Supplementary Data 1. Quantitative ultrasound parameters from radiofrequency data analysis: theoretical background and how to create parametric maps

Tissue Scatter-Distribution Imaging

Tissue scatter-distribution imaging (TSI) a pixel-by-pixel map of the Nakagami parameter, which is the shape parameter of the Nakagami distribution. It depends on the arrangements and concentration of the scatterers [1–3].

The Nakagami parameter can be calculated as follows: " $\text{Nakagami parameter} = \frac{[E(R^2)]^2}{E[R^4]-[E(R^2)]^2}$ ", where R and E(·) represents the backscattered-signal envelope and the expected value, respectively. The Nakagami parameter varied from 0 to 1 when the statistics of the backscattered-signal envelope changed from pre-Rayleigh to Rayleigh distribution. Pre-Rayleigh indicates there are a small number of scatterers randomly distributed in the ultrasound resolution cell, while Rayleigh distribution indicates the high density of randomly distributed scatterers without coherent signal components. When the Nakagami parameter is larger than 1, the backscattered-signal statistics correspond to post-Rayleigh distribution, meaning there are periodic scatterers or local high-concentration scatterer aggregation, in addition to many scatterers randomly distributed in the resolution cell.

To construct a TSI map comprising local Nakagami parameters, the square sliding window (3×3 mm^2) technique is applied through the entire envelope image with the shift of one-pixel step, which assigns a local Nakagami parameter for a new pixel located at the center of the window each time.

Tissue Attenuation Imaging

Tissue attenuation imaging (TAI) is based on the ultrasound attenuation properties of different frequency components in the tissue. As the attenuation of higher frequency components is greater than that of lower frequency components, the power spectrum of radiofrequency signals by using short-time Fourier analysis demonstrates a downward shift of the center frequency along with the depth. Assuming a Gaussian-shaped transmit pulse with invariant variance along with the depth, the relationship between the center frequency shift and attenuation coefficient (β) is given by as following [4,5]: " $\beta(dB/cm/MHz) = -\frac{8.686}{4\sigma^2}\cdot\frac{df_c(z)}{dz}$ ", where z is the depth of the region of interest from the transducer, σ2 is the variance of the transmit pulse, and fc(z) is the center frequency of the power spectrum at depth z. Tissue attenuation imaging parameter (TAI-p) is calculated based on the frequency shift along with the depth which linearly correlates the attenuation coefficient as follows: $\text{TAI-p} = \frac{df_c(z)}{dz}$. The Fourier transform is used to calculate the block power spectrum, and the estimated center frequency is defined as the average frequency in the block power spectrum.

To create a TAI map comprising local center frequency, the sliding window (3 mm x 1 scan-line) technique is applied through the entire radiofrequency signal data with a shift of one-pixel step, and the local center frequency is assigned to a new pixel located at the center of the window each time.

References

1. Shankar PM. A general statistical model for ultrasonic backscattering from tissues. IEEE Trans Ultrason Ferroelectr Freq Control 2000;47:727-736
2. Ho MC, Lee YH, Jeng YM, Chen CN, Chang KJ, Tsui PH. Relationship between ultrasound backscattered statistics and the concentration of fatty droplets in livers: an animal study. PLoS One 2013;8:e63543.
3. Tsui PH, Wan YL. Application of ultrasound Nakagami imaging for the diagnosis of fatty liver. J Med Ultrasound 2016;24:47-49.
4. Kim H, Varghese T. Attenuation estimation using spectral cross-correlation. IEEE Trans Ultrason Ferroelectr Freq Control 2007;54:510-519.
5. Liao YY, Yang KC, Lee MJ, Huang KC, Chen JD, Yeh CK. Multifeature analysis of an ultrasound quantitative diagnostic index for classifying nonalcoholic fatty liver disease. Sci Rep 2016;6:35083.