Development and Validation of Parallel Three-Dimensional Computational Models of Ultrasound Propagation and Tissue Microstructure for Preclinical Cancer Imaging

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High-frequency (20-60 MHz) ultrasound images are sensitive to variations in tissue microanatomy that accompany tumour growth, but the relationships between high-frequency ultrasound backscattering and tumour microstructure are incompletely understood. A parallel 3-D ultrasound simulator and a tissue microanatomical model are developed to investigate these relationships. The simulator runs on computer clusters and uses a 3-D formulation of a *k*-space method to compute wavefront propagation. An allocation algorithm is introduced to divide the computation of each scan line between a group of cluster nodes and employ multiple groups to compute individual lines concurrently. The simulator achieves an error as low as 0.57%. An aperture projection technique is introduced to simulate imaging with a focused transducer using reduced computation grids. This technique is applied to synthesize B-mode images of a tissue-mimicking phantom. The execution time of an image using 20 nodes is 18.6 hours, compared to a serial execution time of 357.5 hours.

The microanatomical model treats tissue as a population of stochastically positioned cells, where each cell is represented as a spherical nucleus surrounded by cytoplasm. The model is employed to represent the microstructure of healthy mouse liver and an experimental liver metastasis that are analyzed using DAPI- and H&E-stained histology specimens digitized at 20× magnification. For each simulated tissue, the spatial organization of cells is controlled by a Gibbs-Markov point process tuned to reproduce the number density and distribution of centre-to-centre spacing of nuclei in the DAPI-stained slides of the corresponding experimental tissue specimen.

The ultrasound simulator is used to synthesize B-mode images of the simulated healthy and tumour tissues. The first-order speckle statistics of the images of each simulated tissue are compared with corresponding experimental images. The simulations show good matching between the images of the simulated healthy tissue and images of healthy liver. Moreover, good matching is achieved between the images of the simulated tumour and matching experimental images when acoustic properties are used that are different from the values assumed for healthy tissue. These simulations suggest that changes in the first-order speckle statistics that accompany tumour progression are related to variations in tissue acoustic and microstructural properties.