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Evaluation of breast tissue characterization by ultrasound computer tomography using a 2D/3D image registration with mammograms

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***Abstract*—Ultrasound Computer Tomography (USCT) is a promising 3D modality for early breast cancer detection, which is expected to provide quantitative imaging. The aim of this paper is to evaluate the quantitative diagnostic value of the USCT images, i.e. sound speed and attenuation images, using X-ray mammograms as ground truth. For this purpose we applied our 2D/3D registration method, which is based on biomechanical modeling of the breast. Mammograms were segmented into fatty, glandular and tumorous tissue. For each tissue, the average sound speed and attenuation in the corresponding USCT images was calculated. Tumorous tissue could be separated from fatty and glandular tissue using a fixed absolute sound speed threshold in all regarded datasets. By combining sound speed and attenuation, the separation between fatty and glandular tissue could be improved. By overlaying sound speed and attenuation information on the mammogram, quantitative and morphological information can be combined for multimodal diagnosis. This may benefit early breast cancer detection in future.**

I. Introduction

Ultrasound Computer Tomography (USCT) is a promising 3D modality for early breast cancer detection [1], [2]. Its purpose is to provide cost-efficient three-dimensional volume imaging of the breast in prone position without exposing the patient to ionizing radiation. The image acquisition is based on numerous ultrasound transducers, which surround the breast in a water bath. The emitted ultrasound is recorded from all directions, allowing for the reconstruction of reflection as well as for transmission images. Reflection images reveal changes in the echo texture, resulting in qualitative imaging of the surfaces of different tissues. Based on the transmission data, attenuation and sound speed images can be reconstructed, which both are expected to provide a quantitative tissue characterization [3].

As USCT is an imaging modality in development, it is of high interest to compare the images with the standard screening method X-ray mammography. For subsequent use in clinical practice it might also be of high interest to combine the diagnostic value of both methods. However, X-ray mammograms image the patient's breast in a considerably different configuration. The patient stands upright, while the breast is compressed between to parallel plates in order to enhance the contrast of the images. From this breast configuration, 2D projection images are acquired. Due to these differences between X-ray mammography and USCT, correlating both imaging methods is challenging. To overcome this challenge, we developed an automatic 2D/3D registration method [4], [5]. It is based on a patient-specific biomechanical model to simulate the huge deformation which is applied to the breast during mammography. The model is built up based on the volume image before the breast deformation is simulated using the Finite Element Method (FEM). The FEM simulation mimics the mammographic compression and results in a deformed volume image, in which the breast is in a similar configuration as in the corresponding mammogram. The projection of the deformed volume image has overlaying circumferences with the mammogram such that both modalities can be compared directly.

The registration method was designed to work with arbitrary volumetric modalities like Magnetic Resonance Imaging (MRI), dedicated breast CT and USCT [6]. In our previous work it was applied to USCT volumes [7]. The resulting registered images served as a basis to carry out an image fusion of sound speed with mammograms [8] resp. a combination of sound speed and attenuation with mammograms [9], which might be beneficial for combined reading in radiological diagnosis. Especially for dense breast tissue, in which the sensitivity of mammograms is limited [10], tissue characterization by quantitative imaging like sound speed and attenuation may provide a guidance for diagnosis of cancerous lesions. In a previous study, we investigated the relevance of sound speed as quantitative measure for tissue characterization [11]. The aim of this paper is now to combine registered sound speed and attenuation images to classify different types of tissue using mammograms as ground truth.

II. Methods

A. Image acquisition and preprocessing

Sound speed and attenuation images were acquired within a clinical study using an experimental USCT device at Karmanos Cancer Institute (KCI), Detroit, USA [12]. The device consists of a ring-shaped aperture which is equipped with 256 ultrasound transducers. The aperture is embedded in a water basin and can be translated in steps of 1 mm. At each translation step, the raw data for one slice is acquired. Afterwards the slice images are reconstructed using an iterative bent-ray ultrasound tomography algorithm [13]. Due to a focusing in elevation direction, the resolution of images is anisotropic with 1 mm in-plane and a slice thickness of 4 mm. The number of acquired slices and the spacing between slices depends on the size of the patient's breast. The USCT images were segmented into background and object using an automatic segmentation algorithm provided by KCI which is based on slice-wise polygon fitting to the boundaries of the breast. Afterwards a scaling and rotation was applied to fit the orientation of the mammogram. In case of a gap between the slices, a linear interpolation was carried out to obtain isotropic voxels.

Mammograms of the same patients were acquired using digital or analog devices. In order to compare morphological structures in the X-ray mammograms with the quantitative information in sound speed and attenuation images, different types of tissue in the X-ray mammogram were manually segmented. In a first step, the breast was separated from the background using thresholding and morphological operations. Afterwards, fatty and fibroglandular tissue was differentiated using an interactive thresholding method similar to [14]. Tumors were manually annotated by an expert using a freehand tool.

For evaluation purposes, only datasets with clearly visible lesions in the X-ray mammogram as well as in the sound speed respectively attenuation image were included in this study.

B. Registration

The preprocessed sound speed and attenuation images were registered to the X-ray mammograms using our automated 2D/3D registration method, which is based on a biomechanical compression simulation as described in [7] resp. [6] (Fig. 1). The geometry of the biomechanical model was specified by a tetrahedral mesh which is built up based on the 3D sound speed image using a tetgen-based meshing algorithm [15]. The physical behavior was defined by applying a material model and boundary conditions. We used an isotropic, nearly incompressible material, for which the stress-strain relationship is defined by a hyperelastic neo-hookean model. Due to the limited effect of more complex models [16], a homogeneous material mimicking fatty tissue was used for the entire breast in this study. Material stiffness parameters were obtained from literature [17].

The mammographic compression was modeled as a contact problem by introducing compression plates, which were moved until a defined compression thickness is reached. Due to simplifications, images did not overlap congruently after this simulation step. Therefore in a second step, the shape of the deformed breast was refined to meet the circumferences of the corresponding mammogram by node displacements. The numerical solution of both simulations is based on FEM and was computed using the commercial FEM package Abaqus [18].

C. Evaluation method

After the registration process was completed, maximum intensity projections of the registered sound speed image and registered attenuation image were created. These projection

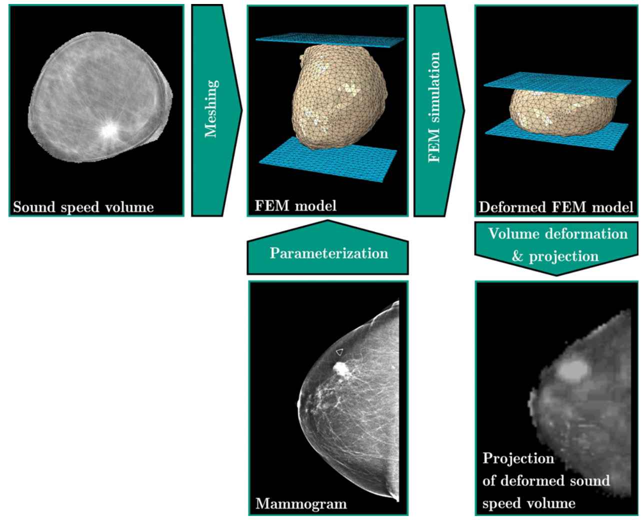

Fig. 1. Simplified principle of the registration process. A FEM model is created based on the segmented sound speed volume using a meshing algorithm. The model is parameterized by information from the mammogram. Afterwards the compression simulation is carried out. Based on the resulting deformed FEM model, the USCT volume is deformed and projected, creating an image directly comparable to the mammogram.

images overlap congruently with the corresponding mammogram. Hence, the segmentation mask of the mammogram can be used to quantify sound speed and attenuation characteristics of the different types of tissue. For each segmented tissue type in the mammogram, the sound speed and attenuation values at the corresponding areas in the projection images were analyzed and the average sound speed and attenuation per tissue type in each dataset was calculated. A linear support vector machine (SVM) [19] was used to calculate separators of a three class problem to distinguish between fatty and glandular respectively glandular and tumor tissue. Furthermore an evaluation of a two-class problem distinguishing tumor tissue from other tissue was carried out. The diagnostic value of sound speed and attenuation values to distinguish tissue types was estimated by the training error of the SVMs and compared to our earlier results, in which solely the sound speed information was used.

For visualization of the diagnostic value of sound speed and attenuation images, an image fusion with the mammogram was carried out. Sound speed values and attenuation values in the maximum intensity projection are combined by a logical operation and color coded. Finally, the color-image is superposed semi-transparently on the gray level X-ray mammogram.

III. Results

The evaluation was carried out with nine datasets. Due to availability of adequate USCT datasets for evaluation, the patient collective was different from our previous study [11]. Each dataset consists of a sound speed image, an attenuation image and the corresponding cranio-caudal mammogram. To estimate the target registration error (TRE), a corresponding lesion in both modalities was annotated manually by an expert

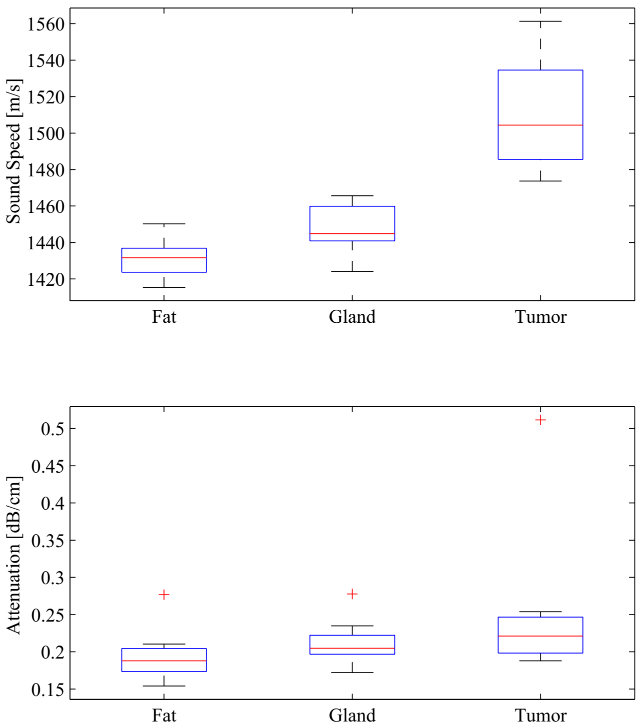

Fig. 2. Box plot of mean sound speed and attenuation values for different types of tissue.

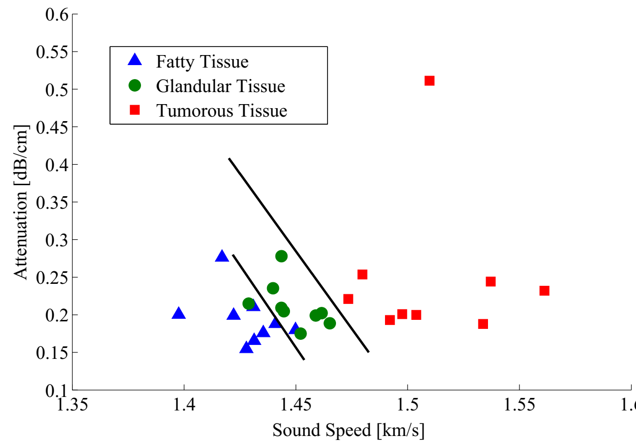

Fig. 3. Scatter plot of the average sound speed and attenuation for fatty, glandular and tumorous tissue in the nine datasets used in this study.

in each dataset and the displacement between the center points of the lesion marking was calculated. The average TRE after carrying out the registration was 6.3 mm ± 3.8 mm.

In the next step, sound speed and attenuation values were analyzed for each tissue type. The average over all the mean sound speed values was 1431 m/s (± 11 m/s) for regions segmented as fatty tissue, 1449 m/s (± 13m/s) for fibroglandular and 1510 m/s (± 29 m/s) for tumorous tissue for the regarded datasets. Accordingly the average over all the mean attenuation values was 0.195 dB/cm (± 0.036 dB/cm) for fatty tissue, 0.212 dB/cm (± 0.030 dB/cm) for fibroglandular and 0.250 dB/cm (± 0.101 db/cm) for tomourous tissue. Fig. 2 presents a boxplot of the reported values.

To evaluate the diagnostic value of the separate as well as the combined sound speed and attenuation values, support vector machines were trained and the training error was evaluated based on the resulting confusion matrix. As expected from the boxplot (Fig. 2), the separation of different tissue by attenuation imaging was less effective than with sound speed. The three class error to distinguish between fatty, glandular and tumour tissue was 11% for the sound speed and 59% for the attenuation. The two class errors were 0% and 29% respectively.

Afterwards sound speed and attenuation were used in combination. Thereby the three class error could be reduced to 7% and the two class error to 0%. Fig. 3 presents a scatter plot of average sound speed and attenuation for fatty, glandular and tumour tissue. Converting the sound speed respectively the attenuation into values relative to the maximal values per patient did not improve the results further, i.e. the best results were achieved using the absolute values.

Finally the image fusion with the X-ray mammogram was carried out. The SVM trained with sound speed and attenuation values in combination was used to threshold the maximum intensity projections of both images before combining them with a logical *AND* operation. The resulting binary masks for the different tissue types were multiplied with the sound speed image at the corresponding position. The sound speed was color-coded since they show a more quantitative diagnostic value. The resulting color image was rendered semi-transparently on the mammogram (Fig. 4). This enables to highlight the location of different tissue types in the mammogram.

IV. Discussion and Conclusion

In this paper we applied our 2D/3D registration method to USCT images. The purpose was to evaluate quantitative sound speed and attenuation images for their ability to separate different types of breast tissue. The registration enables direct comparison and combination of two-dimensional morphological imaging with quantitative three-dimensional imaging. Using the mammograms as ground truth we were able to quantify average sound speed and attenuation values for fat, glandular and tumor tissue. In addition to our previous paper, not only sound speed but also attenuation images and the combination of both images were investigated in this study.

Based on the presented results we can conclude that sound speed seems to have a more quantitative diagnostic value than attenuation imaging. In all cases, the tumor tissue could be separated well from surrounding tissue by a general absolute sound speed threshold. Using sound speed and attenuation in combination may enhance the diagnostic value further: the separation between fatty and glandular tissue improved by taking both images into account. The results are limited by the registration error, since a misregistration of tissue structures

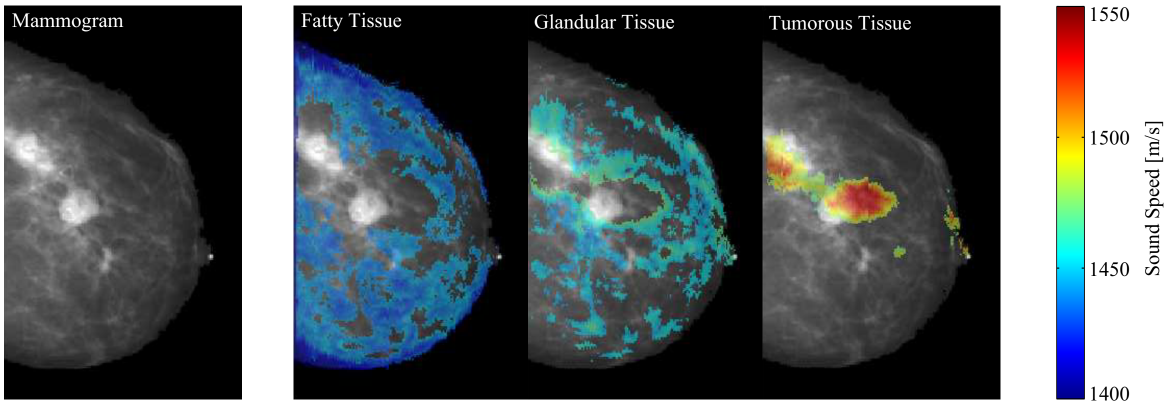

Fig. 4. Semi-transparent overlay of tissue structures separated by sound speed and attenuation. Within the overlay, the sound speed in the particular region is color-coded since it provides a more quantitative diagnostic value than the attenuation.

results in blurring of the obtained sound speed and attenuation values at corresponding image regions. Though a relatively small patient collective with obvious lesions was included in this study, the obtained are promising. Our future work will focus on the evaluation with a higher number of datasets to increase statistical robustness. By overlaying the combined sound speed and attenuation information on the mammogram, tissue structures can be highlighted. As can be seen in the exemplary case in Fig. 4 they tend to clearly follow the morphology visible in the mammogram.

To the best of our knowledge, a quantitative analysis of sound speed and attenuation in correlation with X-ray mammograms has not been carried out before. The method enables comparison of USCT to the standard method X-ray mammography. Quantitative information from sound speed and attenuation can be used in combination with X-ray mammograms for multimodal diagnosis and may be beneficial for early breast cancer detection.

REFERENCES

[1] H. Gemmeke and N. Ruiter, “3D Ultrasound Computer Tomography for Medical Imaging,” *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*, vol. 580, no. 2, pp. 1057 – 1065, 2007.

[2] N. Duric, P. Littrup, L. Poulo, A. Babkin, R. Pevzner, E. Holsapple, O. Rama, and C. Glide, “Detection of Breast Cancer with Ultrasound Tomography: First Results with the Computerized Ultrasound Risk Evaluation (C.U.R.E),” *Medical Physics*, vol. 34, no. 2, pp. 773–785, 2007.

[3] J. F. Greenleaf and R. C. Bahn, “Cinical Imaging with Transmissive Ultrasonic Computerized Tomography,” *IEEE Transactions on Biomedical Engineering*, vol. BME-28, no. 2, pp. 177–185, 1981.

[4] N. V. Ruiter, R. Stotzka, T. O. Mueller, H. Gemmeke, J. R. Reichenbach, and W. A. Kaiser, “Model-Based Registration of X-ray Mammograms and MR Images of the Female Breast,” *IEEE Transactions on Nuclear Science*, vol. 53, no. 1, pp. 204–211, 2006.

[5] T. Hopp, M. Dietzel, P. Baltzer, P. Kreisel, W. Kaiser, H. Gemmeke, and N. Ruiter, “Automatic multimodal 2d/3d breast image registration using biomechanical FEM models and intensity-based optimization,” *Medical Image Analysis*, vol. 17, no. 2, pp. 209 – 218, 2013.

[6] T. Hopp, “Multimodal Registration of X-Ray Mammograms with 3D Volume Datasets,” Ph.D. dissertation, University of Mannheim, 2012.

[7] T. Hopp, M. Holzapfel, N. V. Ruiter, C. Li, and N. Duric, “Registration of X-ray Mammograms and Three-Dimensional Speed of Sound Images of the Female Breast,” in *Proceedings SPIE Medical Imaging*, vol. 7629, 2010, p. 762905.

[8] T. Hopp, J. Bonn, N. V. Ruiter, M. Sak, and N. Duric, “2D/3D Image Fusion of X-ray Mammograms with Speed of Sound Images: Evaluation and Visualization,” in *Proceedings SPIE Medical Imaging*, vol. 7968, 2011, p. 79680L.

[9] T. Hopp, N. Duric, and N. Ruiter, “Automatic Multimodal 2D/3D Image Fusion of Ultrasound Computer Tomography and X-ray Mammography for Breast Cancer Diagnosis,” in *Proceedings SPIE Medical Imaging*, vol. 8320, 2012, p. 83200P.

[10] E. D. Pisano, R. E. Hendrick, M. J. Yaffe, J. K. Baum, S. Acharyya, J. B. Cormack, L. A. Hanna, E. F. Conant, L. L. Fajardo, L. W. Bassett, C. J. D’Orsi, R. A. Jong, M. Rebner, A. N. A. Tosteson, and C. A. Gatsonis, “Diagnostic Accuracy of Digital Versus Film Mammography: Exploratory Analysis of Selected Population Subgroups in DMIST1,” *Radiology*, vol. 246, no. 2, pp. 376–383, 2008.

[11] T. Hopp, N. Duric, and N. V. Ruiter, “Breast tissue characterization by sound speed: Correlation with mammograms using a 2D/3D image registration,” in *2012 IEEE International Ultrasonics Symposium Proceedings*, 2012, pp. 936–940.

[12] N. Duric, P. Littrup, P. Chandiwala-Mody, C. Li, S. Schmidt, L. Myc, O. Rama, L. Bey-Knight, J. Lupinacci, B. Ranger, A. Szczepanski, and E. West, “In-Vivo Imaging Results with Ultrasound Tomography: Report on an Ongoing Study at the Karmanos Cancer Institute,” in *Proceedings SPIE Medical Imaging*, vol. 7629, 2010, p. 76290M.

[13] C. Li, N. Duric, and L. Huang, “Clinical breast imaging using sound-speed reconstructions of ultrasound tomography data,” in *Proc. SPIE Medical Imaging*, vol. 6920, 2008, p. 692009.

[14] J. W. Byng, N. F. Boyd, E. Fishell, R. A. Jong, and M. J. Yaffe, “The quantitative analysis of mammographic densities,” *Physics in Medicine and Biology*, vol. 39, no. 10, p. 1629, 1994.

[15] Q. Fang and D. Boas, “Tetrahedral Mesh Generation from Volumetric Binary and Grayscale Images,” in *IEEE International Symposium on Biomedical Imaging: From Nano to Macro*, 2009, pp. 1142–1145.

[16] T. Hopp, A. Stromboni, N. Duric, M. Zapf, H. Gemmeke, and N. V. Ruiter, “Sound speed based patient-specific biomechanical modeling for registration of usct volumes with x-ray mammograms,” in *Proceedings SPIE Medical Imaging*, 2013, p. 86750L.

[17] P. S. Wellman, R. D. Howe, E. Dalton, and K. A. Kern, “Breast Tissue Stiffness in Compression is Correlated to Histological Diagnosis,” Harvard BioRobotics Laboratory, Technical Report, 1999.

[18] Dassault Systmes, *Abaqus 6.11 Online Documentation*, 2011.

[19] N. Cristianini and J. Shawe-Taylor, *An Introduction to Support Vector Machines and Other Kernel-based Learning Methods*. Cambridge University Press, 2000.