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3D H-scan ultrasound imaging system and method for acoustic scatterer size estimation: Preliminary studies using phantom materials

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***Abstract*—H-scan ultrasound (US) is an innovative real-time imaging technology that depicts the relative size of acoustic scattering objects and structures. The purpose of this research was to develop a novel 3-dimensional (3D) H-scan US imaging approach for tissue classification in volume space. Using a programmable research scanner (Vantage 256, Verasonics Inc, Kirkland, WA) equipped with a custom-built volumetric imaging transducer (4DL7, Vermon, Tours, France), radio frequency (RF) data was collected for offline processing. H-scan US images were constructed after applying a set of convolutional filters based on Gaussian-weighted Hermite polynomials. These functions are related to different sized scattering objects. Preliminary studies were conducted using homogeneous gelatin-based tissue-mimicking phantom materials embedded with acoustic scatterers of varying size (15, 30 or 250 µm) and concentrations (0.1, 0.3, 0.5 or 1.0 %). *In vitro* results indicate that 3D H-scan US imaging can detect acoustic scatterers of varying size ($p < 0.01$) and independent of scatterer concentration ($p > 0.05$). Overall, our preliminary *in vitro* findings reveal that 3D H-scan US imaging allows the visualization of different tissue scatterer patterns.**

***Keywords*—acoustic scatterers; H-scan ultrasound; tissue classification; ultrasound; volumetric imaging**

I. INTRODUCTION

The use of noninvasive ultrasound (US) for quantitative tissue characterization has been the focus of research efforts for several decades now. Herein the challenge is to find hidden patterns in the US data to reveal more information about tissue function and pathology that cannot be seen in conventional US images. Several promising US-based tissue characterization methods have been introduced, namely, backscatter classification, integrated backscatter, spectral feature extraction, and more recently, tissue elasticity imaging. A potential limitation for some of these tissue characterization methods is that they require a complicated calibration step before performing any measurement or use a relatively large kernel (window) of US data during quantification, which can affect spatial resolution and make *in vivo* measurement of local changes problematic.

Bypassing some of the limitations associated with traditional tissue characterization approaches, a new modality has recently emerged for US classification of acoustic scatterers. Termed H-scan US (where the 'H' stands for Hermite or hue), this imaging approach links the mathematics of Gaussian-weighted Hermite (GH) functions to the physics of scattering and reflection from different tissue structures within a standard convolutional model of US pulse-echo systems [1]–[3]. Specific integer orders, termed GH_n, are related to the n^{th} derivative of a Gaussian function. Matched filters employing specific orders of GH_n functions are then used to quickly analyze the spectral content of US backscattered echo signals and to colorize the display. This provides visual discrimination between the major tissue scattering classes at high resolution. In general, lower frequency spectral content is echoed from larger scattering structures whereas higher frequency echo content is reflected by an US wave interacting with small scatterers of scale below the wavelength of the US transmit pulse (i.e. Rayleigh scatterers). In short, H-scan US estimates the relative size and spatial distribution of cellular structures and has shown promise in applications ranging from characterization of thyroid nodules [4] to monitoring cancer response to treatment [5]–[7].

The quality of H-scan US images is directly impacted by attenuation at tissue depth. This progressive reduction in the US signal amplitude manifests as a spectral shift and can compromise analysis of the lower and higher frequency US data content if not corrected. To that end, we recently introduced an adaptive attenuation correction-based approach that uses a K-means clustering algorithm to help improve the quality of H-scan US images. Expanding on this and other research findings, herein we detail development of a novel 3-dimensional (3D) H-scan US imaging system and method for tissue classification in volume space.

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II. MATERIALS AND METHODS

A. Ultrasound Imaging

Volumetric H-scan US imaging functionality was developed using a programmable research scanner (Vantage 256, Verasonics Inc, Kirkland, WA) integrated with a custom-built 3D imaging transducer (4DL7, Vermon, Tours, France). This unique 192-element (0.2 mm pitch) 3D transducer has an 8.5 MHz center frequency and embedded motor for rapidly scanning volume space (Fig. 1). The total scan angle in each volume was 27° (maximum displacement = ± 13.5°) with the acceleration angle set to 0.135° to contained 200 frames of US image data. An US plane wave imaging technique was used to simply radiofrequency (RF) data acquisition.

Fig. 1. Custom three-dimensional (3D) ultrasound (US) imaging transducer that contains a 192-element linear array that is mechanically scanned over a volume of interest.

B. 3D H-scan US Image Processing

All 3D US data underwent scan conversion into a volume of uniform dimension. Two parallel convolution filter kernels were then applied to the acquired RF data sequences to measure the strength of the received signals relative to GH_2 and GH_8 after normalization by the signal energy. During this filtering step, the filter kernels were properly adjusted at depth to overcome the impact of US signal attenuation. Using K-means clustering, the center frequency of the GH_2 and GH_8 kernels were independently and continuously adjusted at depth to maximize spectral coverage [8]. The signal envelope for each of the filtered data sequences was then calculated using a Hilbert transformation. Using an RGB colormap scheme, the relative strength of these filter outputs was color coded whereby the lower frequency (GH_2) backscattered signals are assigned to the red (R) channel and the higher frequency (GH_8) components to the blue (B) channel. The envelope of the original unfiltered compounded dataset is assigned to the green (G) channel to complete the colormap and H-scan US display image [8]-[10].

C. Tissue-Mimicking Phantom Studies

A series of homogeneous tissue-mimicking phantoms were prepared to contain a range of acoustic scatterers of varying size and concentration. Each phantom contained a base mixture of 75 g of gelatin (300 Bloom, Sigma Aldrich, St. Louis, MO, USA), an US scatterer (US Silica, Pacific, MO, USA), and 1 L of H_2O. The diameter (15, 30 or 250 μm) and concentration (0.1, 0.3, 0.5 or 1.0 %) of the spherical scatterers were varied for each phantom produced. Phantom blocks were formed by heating the gelatin solution to 50 ° C and then pouring into a rigid rectangular mold and allowed to cool overnight.

D. Statistical Analysis

For each experimental group, US volumes were summarized as the mean ± SD. To evaluate the impact of scatterer size and concentration on 3D H-scan US imaging, a two-way analysis of variance (ANOVA) test was performed. Any *p*-value less than 0.05 was considered statistically significant.

III. RESULTS AND DISCUSSION

3D H-scan US imaging was evaluated using a series of *in vitro* phantom experiments. During these studies, the impact of US scatterer size and concentration were evaluated. A representative set of 3D H-scan US image reconstructions are depicted in Fig. 2. Collectively, these results indicate there is a progressive red color (hue) shift as the size of the acoustic scatterers are increased. This agrees with the H-scan US theory whereas larger scatterers dominate the blue (low frequency) spectrum and smaller scattering objects the red (high frequency) spectrum [3]. Additionally, the spatial distribution of the scatterer population can be clearly detected throughout the entire 3D H-scan US volume space. The H-scan volume color appears similar when only concentration varies (from left to right), which suggests imaging is much more sensitive to scatterer size rather than concentration.

To further evaluate sensitivity of the 3D H-scan US imaging technology to scatterer size and concentration, the mean signal intensity for each volume with different scatterer size (15 to 250μm) and concertation (0.1, 0.3, 0.5 and 1%) was compared, Fig 3. Analysis of the red channel in Fig 3A shows that H-scan US imaging can detect the lower frequency information from the different-sized scatterers ($p < 0.05$), while the impact of scatterer concentration on H-scan US imaging was not statistically

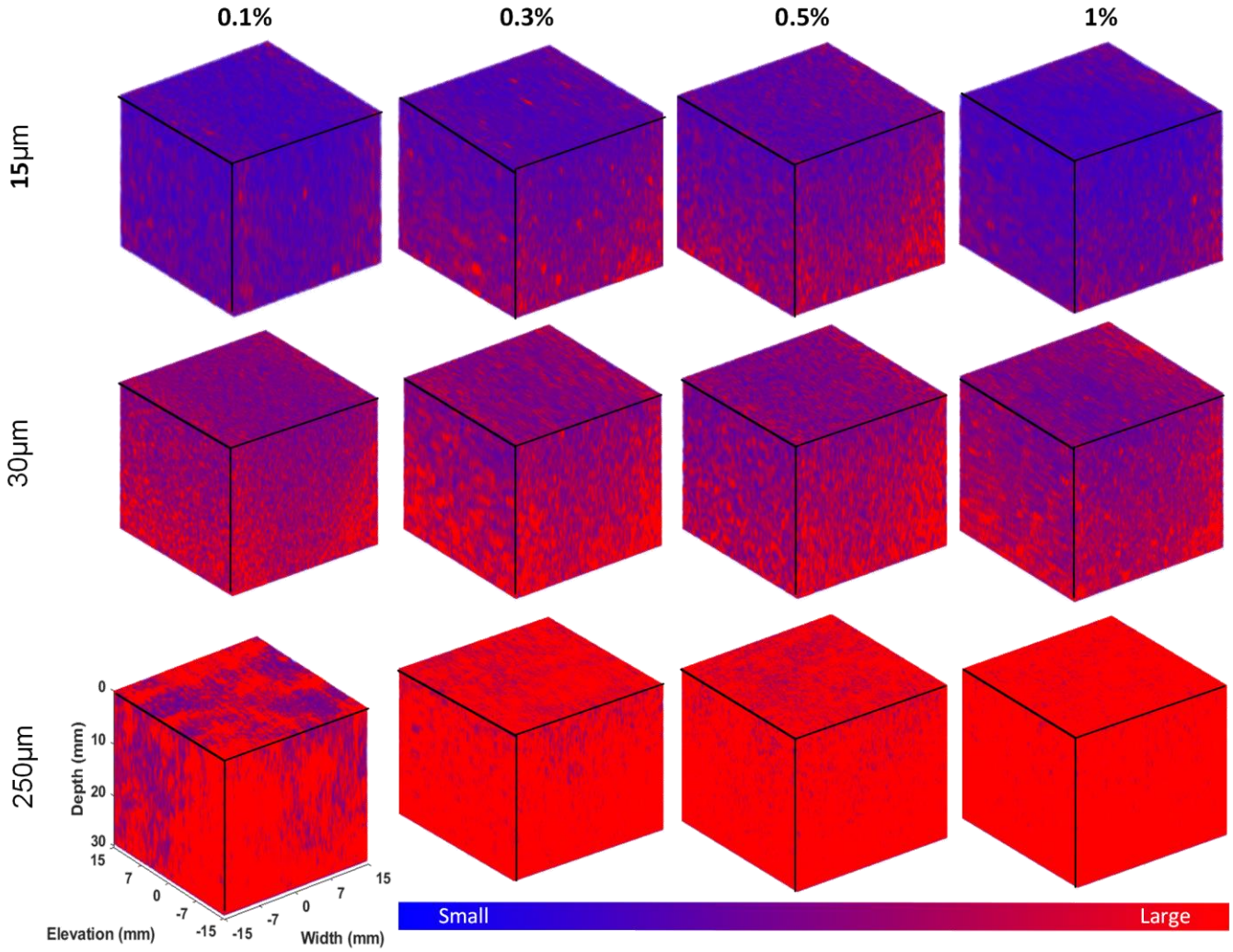

Fig. 2. Representative H-scan US volumes from a series of tissue-mimicking phantom materials containing a homogeneous distribution of silica spheres, namely, 15, 30, or 250 µm-sized scatterers. Scatterer concentration was either 0.1, 0.3, 0.5 or 1.0 %. Note the color shift from blue to red with increasing scatterer size. Note the H-scan US image intensity increases considerably with increased scatterer size but not with scatterer concentration used to fabricate the different phantom materials.

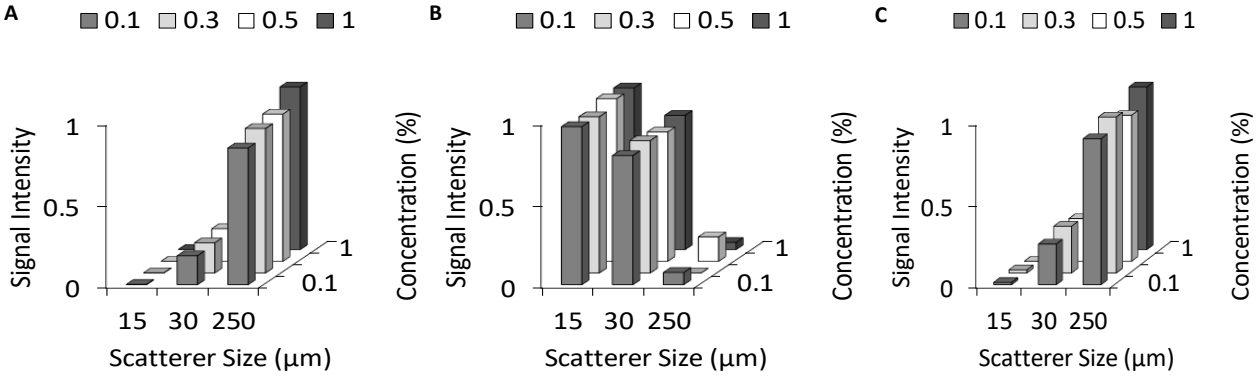

Fig. 3. Volume summary of the mean (A) red and (B) blue channel signal intensities used to create the final H-scan US images. (C) Mean image intensity analysis reveals that this new technique able to detect the changes of scatterer sizes. Note that the higher frequency signal is decreasing with increased scatterer size and vice versa for the lower frequency signal.

significant (p = 0.43). Since the H-scan US image processing isolates both the lower and higher frequency information backscattered from different-sized scatterers to achieve size estimation, the same analysis was repeated on the higher frequency information. Results show that scatterer size also has a significant effect on the blue channel image intensity (p < 0.03), whereas varying the scatterer concentration does not (p = 0.395). Analysis of the mean H-scan US image intensities in Fig. 3C also reveals a dependence on scatterer size (p < 0.01) but not concentration (p > 0.05). To assess both H-scan and B-scan US image quality more closely, a different volume region and random slice were selected for comparison, Fig. 4. H-scan US shows a rapid change in image intensity with increased scatterer size (> 200%, p < 0.03) as compared to only a slight increased observed in the B-mode US images (< 60%, p > 0.05), which suggests H-scan US imaging is more sensitive to changes in scatterer size.

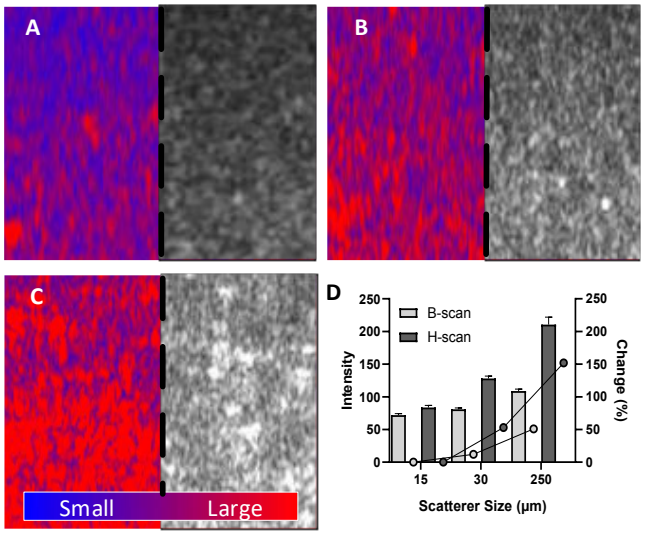

Fig. 4. Representative H-scan US images with co-registered B-scan US slices for comparison. US images were acquired in phantom materials embedded with either (A) 15, (B) 30, or (C) 250 μm-sized acoustic scatterers. Note the (D) progressive shift in the H-scan US image intensity, which is much less pronounced in the B-scan US image sequence.

IV. CONCLUSION

3D H-scan US is a novel imaging technology that can be used to visualize the relative size of scattering objects or structures in volume space. Preliminary results were encouraging, and future work will involve investigating preclinical applications and *in vivo* system performance.

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