Influence of prostate perfusion on high-intensity focused ultrasound cancer ablation: a first-pass MRI study

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Rationales and objectives: Transrectal high-intensity focused ultrasound (HIFU) is a new minimally invasive treatment for prostate cancer, inducing coagulation necrosis by tissue heating (1-2). According to bio-heat transfer simulations, prostate perfusion should have a major impact on the formation of HIFU-induced lesions, with increasing levels of regional blood flow leading to reduced heat deposition. However, the influence of prostate perfusion on the clinical outcome of HIFU treatment has never been precisely evaluated. The bolus tracking technique represents the more widely used protocol in MR perfusion studies but leakage of approved low-molecular gadolinium chelates from the capillaries into the interstitial space could be an obstacle to absolute quantification of blood flow. In this paper we propose a new modeling approach that takes contrast agent leakage into account. Our specific aim was to test the hypothesis that pre-HIFU perfusion level is of predictive value for patient responsiveness to treatment.

Methods: Forty-eight patients with clinical stage T1-T2 prostate cancer were treated by HIFU (ABLATHERM, EDAP S.A.). Neo-adjuvant hormonal therapy was previously administered to 37 of these patients. Dynamic contrast-enhanced MRI was performed in all patients using a T1-weighted Turbo-FLASH imaging sequence (TR/TE: 238/2.75-ms; time of inversion: 500-ms; flip angle: 10°; field of view: 24x38-cm; matrix 160x256 voxels; slice thickness: 5-mm; slice number: 3; 25 images per slice obtained at intervals of 2.5-s) during intravenous bolus injection of gadolinium at the dose of 0.1-mmol/kg. Regional prostatic blood flow (rPBF) was estimated by deconvolution of the whole prostate curve with an arterial input function. We constrained deconvolution by introducing the following apparent residue function: $Rapp(t)=K^{PS}+rPBF.\exp(-t/MTT)$ where K^{PS} is the transendothelium transfer coefficient and MTT the mean transit time in the vascular compartment. This new method, referred as « monoexponential plus constant » (MPC), was evaluated in comparison to two well known techniques: one semi-quantitative (normalized mean gradient (3)) and one quantitative, using a Fermi function, that was validated in the myocardium (4). Response to treatment was divided into two groups according to a post-HIFU PSA nadir cutoff of 0.2 ng/ml, indicative of residual cancer (5).

Results: rPBF values obtained using MPC deconvolution were in good agreement with published values obtained with PET studies in the prostate (6) and in the muscle taken as a tissue of reference (7), whereas the Fermi method underestimated rPBF (Table). Patients with PSA nadir>0.2 ng/ml had a significantly higher pre-HIFU rPBF estimated with both quantitative approaches (Table). The semi-quantitative data showed the same trend but the difference was not significant (Table). The sub-group of patients who received neo-adjuvant hormonal therapy had a pre-operative rPBF statistically lower compared to patients who did not (MPC deconvolution: 11±7 vs 17±9 ml/min/100g, p=0.02). In this subgroup also, patients with PSA nadir>0.2 ng/ml had a significantly higher pre-operative rPBF (MPC deconvolution: 9±5 vs 16±9 ml/min/100g, p=0.007).

	PSA nadir< 0.2 ng/ml (N=31)	PSA nadir> 0.2 ng/ml (N=17)	Muscle (N=48)
rPBF Fermi (ml/min/100g)	6 ± 3	10 ± 6*	3 ± 2
rPBF MPC (ml/min/100g)	10 ± 6	16 ± 9*	5 ± 3
Normalized mean gradient (10^5 s^{-1})	41 ± 15	59 ± 29	19 ± 13

Table- Perfusion estimates obtained using 3 different methods in the two groups of patients with PSA nadir< or >0.2 ng/ml. Data are expressed as mean ± standard deviation. * *p<0.05 Student t test*

Conclusion: Dynamic MRI during first-pass of conventional contrast agent and appropriate modeling allows prostate perfusion estimation. This *in vivo* study confirms simulation results showing that perfusion level is one of the factors influencing treatment outcome. These findings could have important implications for the management of patients on an individual basis.

References:

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