

PhD Thesis Title: 'Methods and algorithms for the quantification of blood flow in the microcirculation with contrast enhanced ultrasound'

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ABSTRACT:

Dynamic contrast enhanced ultrasound (DCEUS) holds great promise as a clinical tool for the analysis and quantification of tissue perfusion. It can provide valuable insight into the development of disease neovascularization. Specifically, the progress of diseases such as malignant liver lesions, renal carcinomas and carotid atherosclerotic plaques can be monitored using quantitative DCEUS. However, the reliable implementation of quantitative DCEUS has several limitations, like operator dependence, signal saturation, physiological motion, and speckle noise. In this thesis, a novel automatic respiratory gating (ARG) algorithm is developed to address challenges in the use of indicator dilution models for the quantification of tissue perfusion, which exhibits a high amount of blood flow such as liver lesions. Contrary, carotid plaques exhibit very low blood flows, making the use of indicator dilution models inaccurate in the quantification of perfusion. To overcome this limitation a new method is formulated that calculates the percent perfusion coverage of the plaque's area.

The novel ARG algorithm developed overcomes many of the limitations of respiratory compensation methods published in the literature demonstrating efficiency in removing in-plane, as well as, out-of-plane motion. The algorithm also exhibits high computational speed by processing a 2 minute DCEUS acquisition in less than 10 seconds. The increase in the reliability of liver lesion DCEUS quantification with the use of ARG is demonstrated using clinical data with a significant increase in the quality-of-fit of perfusion modeling ($p < 0.05$).

A respiratory motion simulation model (RMSM) is constructed to investigate the efficiency of ARG in reducing the percentage error of DCEUS quantification parameters from their true values. The RMSM demonstrates a decrease in the maximum percentage error of DCEUS quantification parameters from 32.3% to 6.2% with the use of ARG. The implications of the presence of multiplicative noise in liver lesion DCEUS acquisitions are also studied and quantified using the RMSM.

An algorithm is developed for the calculation of the percent perfusion coverage of carotid atherosclerotic plaques from DCEUS acquisitions. Visual scores of carotid plaque perfusion are used to validate the results from the DCEUS quantification analysis. Both, the percent perfused area with DCEUS quantification analysis and the

qualitative scores, demonstrate that the extent of carotid plaque perfusion for symptomatic patients is significantly less than asymptomatic ($p < 0.05$). Percent perfusion coverage has the potential to identify the perfusion characteristics of vulnerable carotid plaques and to also assess changes in the microflow caused by anti-atherosclerotic therapies.

References to author publications that relate specifically to the dissertation:

D. Christofides, E. Leen, and M. A. Averkiou, "Improvement of the accuracy of liver lesion DCEUS quantification with the use of automatic respiratory gating," *European Radiology*, vol. 26, no. 2, pp. 417–424, Feb. 2016.

D. Christofides, E. Leen, and M. A. Averkiou, "Evaluation of the accuracy of liver lesion DCEUS quantification with respiratory gating," *IEEE Trans Med Imaging*, [Epub ahead of print] doi: 10.1109/TMI.2015.2487866, 2015.

D. Christofides, E. Leen, and M. A. Averkiou, "Automatic respiratory gating for contrast ultrasound evaluation of liver lesions," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 61, no. 1, pp. 25–32, Jan. 2014. (front cover image)