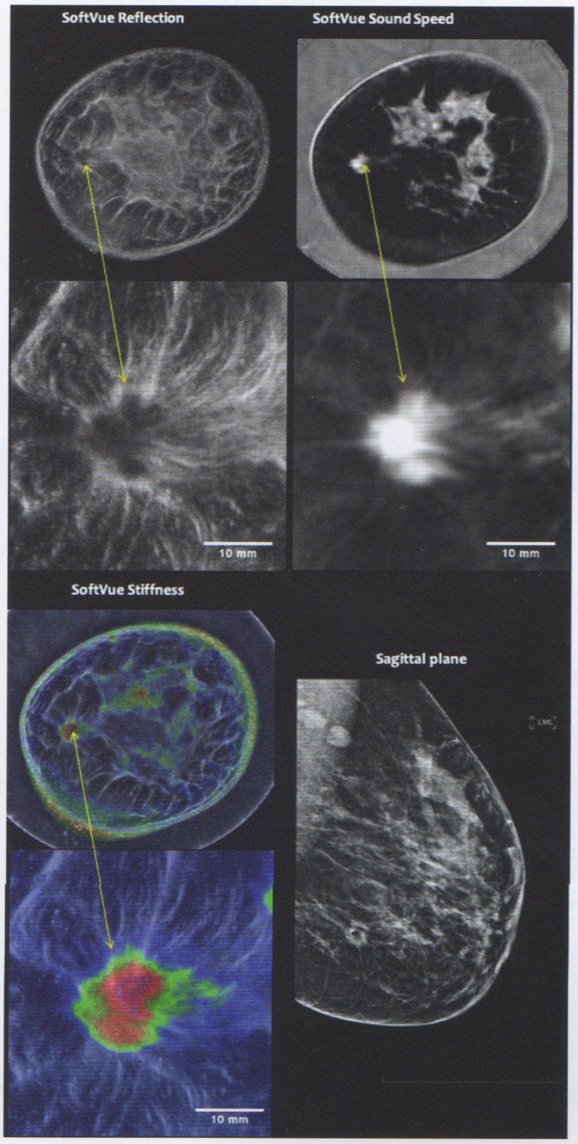
Ultrasound Tomography (UST): a potential new breast screening modality?

By Preena Patel, Morgan Roberts and Ben Cox

The diagnostic imaging gap

As of 2016, breast cancer is the most commonly diagnosed cancer amongst women in the UK and globally, it is the second most common cause of cancer-related death[1]. The current breast cancer screening programme of mammography involves compression of the breast to produce X-ray projection images from two orthogonal planes, which can reveal suspicious lesions [2, 3]. However, in women with dense breasts, the shadow of a breast tumour can easily be hidden within the complicated background structure of the glandular tissues and hence its sensitivity in these women decreases significantly[4]. This is particularly noteworthy, as women with dense breasts are at higher risk of breast cancer[4] and because there is no clinical biomarker of breast density until a mammogram has been done, there is no way to predict whether a woman has dense breasts or not.



Below: Figure 1: Reflection, sound speed and stiffness images of a human breast using the SoftVue System (Image courtesy of Dr Neb Duric)

Other weaknesses of mammography include the pain associated with breast compression, the psychological trauma of over-diagnosis, and the use of ionising radiation[2]. For these reasons, despite the reduction in mortality shown due to screening, there is still controversy as to whether breast screening does more harm than good and most breast imaging experts would agree there is scope for improvement[2]. Nevertheless, whilst mammography is imperfect, it currently remains the most practical and cost-effective approach for breast cancer screening. However, the above drawbacks continue to drive the development of alternative screening modalities.

Magnetic resonance imaging (MRI) has been demonstrated to have superior sensitivity compared to mammography in younger, high-risk women[5]. However, it is probably not cost-effective for breast screening in large populations. A cheaper alternative of 'Fast MRI' is being explored, however a significant proportion of individuals do not tolerate MRI scans due to claustrophobia (approximately 15%) [3]. Diffuse optical imaging techniques are currently limited by the fact that light scatters significantly while propagating through the breast, thus the spatial resolution is too low to detect small, early tumours[6]. Several photoacoustic tomography systems (whole breast and hand-held) in many stages of development are also showing promising results[18].

Conventional ultrasound (US) imaging of the breast is currently used in the diagnostic pathway if a suspicious lesion is identified on a mammogram[1]. It aids differentiation of soft tissue masses and cysts. As US does not use ionising radiation, it provides scope for screening younger patients, on a larger scale, more often. However, few studies have demonstrated that ultrasound imaging by itself can match the sensitivity of mammography[3]. In addition to this, it is time consuming and requires an experienced practitioner, which subsequently increases the cost above that of a screening tool. To overcome this, automated breast ultrasound systems (ABUS) have been developed. They can generate reproducible qualitative images of the whole breast using a mechanical scanning device which holds the transducer and produces a stack of images of the screened area[7]. In these devices, scanning is accomplished by mechanically moving the probe over the breast in a way similar to that used for hand-held US[7]. The main advantages of these systems include a reduction in variability in examination performance due to less operator dependence, and reduced physician time. These systems have received FDA approval for breast screening in the USA and large multi-centre clinical trials are currently ongoing[7]. P52

Ultrasound tomography (UST), like ABUS, is an operator independent ultrasound imaging technique. However, it can produce quantitative images[8]. The quantitative nature of these images allows for objective (rather than subjective) interpretation of images, development of diagnostic standards/cut-offs, and scope for additional research into correlations between images and pathology. Additionally, in UST, several slices of the 3D breast volume are produced[8] such that the effect of overlying and underlying anatomical tissue can be effectively removed when viewing individual slices. The detrimental problem of superposition in mammography of dense breasts can hence be avoided.

In 1974, Greenleaf et al. recognised the potential advantages of using a non-ionising tomographic method that removes operator dependence and gives quantitative images, and they introduced the fundamental concepts and initial experiments of UST[9]. But only within the past decade or so has the increasing availability of affordable high performance computing facilities and multi-channel data acquisition systems led to renewed interest in UST, and the development of clinically useful devices.

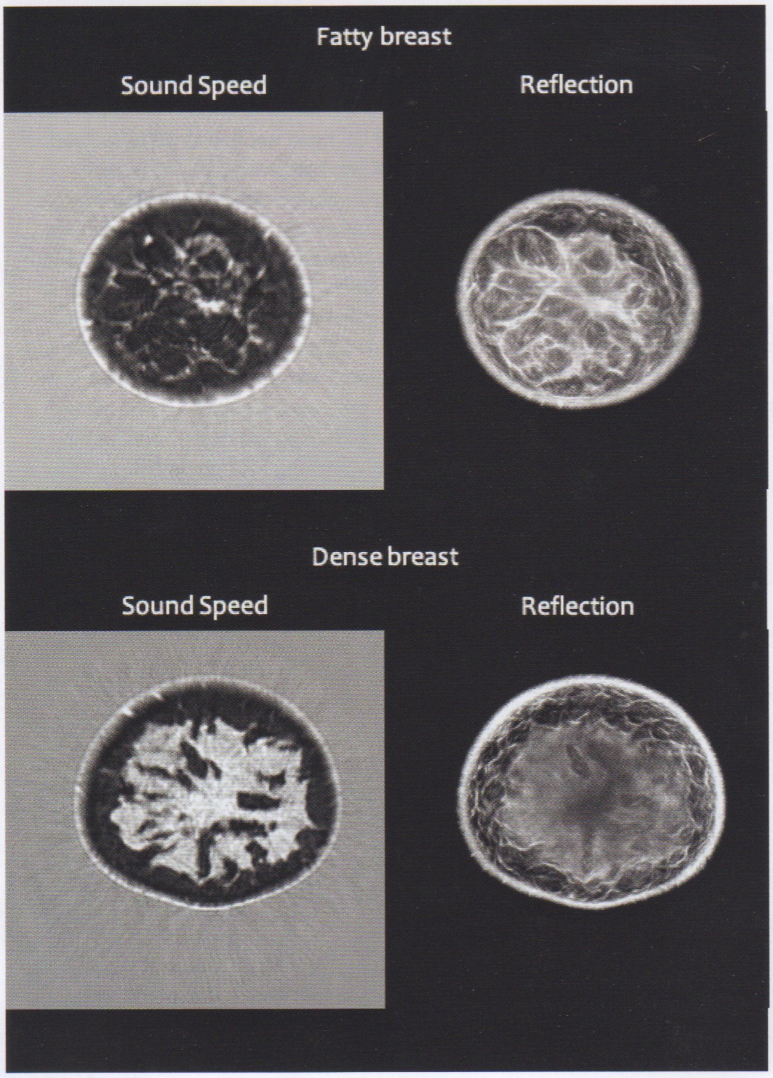
Ultrasound tomography

UST systems comprise a patient bed on which the patient lies prone[10]. The patient's breast is suspended through an opening in the bed into a water tank underneath the bed[10]. There is therefore no painful breast compression. The breast is surrounded by a ring or bowl array of ultrasound transducers. (The water is a coupling medium between the transducers and the breast.) Scanning typically involves sending pulses of ultrasound into the breast from one or more of the transducers and measuring the reflected and transmitted pulses on some or all of the remaining transducers. Some systems then physically rotate and repeat the measurements at multiple angles.

Acoustically, the breast can be considered as an inhomogeneous medium containing numerous structures (glands, lobules, muscle, fat etc) that result in spatial variations in sound speed, density and acoustic absorption. As a sound wave propagates through such a medium, it will be scattered, refracted and attenuated, resulting in measured signals that contain information about the distribution of acoustic impedance, sound speed, and attenuation. These measurements can therefore be used to form images of these quantities, the acoustic impedance depending primarily on the scattered waves, and the sound speed and attenuation on the through-transmitted parts of the signal[9].

The earliest approaches to image reconstruction made an analogy with X-ray computed tomography, in which the measurements are line integrals of the X-ray absorption[9]. If the sound is assumed to travel along rays between emitters and receivers, then the measured drop in signal amplitude can be related to the line integrals of the attenuation along those rays. Furthermore, the time it takes the sound to pass from an emitter to a receiver can be linked to the line integral of the sound speed along the ray joining the two. The simplest algorithms assume that the rays are straight; more advanced algorithms can include the refraction of the rays[19]. Either way, quantitative images of the sound speed and attenuation can be recovered from the line integrals. Reflection images, which are closer to conventional B-mode images can also be obtained. More recently, there has been a move towards reconstruction approaches known as full-wave inversion approaches, in which a numerical model of acoustic propagation is iteratively updated, e.g. the sound speed distribution is updated, until the output matches the measurements[20], [21], [22]. This approach to recovering the sound speed or attenuation maps makes fewer assumptions, and is more flexible, than ray-based approaches and higher quality images can be obtained in this way. However, it is non-trivial and can be very computationally expensive, especially in 3D.

The resulting images, particularly the quantitative images of sound speed and attenuation, provide different contrasts, which can help differentiate between different P54



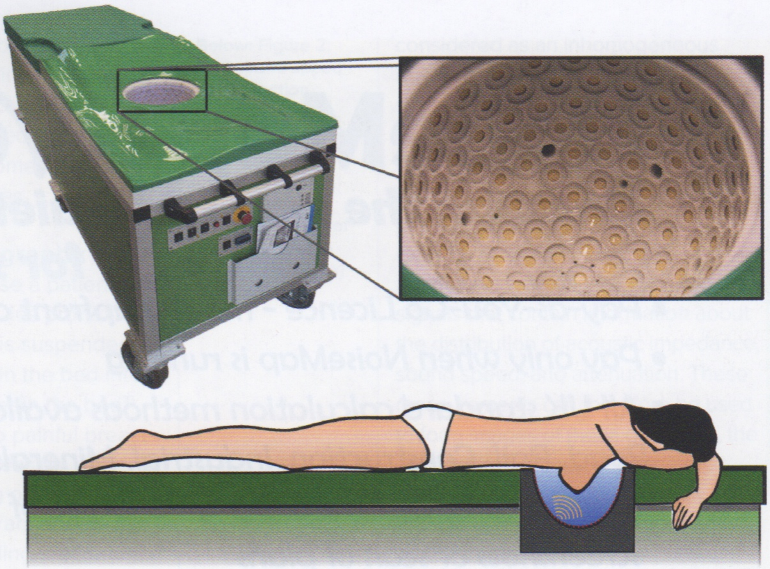
Below: Figure 2: UST sound speed and reflection images of a fatty human breast and a dense human breast using the QTUS system (Image courtesy of Dr James Wiskin and Dr Bilal Malik) tissue types, for example between benign and malignant soft tissue masses, cysts and background breast tissue. Furthermore, the quantitative nature of the images will facilitate comparisons over time. The production of images which show quantitative distributions of multiple acoustic parameters, increases the ability to differentiate structures and provides an opportunity for fusion images which may be useful in lesion detection.

Current systems

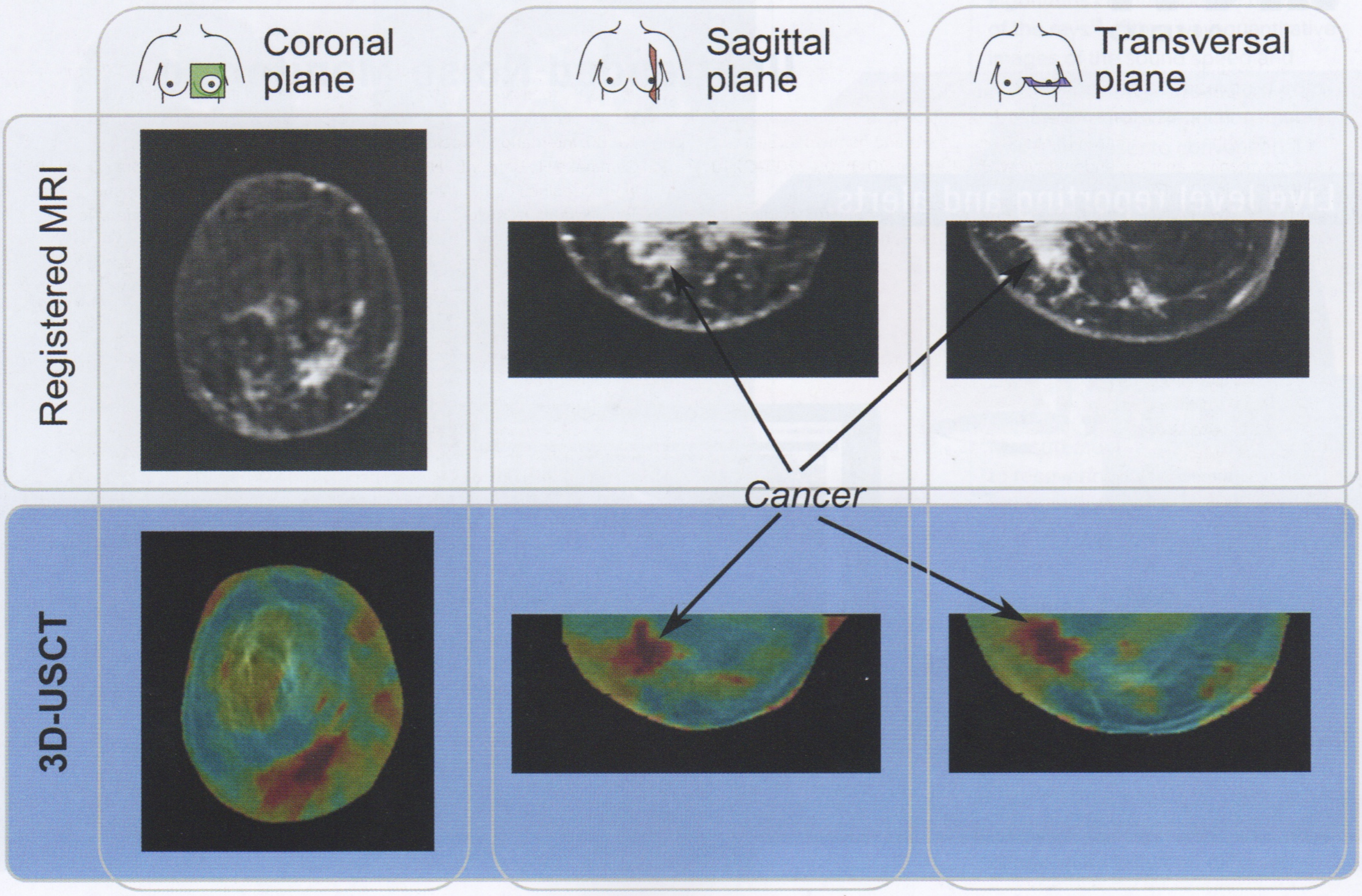
Several UST systems have been developed by research groups to carry out pilot clinical work. For UST, transducer elements are ideally distributed around an aperture to achieve full coverage of the breast, but research groups have met this criteria using many different configurations.

The SoftVue system has been developed by Delphinus Medical Technologies (Karmanos Cancer Institute). It acquires 2D coronal slices of the breast using a ring array of 2048 identical transducer elements, which focus energy into a narrow plane[11]. The ring is mounted on a motorised gantry which moves from the chest wall all the way to the nipple, and acquires multiple slices which can then be stacked to form a pseudo-3D/2.5D volume[11]. Figure 1 shows as image obtained using the Soft~Vue system.

The QT Ultrasound Breast Scanner is a breast scanner which acquires data using separate arrays for transmission and reflection mode[12]. For transmission mode, a large single-element transmitter generates an unfocused plane wave that propagates through the breast and is detected by a 2048-element rectangular receiver array[12]. In reflection mode, there are three linear arrays which are focused at different depths within the breast, these acquire data in a manner similar to standard B-mode imaging[12]. The scan head rotates and translates the arrays to achieve full coverage of the breast, and uses fully 3D methods to reconstruct images[12]. Although, its FDA clearance is for use as an adjunct to mammography, the company is generalising this imaging modality for use in other parts of the body,



Right: Figure 3: Schematic of the KIT 3D UST system (Image courtesy of Dr Torsten Hopp) These images can also be found in: T. Hopp, M. Zapf, E. Kretzek, J. Henrich, A. Tukalo, H. Gemmeke, C. Kaiser, J. Knaudt, N. V. Ruiter, "3D ultrasound computer tomography: update from a clinical study," Proc. SPIE 9790, Medical Imaging 2016: Ultrasonic Imaging and Tomography, 97900A (1 April 2016); **https://doi.org/10.1117/12.2216686**



Below: Figure 4: 3D UST fusion (reflectivity and sound speed) images of a human breast using the KIT 3D UST system. The cancer can be seen as an uptake of contrast agent in the MRI images. The MRI images are registered to the UST images such that it has the same shape (Image courtesy of Dr Torsten Hopp) and have demonstrated that quantitative transmission tomography can still be used in the presence of bone and air, which generate large reflections. An example QT scan of the human breast is shown in Figure 2.

The Karlsruhe Institute of Technology (KIT) have designed a system which uses a semi-ellipsoidal bowl aperture, shown in Figure 3. There are 2041 small omnidirectional elements distributed over the bowl surface, which emit spherical waves so that a 3D reconstruction method can be used[13]. The bowl can also be rotated and translated to acquire data from more positions. Images from a clinical study using the KIT system are shown in Figure 4. The KIT group is currently developing another system, 3D UST III, which will have a larger aperture to accommodate fatty breasts which spread horizontally due to buoyancy[14]. They are also improving the distribution of transducers on the surface of the bowl, which reduces the number of rotations needed and therefore the acquisition time, which reduces the image artefacts that arise from patient motion[14].

Finally, Wroclaw University of Technology have designed an ultrasound transmission tomography system which also uses a solid-state ring array. Their design is such that it uses printed circuit boards and simplifies production of the system leading to reduced cost and time to manufacture[15], [16]. They have also developed an approach to recognising lesions within an UST image based on the characteristic of transmission, reflection and fusion images, based on in vivo xamination of breast lesions[17]. This method of interpretation for clinicians helps translate this modality into routine clinical practice.

Summary

Shortly after the inception of X-ray computed tomography, Greenleaf et al. introduced UST in 1974, by using an analogous approach with ultrasound. Now, UST is a rapidly emerging technology for medical imaging which is gaining greater interest for a wide range of applications. Recently, the 2nd International Workshop on Medical Ultrasound Tomography (MUST) was hosted in Detroit, which discussed recent work in system design, reconstruction and translation towards routine clinical use. It bought together a growing community of researchers to exchange ideas and research results. The work presented at the conference demonstrated progress towards UST as a routine breast screening imaging modality which produces quantitative images in an ionising radiation and pain-free manner.

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References

1. Cancer Research UK. Breast Cancer Statistics. **https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer#heading-Zero** (Accessed July 25, 2019).
2. Marmot M., Altman D., Cameron D. et al. The benefits and harms of breast cancer screening: an independent review. Br J Cancer (2013) 108 2205–2240 doi:10.1038/bjc.2013.177.
3. Boone J.M., Kwan A.L.C., Yang K. et al. Computed Tomography for Imaging the Breast. J Mammary Gland Biol Neoplasia (2006) 11 103. **https://doi.org/10.1007/s10911-006-9017-1**.
4. Brem R.F., Lenihan M.J., Lieberman J. et al. Screening Breast Ultrasound: Past, Present, and Future. American Journal of Roentgenology (2015) 204 234-240 doi: 10.2214/AJR.13.12072.
5. Leach M.O., Boggis C.R., Dixon A.K., et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). Lancet (2005) 365 1769–78 doi: **https://doi.org/10.1016/S0140-6736 (05)66481-1**.
6. Agnese D.M. Advances in breast imaging. Surg Technol Int (2005) 14 51–6.
7. Kaplan S.S. Automated Whole Breast Ultrasound. Radiologic Clinics, (2014) 52 539 – 546.
8. Li C., Duric N., and Huang L. Clinical breast imaging using sound-speed reconstructions of ultrasound tomography data. Proc SPIE. (2008) doi:10.1117/12.771436.
9. Greenleaf J., Johnson S., Lee S., et al. Algebraic reconstruction of spatial distributions of acoustic absorption within tissue from their two-dimensional acoustic projections. Springer US (1974) 5 591–603.
10. Duric N., Littrup P., Li C et al. Breast ultrasound tomography: bridging the gap to clinical practice. Progress in Biomedical Optics and Imaging - Proceedings of SPIE (2012) 8320. doi: 23.10.1117/12.910988.
11. Duric N., Littrup P., Schmidt S. et al. Breast imaging with the SoftVue imaging system: First results. In Medical Imaging 2013: Ultrasonic Imaging, Tomography, and Therapy (2013) 8675, 86750K. International Society for Optics and Photonics, 2013.
12. Malik B., Terry R., Wiskin J., and Mark Lenox. Quantitative transmission ultrasound tomography: Imaging and performance characteristics. Medical physics (2018) 45 7 3063–3075.
13. Stotzka R., Widmann H., O Mueller T., et al. Prototype of a new 3d ultrasound computer tomography system: transducer design and data recording. In Medical Imaging 2004: Ultrasonic Imaging and Signal Processing. 5373, 70–80. International Society for Optics and Photonics.
14. Gemmeke H., Berger L., Hopp T., et al. The new generation of the KIT 3D UST. In Proceedings of the International Workshop on Medical Ultrasound Tomography: 1.- 3. Nov. 2017, Speyer, Germany. 271–282. KIT Scientific Publishing, Karlsruhe, 2018.
15. Opieli´nski K.J., Pruchnicki P., Gudra T., et al. Ultrasound transmission tomography imaging of structure of breast elastography phantom compared to US, CT and MRI. Archives of Acoustics (2013) 38(3):321–334.
16. Opieli´nski K.J., Pruchnicki P., Gudra T., et al. Imaging results of multi-modal ultrasound computerized tomography system designed for breast diagnosis. Computerized Medical Imaging and Graphics (2015) 46 83 – 94. Information Technologies in Biomedicine.
17. Opieli´nski K.J., Pruchnicki P., Szymanowski P. et al Multimodal ultrasound computer-assisted tomography: An approach to the recognition of breast lesions. Computerized Medical Imaging and Graphics (2018) 65 102–114.
18. Manohar, S., Dantuma, M. Current and future trends in photoacoustic breast imaging. Photoacoustics. (2019). 16 100134.
19. Li S., Jackowski, M., Dione D.P., et al. Refraction corrected transmission ultrasound computed tomography for application in breast imaging. Medical physics, (2010) 37 5 2233-2246.
20. Wiskin, J., Borup, D.T., Johnson, S.A., & Berggren, M. Non-linear inverse scattering: High resolution quantitative breast tissue tomography. The Journal of the Acoustical Society of America, (2012) 131 5 3802-3813.
21. Wang, K., Matthews, T., Anis, F., et al. Waveform inversion with source encoding for breast sound speed reconstruction in ultrasound computed tomography. IEEE Trans. Ultrason. Ferroelectr. Freq. Control (2015) 62, 475–493.
22. Proceedings of the International Workshop on Medical Ultrasound Tomography. 1.- 3. Nov. 2017, Speyer, Germany. Hrsg.: T. Hopp,. KIT Scientific Publishing, Karlsruhe, 2018.