Estimating Scatterer Properties in Rat Fibroadenomas Using Various Mathematical Form Factors

Zachary T. Hafez¹, Lauren A. Wirtzfeld¹, Andrew Battles¹, Rita J. Miller¹, Sandhya Sarwate¹, Michael L. Oelze¹, Timothy J. Hall², William D. O’Brien Jr.¹

¹Bioacoustics Research Laboratory, Department of Electrical and Computer Engineering University of Illinois, Urbana, Illinois, 61820
²Department of Medical Physics, University of Wisconsin, Madison, WI, 53706
Email: lwirtz@illinois.edu

Abstract—Quantitative ultrasound (QUS) imaging is a model-based approach aimed at lesion detection and classification. In this study, the RF backscattered signals from rat fibroadenomas were fit to various mathematical models to yield effective scatterer diameter (ESD) estimates which are tied to tissue microstructure. In contrast to conventional B-mode imaging that provides primarily qualitative images of tissue, QUS aims to extract quantitative values associated with tissue micro-structure, such as the effective scatterer diameter (ESD). In this study, RF backscattered signals from rat fibroadenomas were fit to various mathematical models to yield ESD estimates which are tied to tissue microstructure. The goals of these experiments were to understand potential sources of scattering in live tissue across a wide frequency range and how results from different models compare to one another.

The ESD was computed from the RF backscattered signals from Sprague Dawley rats with fibroadenoma tumors ranging in size from 1 to 6 cm in diameter. The tumors were scanned using three single-element transducers with center frequencies of 3.5, 7.5 and 13 MHz with a collective -10-dB frequency bandwidth of 1.4 to 18 MHz. Theoretical models of scattering, i.e., form factors, were used to estimate the average ESD of each tumor. Glass bead (Faran), fluid-filled sphere and spherical Gaussian form factors were used, allowing for a comparison between different models.

Sixteen histologically confirmed fibroadenomas were included in the analysis. The ESD values were highest for the spherical Gaussian form factor and were 250 µm ± 63 µm, 115 µm ± 38 µm and 52 µm ± 25 µm for 3.5 MHz, 7.5 MHz, and 13 MHz respectively.

A trend of decreased ESD with increased frequency was observed for all three form factors, which fits with theory that the scattering at higher frequencies is due to smaller scatterers. The range of values obtained across the form factors and frequencies resulted in ESDs in the typical range of the acini of the rat fibroadenomas, which range in cross sections from 10s to 100s of micrometers. This work was supported by NIH Grant R01CA111289.

I. INTRODUCTION

Fibroadenomas are the most common benign tumor of the breast. The ability to differentiate fibroadenomas from malignant tumors through ultrasound imaging would reduce the need for biopsies and subsequent wait times for a diagnosis. In order to study the feasibility of using quantitative ultrasound (QUS) to provide information about the structure of breast fibroadenomas, a study was performed with rat mammary fibroadenomas. QUS imaging is a model-based approach aimed at lesion detection and classification. In contrast to conventional B-mode imaging that provide primarily qualitative images of tissue, QUS aims to extract quantitative values associated with tissue micro-structure, such
mounted within a single holder with their centers vertically aligned to each other. This allowed for the use of an automated method of data acquisition that sequentially scanned the exact same area with all transducers.

After scanning the animal with all three transducers, the animal was euthanized and scanned again using the same settings as the previous live scans. After the euthanized scans, the tumors of the animals were then excised, fixed in 10% formalin, trimmed for histology and then sent for pathology.

Reference scans were acquired for each transducer from a Plexiglas reflector, using the same equipment settings as for the tumor imaging.

**B. Data analysis**

The region of the tumor to be analyzed was manually segmented within each B-mode image. This region was automatically divided into square regions of interest (ROIs) that were 15 by 15 wavelengths long and overlapped each other by 75% in both axial and lateral directions (Figure 2). In addition, the water-tumor interface was outlined to delineate the water from the tissue in order to appropriately take into account the signal attenuation along the water path.

Within each ROI, the backscatter coefficient (BSC) was computed as a function of frequency. The BSC was reduced and then fit to form factors, mathematical models of scattering. The effective scatterer diameter (ESD) was estimated by minimizing the mean square error between the theory and reduced BSC. Three different form factors were fit to the data,

![Image](image1.png)  
**Fig. 1.** An example Bmode image of a tumor acquired with the 7.5 MHz transducer.

![Image](image2.png)  
**Fig. 2.** The same tumor as figure 1 with the overlayed manual outline of the tumor and the ROI placement.

![Image](image3.png)  
**Fig. 3.** The example tumor with the estimated effective scatterer diameter (ESD) based on the fluid filled sphere form factor, for each ROI superimposed on the Bmode image.
1) the form factor for scattering from glass beads including the effects of shear wave [1], 2) the fluid-filled sphere [2], and 3) the spherical Gaussian [2].

An ESD was calculated for each ROI, allowing for parametric images, see figure 3, to be displayed. The average ESD was also computed across the five image slices and compared across form factors and transducer frequencies. An ANOVA was performed to determine statistically significant differences between ESD across form factors and transducer frequencies.

III. RESULTS

Sixteen histologically confirmed fibroadenomas were included in the analysis. The ESD values calculated are for the 3.5 MHz, 7.5 MHz, and 13 MHz transducers respectively. The ESD values for the glass bead form factor for all tumors were $109 \pm 66 \mu m$ (mean ± standard deviation), $80 \mu m \pm 45 \mu m$, and $59 \mu m \pm 19 \mu m$. The fluid filled sphere form factor ESD values were $195 \mu m \pm 25 \mu m$, $97 \mu m \pm 33 \mu m$ and $46 \mu m \pm 14 \mu m$ (see figure 6). The Gaussian form factor ESD values were $250 \mu m \pm 63 \mu m$, $115 \mu m \pm 38 \mu m$ and $52 \mu m \pm 25 \mu m$. Figure 4 shows the ESD for each frequency and each form factor.

The 2-way ANOVA of the ESD indicated there were statistically significant interactions between the frequency and form factor ($p < 0.001$) as well as frequency ($p < 0.001$) and form factor ($p < 0.001$). Bonferroni post-hoc tests show no significant differences in estimates between the three form factors at 13 MHz, significant differences between all three estimates at 3.5 MHz and only a significant difference between the Gaussian and glass bead form factors at 7.5 MHz.

IV. DISCUSSION

For all three form factors a trend of decreased average ESD with increased transducer frequency was observed. This suggests that the BSC is sensitive to smaller structures within the fibroadenomas when the higher frequency transducers are employed. The ESDs across the form factors were in the same range, however, the spherical Gaussian estimates were consistently the highest and the glass bead estimates the lowest. As the spherical Gaussian form factor does not have a defined scatterer boundary, it would be consistent to obtain the highest estimates from this model. The fluid filled sphere estimate would be expected to be the most realistic as tissue microstructure has fluid like parameters and most structures of interest would have defined borders rather than being continuous.

While it is difficult to determine a particular size or size distribution of anatomical features within the fibroadenoma, structures corresponding to the range of ESDs obtained can be observed within the histological slides. The acini range in size from 10s to 100s of microns in diameter and could be the predominant scattering sites within this tissue. Further evaluation and comparison of individual tumor ESD estimates and the specific histology would be required to determine if there is a direct correlation between sizes of structures observed histologically and the QUS size estimates.

V. CONCLUSION

The high level agreement across a reasonable number of tumors, suggest that the methodology is able to pick-up on a particular structural feature within the tissue, which could be used to classify fibroadenomas.

ACKNOWLEDGMENT

The authors would like to thank Michael Tu, David Hruska and Michael King for their assistance with experiments and data processing code. BRP support from NIH/NCI RO1CA111289.

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