increased from 58% to 74%, while specificity was statistically unchanged.

Although there are clear-cut benefits of employing FFDM followed by ABUS as a screening strategy, this approach has three distinct drawbacks.
First, the breast is in a different orientation and degree of compression for the two modalities, which complicates the interpretation and co-registration of the X-ray and ultrasound images.
Second, the time required to prepare the patient and gather separate images is at least 30 minutes, compared with just 10 minutes for FFDM alone.
Third, there is the considerable capital expense to acquire separate FFDM and ABUS systems.
All this begs the obvious question: is it possible to integrate the two modalities into a single platform? The potential for combining the modalities was hinted at over thirty years ago during the analogue imaging era by Novak [6].

Ideally, a dual-modality platform should include the following five functional attributes:

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(1) the breast to be in same orientation and degree of compression when FFDM and ABUS images are obtained;
(2) images to be acquired simultaneously, thus minimising the time the woman's breast is held stationary;
(3) ABUS images of the whole breast to be obtained in a single scan;
(4) radiation dose exposure to the woman to be minimised;
(5) the design to accommodate acquisition of both X-ray and ultrasound images in 3D.

A review of the field of dual-modality imaging – combining X-rays and ultrasound to detect breast cancer – shows that there are four basic design concepts that have been described in the literature.

• In **design one**, FFDM images are captured by a flat panel X-ray detector located underneath the breast while an ultrasound probe, located on top of the compression paddle, moves under automated control [7].
• In **design two**, researchers from the USA [8] and Germany [9] have adapted design one by replacing FFDM with digital breast tomosynthesis (DBT), the technique that enables 3D X-ray images of the breast to be reconstructed. Although the clinical results were encouraging, enabling lesions to be co-registered on the DBT and ABUS images, the design had a major drawback: the images were gathered sequentially rather than simultaneously because the ultrasound scanner had to be moved out of the X-ray field of view, meaning that the patient's breast was compressed for too long.
• **Design three** employs a slot-scanning approach to acquire FFDM images, with an X-ray camera scanning beneath the breast, and an ultrasound probe moving in parallel to the camera [10], enabling both FFDM and ABUS images to be acquired simultaneously. However, because the researchers were unable to acoustically couple the probe to the breast, they could not gather clinical images.
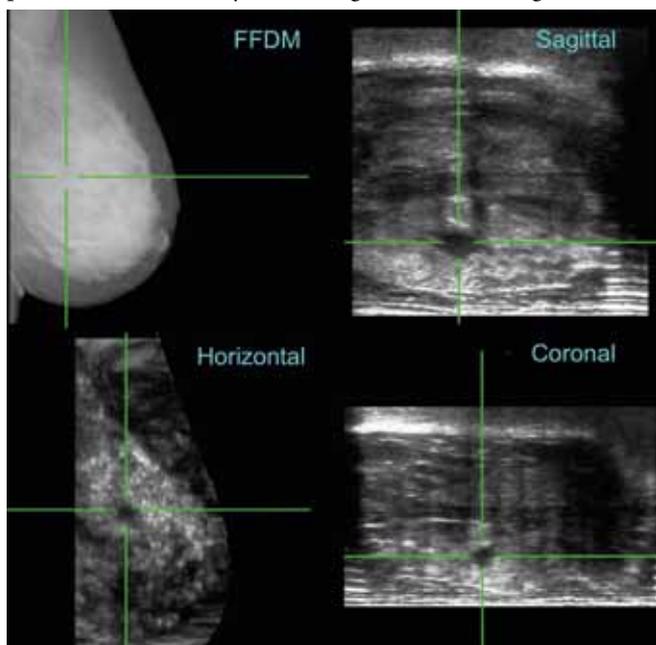
• In **design four,** the patient lies prone on her stomach with her breast protruding through an opening in the bed [11]. Both the X-ray and ultrasound systems are located beneath the support and rotate around the breast through 360 degrees, enabling 3D images to be gathered for both modalities. To date, this design has not been built and clinically tested.

Figure 1. The Aceso dual-modality breast imaging system, showing the digital X-ray camera (right) and the linear ultrasound probe (left) immersed in mineral oil in a hermetically sealed breast platform [13, 14].

DUAL MODALITY ACESO SYSTEM

Named after the Greek goddess of healing, our dual-modality Aceso system is based on design three, in which FFDM is accomplished via a slot-scanning geometry, while ABUS is implemented by positioning a linear ultrasound probe parallel to the X-ray camera [12]. As illustrated in Figure 1, acoustic coupling is enhanced by locating both the probe and camera in a hermetically sealed breast platform filled with mineral oil [13]. Two clinical trials have been conducted on 83 women – 65 healthy volunteers and 18 patients referred by clinicians at Groote Schuur Hospital – and the findings have demonstrated the potential of an integrated dual-modality system to detect breast cancer [14, 15].

The average time spent by the 83 women in the imaging room for the radiographer to acquire a full set of dual-modality images – FFDM and ABUS of both breasts in CC and MLO views – was just 10 minutes. This is comparable to standard screening mammography times and considerably less than the 30 minutes required when the two modalities are performed sequentially. While the FFDM image is gathered in the horizontal plane (parallel to the breast platform), the ABUS images are acquired in the sagittal plane and multiple slices may be reconstructed to form a 3D data set. Because the FFDM and ABUS data have a common origin and coordinate system, and are acquired simultaneously with the breast in the same orientation and degree of compression, co-registration of the images is straightforward.

CLINICAL EXAMPLES

Some of the subjects in our first clinical trial had extremely dense breasts (BI-RADS d) and here we feature a 42-year-old healthy volunteer with no prior history of breast pathology [14]. The FFDM image for the left LMO view confirmed no evidence of pathology. However, when the ABUS images in the sagittal plane were viewed as a video clip, the animation revealed the brief appearance of a dark well-defined lesion close to the breast platform. As seen in Figure 2, the four views illustrate the co-registration of the FFDM and ABUS images, while the green crosshairs identify the location of
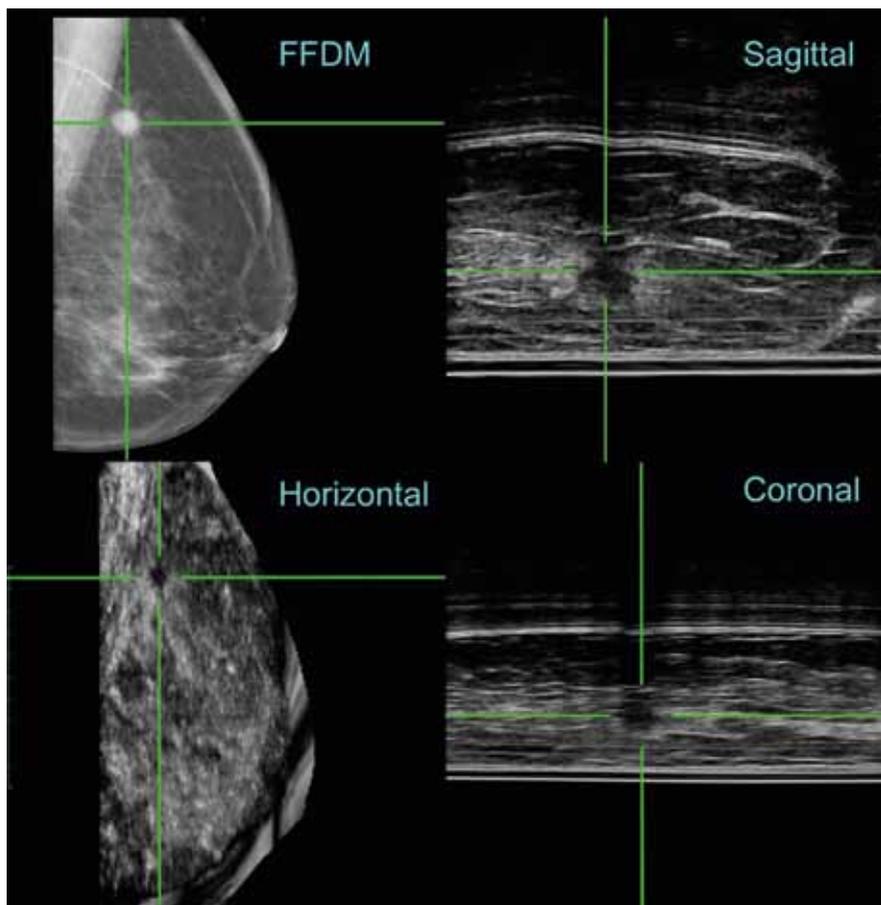

Figure 2. Co-registration of the FFDM in the horizontal plane and the ABUS images in the horizontal, coronal, and sagittal planes for a 42-year-old volunteer [14]. A lesion (benign cyst) has been highlighted by green crosshairs in the ABUS views, but the lesion is occult in the FFDM image. Note that for the ABUS images, the sagittal plane view is the acquired image, whereas the coronal and horizontal plane views have been reconstructed.

Figure 3. Co-registration of the FFDM in the horizontal plane and the ABUS images in the horizontal, coronal, and sagittal planes for a 61-year-old patient [15]. A malignant lesion has been highlighted by green crosshairs in the ABUS views and is clearly co-registered in the FFDM image. Note that for the ABUS images, the sagittal plane view is the acquired image, whereas the coronal and horizontal plane views have been reconstructed.

the lesion that is clearly occult in the FFDM image. Follow-up evaluation revealed a benign cyst. Since the ABUS images were not of sufficient quality, we developed a custom linear ultrasound probe – 192mm long, 0.5mm element pitch, 6.5MHz centre frequency for our second clinical trial [15].

Our second clinical example is a 61-year-old woman who presented with a four-week history of a painless left breast lump [15]. There was no familial history of breast cancer, she had not used hormone replacement therapy, and when examined clinically, a 2cm suspicious, hard, irregular mass was palpated. The FFDM image for the left MLO view revealed a spiculated lesion in the outer quadrant. The 3D location of the lesion, identified by the green crosshairs in Figure 3, is highlighted by co-registration of the FFDM and ABUS images generated by Aceso. An invasive ductal carcinoma was confirmed following needle biopsy, cytology and histology. The patient underwent breast preservation surgery and axillary node clearance, followed by adjuvant radiotherapy and hormonal therapy. As can be seen by comparing the ABUS images in Figures 2 and 3, the quality of the ultrasound was significantly improved in the second clinical trial [Figure 3].

CONCLUSION

Although FFDM may still be considered the gold standard for early detection of breast cancer, if a woman has dense breast tissue, lesions are often mammographically occult. A false negative finding can be devastating because a later diagnosis will inevitably lead to more expensive treatment and a poorer prognosis. Although other imaging modalities such as digital breast tomosynthesis (DBT) have demonstrated success in women with dense breasts, even DBT misses some lesions. Our second-generation Aceso system, with its improved quality FFDM and ABUS images [15], has proven its potential as a screening system for early detection of breast cancer in a busy clinic.

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DISCLOSURE