ULTRASOUND SCATTERER SIZE ESTIMATION TECHNIQUE BASED ON A 3D ACOUSTIC IMPEDANCE MAP FROM HISTOLOGIC SECTIONS.

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Abstract—

Identifying the scatterers and obtaining accurate estimates of ultrasonic scatterer sizes are beneficial adjuncts to characterize (diagnose) disease from ultrasonic backscatterer measurements. A new scatterer size estimation technique has been developed that is based on a 3D acoustic impedance map. Ultrasonic scatterer estimation techniques rely extensively on form factor functions to obtain estimates, and 3D impedance maps can be used to derive independently form factors. The 3D acoustic impedance map is derived from a 3D histological data set of tissue, and is independent of ultrasonically acquired data. A rat fibroadenoma and a mouse 4T1 mouse mammary tumor (MMT) were fixed (10% neutral-buffered formalin), embedded in paraffin, serially sectioned at 10 μm and 5 μm respectively, and stained with H&E for histologic evaluation. Each section was digitally photographed through the light microscope. Tissue structures in each section were assigned distinct acoustic impedance values. The images from serial sections were aligned to yield two 3D impedance data set. A Gaussian form factor was used to estimate scatterer size and acoustic concentration. The scatterer size estimates were compared to previous values that were obtained from ultrasonic backscatterer measurements (also using a Gaussian form factor). For both 3D impedance maps, the relative difference between the size estimates were below 10%. The optimization scheme was also conducted on two simulated medium and led to relative errors below 1% for the scatterer size. This approach demonstrates that the use of 3D impedance maps has significant potential for improving parametric imaging by evaluating form factor functions.

I. INTRODUCTION

The echoes or backscattered signals received by an ultrasonic transducer used to image tissues are due to small spatial variations in the mechanical properties of the tissues. Ultrasonic parametric images try to improve conventional ultrasonic B-mode images by obtaining information about structures smaller than the wavelength. Parametric techniques retrieve information about tissue microstructures from the frequency-dependent information [1] contained in the backscattered signals. Usually two main parameters are estimated from the spectrum of the backscattered signals, the scatterer size and the acoustic concentration[2]. The estimates depend on the chosen model to describe the scatterers. The functions that describe the scattering structures are called form factors. A more accurate form factor will lead to improved quality in parametric images.

A method is proposed to obtain estimates of the scatterer size and acoustic concentration that is totally independent of the ultrasonic measurements. This method involves the development of a 3D impedance volume of tissue. The 3D impedance volume can also be used to obtain realistic form factors.

II. METHODS

A. 3D Impedance Maps

A 3D impedance map can be seen as a computational phantom. It is essentially a 3D matrix that describes the acoustical properties of a 3D medium; the elements are the values of the acoustical impedance of the medium.

3D impedance maps can be used to derive independently form factors. Form factors are obtained from the Fourier transform of the 3D spatial autocorrelation function (SAF) of 3D impedance maps.

The 3D impedance maps are derived from 3D his-

tologic datasets. Impedance maps are independent of ultrasonically acquired data. Tissue was fixed by immersion in 10% neutral-buffered formalin, embedded in paraffin. The tissue was then stained by H&E. The 3D histological data volume is obtained by aligning light microscopy images of sections to make a 3D volume.

The next step consists in assigning acoustic impedance value at every single point in the volume. The result of this operation yields the 3D impedance map. The acoustic values are obtained by recognizing tissue histology, using a look-up table of acoustical properties of tissues and thresholding the color coded histology images.

In this study two tumors were used, a rat fibroadenoma and a 4T1 MMT. The rat fibroadenoma was of size $640\mu m * 480\mu m * 390\mu m$. It was obtained from 39 slices of size $640\mu m * 480\mu m$. Each slice had a thickness of 10 μm. The 4T1 MMT was of size $220\mu m * 165\mu m * 330\mu m$. It was obtained from 66 slices of size $220\mu m * 165\mu m$. Each slice had a thickness of 5 μm.

The 3D histology and 3D impedance maps can be found in the top of Figure 1 for the fibroadenoma and on the top of Figure 2 for the MMT.

B. Estimation

The backscattered intensity, I_{bs}, due to an incident plane wave on a weakly inhomogeneous medium can be written as[3]:

$$I_{bs} = Ak^4 S(2k) \quad \text{where} \tag{1}$$

$$S(2k) = \left| \int\int\int_{V_0} \frac{\Delta(z)}{z} e^{-2jkr_0} dv_0 \right|^2. \tag{2}$$

A is a proportionality constant. Hence, the power spectrum of the relative impedance variations can be easily extracted from the backscattered intensity.

A Gaussian form factor was chosen to describe the scatterering structures because it is the form factor usually chosen for the ultrasonic measurements. Using the Gaussian form factor allows for direct comparison with estimates obtained using the 3D impedance map and the ultrasonic backscatter measurements [2]. The Gaussian form factor is defined by [1], [4]:

$$F_a(2k) = e^{-0.827k^2 a_{eff}^2}. \tag{3}$$

The subscript eff in Eq. (3) stands for effective because the Gaussian form factor describes a continuous distribution, the subscript will be omitted in the reminder of the paper.

The 3D impedance map is divided into smaller 3D volumes called regions of interest (ROIs). The power spectrum, $S(2k)$, of each ROI is computed by taking the magnitude squared of the Fourier transform of the ROI. Then, an optimization scheme is ran to fit F_a on $S(2k)$. The scheme consists in minimizing $E(a, G)$ defined by:

$$E(a, G) = \int_{k_{min}}^{k_{max}} \left[log(S(2k)) - log(GF_a(2k)) \right]^2 dk \tag{4}$$

This leads to two estimates, a radius estimate a^* and a gain estimate G^*. The scatterer size (diameter) estimate is then $2a^*$. The acoustical concentration estimate, C^*, is related to G by[1]:

$$C^* = G^*/V_s^2, \text{ where } V_s = \frac{4}{3}\pi a^{*3}. \tag{5}$$

The acoustical concentration may have large variation from one ROI to the other, it is therefore usually transformed into a log scale through $C_{dB} = 10 * \log(\mathrm{C}[mm^-3])$.

This estimation scheme has no limitation over the chosen frequency range; therefore, it has the advantage to be able to potentially find a scatterer of any size. Ultrasonic measurements are dependent upon the bandwidth of the transducer which limits the range of scatterer size that can be detected.

III. RESULTS

A. Simulated 3D impedance maps

Two 3D impedance maps were simulated. They contained randomly positioned single sized spherical scatterers of diameter $40\mu m$ and $80\mu m$ respectively. The background impedance was fixed to 1.0 Mrayl and the scatterer impedance was fixed to 1.1 Mrayl for both medium. Both 3D impedance volumes were cubic with side lengths of 256 μm.

The estimation scheme was conducted on the two simulated 3D Impedance maps. The estimated size (diameter) found were 39.6 μm and 79.8 μm for the first and second simulated medium respectively. The relative error between the estimated and actual concentration were in both cases around -8%.

These results tend to demonstrate the ability of the 3D impedance map methodology to find scatterer of very different sizes.

TABLE I
3D IMPEDANCE MAP ESTIMATES

	Rat fibroadenoma	Mouse 4T1 MMT
Impedance values used (Mrayl)	1.0 - ephitelial cells 1.1 - mammary duct 1.3 - connective tissue	1.45 - fat 1.50 - cytoplasm 1.51 - nuclei 1.51 - red blood cells 1.60 - connective tissue
Impedance Map Estimates	Size: $95 \pm 27\mu m$ Concentration: $-11.4 \pm 7dB(mm^{-3})$	Size: $30.5 \pm 5.8\mu m$ Concentration: $-7.1 \pm 4.8dB(mm^{-3})$
Ultrasound Estimates	Size: $105 \pm 25\mu m$ Concentration: $-15.6 \pm 5dB(mm^{-3})$	Size: $30.0 \pm 9.6\mu m$ Concentration: $10.6 \pm 6.9dB(mm^{-3})$

B. Mammary tumors

The estimation scheme was then conducted on the 3D impedance maps of the rat fibroadenoma and of the 4T1 MMT. The 3D impedance maps were first divided into 4 region of interest (ROI) and the estimation was processed independently on each ROI. The way the 3D impedance volumes were divided into 4 ROIs is shown on the image B) of Figures 1 and 2.

The estimated values obtained for the scatterer sizes and acoustical concentrations are shown on the two bottom plots of Figure 1 for the rat fibroadenoma and on the two bottom plots of Figure2 for the 4T1 MMT. Also, the average values and standard deviations of the estimates were computed and can be found on Table I. The first row of Table I shows the values of the impedances used for the two tumors, the second rows displays the estimates obtained using the 3D impedance map technique and the third row displays the estimates obtained by ultrasonic backscatter measurements[2].

The relative difference between the size estimates obtained by the 3D impedance methodology and the backscatter measurements for both tumors is smaller than 10 %. It tends to demonstrate that the 3D impedance map is a powerful tool to obtain estimates. However the acoustic concentration values obtained are very different and need to be further investigated.

IV. CONCLUSIONS

A method was proposed to obtain estimates of ultrasonic scatterer properties: the scatterer size and the acoustic concentration. This method involves the development of a 3D impedance map from histologic sections of tissues.

The methodology was used on two simulated volumes. For both simulated media the relative error in the scatterer size was less than 1%. The relative error in the acoustical concentration was less than 10%. These results tend to demonstrate that the 3D impedance map is a powerful tool to obtain estimates.

The estimation scheme does not have a preferred frequency band. The same algorithm was able to find scatterers of sizes 40 μm and 80 μm. To detect scatterers of these two different sizes ultrasonically one would likely have to use different transducers with two different bandwidths. The 3D impedance map estimation scheme may therefore also have the potential to find multiple populations of scatterers.

The methodology was used with two 3D impedance map derived from two different mammary tumors, a rat fibroadenoma and a 4T1 mouse mammary tumor. The estimates were compared to the ultrasonically obtained estimates. For both tumors the relative difference for the size were less than 10 %.

The good agreement between the estimated sizes for both techniques demonstrates that the 3D impedance map may have potential to help in deriving more accurate form factors.

V. ACKNOLEDGEMENT

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VI. REFERENCES

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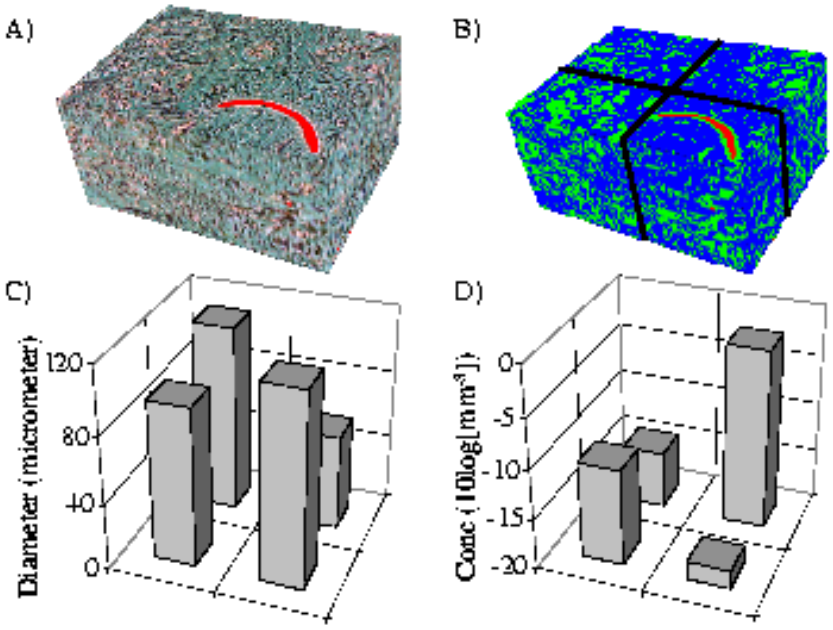

Figure 1

RAT FIBROADENOMA TUMOR. A) IS THE 3D HISTOLOGY MAP. B) IS THE DEDUCED 3D IMPEDANCE MAP. THE BLACK LINES SHOWS HOW THE VOLUME WAS DIVIDED INTO 4 ROIS. C) SHOWS THE SCATTERER SIZE ESTIMATES FOR THE 4 ROIS. D) SHOWS THE ACOUSTIC CONCENTRATION ESTIMATES FOR THE 4 ROIS.

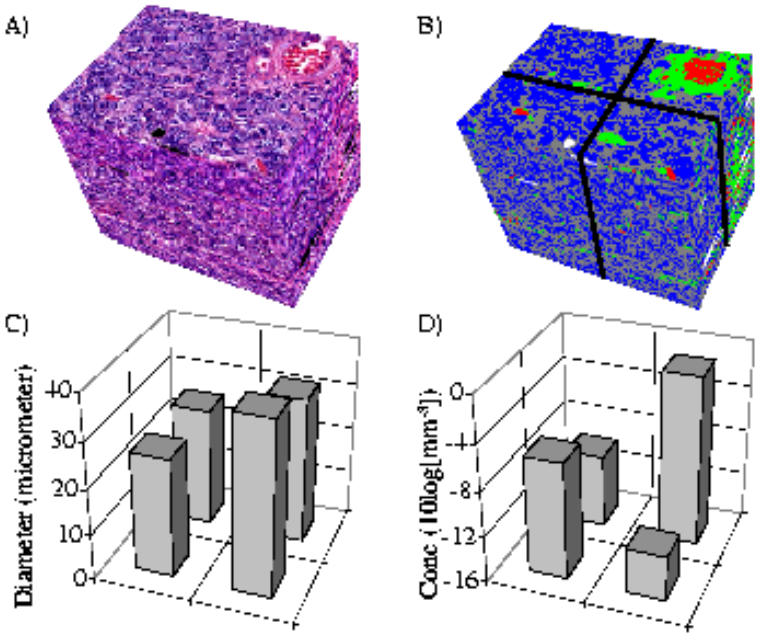

Figure 2

MOUSE 4T1 MAMMARY TUMOR. A) IS THE 3D HISTOLOGY MAP. B) IS THE DEDUCED 3D IMPEDANCE MAP. THE BLACK LINES SHOWS HOW THE VOLUME WAS DIVIDED INTO 4 ROIS. C) SHOWS THE SCATTERER SIZE ESTIMATES FOR THE 4 ROIS. D) SHOWS THE ACOUSTIC CONCENTRATION ESTIMATES FOR THE 4 ROIS.