BREAST IMAGING

Recent developments in breast cancer imaging: combination of 3D automated breast ultrasound and digital breast tomosynthesis in the FUSION-X-US prototype

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In this article we present a novel approach to breast cancer imaging. In response to the growing importance of breast sonography and digital tomosynthesis, the FUSION-X-US prototype has been developed to enable the carrying out of both automated breast volume scan (ABVS) and tomosynthesis in one, combined workflow.

There is a pressing need for improvement in current methodologies of breast cancer screening, since it is well establsihed that mammography alone does not provide sufficient diagnostic accuracy for all patients. The management of patients with dense breast tissue is particularly challenging, not only because the risk of developing breast cancer is significantly higher in such patients but also because in women with dense breasts, lesions are more likely to be missed in breast cancer screening [1].

Mammography and breast ultrasound are currently the basic imaging modalities used in routine breast cancer screening and have undergone continued development over the last few years [2].

One such developement is tomosynthesis, the 3D-procedure using low-dose digital x-ray projections. Compared to 2D-mammography, tomosynthesis has been shown to increase the sensitivity and specificity of breast cancer detection, especially in high risk patient groups with dense breast tissue [3-5].

Hand held ultrasound (HHUS) is able to detect additional malignancies compared to mammography alone, but is a procedure that is both time-consuming and highly examiner-dependent [6]. Automated 3D-ultrasound imaging of the whole breast (ABVS) has been shown to not only reduce the examination and interpretation time compared to HHUS, but also to yield higher inter-observer reliability [7-11].

Both ABVS and tomosynthesis are thus playing an increasingly important role in modern breast cancer diagnostics [12-14].

It is against this background that recently research and development efforts have been undertaken with the aim of combining tomosynthesis and ABVS in one device for the improved detection and classification of breast lesions [15-21].

THE FUSION-X-US PROTOTYPE

This is one of the first devices combining tomosynthesis and ABVS that has been developed to the level of testing on patients in a clinical setting. Based on the well-established ACUSON S2000 ultrasound system and the Mammomat Inspiration mammography/tomosynthesis system (both from Siemens Healthineers), the new FUSION-X-US system allows both ABVS und tomosynthesis to be carried out in only a few minutes, in one single workflow procedure without decompression of the breast or change of position

In the procedure, the breast compression involves the use of a flexible gauze, which is transparent to X-rays

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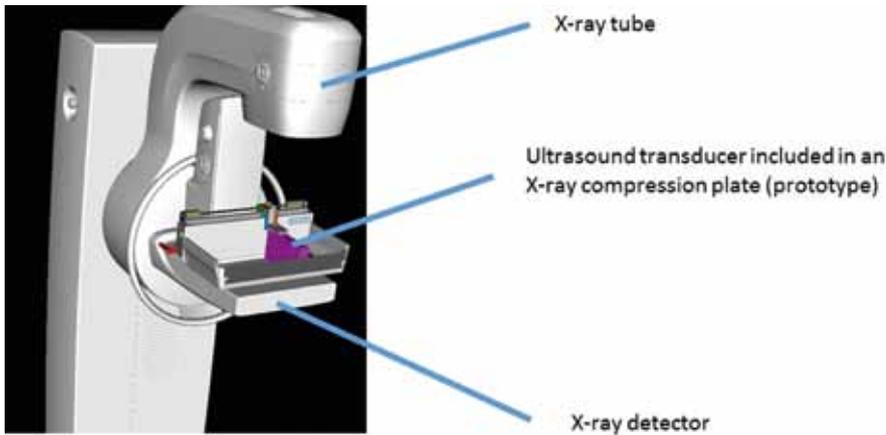michael.golatta@med.uni-heidelberg.de

Figure 1: Schematic view of the X-US prototype. An ultrasound transducer is incoporated into a prototype compression plate of a standard MAMMOMAT Inspiration system. During normal x-ray imaging (mammography or tomosynthesis) the transducer is "parked" outside the x-ray field at the edge of the compression plate. Directly after acquisition of the x-ray images, the transducer then moves automatically from right to left to perform the ultrasound scan.

and also allows the full functioning of the ultrasound transducer head.

In the first step of the procedure, tomosynthesis is carried out as usual in mediolateral (ML), mediolateral-oblique (MLO) or craniocaudal (CC) views.

While the breast remains under compression and without any change of position, the ultrasound transducer then moves over the gauze to acquire the ultrasound scans. The data are processed in separate computer software systems; the regions of interest can be analyzed side-by-side by matching the 3D image position data from tomosynthesis and ABVS [Figures 1,2].

A feasibility study of the new system was performed in 2015 with 23 non-selectively recruited patients who had been referred to our breast unit with an indication for tomosynthesis. All patients underwent the standard diagnostic work-up according to current guidelines, namely physician-performed clinical examination, 2D-digital mammography and hand held 2D-ultrasound [22]. This procedure was then complemented with tomosynthesis and ABVS examinations, which were carried out using the FUSION-X-US prototype system and interpreted in conjunction with the other examinations.

In this study, two radiologists, both of whom were blinded to the results of the standard workup, were presented with only the ABVS and tomosynthesis images from the FUSION-X-US prototype. The examining radiologists were instructed to classify any lesions according to the Breast Imaging-Reporting and Data System (BI-RADS®) [23].

The objective of this separate evaluation of the tomosynthesis and ABVS data, was to determine whether the images acquired using the FUSION-X-US prototype alone were sufficient for the detection of malignant lesions.

RESULTS

The scanning process was well tolerated by all patients. and worked flawlessly, taking 25 sec for the tomosynthesis scan and 80 sec for ABVS.

The 3D reconstruction allowed direct correlation of ABVS and tomosynthesis slides in all cases. The investigators spent approximately two minutes interpreting the tomosynthesis image and another two to three minutes on the ABVS interpretation. There was no significant difference between the interpretation time spent by both investigators [Table 1].

In the whole patient cohort in this evaluation [see Supplementary Table for patient details], a total of 29 lesions were found (23 benign lesions, including three with microcalcifications, and six malignant lesions). All six malignant lesions were identified by both investigators in tomosynthesis and were classified as either unclear (BI-RADS® 0) or suspicious (BI-RADS® 4-5) [see Table 2], so no malignant lesion was missed [see Table 3]. However, only in a few cases (3/6, 50.0%, investigator 1; 4/6, 66.6%, investigator

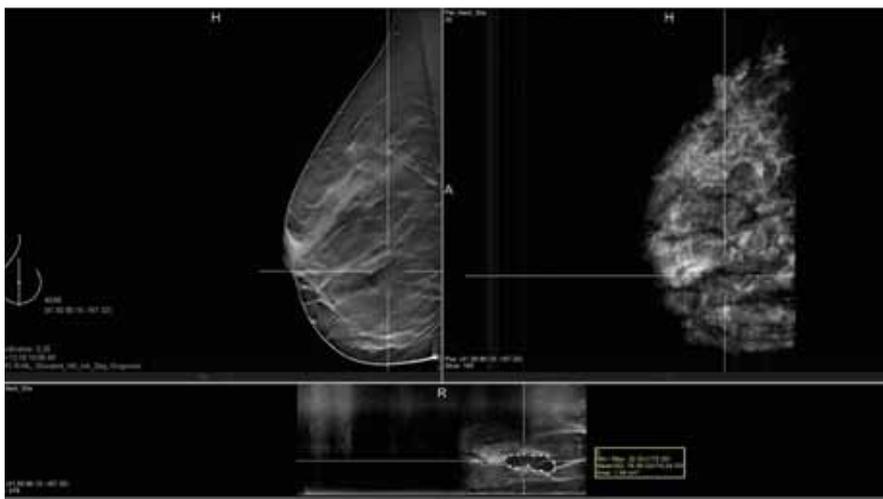**Figure 2**: Close up of the transducer unit and compression plate

Figure 3: Screenshots showing a benign solid lesion on corresponding images of tomosyntesis in mediolateral orientation (upper left), 3D-ABVS reconstruction (upper right-hand side) and 2D-ABVS ultrasound image (note: the bottom of the image is oriented towards the ultrasound transducer)

2), was the lesion also seen in ABVS. No lesion was detected only in ABVS.

In six cases, the ABVS image of a lesion that was classified in tomosynthesis as unclear or suspicious (BI-RADS® 0, 4b or 5) was identified as benign (BI-RADS® 2). Figure 3 shows a screenshot of one of these cases in which the ABVS image led to the correct identification of a benign lesion as a fibroadenoma (BI-RADS® 2), which had been

classified as suspicious (BI-RADS® 4b) by tomosynthesis.

The average area of the breast covered in ABVS (99.7 cm², SD 25.4) was significantly smaller than in tomosynthesis (150.3 cm²; SD 37.9; p<0.001). An improved ABVS coverage is one of the major development priorities for future systems.

CONCLUSION
Our descriptive feasibility study showed that the FUSION-X-US system

can perform tomosynthesis and ABVS in a single, one-time and efficient workflow procedure with direct correlation of imaging findings from both modalities. Suspicious findings were reliably detected by two independent investigators.

Since no additional lesions were detected in ABVS, there was no increase in sensitivity compared to tomosynthesis alone. Thus, our analysis of this relatively small cohort of patients did not show any clear benefit of the additional ABVS. A larger study with higher patient numbers is needed to test the potential benefit of the additional ABVS.

The main technical challenges of the integrated ABVS/tomosynthesis system are breast coverage and image quality. Against these criteria, the FUSION-X-US prototype currently does not come up to the performance of a stand-alone ABVS device. On average, only 66.0% of the area covered by tomosynthesis was covered by ABVS, so not all regions of interest could be examined in both modalities. One reason for the limited coverage of ABVS is the fact that the ultrasound transducer was embedded in a housing with a thickness of about 1 cm on each side, thus limiting coverage of peripheral regions. Development efforts to produce ultrasound transducers with a thinner housing that are better adapted to the specifications of the prototype should help to overcome this issue.

The quality of the tomosynthesis images of the prototype device was

	Investigator 1	Investigator 2	T-test significance
Tomosynthesis	122.7 sec (st.dev. 95.7 sec)	151.3 sec (st. dev. 55.3 sec)	p = 0.221
ABVS	149.4 sec (st. dev. 69.6 sec)	141.2 sec (st. dev. 44.1 sec)	p = 0.638

TABLE 1: Time spent by both investigators for the interpretation of ABVS and tomosynthesis images produced by the FUSION-X-US-prototype

Case nr	Standard Work-up			Lesion Size			Investigator 1		Investigator 2	
	BI-RADS (Mammo)	BI-RADS (HHUS)	Pathology	cm² as measured in mammo (standard work-up)	cm² as measured in tomo (Invest 2)	cm² as measured in tomo (Invest 1)	BI-RADS (Tomo)	BI-RADS (ABVS)	BI-RADS (Tomo)	BI-RADS (ABVS)
1	5	5	Her2 +	20.1 (6.1 x 3.3)	18.1	22	4c	0	5	5
2	4	5	Basal-Like (TNBC)	2.5 (2.1 x 1.2)	2.4	5.4	4b	Not covered	4c	Not covered
3	4c	4c	Luminal B	2.0 (1.3 x 1.5)	2.3	3.9	0	No lesion detected	5	4b
4	4b	4b	Luminal B	1.1 (1.1 x 1.0)	0.7	1.8	0	Not covered	5	Not covered
5	4b	4b	Luminal B	16 (4.0 x 4.0)	5.1	5.1	4b	0	5	4a
6	4c	4c	Luminal B	13.3 (3.4 x 3.9)	11.2	8.5	0	4b	5	5

TABLE 2: Malignant lesions case-by-case

		Investigator 1				Investigator 2			
	n=	Detected in Tomo	%	Detected in Tomo + ABVS	%	Detected in Tomo	%	Detected in Tomo + ABVS	%
malignant	6	6	100.0	3	50.0	6	100.0	4	66.7
benign	23	18	78.3	11	47.8	19	82.6	8	34.8
of which contain microcalcifications	3	3	100.0	0	0.0	2	66.7	0	0.0

TABLE 3: Detection of lesions

Supplementary Table . Description of patient cohort

comparable to those of standard tomosynthesis, but the ABVS image quality was lower than in a stand-alone ABVS system. This limitation probably contributed to the relatively high rate of unclear (BI-RADS® 0) cases in ABVS. Also, the software for the ultrasound measurements was optimized for standard ABVS measurements and not for the special case of the prototype, resulting in suboptimal image quality. In future studies, a parameter optimization for the interpretation of the ABVS data produced by the prototype device will be performed.

3D tomosynthesis and additional ultrasound examinations have a growing diagnostic importance, especially in high-risk patient groups with dense breast tissue.
With further technical improvements, combined ABVS and tomosynthesis systems could be valuable tools for improved breast cancer diagnostics.

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