SUPPLEMENTARY MATERIALS

Technical Background and Principle of NLV

Normalized local variance (NLV) is a regional analysis used to quantify the homogeneity of the speckle patterns in B-mode images. NLV analyzes the spatial echo pattern of a grayscale image from the receiving echo signal amplitude within a certain region of interest (ROI) during normal ultrasound (US) examination. The system looks deeper into the US echo signal information, at more than 100 x higher resolution, and operates in the background with the raw data from this ROI. Then, it extracts parameters and their complete probability distribution related to the "homogeneity" or "smoothness" of the structures reflecting the US beam sent by the machine into the body. The measured variance by this process is compared to a normalized variance of normal or reference liver tissue.

This is to standardize the variance of the echo signal of the micro-ROIs, which were automatically placed within the analytical ROI. The formula to calculate NLV is as follows:

$$NLV = \left(\frac{\pi}{4-\pi}\right)\frac{\sigma_m^2}{\mu_m^2}$$

$x = amp$

$\sigma_m^2 = E\left[(x-\mu)^2\right]$: Measured local variance of amp

$\mu_m = E[x]$: Normalized by measured average of amp

According to this equation, when the speckle pattern is homogeneous, the NLV value is 1, which means that the amplitude distribution becomes the Rayleigh distribution. Scattering is diffuse reflection of US waves at interfaces that are typically equal to, or smaller than the wavelength. Rayleigh scattering occurs at interfaces that are several times smaller than the wavelength; thus, a homogeneous speckle pattern, like a fatty liver, is in agreement with the Rayleigh scattering distribution.

Furthermore, when inhomogeneous structures, like a blood vessel wall in a normal liver, are included in the analytical ROI, because other interactions of US waves occur in the liver tissue, such as specular reflection, the NLV is greater than 1.

Because NLV is based on the raw signal data of a grayscale that is collected before a scan converter, the gain for local intensity variance is independent.