UBID: Ultrasound Breast Imaging with Deep Learning

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ABSTRACT

Breast cancer is the most common cancer in women worldwide. Early detection, if the cancer is in the localised stage, has a 5-year survival rate of 100%. Systematic screening is the main tool for early detection, and it relies almost entirely on imaging with mammography, which exposes women to harmful ionising radiation. We present an alternative ultrasound imaging modality that is safe, universally applicable, and does not suffer from the limitations that mammography or MRI have. The incorporation of deep learning in the image reconstruction algorithm, based on full-waveform inversion, provides a complement and potentially a replacement to existing imaging methods.

Keywords: ultrasound computed tomography; full-waveform inversion; breast imaging; deep learning

1. INTRODUCTION

Breast cancer is the second most common cancer worldwide and the main cause of cancer-related mortality in Europe [1]. Despite its success in reducing breast cancer mortality in the last 5 decades, mammography suffers from two important drawbacks: it exposes the patient to potentially harmful ionising radiation and has low sensitivity and specificity in patients with dense breasts [2]. MRI does not suffer from these limitations, but it is less used due to its significantly higher deployment and maintenance cost and limited applicability [3].

Ultrasound imaging has the potential to overcome the limitations of mammography and MRI, but conventional modalities based on pulse-echo fail to deliver images with enough information to be diagnostically useful due to the limited data available for the reconstruction. If more data were available it would be possible to use more sophisticated reconstruction algorithms, and this fact, combined with an increase in computational capacity has sparked the development and growth of ultrasound computed tomography (USCT) for breast imaging over the last decades [4,5]. USCT devices acquire not only reflected but also transmitted ultrasound energy through the breast, providing a more reliable source of information to derive physical properties of breast tissues.

Even though the most common form of USCT imaging relies on time-of-flight (TOF) tomography, we advocate the use of a more sophisticated technique that produces images at much higher resolution (up to sub-millimetre scale at 1MHz) called full-waveform inversion (FWI) [6] as an ideal complement - and potential replacement - for mammography and MRI. FWI is much more computationally intensive than its TOF counterpart, and it requires low frequency content in the data that is not readily available in most USCT acquisition devices.

The objectives of the project are two-fold. First, to demonstrate the potential of FWI to reconstruct high-fidelity and high-resolution breast images from high-frequency USCT data. Second, to identify the limitations of our method and use this information to design the next generation of acquisition devices and algorithms that will be used in a clinical setting.

The results presented in the paper confirm that FWI is a suitable modality for breast imaging, but acquisition devices need to be re-designed to be more robust, as the position of the ultrasound probes during the experiment introduces a level of uncertainty that hinders the performance of the reconstruction algorithm. Finally, we use CT-scans and MRI images to validate our results and to combine them to produce a multi-modality registered reconstruction.

2. STATE OF THE ART

The first speed-of-sound (SoS) images from TOF measurements were presented in 1975 by J.F. Greenleaf et al. [7]. Nevertheless, the image quality of those initial studies was low, and the technique remained unexplored until recent years, when several companies and research groups developed USCT scanners and started to demonstrate the capacities and potential of this technique, including several clinical studies. The first international conference devoted entirely to this technique was hold in Speyer in 2016 [8]. The renaissance of USCT is mostly due to the capacity of modern equipment of acquiring, processing and reconstructing the large amounts of data generated in these studies.

Despite these recent advances, USCT still has to demonstrate its capacity of obtaining artifact-free, quantitative, high-resolution images fast enough for its routine use in clinical practice. The use of higher-frequencies in the ultrasound transducers allows getting reflectivity images with better resolution, but for transmission images, the use of higher frequencies increases the amount of acquired data and the complexity of the models to a point that the best reconstruction algorithms such as FWI cannot be directly applied. Therefore, there is a need for new high-quality reconstruction methods able to deal with medium and high-frequency ultrasound transmission tomography to fully exploit the potential of this technique.

In the last decade, deep-learning methods have demonstrated their capacity to overcome many different technical problems, usually by obtaining models, trained from a large set of data pairs, that allows transforming data from an input space into data of an output space.

3. BREAKTHROUGH CHARACTER OF THE PROJECT

An experimental multi-modality ultrasound breast imaging platform (MUBI) [9] developed by CSIC was used for the experimental validation of the project (Fig. 1a). It consists of a water-tank with two motorized ultrasound probes, capable of obtaining pulse-echo and through-transmission signals in arbitrary positions around the imaging zone. The probes (Prosonic, Korea) are 3.5 MHz centre frequency, 70% bandwidth, 128 elements with 0.22 mm pitch and 80 mm depth elevation focus, and the ultrasound system (DASEL SL, Spain) is a full-parallel equipment with 128 channels, 40 MSPS sampling rate at 16 bits resolution.

By sequentially moving the probes with two high-resolution stepper motors, the system simulates the behaviour of a ring with 20 phased-array probes, which is the foreseen configuration for the breast imaging system to be developed for clinical tests during ATTRACT Phase 2. The acquisition scheme includes pulse-echo sector scan images for generating the full angle spatial compound reflectivity images [10] (Fig. 4, lower left), and element-to-element acquisition for FWI.

The phantom used to demonstrate the imaging capabilities of ultrasound FWI during the project was model 073 from CIRS (Fig. 1b), a multi-modality breast phantom with cyst, dense masses and micro-calcification lesions. It is compatible with ultrasound, magnetic resonance (MRI), X-ray mammography and computed tomography (CT).

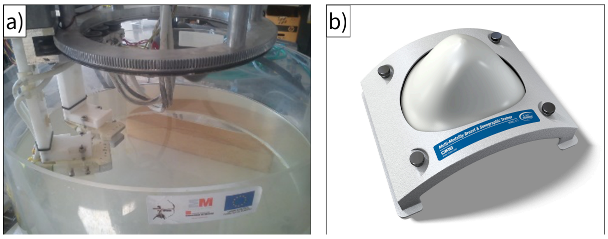

Fig. 1. a) MUBI platform; b) breast phantom used in the experiments.

The image reconstruction was based on a combination of FWI and deep learning algorithms. FWI is a technique that uses all available information present in the time-series data, and iteratively updates a model of acoustic properties - acoustic speed of sound in our case - that is used to produce numerically generated data (predicted) that mimics that corresponding to the laboratory experiment (observed). An optimisation problem is then designed to minimise an objective function that represents the misfit between the two datasets (typically as an L2 norm of the sample-by-sample difference), and the model of acoustic properties is iteratively updated to reduce this objective function at every step, where the frequency increase as iterations proceed to mitigate mis-convergence to local minima. The FWI reconstruction algorithm has been developed at Imperial College London (originally designed for Earth imaging purposes and extended to medical applications over the last 5 years) [6,11].

4. PROJECT RESULTS

As a local optimisation method, FWI relies on being able to converge to the global minimum of its solution space. In order to automate the breast reconstruction process as much as possible, one would ideally start the inversion process without requiring any prior information, namely with a starting model that was homogeneous and had the acoustic properties of water. In order to achieve this, frequencies below 500 kHz are usually required to avoid converging to a local minimum, but such low frequencies are not present in most USCT datasets due to the design of the ultrasound probes. Our approach is to extrapolate the missing low frequencies using convolutional neural networks (CNN) that have been trained with numerically generated datasets containing such missing low frequencies [12]. This enables FWI to reconstruct images without any prior information (i.e., starting the reconstruction from water).

The effects of not having sufficient low frequencies result in a phenomenon known as cycle-skipping, where the reconstructed image does not correspond to the ground truth (Fig. 2a). Fig. 2b shows the impact of cycle-skipping in an in-silico [13] reconstruction where FWI starts at a frequency of 500 kHz. The data inverted does not have energy below this frequency, and therefore the reconstruction fails (converges to a local minimum).

In contrast, using data with low frequencies extrapolated with our trained CNN (Fig. 2d-f) and starting FWI at 150 kHz successfully recovers the ground truth acoustic values of the target (Fig. 2c).

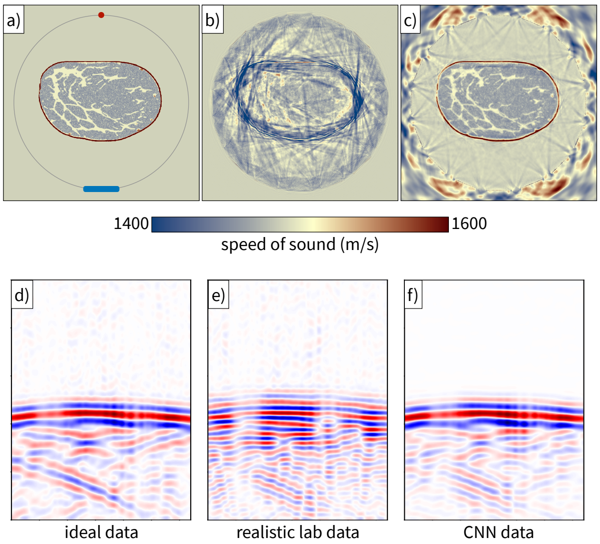

Fig. 2. Coronal slices through a numerical synthetic model: a) ground truth; b) FWI using starting at 500 kHz and using the dataset shown in e) clearly fails to recover the ground trught model; c) FWI starting at 150 kHz and using the dataset shown in f) recovers the ground truth model. Data corresponding to the emitter shown in red and the receivers shown blue in panel a) for: d) ideal full-bandwidth data used in the CNN training; e) synthetic data with a realistic amplitude spectrum missing low frequencies; f) data with extrapolated low frequencies. All data has realistic noise added to better simulate laboratory conditions.

However, while in-silico experiments confirm the validity of our approach under ideal conditions, they do not guarantee its robustness in real laboratory experiments. We acquired a dataset consisting of 25 slices through the breast phantom, each with 320 and 1280 unique emit and receive positions respectively. As in the in-silico case, the lowest frequency available in the data is 500 kHz. We apply minimal pre-processing; we low-pass filter the data below 2 MHz to avoid dispersion in our wave equation numerical modelling solver, we remove anomalously high noise and dead traces and apply a mute to remove high-amplitude frequency noise at early times. Then, we derive a source wavelet directly from the data, and use a watershot (dataset acquired in a water bath without phantom) to calibrate the positions of the transducers, and assume that these positions are repeatable (as we will discuss below they are not, which significantly degrades the quality of the FWI results). The starting model for all reconstructions is homogeneous and with a value of 1488 m/s (derived speed of sound of the water bath).

As expected, in line with the in-silico results, the reconstruction fails when FWI starts at 500 kHz as shown in Fig. 3a. The low velocity circular zone inside the breast is an artifact due to cycle-skipping and has a similar structure to the artifact in the in-silico results shown in Fig. 2b.

Using the low-frequency extrapolated dataset (Fig. 3c) allows us to start the reconstruction at 150 kHz. In this case, the model converges to the global minimum without cycle-skipping artifacts (Fig. 2b), but the final image presents some spurious features and a lack of sharpness in some areas, particularly in the outer layer of the phantom, in blue in Fig. 2b, where it is not possible to identify a clear boundary between water and the external boundary of the phantom. These reconstruction problems arise because the geometry of the experiment is not sufficiently accurate (FWI requires errors in positions of less than a tenth of a wavelength) and the errors in positions are mapped in the speed of sound model in an attempt to match the observed arrival times.

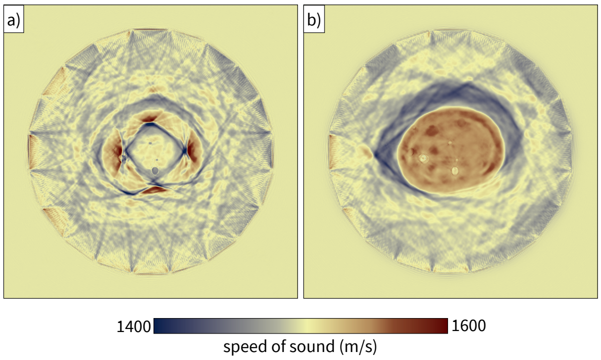

Fig. 1. a) Starting FWI at 500 kHz using data without low frequency extrapolation results in misconvergence due to cycle-skipping; b) starting FWI at 150 kHz with data pre-processed by the low-frequency extrapolation network succeeds in recovering coherent features compatible with CT-scans and MRI images.

Nonetheless, the obtained results present a good match to the structures observed in the MRI and CT-scans of the same breast phantom (Fig. 4). A surprising feature observed in the CT-scans is the presence of air pockets (white spots in the CT-scan shown in Fig. 4) which have a negative effect on our FWI reconstructions as we cannot affordably simulate wave propagation through air.

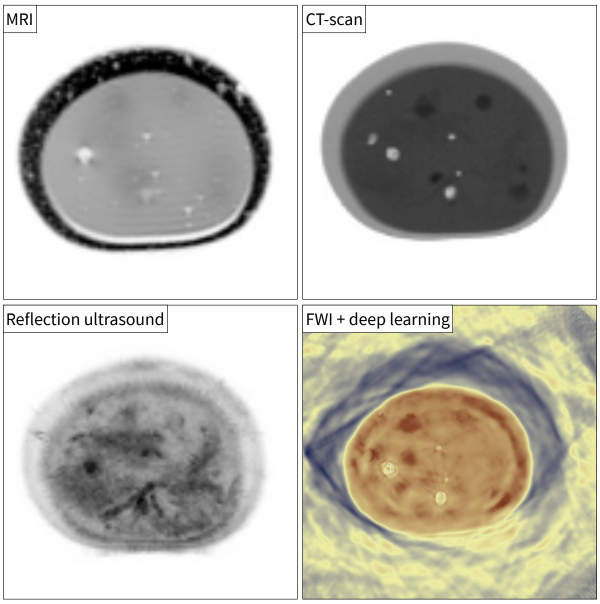

Fig. 4. Comparison between different imaging modalities. The high degree of correlation between the CT-scan and the FWI images confirms that our reconstruction has converged to the global minimum. In particular low (and high) density anomalies shown in white (and dark grey) in the CT-scan correspond to low (and high) speed of sound inclusions shown as yellow (and dark red) circles inside the phantom.

5. FUTURE PROJECT VISION

5.1. Technology Scaling

The UBID project is now at a TRL 3-4. The next phase of the project will focus on the redesign of the ultrasound acquisition device to improve its robustness. As mentioned in section 2, the new device will be a fully populated ultrasound ring without moving parts. This design will eliminate the positioning errors introduced in our original prototype and produce data with the quality and consistency required by our reconstruction algorithm.

The algorithmic development will be focused on the computational optimisation of the reconstruction algorithms to enable affordable and fast 3D breast reconstructions at the cost and speed demanded by clinical applications.

Both hardware and software are considered medical devices, and therefore will have to comply with CE regulations and be certified before they can be deployed in a relevant environment. This certification process will be the final step to be able to scale our technology to a TRL 5-7.

5.2. Project Synergies and Outreach

Central to the ability to advance to the desired TRL is the access to partners that are closer to the end-user of our technology. We have engaged with a team of breast cancer radiologists in one of the biggest hospitals in Spain that will, not only provide the best platform to test and validate our imaging system with volunteers and patients, but also contribute with invaluable feedback during the development and redesign of our platform. In parallel, we have established contact with various ultrasound sensor manufacturers to assist us in the development of the new prototype transducers.

We anticipate that, if successful, the final product of the consortium will have significant societal, scientific and commercial impact, as a complement and eventually a replacement for mammography and MRI. As such, we would like to organise a joint press-release between ATTRACT and all the partner institutions to announce the launch of Phase 2. Following this initial announcement, we plan to set up a web-based platform to provide and up-to-date record of the project progress, have an active social presence, and contribute to events organised by ATTRACT and other international scientific and medical conferences.

5.3. Technology application and demonstration cases

Our project goal is to improve the wellbeing and health of women by providing a better alternative to current screening and monitoring breast imaging modalities. Tests with volunteers and subsequent clinical trials will provide the demonstration cases required to validate our technology. The initial tests with healthy volunteers will be integrated in the development of the new prototype, where we will use other imaging modalities (MRI and mammography) to corroborate our reconstructed images and use this information to adapt the hardware and software of our prototype. Upon completion of this initial testing we will, after the appropriate EU certification process, proceed to clinical trials to demonstrate the efficacy of this new imaging modality. At this point, we expect to be able to attract interest from other partners that will contribute towards the commercialisation of the product.

Our project will contribute to the Research Infrastructure communities by providing a new medical imaging device that will help better understand and study breast-related diseases.

5.4. Technology commercialization

In line with the translational spirit of the ATTRACT initiative, we have started to build the infrastructure to commercialise the outcomes of our project. At this stage, we have set up a start-up company in collaboration with a venture accelerator that provides the seed investment to kick-start the company. Our vision is to have a working scanning system ready for clinical trials in the next two years, at which stage we will engage with a variety of private partners to accelerate the commercialisation and route to market of our product.

5.5. Envisioned risks

Phase 2 will have to overcome two main challenges. The first one is our ability to design a new prototype that is suitable for clinical trials. The main risk here is time, we need to have enough resources to build the new acquisition system within the first year of the project. Our mitigation strategy is to relax the demands of the device by improving our data pre-processing and reconstruction algorithms. We have already started this development by implementing a deep learning solution that replaces our existing source extraction and position calibration algorithms. We are also working in the design of a new sensor ring to improve the elevation resolution, which is the main limitation of current USCT systems. As another differential aspect, we plan to include ultrasound elastography imaging modality, a very specific technique for lesions malignancy quantification.

The second challenge is the performance of our reconstruction FWI algorithm in living patients that move and breath during data acquisition. It is possible, but not certain, that such patient movements will create small discrepancies in the data due to changes in the breast position and shape. If this is the case, we will implement registration as a pre-processing step in order to remove these effects from the data.

5.6. Liaison with Student Teams and Socio-Economic Study

Several master and undergrad female students have participated in this project. Their contribution has facilitated achieving the ambitious goals of the project in this very short period of time. We are collaborating in the International Mentoring Program of IMFAHE's Foundation (www.imfahe.org), which connect outstanding students about to finish their undergrad and PhD studies with researchers working at the best universities and research centres in the world. Joaquin L. Herraiz is the director of the engineering section of this program, and this project has created the connection with Lluís Guasch and Oscar Calderón, who are now program mentors. The program has a networking platform, and we will use it to gain more exposure for our project as part of the ATTRACT dissemination strategy, as well as to recruit more MSc. students.

6. ACKNOWLEDGEMENT

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7. REFERENCES

[1] J. Ferlay, I. Soerjomataram, R. Dikshit, S. Eser, C. Mathers, M. Rebelo, D. M. Parkin, D. Forman, and F. Bray, "Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012," Int. J. Cancer, vol. 136, no. 5, pp. E359– E386, Mar. 2015.

[2] M. Løberg, M. L. Lousdal, M. Bretthauer, and M. Kalager, "Benefits and harms of mammography screening," Breast Cancer Res., vol. 17, no. 1, pp. 1–12, 2015.

[3] S. V. Sree, Y.-K. E. Ng, R. U. Acharya, and O. Faust, "Breast imaging: A survey," World J. Clin. Oncol., vol. 2, no. 4, pp. 171– 178, Apr. 2011.

[4] N. V. Ruiter, T. Hopp, M. Zapf, A. Menshikov, C. Kaiser, and H. Gemmeke, "3D ultrasound computer tomography for breast cancer diagnosis at KIT: an overview," in Proceedings of the International Workshop on Medical Ultrasound Tomography, 2018, pp. 205–216.

[5] R. G. Pratt, L. Huang, N. Duric, and P. Littrup, "Sound-speed and attenuation imaging of breast tissue using waveform tomography of [35] transmission ultrasound data," in Proceedings SPIE, 2007, vol. 6510, pp. 1–12.

[6] Guasch, L., Agudo, O. C., Tang, M. X., Nachev, P., & Warner, M. (2020). Full-waveform inversion imaging of the human brain. NPJ digital medicine, 3(1), 1-12.

[7] Greenleaf, J. F., Johnson, S. A., Samayoa, W. F. and Duck, F. A. (1975) Algebraic reconstruction of spatial distribution of acoustic velocities in tissue from their time-of-flight profiles. In Acoustical Holography, Vol. 6 (Ed. N. Booth), Proc Int Symp **Feb**,1975, 71-90. Plenum Press, New York

[8] https://indico.scc.kit.edu/event/307/overview

[9] J. Camacho; J. F. Cruza; N. González-Salido; C. Fritsch; M. Pérez-Liva; J.L. Herraiz; J.M. Udías. A Multi-Modal Ultrasound Breast Imaging System. Proceedings of the International Workshop on Medical Ultrasound Tomography: 1.- 3. Nov. 2017, Speyer, Germany. pp. 119 - 130. KIT Scientific Publishing, Karlsruhe, 11/2017. ISBN 9783731506898

[10] L. Medina; J. Camacho; C. Fritsch. A characterization of ultrasonic full angle spatial compounding as a possible alternative for breast cancer screening. Archives of Acoustics. 40, 3, pp. 301 – 310. ISSN 0137-5075

[11] Warner, M., Ratcliffe, A., Nangoo, T., Morgan, J., Umpleby, A., Shah, N., ... & Conroy, G. (2013). Anisotropic 3D full-waveform inversion. Geophysics, 78(2), R59-R80

[12] Sun, H., & Demanet, L. (2020). Extrapolated full-waveform inversion with deep learning. Geophysics, 85(3), R275-R288.

[13] Lou, Y., Zhou, W., Matthews, T. P., Appleton, C. M., & Anastasio, M. A. (2017). Generation of anatomically realistic numerical phantoms for photoacoustic and ultrasonic breast imaging. Journal of Biomedical Optics, 22(4), 041015.