Automated correction method allowing phase-based detection of contrast enhancement in DCE-MRI

Ellis Beld[1], Frank F.J. Simonis[1], Johannes G. Korporaal[1], Uulke A. van der Heide[2], and Cornelis A.T. van den Berg[1]
[1]*Radiotherapy, UMC Utrecht, Utrecht, Netherlands,* [2]*Radiotherapy, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Amsterdam, Netherlands*

Introduction Measurement of an accurate arterial input function (AIF) is essential in dynamic contrast-enhanced (DCE) MRI. The measurement of patient individual AIFs using magnitude data is challenging due to various experimental difficulties such as inflow, B_1 non-uniformity and saturation effect. Phase-based measurements of the AIF are insensitive to aforementioned difficulties and display an attractive linear relationship between contrast agent concentration and phase shift[1-3]. Unfortunately, one major difficulty is that phase sensitive MR procedures are affected by spatially and temporally varying B_0 inhomogeneities. The two main sources of the background field (ΔB_0) fluctuations are: field drift inherent to the MR system itself and a contrast agent induced change of the effective susceptibility on the whole body. In a previous study on phase-based AIFs, a zeroth order background field correction was used[3]. Here, a method (derived from MR thermometry[4]) is described that determines higher order background fields for a more accurate and reliable correction. This enables phase correction not only at the location of the vessel where the AIF is taken, but over the whole field of view. We also demonstrate that the correction allows detection of contrast induced phase modulation in tissues. Here, we apply this new methodology for 3T DCE-MRI of the prostate.

Materials and methods DCE-CT and -MR data of a previous clinical study for prostate cancer patients were used[3]. The DCE-MRI exams were performed on a 3T MR scanner (Achieva, Philips Healthcare), using a 3D spoiled gradient echo sequence (20 transverse slices, slice thickness 5.0 mm, TR/TE 4.0/1.7 ms, acq. matrix 160 x 160, FOV 40 cm, flip angle 8º, 120 dynamics at 2.4 s time interval). In each patient 0.1 mL/kg gadobutrol (1.0 M Gadovist) was injected with a power injector (1 mL/s or 2 mL/s), followed by a saline flush. Phase difference images were corrected for ΔB_0, by subtracting a near-harmonic 2D reconstruction of the background phase (see figure 1b for an example). This reconstruction of the background phase was created by manually selecting a continuous layer of subcutaneous fat (see figure 1a) and using it as boundary condition of a classic Dirichlet problem, to calculate the field inwards[4]. The phase of subcutaneous fat was chosen for this purpose, as we observed a negligible uptake of contrast agent in fat in the magnitude data. This means that the fat phase reflects only ΔB_0. The fat layer needs to be sufficiently thick and principally needs to fully surround the body. However, we found that small gaps could be compensated. The correction method cannot compensate for phase disturbances due to motion. For the AIF determination vascular voxels of the right femoral artery (see figure 1a) were selected from a cumulative enhancement magnitude image obtained by summing the enhancement over time. Voxels with intensities higher than 90% of the maximum were included. This was done for three subsequent slices and a mean AIF over time was obtained. The corrected AIF phase difference $\Delta\varphi$ was converted to the concentration of gadobutrol C, using the following equation: $C(t) = \frac{\Delta\varphi(t)}{\omega_0 \cdot \chi_M \cdot F \cdot TE}$, where ω_0 is the resonance frequency, χ_m the molar susceptibility of the contrast agent, F a geometry factor of the artery and TE the echo time[2,3]. AIFs measured from DCE-CT in the same patients were used as gold standard. The DCE-CT exams (120 kV, 200 mAs) were performed with a 256-slice CT scanner (Brilliance iCT, Philips Healthcare) and an iodine contrast agent (Ultravist 300) was injected (60 ml, 6 ml/s), followed by a saline flush. For comparison of $AIF_{MR\text{-}phase}$ with AIF_{CT}, both AIFs were normalized to the injected amount of contrast agent. For one patient, the phase signal enhancement in the prostate was determined, by averaging the phase signal over time. The phase enhancement pattern was compared with the cumulative enhancement of the magnitude signal.

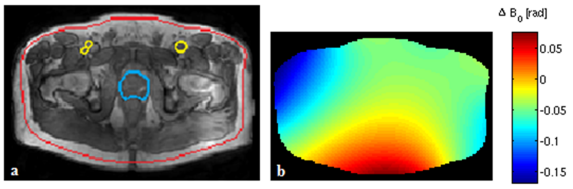

Fig. 1. *a) Example of an axial slice in which the background phase correction can be applied. The prostate (yellow) and the right and left femoral artery (blue) are delineated. In red, the selected boundary in the subcutaneous fat layer is indicated. b) An example of a fitted background phase (ΔB_0) for correction.*

Results and discussion Figure 2 shows three examples of the uncorrected and corrected dose normalized $AIF_{MR\text{-}phase}$ and AIF_{CT}. The applied ΔB_0 correction strongly improved the shape of $AIF_{MR\text{-}phase}$. The main improvements were seen in the AIF tail, correcting physically impossible, negative concentrations. Some small differences were still observed between the peak heights of the corrected $AIF_{MR\text{-}phase}$ and AIF_{CT}. This can be explained by missing the real peak height due to undersampling. The higher noise in the $AIF_{MR\text{-}phase}$ can be attributed to pulsatile flow in the artery, generating small phase differences. Figure 3 shows the cumulative phase enhancement in the prostate and the corresponding cumulative enhancement of the magnitude signal. Although small differences between the two maps are observable, the averaged phase difference and averaged magnitude enhancement show similarities. It is important to mention that the enhancement on the phase and magnitude images are based upon different physical processes; phase enhancement will be modulated by susceptibility gradients, while T_1 enhancement modulates the steady state magnetization. Therefore, T_1-based and phase enhancement have different relations with the underlying microvascular properties. Converting the phase enhancement to concentration would require techniques from Quantitative Susceptibility mapping which is outside the scope of this study.

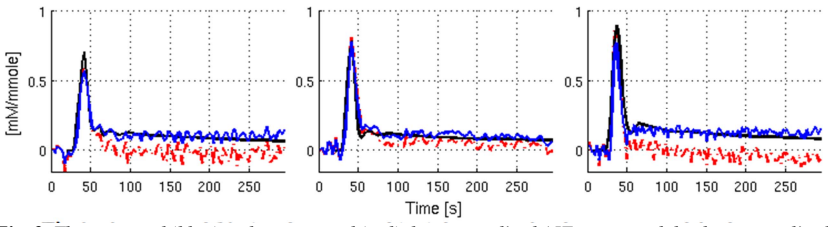

Fig. 2. *The corrected (blue) and uncorrected (red) dose normalized $AIF_{MR\text{-}phase}$ and the dose normalized AIF_{CT} (black), measured in the femoral artery in three prostate cancer patients.*

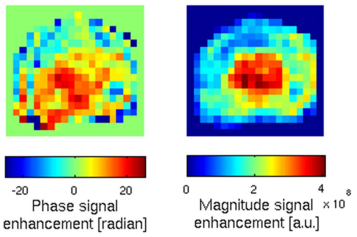

Fig. 3. *a) Cumulative phase signal enhancement and b) cumulative magnitude signal enhancement in the prostate.*

Conclusion Higher order background phase corrections can be applied to MR phase signals from DCE-MRI. The background phase is calculated inwards with a near-harmonic 2D reconstruction starting from the subcutaneous fat layer. This allows measurement of the AIF and detection of contrast induced phase modulation in tissues, for example the prostate. Current limitations of the method are that the fat layer needs to be sufficiently thick and that the methodology cannot compensate for phase disturbances due to motion. The phase enhancement in tissue has a different relation to underlying microvascular- and tissue structure than T_1 enhancement. Both methods could be combined in a synergistic manner to extract more information on tumor characteristics. Because of the minimal user interaction the method could be useful for clinical usage. We will test the correction method on a larger group of patients to confirm its applicability.

References 1) Akbudak E. et al, MRM 1996; 36:809-815. 2) Garpebring A. et al, Magn Reson Mater Phy 2011; 24:233-245. 3) Korporaal J.G. et al, MRM 2011; 66:1267-1274. 4) Salomir R. et al, IEEE Trans Med Imaging 2012; 31:287-301.