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Theoretical and phantom based investigation of the impact of sound speed and backscatter variations on attenuation slope estimation

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ABSTRACT

Quantitative ultrasound features such as the attenuation slope, sound speed and scatterer size, have been utilized to evaluate pathological variations in soft tissues such as the liver and breast. However, the impact of variations in the sound speed and backscatter due to underlying fat content or fibrotic changes, on the attenuation slope has not been addressed. Both numerical and acoustically uniform tissue-mimicking experimental phantoms are used to demonstrate the impact of sound speed variations on attenuation slope using clinical real-time ultrasound scanners equipped with linear array transducers. Radiofrequency data at center frequencies of 4 and 5 MHz are acquired for the experimental and numerical phantoms respectively. Numerical phantom sound speeds between 1480 and 1600 m/s in increments of 20 m/s for attenuation coefficients of 0.3, 0.4, 0.5, 0.6, and 0.7 dB/cm/MHz are simulated. Variations in the attenuation slope when the backscatter intensity of the sample is equal, 3 dB higher, and 3 dB lower than the reference is also evaluated. The sound speed for the experimental tissue-mimicking phantoms were 1500, 1540, 1560 and 1580 m/s respectively, with an attenuation coefficient of 0.5 dB/cm/MHz. Radiofrequency data is processed using three different attenuation estimation algorithms, i.e. the reference phantom, centroid downshift, and a hybrid method. In both numerical and experimental phantoms our results indicate a bias in attenuation slope estimates when the reference phantom sound speed is higher (overestimation) or lower (underestimation) than that of the sample. This bias is introduced via a small spectral shift in the normalized power spectra of the reference and sample with different sound speeds. The hybrid method provides the best estimation performance, especially for sample attenuation coefficient values lower than that of the reference phantom. The performance of all the methods deteriorates when the attenuation coefficient of the reference phantom is lower than that of the sample. In addition, the hybrid method is the least sensitive to sample backscatter intensity variations.

1. Introduction

Radiofrequency (RF) data has been used for the determination of quantitative ultrasonic (QUS) features such as speed of sound (SOS), backscatter coefficient (BSC), attenuation coefficient and the non-linearity parameter [1–8]. QUS features such as the attenuation slope may provide valuable insights into tissue pathology [8,9], and attenuation imaging is envisioned as an optional modality to augment standard B-mode imaging [10]. These tissue features are used to quantify the underlying tissue pathology using ultrasound pulse-echo imaging, for eventual use in clinical diagnosis [11,12]. For example, Strowitzki et al. [13] analyzed attenuation and backscatter values of brain tissue for potential intraoperative discrimination between normal and pathologic areas which could be of interest to the surgeon. Taylor et al. [14] estimated ultrasound attenuation in liver based on amplitude and frequency changes as a function of depth. They compared their QUS results with histological data indicating that the presence of fat alone accounted for the increased attenuation associated with cirrhosis, and similar high attenuation values were found in patients with fatty infiltration. Landini et al. [15] showed the feasibility of using an index derived from the slope of the frequency-dependent ultrasonic attenuation to provide quantitative information on normal and pathological breast tissue. Pre-term birth is also investigated by evaluating variations in attenuation during the ripening of the cervix [16]. Bigelow et al. [17] have performed computer simulations as well as *in vivo* studies on rats by detecting the attenuation decrease of the ripened cervix versus an unripened cervix.

Sound speed changes in biological tissue have also been measured *ex-vivo* [18,19] and *in vivo* [20,21]. Keshavarzi et al. [22] measured the attenuation and SOS variations in fresh human uterine fibroids and myometrium as a function of frequency. Frequency

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dependent backscatter variations have also been measured for example, Garra et al. [23] measured spectral centroid shift from ultrasonic backscatter signals from the spine *in vivo*, where measurements were made through the abdomen. Imaging scatterer size in thyroid nodules has also been investigated using the frequency dependence of backscatter [12]. In soft tissue, such as liver, it has been shown that the mean backscatter coefficient of patients with fatty liver infiltrations is higher than that of normal patients [9]. Attenuation and backscatter indices may also be effective in determining normal versus abnormal liver and "pure" fatty versus healthy liver [24]. Gaitini et al. [24] demonstrate that backscatter indices are better than ultrasound texture based indices using receiver operating characteristic (ROC) analysis, with an area under the curve (AUC) of 0.86 to discriminate abnormal versus normal livers, 1.0 to discriminate "pure" fatty versus healthy livers, and 0.92 to discriminate "pure" fatty versus mixed livers.

Both time and frequency domain approaches for estimating the attenuation coefficient have been developed [25,26]. Frequency domain approaches primarily rely on the estimation of the shift of the power spectrum towards lower frequencies due to the increased attenuation of the higher frequency content, and/or subsequent reduction in the signal/spectral amplitude with propagation depth. The centroid downshift method or spectral shift method evaluates the variation in the spectral centroid with depth from the backscattered RF data [27]. Attenuation is estimated from the decay with depth of the spectral centroid due to the increased attenuation of higher frequency signals of the backscattered RF data when compared to the lower frequencies. The reference phantom method (RPM) or the spectral difference method, on the other hand utilizes backscattered RF signals to calculate the amplitude decay of the power spectra with depth [25]. This method uses a well-characterized tissue mimicking (TM) phantom as a reference with known attenuation, sound speed and backscatter characteristics, to reduce system and transducer dependencies. An attenuation slope estimation method termed the hybrid spectral domain method which incorporates advantages of both the spectral shift and the spectral difference method, while overcoming their limitations, has also been developed [28]. Spectral shift methods are sensitive to local spectral noise artifacts and have difficulty in compensating for diffraction effects due to beam focusing. Spectral difference methods on the other hand, fail to accurately estimate attenuation coefficient values at tissue boundaries that also include variations in the backscatter. The hybrid method uses a spectral difference method to reduce the impact of system dependent parameters such as diffraction by normalizing the power spectra obtained at different depths using a reference power spectrum. The normalized spectra is then filtered using a Gaussian filter centered on the transmit center frequency of the ultrasound system. A spectral shift method using spectral cross-correlation [29] is then performed on the filtered bandpass signal to estimate the attenuation coefficient.

In this paper we investigate the impact of SOS and backscatter intensity variations on attenuation estimation by comparing attenuation slope estimated using the three different frequency domain attenuation slope estimation methods; namely the reference phantom, centroid downshift, and the hybrid method, using numerical and experimental TM phantoms. Typical attenuation slope values of soft tissue, fat, liver and breast tissue are around 0.54, 0.48, 0.5 and 0.75 dB/cm/MHz, respectively [30]. Attenuation slope estimates for sample phantoms whose backscatter intensity variations are different from that of the reference phantom are also presented. The next section presents details on the numerical ultrasound simulation, and acquisition of experimental data on TM phantoms. A description of the three attenuation methods along with data processing is also presented. The Section 3 presents the numerical and experimental results, which are then summarized in Section 4. Finally, the conclusions of this paper are presented.

2. Materials and methods

2.1. Ultrasound simulation

Numerical phantoms were generated using a frequency domain simulation program based on the linear diffraction theory of continuous waves [31,32]. A linear-array transducer was modeled consisting of rectangular elements of dimensions 0.18 mm by 10 mm, with a center to center element separation of 0.2 mm. Each beam line was formed using 128 consecutive elements which form the transducer aperture, and 170 A-lines over a 34 mm lateral width were generated. A fixed elevational focus is applied using an acoustic lens on the top surface of the transducer. The elevational focus is set to be equal to the lateral focus in order to avoid the effect of different elevational and lateral foci in the analysis. Dynamic receive focusing and dynamic aperture was used on receive such that the F number is fixed at 2. The field strength in the focal plane was set to be the field strength at all the depth planes in order to avoid a varying signal density due to the focusing effect. The incident pulse was simulated as a Gaussian-shaped pulse with center frequency of 5 MHz and 80% bandwidth.

All numerical phantoms generated in this paper were 34 mm wide with a depth of 80 mm and a thickness of 10 mm. The uniformly attenuating phantoms were simulated numerically by assuming a random distribution of 25 μm glass beads in a medium having a sound speed of 1540 m/s, which is the average sound speed for soft tissue. Most tissues of interest for medical ultrasound imaging have sound speeds within 2–3% of this value [33]. The glass beads generate backscattered echo signals with the propagation of the ultrasound pulse. A scatterer number density of approximately 10 per cubic millimeter was used to ensure Rayleigh scattering statistics [34]. Rayleigh scattering statistics are commonly associated with ultrasonic backscattered signals [35]. Adjacent beam lines were separated by a 0.2 mm distance, equal to the element pitch. The sample and the reference phantoms were assumed to be in direct contact with the transducer. A single transmit focus set to 40 mm was utilized with the elevational focus also set to 40 mm. The sampling rate was set to 40 MHz and no time gain compensation (TGC) was assumed.

In order to investigate SOS variations, the first set of numerical phantoms had identical acoustic properties with only variations in the material SOS simulated, ranging from 1480 to 1600 m/s at 20 m/s intervals (seven phantoms). Two additional sets of numerical phantoms with similar sound speed values and incorporating backscatter intensities 3 dB higher and 3 dB lower were also constructed to investigate the effect of backscatter intensity variations. The scatterer density parameter was varied to introduce the variations in the backscatter intensity. Scatterer density was doubled to obtain the 3 dB increase and halved for the 3 dB lower backscatter intensity phantoms. In addition, phantoms with attenuation coefficient values ranging from 0.3 to 0.7 dB/cm/MHz at 0.1 dB/cm/MHz increments were also simulated at a sound speed of 1540 m/s, Table 1 lists the acoustic properties of the reference and sample phantoms generated.

The SOS parameter is encountered in two different sections of the ultrasound simulation program: in the construction of the numerical phantoms, and during transmit and receive beamforming. The ultrasound system SOS was fixed at a value of 1540 m/s, and was used to generate the transmit focal zone, and for receive beamforming. The SOS variation described in this paper refers only to the tissue material SOS variation. The numerical simulation would therefore mimic this case, where an ultrasound system