# Clinical evaluation of dispersion MRI for prostate cancer localization: a multicenter study

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**Introduction:** Multiparametric magnetic resonance imaging (mpMRI) has emerged as a promising tool for prostate cancer (PCa) localization. Due to the complex acquisition procedure and analysis, along with a questioned diagnostic contribution, the inclusion of DCE-MRI in the updated Prostate Imaging and Reporting Data System (PI-RADS2) has been limited to qualitative assessment only, with a marginal weight on the final score[1]. However, lower diagnostic performance has been reported for PI-RADS2 compared to original PI-RADS, evidencing the need to reconsider the role of DCE-MRI[2]. Recently, dispersion MRI (dMRI) has shown promise for quantitative DCE-MRI of the prostate[3, 4]. In dMRI, the adopted pharmacokinetic (PK) model includes a description of the contrast agent intravascular transport, enabling additional assessment of the microvascular architecture. Compared to standard PK analysis in MRI, separate estimation of an arterial input function (AIF) is no longer necessary, facilitating the clinical routine. Here we evaluate the diagnostic performance of dMRI for PCa localization compared to standard PK analysis by the Tofts model (TM) in a retrospective study including 80 patients from three different Dutch institutions.

**Methods**

In dMRI, the intravascular transport kinetics of an extravascular contrast agent is described as a convective-dispersion process by the modified local density random walk (mLDRW) model. Under the adiabatic approximation, by which the intravascular transport is assumed to be much faster than the extravascular leakage, the mLDRW model is combined with the TM, replacing the AIF, and obtaining the reduced dispersion model (RDM) as[3, 4]

$$C_t(t) = A\left(\sqrt{\frac{k_d}{2\pi t}}e^{-\frac{k_d(t-T_i)^2}{2t}}\right) * e^{-k_{ep}t}, \quad (1)$$

where the symbol * indicates a convolution; $C_t(t)$ represents the total contrast concentration; $T_i$ is the intravascular mean transit time; $k_{ep}$ is the flux rate constant between blood plasma and extravascular space, as in the TM; $A$ is an amplitude parameter; and $k_d$ is the dispersion parameter given by the local ratio between the squared velocity, $v^2$, and the dispersion coefficient, $D$. Similar to a dispersion process through porous media, $k_d$ reflects the porosity and tortuosity of the medium and is adopted to characterize the microvascular architecture. Fitting the model in eq. (1) to measured concentration-time curves provides assessment of the microvascular architecture, by the dispersion parameter $k_d$, and of the microvascular leakage, by the flux rate $k_{ep}$, without need for a separate estimation of the AIF.

Validation was performed in 80 patients from three different institutes in the Netherlands with biopsy-proven prostate cancer, referred for radical prostatectomy. MRI examinations were performed with different protocols depending on the institution. DCE-MRI parameters were extracted from dMRI analysis (dispersion parameter $k_d$, flux rate $k_{ep}$, mean transit time $T_i$) and TM analysis (transfer constant $K^{trans}$, flux rate $k_{ep}$, extravascular volume fraction $v_e$). Regions-of-interest representing benign and malignant tissue were drawn on each DCE-MRI slice according to the histopathology, and the performance of the estimated parameters for PCa diagnosis were evaluated by 5-fold cross validation and by receiver-operating-characteristic (ROC) curve analysis.

**Results**

As shown in Table 1 and Fig.1, the dispersion parameter $k_d$ from dMRI significantly outperformed all the other PK parameters, providing the best diagnostic performance, evaluated by 5-fold cross validation, and the highest AUC of the ROC analysis ($p$-value<<0.01).

**Table 1 Result of 5-fold cross-validation**

| | SENS (%) | SPEC (%) | ACC (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|---|
| $k_d$ **(dMRI)** | 78 ± 9 | 91 ± 7 | 85 ± 5 | 90 ± 7 | 81 ± 6 |
| $k_{ep}$ **(TM)** | 72 ± 14 | 75 ± 14 | 73 ± 6 | 76 ± 9 | 74 ± 8 |
| $K^{trans}$ **(TM)** | 63 ± 14 | 74 ± 14 | 68 ± 6 | 72 ± 9 | 67 ± 7 |
| $k_{ep}$ **(dMRI)** | 60 ± 14 | 68 ± 15 | 64 ± 7 | 66 ± 10 | 63 ± 7 |
| $T_i$ **(dMRI)** | 58 ± 14 | 64 ± 15 | 61 ± 7 | 63 ± 9 | 61 ± 7 |
| $v_e$ **(TM)** | 54 ± 17 | 61 ± 20 | 58 ± 6 | 60 ± 10 | 57 ± 7 |

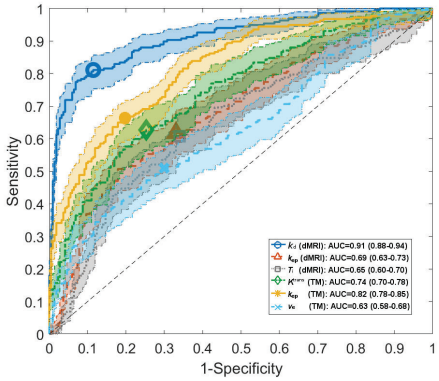


**Fig. 1 ROC curves calculated on the full 80-patient dataset.**

**Discussion**

In this study, we showed the promise of dMRI for quantitative DCE-MRI of the prostate. Moreover, dMRI eliminates the need for a separate AIF measurements, reducing technical hurdles and sources of inaccuracies in the estimated PK parameters. In the context of PI-RADS scoring, dMRI may improve mpMRI performance and workflow by providing a quantitative DCE-MRI method with higher diagnostic accuracy and a simpler quantification protocol. In fact, recent studies suggests that PI-RADS2 is still not optimal, and that the role of quantitative DCE needs to be reviewed.

**Conclusion**

MRDI improves the diagnostic performance of standard DCE-MRI for PCa localization with a simpler quantification protocol, not requiring separate AIF estimation. In the context of mpMRI, it may represent a valuable option for integrating quantitative DCE-MRI, possibly improving standardization and overall performance of PI-RADS scoring. In the future, the potential added value of MRDI to mpMRI will be investigated by comparing the diagnostic performance of PI-RADS2, dMRI, and the combination of the two.

**References**

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