Prostate cancer localization by magnetic resonance dispersion imaging

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Introduction

In the United States, prostate cancer (PCa) is the first and the second form of cancer for incidence (28%) and mortality (10%) in men, respectively[1]. Current PCa diagnosis still relies on repeated systematic biopsies, hampering the efficient management of the disease by e.g. targeted biopsies, focal therapy, and active surveillance. Extensive research is therefore focused on the development of imaging methods for reliable PCa localization. The crucial role of angiogenesis in cancer growth and development is today well established[2]. Angiogenic microvasculature is characterized by a dense network of irregular and tortuous microvessels, exhibiting arteriovenous shunts and a higher permeability. In response, several imaging methods have been proposed to detect those microvascular changes resulting from cancer angiogenesis. Dynamic contrast-enhanced (DCE) MRI provides an opportunity to detect the increase in vascular permeability. The adopted gadolinium-based contrast agents leak across the vascular wall into the extravascular space. Assuming a dominant contribution of the extravascular contrast concentration, this transport process can be described by the compartmental model introduced by Tofts *et al*[3] as

$$C_t(t) = K^{trans} AIF(t) * e^{-k_{ep}t}, \qquad (1)$$

where $C_t(t)$ is the measured tissue contrast concentration, the symbol * indicates a convolution, and AIF(t) (Arterial Input Function) is the intravascular contrast concentration, which needs to be estimated separately. Fitting this model to measured concentration-time curves (CTCs) provides assessment of the extravascular leakage in terms of the volume transfer coefficient, K^{trans}, and the flux rate, $k_{ep}=K^{trans}/v_e$, with v_e being the extravascular volume fraction. This model does not address angiogenic changes in the microvascular architecture. Assuming an increase in blood supply as a result of increased microvascular density, many authors have investigated intravascular blood perfusion as a potential marker of cancer angiogenesis. However, while the lack of vasomotor control and increase in arteriovenous shunts may result in low flow resistance, this may be opposed by the high vessel irregularity and tortuosity, as well as by the increased interstitial pressure due to extravascular leakage, resulting in unreliable characterization of the microvascular architecture by perfusion analysis[4]. Recently, analysis of the intravascular dispersion kinetics of a contrast agent has been proposed as better approach to characterize the microvascular architecture and detect angiogenenic changes related to cancer growth. This method was validated by means of intravascular contrast agents in the context of DCE ultrasound[5]. Although this method relies on the kinetics of intravascular contrast agents, the underlying dispersion model could also be considered to characterize the intravascular phase of an extravascular agent. Therefore, this work investigates the feasibility and accuracy of DCE-MRI dispersion imaging for PCa localization by a standard extravascular agent.

Methods

Following the intravenous injection of a Gadobutrol contrast bolus, intravascular dispersion is assessed at each voxel by fitting the modified Local Density Random Walk (mLDRW) model to the measured CTC[5]. This yields the estimation of a local dispersion parameter, $\kappa = v^2/D$, which represents the ratio between intravascular contrast convection (squared velocity v^2) and dispersion (D), where dispersion is dominated by the transit-time distribution of the contrast molecules, determined by the underlying microvascular architecture[6]. Combination of the intravascular dispersion model and the Tofts extravasation model results in the following representation for the tissue concentration:

$$C_t(t) = A\left(\sqrt{\frac{\kappa}{2\pi t}}e^{-\frac{\kappa(t-\mu)^2}{2t}}\right) * e^{-\kappa_{ep}t}, \qquad (2)$$

where μ is the contrast mean transit time, and $A = \alpha K^{trans}$, with α being the time integral of the intravascular CTC. Fitting is performed by a Trust-Region Reflective method, with parameter initialization based on the neighboring voxels. An initial validation was performed with 90 MRI slices recorded with a Magnetom Avanto 1.5-T scanner (Siemens) in 15 patients referred for radical prostatectomy at the Academic Medical Center, University of Amsterdam, the Netherlands. A 2D multislice spoiled GRE sequence with voxel size 1.67x1.67x4 mm^3 at a temporal resolution of 2 s/volume was used. To obtain a quantitative CTC measurement, T1 mapping was performed in each patient by an IR sequence with five different inversion times (TI) prior to contrast injection. For each slice, two regions representing malignant and benign tissue were determined according to the histology. Voxel classification on these regions by the proposed dispersion parameter, κ, and the standard leakage parameter, K^{trans}, was compared. The AIF for application of the Tofts' model in Eq. (1) was measured in the femoral artery and fitted by a dedicated model[7]. A 5-fold cross-validation on the 15 patients was used to assess the classification performance of the methods. Figure 1 shows maps of K^{trans} and κ with corresponding histology.

Results

Voxel classification by κ maps yielded sensitivity, specificity, and ROC curve area equal to 84.4%, 85.8%, and 0.93, respectively, outperforming classification by the Tofts leakage parameter, K^{trans}, which resulted in sensitivity, specificity, and ROC curve area equal to 63.8%, 72.5%, and 0.77, respectively.

Discussion

The proposed method provides accurate localization of PCa by the intravascular dispersion parameter κ. The changes in the microvasculature architecture and permeability associated with tumor angiogenesis are simultaneously addressed, without the need for a separate estimation of the AIF. In addition, a contribution of this method to the performance of multiparametric (mp) MRI can also be envisaged, providing the currently-lacking information on the microvascular architecture.

Conclusion

The obtained results are promising, encouraging further research to establish the additional value of MRI dispersion imaging in the context of mpMRI for PCa localization and to extend its use to other forms of cancer where angiogenesis is involved.

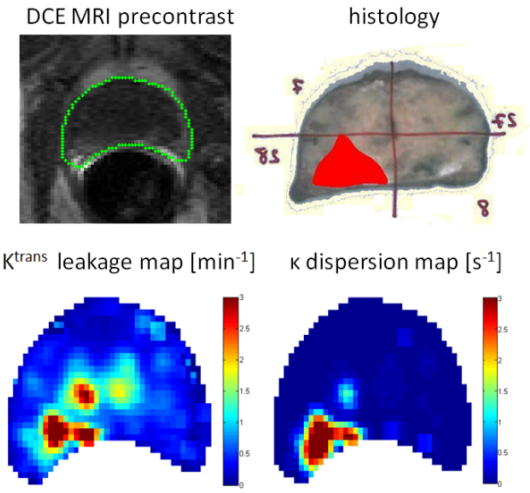

Figure 1. Parametric maps of dispersion, κ, and leakage, K^{trans}, with corresponding histology.

References

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