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Background: Quantitative spectrum analysis is a unique ultrasound technology which involves quantification of spectral parameters and enables objective tissue characterization. This has been proven to be effective in distinguishing and detecting malignant tumors from normal tissue in breast and pancreas cancer patients. However, the technology has not been applied for localization of lung tumors during the use of the thoroscopic ultrasound, and the factors which significantly influence the spectral parameters remain unclear. The aim of this study was to demonstrate the feasibility of spectrum analysis for localization of lung malignancy using multiple animal models and to identify the cytological factors which reflect the spectral parameters.

Methods: Lung cancer tissues were evaluated using a convex probe endoscopic ultrasound and an ultrasound scanner (EU-Y0005, Olympus, Tokyo, Japan) with software capable of calculating the spectral parameters. Initially, the rabbit orthotopic VX2 lung tumor models were used to distinguish tumor from lung parenchyma. Regions of interest were selected within ultrasound images captured from the model. Three spectral parameters including midband-fit (dB), intercept (dB), and slope (dB/MHz) were calculated and compared between the tumor and the lung. Thereafter, the nude mice subcutaneous tumor models made with three human lung cancer cell lines, normal pig mediastinal lymph nodes, and normal rabbit lung were used to compare cytological findings, mainly nucleus size in each tissue, to the spectral parameters in each region of interest.

Results: In the rabbit tumor model (n=5), the B-mode showed similar ultrasound contrast in both the tumor and the lung, however, spectral parameters of the tumors revealed a significantly lower midband-fit and intercept, as well as a higher slope than normal lungs ($p<0.001$). The subcutaneous tumors (n=3 in each cell lines) showed a significantly lower intercept, a higher slope, and a larger nucleus size than those of the pig lymph nodes and rabbit lungs (n=3) ($p<0.001$). Intercept and slope showed statistically significant correlation with the nucleus size of the tissues ($r=-0.49$, $p<0.001$ for intercept and $r=0.60$, $p<0.001$ for slope).

Conclusion: Spectral parameters showed a significant difference between tumors and normal lung tissue. Slope represented moderate correlation with the nucleus size of the target tissues. Spectrum analysis is a feasible way to identify malignant tumors in the normal lung which may improve detectability of small-sized malignant lung tumors using ultrasound technology.

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