DCE-MRI of prostate cancer: perfusion quantification with Tofts model vs. shutter-speed model. Initial experience.

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Target audience: Radiologists, physicists and technologists with interest in prostate imaging and perfusion imaging.

Purpose: DCE-MRI can be used to quantify prostate tumor perfusion parameters with the use of pharmacokinetic (PK) models[1], such as the Tofts Model (TM). However, the TM assumes infinitely fast equilibrium inter-compartmental water exchange kinetics, which might not hold true when there is significant contrast agent (CA) extravasation during CA bolus passage through the tissue of interest. The Shutter-Speed model (SSM) [2] takes into consideration the finite water exchange kinetics and the two-compartment SSM version introduces a parameter in addition to the K^{trans} and v_e parameters, the mean intracellular water molecule lifetime, τi, to account for the transcytolemmal exchange. Currently, there is no consensus regarding the pharmacokinetic model that should be used to quantify prostate perfusion parameters [3], with little experience on SSM in prostate imaging [4]. The purpose of this study is to report our initial experience with the use of SSM compared to a conventional TM to quantify normal prostate tissue and prostate cancer (PCa) perfusion with DCE-MRI with prostatectomy specimens used as reference standard.

Methods: Patients with PCa who underwent DCE-MRI of the prostate at 3T (Skyra, Siemens) before prostatectomy were included in this retrospective IRB approved study. DCE-MRI data was acquired using axial 3D-FLASH sequence covering the whole prostate (TR/TE/FA 4.9/1.9/12°, 192x154, slice thickness 3.5 mm, temporal resolution 4.5s, 65-70 volumes acquired) before and after injection of 0.1 mmol/kg of Gadobutrol (Gadavist). One radiologist placed ROIs in PCa lesions and normal peripheral zone (PZ) using prostatectomy maps as a guidance. A constant value of T1 was assumed over the prostate gland (1597 ms)[5]. The arterial input function (AIF) time course was obtained from the external iliac artery and considered as single vascular input function for PK modeling. Signal intensity (SI) time-courses were obtained. The normal PZ and PCa lesion SI time- course data were analyzed using TM and fast-exchange-regime-allowed version of SSM to extract K^{trans}, v_e, k_{ep} ($=K^{trans}/v_e$), and τi (SSM only). The parameters that were obtained with both models (K^{trans}, v_e and k_{ep}) were compared using Wilcoxon test. Reference standard was provided by surgical pathology and tumors were classified according to total Gleason grade scores. The correlation between PK parameters and total Gleason scores were analyzed with Spearman test.

	Normal PZ	PCa	*p*
K_{TM}^{trans} (min^{-1})	0.14 ± 0.06	0.41 ± 0.22	**0.009**
K_{SSM}^{trans} (min^{-1})	0.15 ± 0.07	0.41 ± 0.20	**0.009**
p	**0.003**	0.12	
v_e^{TM}	0.29 ± 0.09	0.34 ± 0.14	0.27
v_e^{SSM}	0.43 ± 0.19	0.47 ± 0.19	0.27
p	**0.009**	**0.009**	
k_{ep}^{TM} (min^{-1})	0.49 ± 0.23	1.4 ± 1.1	**0.009**
k_{ep}^{SSM} (min^{-1})	0.37 ± 0.18	1.0 ± 0.78	**0.009**
p	**0.009**	**0.009**	
τi (s)	0.13 ± 0.12	0.1 ± 0.001	1

Perfusion parameters of normal PZ and prostate cancer (PCa) lesions estimated in 11 patients, using TM and SSM.

Results: Initial data for 11 patients (mean age 62 y, 49-74 y) with 11 surgically resected PCa lesions in the peripheral zone (total Gleason score: G7=8, G9=3) were included. **Table** shows estimated perfusion parameters in normal PZ and PCa (K_{TM}^{trans}, v_e^{TM} and k_{ep}^{TM} for TM and K_{SSM}^{trans} v_e^{SSM} and k_{ep}^{SSM} for SSM). K^{trans} and k_{ep} showed significant differences between normal PZ and PCa lesions. No differences were noted on τi between normal PZ and PCa lesions. PCa and PZ K^{trans}, v_e and k_{ep} were significantly different when compared with their SSM counterparts, with the exception of K^{trans} in PCa lesions. A significant negative correlation was observed between K^{trans} *and* Gleason scores (r=-0.64, p=0.03), while there was no correlation with other parameters for both PK models.

Discussion: Our initial data shows that both the TM and the SSM produced significantly different parameters (K^{trans} and k_{ep}) when comparing PCa lesions to normal PZ, as previously reported. However, no differences were noted for τi between normal PZ and tumors. Significant differences in v_e and k_{ep} perfusion metrics were noted when computed with the TM and the SSM for normal PZ and PCa lesions, with v_e and k_{ep} being significantly lower and greater for the TM compared to the SSM respectively. Greater K^{trans} were observed for normal PZ using SSM versus TM, however no differences were noted for K^{trans} between the two PK models. These results are in disagreement with a prior study by Li et al. [4] who found that SSM returns greater K^{trans} and τi in prostate cancer when compared to the TM due to the modeling of the finite equilibrium transcytolemmal water exchange kinetics. The values of K^{trans} for PCa lesions and normal PZ reported in this study are similar to prior published values. Fennessy et al [6] found a baseline K^{trans} distribution for PCa lesions between 0.27-0.41min^{-1} and 0.09-0.15min^{-1} for normal PZ using DCE-MRI. A significant negative correlation was observed between Gleason scores and K^{trans} in our initial data. Prior reports have shown conflicting results. Langer et al [7] observed that Gleason 6 had higher K^{trans} compared to Gleason 7 tumors, however this difference was not significant. Conversely, Vos et al [8] showed that K^{trans} correlated significantly with aggressiveness in PZ tumors. The range of Gleason scores in our initial cohort of patients were limited, with only high grade tumors included. Therefore, pending analysis of larger number of cases with histopathologic correlation is needed.

Conclusion: Initial data shows differences in perfusion metrics when computed with the TM and the SSM. Both PK models could be used to quantify differences in normal prostate tissue and PCa perfusion. However, no differences were observed in τi between PCa and normal prostate tissue using the SSM, which questions the need for the use of SSM. However, more data should be analyzed to confirm these findings.

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