Prostate cancer localization through convective-dispersion estimation in three-dimensional contrast ultrasound

R. R. Wildeboer¹, R. J. G. van Sloun¹, S. G. Schalk¹,², C. K. Mannaerts³, J. C. van der Linden³, P. Huang⁴, H. Wijkstra¹,², M. Mischi¹

¹ Department of Electrical Engineering, Eindhoven University of Technology, The Netherlands
² Department of Urology, Academic Medical Centre, University of Amsterdam, The Netherlands
³ Department of Pathology / DNA laboratories, Jeroen Bosch Hospital, ‘s-Hertogenbosch, The Netherlands
⁴ Second Affiliated Hospital of Zhejiang University, Hangzhou, China

Introduction

Detection and localization of prostate cancer (PCa) is still a challenge in today’s clinical practice. Despite being the most occurring type of malignancy aside skin cancers in western men, PCa diagnosis still relies on systematic biopsy [1]. A shift towards imaging-guided targeted biopsy would reduce the risk of underdiagnosis and overtreatment, whilst alleviating the burden on patients with no or insignificant PCa [2]. However, sufficiently reliable imaging is not only of paramount importance for reducing the risks associated with the systematic biopsy procedure, it is also essential for follow-up in active surveillance protocols [3] and for selection and monitoring of focal treatment [4].

Dynamic contrast-enhanced ultrasound (DCE-US) is a promising tool in PCa diagnosis that enables investigation of the vascularity. As significant PCa exceeding a size of 1 mm³ requires neovascularization and angiogenesis [5], several DCE-US analysis methods have been developed to capture the differences between benign and malignant (micro)vascular architectures. These methods were initially implemented in two dimensions (2D), quantifying dispersive effects in the contrast concentration kinetics at each pixel of the DCE-US image by e.g. model-based fitting [6] or similarity analysis [7]. As three-dimensional (3D) imaging became available, these techniques were expanded to three dimensions [8].

A 3D approach does not only prevent us from missing tumours outside the 2D imaging plane while reducing the number of bolus injections required, it also relaxes some major constraints of 2D modelling. Whereas direct 2D estimation of dispersion and velocity through system identification required strong assumptions on out-of-plane directionality [9], 3D data can be completely modelled by the convective-dispersion equation. In this work, we aim at estimating convective dispersion and velocity in a 3D DCE-US video by solving the least-squares formulation of the convection-dispersion equation.

Materials & Methods

In this analysis, we take a macroscopic view of the concentration kinetics of contrast agents spreading through the prostate. To this end, we consider the concentration C in x, y, z, and t to be governed by the convective-dispersion equation [10].
where the D- and v-elements are coefficients of dispersion and velocity, respectively.

To avoid high-frequency noise amplification during the computation of derivatives, we adopt an approach in which the concentration gradients are computed through convolution with four-dimensional Gaussian derivatives with a standard deviation \( \sigma \) and \( \sigma_t \) in space and time, respectively [11].

Assuming the D-coefficients in the dispersion tensor and the v-coefficients in the velocity vector to be locally constant, Equation (1) can be formulated as a linear least-squares problem. To avoid issues with ill-conditioning, we add an \( l_2 \)-norm regularization term to the problem with a regularization parameter \( \lambda \), with \( n \) the number of voxels in the analysis.

We successively perform the regularized minimization in a moving spherical kernel with a diameter of 7 voxels, \( \sigma = 1.5 \text{ mm (isotropic)} \) and \( \sigma_t = \Delta t \). The approach was implemented in an elastic-net fashion using the QR factorization procedure in Matlab™ (Mathworks, Natick, MA, USA) with a regularization parameter, \( \lambda \), and \( \rho \) the number of voxels in the analysis.

The diagnostic performance of \( D_{ADC} \) and \( v \) for the localization of PCa is assessed in six patients that underwent a two-minute 3D DCE-US recording prior to radical prostatectomy at the Second Affiliated Hospital of Zhejiang University (Hangzhou, China). The scanning procedure comprised a 2.4 mL SonoVue® (Bracco, Milan, Italy) bolus injection and a DCE-US acquisition with a RIC9-5 probe on a LOGIQ E9 scanner (GE HealthCare, Wauwasota, WI, USA). Subsequently, the data was spatially downsampling and linearized to a volumetric video with cubic 0.75-mm sized voxels and a frame rate of \( \sim 0.25 \) Hz. As a reference standard, the radical prostatectomy specimens were histopathologically examined, 3D reconstructed [13], and registered to the prostate [14]. Voxels from benign and malignant tissue, excluding those in a 3.6-mm error margin from the region boundaries, were included in a Receiver Operating Characteristic (ROC) curve analysis.

Results

Figure 1 depicts the result of the convective-dispersion analysis, showing an example case of the parametric maps of \( D_{ADC} \) and \( v \), along with the corresponding histopathologic ground truth. The ROC curve analysis yielded areas under the curve of 0.71 and 0.79 for \( D_{ADC} \) and \( v \), respectively, over the entire set of patients.
Discussion and Conclusion

In this work, we estimated the $D_{ADC}$ and $v$ by solving the regularized least-squares problem of the convective dispersion equation. Despite the limited number of patients included, ROC curve analysis reveals the potential of these parameters as markers for the localization of PCa. In contrast to the previous parameters related to dispersion [6, 7, 15], $D_{ADC}$ seems to increase in malignant tissue. An explanation for this might be that $D_{ADC}$ includes directional effects rather than the point-to-point dispersion of quantified in previous work. This effect, as well as the feasibility of multiscale analysis, effective combination of parameters, and index-tumour detection, remains to be tested in future work.

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References


