Delay and dispersion correction for simultaneous quantification of perfusion and permeability in the prostate using DCE-MRI with a dual-contrast sequence

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Introduction

Contrast enhancement of the prostate in dynamic MR imaging can be used to assess perfusion and permeability using a low-molecular-weight contrast medium (CM). The arterial input function (AIF) is subject to delay and dispersion during its passage from the point of measurement to the target voxel [1]. The dispersion is inherently coupled to the delay. Whereas the delay can easily assessed the bolus dispersion is caused by two processes, the dispersion during its passage from the point of measurement to the tissue and the dispersion by the tissue passage expressed by the mean transit time (MTT).

Material and Methods

A sequence was designed for the dynamic acquisition of two FLASH images ($\alpha = 30°$, matrix size: 128×90, FoV: 228×228 mm) every 1.65 sec: first a T1-weighted image (TE1 = 2.1 ms) using global inversion preparation (TI = 280 ms) and then a T2*-weighted image (TE2 = 27 ms). The echo time of the first image was chosen as short as possible and the echo time of the second image was adjusted to depict the passage of the contrast medium (CM) bolus. Non-slice-selective inversion preparation was used to improve the contrast-to-noise ratio (CNR) and was adjusted to suppress signal contributions from unenhanced arterial blood. For dynamic MRI a transverse 5-mm slice through the prostate was chosen. A bolus of 24 ml gadopentetate dimeglumine was infused intravenously at a flow rate of 6 ml s^{-1} followed by a 20-ml saline flush. Retrospective signal intensity homogenization of the dynamic MRI data sets was performed in order to eliminate signal inhomogeneities caused by the use of multiple surface coils for data acquisition.

The AIF was quantitatively determined in the external iliac artery from the signal intensity time courses of both, the T1- and T2*-weighted images, and modeled as a gamma variate function. The estimated AIF ($C_a^{(est)}$) is subject to delay and dispersion during its passage from the point of measurement (external iliac artery) to the target voxel [1]. A delay can be introduced by increasing the arrival time (t_0) by replacing with ($t_0 + \delta t_0$). Dispersion can be described mathematically as a convolution with a vascular transport function $h(t)$ from the site of measurement to the target voxel, i.e.: $C_a(t) = C_a^{(est)}(t+\delta t_0) \otimes h(t)$. The transport function is given by: $h(t) = \beta \cdot e^{-\beta t}$.

The quantification of perfusion is based on the indicator dilution theory, and requires determination of the AIF (C_a) for deconvolution of the blood concentration-time curve in tissue capillaries, $C_b(t)$: $C_b(t) = F \cdot C_a(t) \otimes R(t)$, where F is perfusion and $R(t) = e^{-t/MTT}$ the residue function, MTT is the meant transit time through the tissue. Perfusion can be calculated from mean transit time MTT and blood volume v_b, $F = v_b / MTT$. The resulting tissue concentration can therefore be expressed as [1]: $C_b(t) = F \cdot C_a(t) \otimes R(t) = F \cdot (C_a^{(est)}(t+\delta t_0) \otimes h(t)) \otimes R(t)$

Tracer uptake was described by a mixed flow- and permeability-limited [2]: $\frac{dC_e}{dt} = \frac{EF\rho}{v_e}(1-Hct)(C_p - C_e)$, where C_e is the contrast medium concentration in the extravascular extracellular space, $C_p = C_a/(1-Hct)$ tracer concentration in arterial blood plasma, Hct hematocrit fraction in whole blood, v_e fractional extravascular extracellular volume per unit volume of tissue, ρ density of tissue, and E extraction fraction. The extraction fraction is the fractional reduction of the capillary blood concentration as it passes through tissue: $E = 1 - e^{-PS/F(1-Hct)}$, where PS is the permeability surface area. The tissue signal I_t consists of two contributions, the vascular I_b and the extravascular I_{ev}: $I_t = v_b I_b + (v_e + v_c) I_{ev}$, where v_c is the fractional cellular volume.

13 patients with a histological defined prostate tumor were imaged. A tumor and a healthy prostate ROI were evaluated by using the above described model with and without dispersion correction. All parameters were calculated and the F-test applied to decide which model is more appropriate. Statistical significance was tested using the paired Wilcoxon signed rank test

Results

The F-test yielded a mean value over all ROIs of 44.7 with P=0.02, indicating that dispersion correction significantly improves fitting accuracy. Additionally, the methodical difference is significant for all parameters. Both statistical evaluations yielded similar P-values for most parameters but the differences between tumor and prostate were generally more significant using dispersion correction. $C_a^{(est)}$ was significantly delayed and dispersed on the way from the iliac artery to the prostate before entering the tissue, resulting in a local AIF, C_a. $C_a^{(est)}$ was delayed by a median of 13.1 s in prostate tissue and by 9.2 s in prostate tumor. The dispersion coefficients were 14.8 s for prostate tissue and 9.6 s for prostate tumor. The mean transit time was significantly different between tumor and prostate with dispersion correction while it was not without (P(MTT)=0.039 with dispersion correction and P(MTT)=0.311 without). The blood volume and perfusion differed significantly between tumor and prostate for both models (P(v_b)=0.019/ P(F)=0.004 with dispersion correction and P(v_b)=0.011/ P(F)=0.016 without). Tumor perfusion was more than five times higher than tissue perfusion, 1.38 ml/(min·cm^3) vs. 0.23 ml/(min·cm^3); blood volume approximately two times higher, 1.9 % vs. 0.7 %; and mean transit time in tumors approximately half that of normal prostate tissue, 2.88±2.30 s vs. 4.88±3.21 s.

Conclusions

Delay and dispersion are so large that they must be taken into account to accurately estimate perfusion and extravasation in the prostate.

References

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