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Contrast ultrasound dispersion imaging in prostate cancer: an update

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In Western countries, Prostate Cancer (PCa) is the most common form of cancer in men, accounting for 26% of new cancer cases and 9% of cancer-related deaths; yet the available diagnostic options are limited by the lack of reliable imaging solutions [1]. Dynamic Contrast-Enhanced UltraSound (DCE-US) is a diagnostic tool that is suitable for analysis of the vascularization, by imaging an intravenously-injected bolus of ultrasound contrast agents. The localization of angiogenic vascularization associated with cancer growth is of particular interest for the diagnosis of aggressive cancer [2]. Recently, methods for the analysis of the bolus convective-dispersion process have shown promise to localize angiogenesis. These are implemented by fitting the modified local density random walk model to time-intensity curves (TICs) measured at each pixel [3], or by estimating the similarity between neighboring TICs [4-6]. Several similarity measures have been adopted ranging from spectral coherence [4-5], to temporal correlation [6], up to nonlinear measures such as mutual information [7]. More recently, extension to 3D has also been shown, enabling the analysis of the full prostate volume by the injection of a single bolus of ultrasound contrast agents [8].

By all these methods, independent estimation of dispersion was not possible due to the ambiguity between convection and dispersion. Here a new method is presented that provides the separate estimation of convection and dispersion by identification of the local (linear) dilution system. To this end, model-based parameter estimation is employed. The method also permits generating maps of the Péclet number (Pe), a physics parameter characterizing the dilution system [9]. Clinical evaluation using data recorded from 25 patients (61 planes) at the Academic Medical Center, University of Amsterdam (the Netherlands), shows that the proposed method can be applied effectively to DCE-US, and is able to locally characterize the hemodynamics, yielding promising results for prostate cancer localization. Comparison of the resulting Pe maps with the histological results following radical prostatectomy showed an area under the ROC curve of 0.84, superior to all the other methods.

In addition, use and modeling of ultrasound contrast agents that are targeted to angiogenic expressions (BR55, Bracco Suisse), such as the vascular endothelial growth factor receptor 2 (VEGF-R2), are tested in rat models of human prostate cancer. A convective-dispersion model is used to describe the kinetics of circulating bubbles while a single-compartment model is used to describe bubble binding/unbinding kinetics. Identification of the proposed analytical model enables the assessment of both vascular and molecular features, determined by the dispersion and binding kinetics of the agent, showing promise for future applications aimed at PCa localization. In general, the proposed methods for angiogenesis imaging are not specific to prostate cancer only, and future extension to other types of cancer can also be envisaged.