VALIDATION WITH DCE-CT PROVES THAT THE DCE-MRI PHASE SIGNAL CAN BE USED FOR ROBUST MEASUREMENT OF THE ARTERIAL INPUT FUNCTION (AIF) IN THE ILIAC ARTERIES

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OBJECTIVE

The measurement of an accurate arterial input function (AIF) is needed for reliable analysis of DCE data with a tracer kinetic model. However, measurement of an AIF directly from the MR magnitude signal (AIF_{MAGN}) can be challenging due to T_2^*-effects at higher concentrations, B_1-field inhomogeneities and inflow effects [1,2]. As an alternative to the magnitude signal, the AIF can also be measured from the phase signal (AIF_{PHASE}) [3,4]. Advantageous are the linear relationship between phase shift and contrast agent concentration and the insensitivity to the previously mentioned artifacts that influence the measurement of AIF_{MAGN}. We chose dynamic contrast-enhanced CT (DCE-CT) for the validation of AIF_{PHASE}, since CT does not suffer from the MR artifacts and a linear relationship exists between Hounsfield units (H.U.) and contrast agent concentration. The purpose of this study is to validate AIF_{PHASE} with the AIF as measured on DCE-CT (AIF_{CT}) in the iliac arteries of prostate cancer patients.

METHODS

The study was approved by the local medical ethical research board and all patients gave written informed consent. Twelve patients (mean age 67.8, range 56–84 years) with biopsy proven prostate cancer were included, that did not have a contraindication for the CT contrast agent and/or the MRI exam and MRI contrast agent. Patients underwent a DCE-CT and a DCE-MRI exam (median 11.5 days apart, range 0-15) prior to radiotherapy treatment (≥77 Gy). MRI acquisitions were performed on a 3 Tesla MR scanner. The DCE-MRI exam consisted of a T1-weighted 3D spoiled gradient echo sequence (20 transverse slices, slice thickness 5.0 mm, TR/TE 4.0/1.7 ms, acquisition matrix 160x160, FOV 40 cm, flip angle 8º). A total of 120 scans were obtained at a 2.4 s time interval. In each patient 0.1 ml/kg gadobutrol (1.0M Gadovist) was injected with a power injector (1ml/s or 2ml/s), followed by a saline flush. DCE-CT scans (120kV, 200mAs, CTDI 13.3mGy per time point) were performed on a 128-slice CT scanner and consisted of acquisitions at 42 time points (2.4 s time interval during first 24 acquisitions) within a time window of 5 minutes. The injection of iodine contrast agent (Ultravist 300) was performed with a power injector (60 ml, 6 ml/s), followed by a saline flush. AIF_{CT} in the iliac arteries was converted from H.U. to concentration iopromide with the aid of a calibration phantom. AIF_{PHASE} was measured from the phase evolution over time in manually selected voxels in the iliac arteries. The phase signal ($\Delta\varphi$) at a certain time point can be converted from radians to concentration gadobutrol, C, using the following equation [4]:

$$\Delta\varphi = \gamma \frac{\Delta\mathbf{B}\cdot\mathbf{H}_0}{\|\mathbf{H}_0\|} TE = \omega_0 \cdot \chi_M \cdot C \cdot F \cdot TE \ ,$$

with γ the gyromagnetic ratio, $\Delta\mathbf{B}$ the change in the magnetic induction vector, $\mathbf{H}_0$ the static external magnetic field vector, TE the echo time of the DCE-MRI sequence and ω_0 the resonance frequency ($8.03\cdot10^8$ rad/s at 3T). The molar susceptibility of the contrast agent, χ_M, was calculated from the Langevin equation, yielding a value of 320 ppm/M at 310 K in vivo. The geometry factor of the susceptibility compartment, F, was assumed to be an infinite cylinder, adjusted to the angle of the iliac arteries with the B_0-field [4]. As the amplitudes (mM) of AIF_{CT} and AIF_{PHASE} are proportional to the amount (mmol) of contrast agent injected [5,6], the AIFs were divided by the amount of contrast agent injected to obtain a single, dose normalized unit (mM/mmol) for direct comparison between AIF_{PHASE} and AIF_{CT}. We tested with a paired Student's t-test for differences in the area under the curve of the first pass peak (AUC_{FPP}), the peak height, full-width-at-half-maximum (FWHM) and the signal 180 seconds after the peak (SI_{180}), between the dose normalized AIF_{PHASE} and AIF_{CT} in the right iliac artery. The within-subject standard deviation (wSD) [7] and within-subject coefficient of variation (wCV), the wSD as percentage of the mean, were calculated to quantify the consistency of the AIF_{PHASE} and AIF_{CT} measurements between the left and right arteries.

RESULTS AND DISCUSSION

Figure 1 shows examples of dose normalized AIF_{CT} and AIF_{PHASE} in four patients, together with the concentration-time curve of AIF_{MAGN}. AIF_{MAGN} shows an anomalous shape and incorrect amplitude, due to signal saturation, T_2^*-effects, B_1-field inhomogeneities and inflow effects. Despite these problems with AIF_{MAGN}, for all patients the shape of AIF_{PHASE} is very similar to the shape of AIF_{CT}. Furthermore, no significant differences were found in AUC_{FPP} and SI_{180} between AIF_{PHASE} and AIF_{CT} (Table 1). AIF_{PHASE} shows a somewhat narrower and higher first pass peak compared to AIF_{CT} (Table 1), possibly reflecting differences in injection protocol. The consistency of AIF_{PHASE} measurements between the left and right iliac arteries is in the same order of magnitude as AIF_{CT} (Table 2), except for SI_{180}. This is caused by drift of the B_0-field, which may cause errors in the tail of AIF_{PHASE} for individual patients.

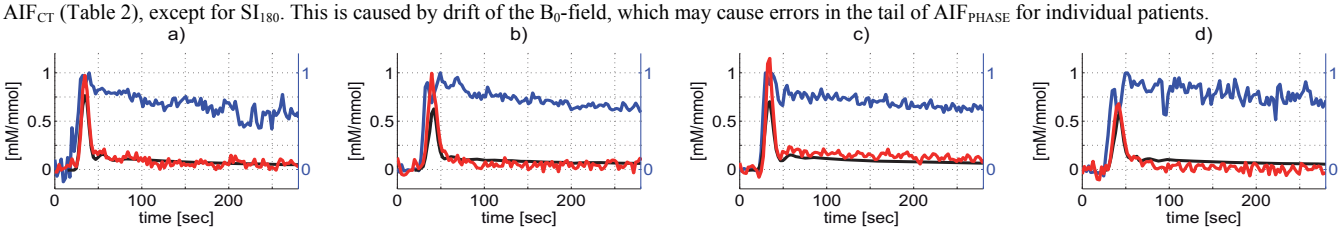

***Figure 1**: Examples of AIF_{CT} (black), AIF_{PHASE} (red) and AIF_{MAGN} (blue, scaled between 0 and 1) in four prostate cancer patients.*

TABLE 1 (N=12)	AIF_{PHASE} mean ± std	AIF_{CT} mean ± std	t-test p-value
AUC_{FPP} [mM/mmol*s]	8.0 ± 2.6	7.7 ± 0.9	n.s.
Peak height [mM/mmol]	0.86 ± 0.18	0.64 ± 0.08	*0.0009
FWHM [s]	10.1 ± 2.5	11.8 ± 1.1	*0.031
SI_{180} [mM/mmol]	0.05 ± 0.11	0.07 ± 0.01	n.s.

***Table 1**: Peak characteristics and differences between AIF_{PHASE} and AIF_{CT}*

TABLE 2 (N=12)	AIF_{PHASE} wSD	AIF_{PHASE} wCV	AIF_{CT} wSD	AIF_{CT} wCV
AUC_{FPP} [mM/mmol*s]	1.4	17.2%	0.2	2.9%
Peak height [mM/mmol]	0.05	6.3%	0.01	2.5%
FWHM [s]	0.7	7.3%	0.4	3.1%
SI_{180} [mM/mmol]	0.08	239.6%	0.01	17.0%

***Table 2**: Measurement consistency between the left and right iliac arteries*

CONCLUSION

Even when the AIF measured from the magnitude signal was very poor due to signal saturation, T_2^*-effects, B_1-field inhomogeneities and inflow effects, we could reliably measure the AIF from the phase signal, in view of the good agreement in both shape and amplitude with AIF_{CT}. This indicates that AIF measurements from signal phase are more robust than AIF measurements from the magnitude signal. From indicator dilution theory it can be explained that AUC_{FPP} is the same for both imaging modalities, irrespective of differences in injection protocol that are reflected by the inverse relationship between peak width and peak height. The phase drift in the tail of AIF_{PHASE} is a hardware problem and may need correction in some individual cases. In conclusion, AIF_{PHASE} shows good agreement in both shape and amplitude with AIF_{CT}.

REFERENCES

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