Re-use of subject-specific AIFs are warranted in longitudinal DCE-MRI

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TARGET AUDIENCE: Clinicians, physicists and researchers involved in imaging studies and clinical trials with longitudinal monitoring of tumor permeability.

PURPOSE: Dynamic contrast-enhanced (DCE)-MRI is widely used for assessment of tumor permeability by the capillary permeability transfer constant K^{trans} [1]. For this technique to be a valuable biomarker of response in clinical trials with repeated imaging [2], high intra-patient reproducibility is crucial to detect subtle treatment effects [3]. Because of subject-specific variations in systemic circulation, a decisive step in the estimate of K^{trans} is the selection of the arterial input function (AIF). The accuracy and reproducibility of the AIF section and subsequent K^{trans} estimation are challenged by user-dependent variations, partial volume effects, image quality and choice of analysis method [1]. We hypothesize that intra-patient reproducibility of the K^{trans} estimate is maximized by re-use of a single, subject-specific AIF in comparison to traditional re-estimation at each scan or a population based AIF.

METHODS: DCE-MRI was performed at 3T (TimTrio Siemens, Germany) with axial, fast gradient-echo images with repetition-time 5.7ms, echo-time 2.73ms, slice-thickness 2.1mm, inter-slice distance 0.4mm, in-plane resolution 2.90:2.00mm, matrix size 128:87 and 20 slices. After approximately 52s of imaging, a 0.1mmol/kg dose of gadopentetate-dimeglumine (Magnevist, Bayer Schering Pharma AG, Germany) was injected at 5cc/s. To exclude effects from T_1 variations, the T_1 values in blood and tumor were fixed at 1650ms and 1450ms, respectively. Twenty-two adult patients with recurrent glioblastoma received two baseline scans approximately four days apart with absence of intervening treatment (clinicaltrials.gov, NCT00305656) [2]. Estimates of K^{trans} were calculated in four ways: (a) with the AIF semi-automatically determined [4] at each scan (scanAIF), (b) with the AIF determined at the first scan, representing an AIF particular to the patient (patAIF), (c) with an AIF obtained as the average over all patients and scans, representing a population based AIF (popAIF) and (d) with a pre-defined and synthetic AIF (syntAIF) created in *JSim* (National Simulation Resource Physiome initiative) [5]. Values of K^{trans} between visits 1 and 2 were compared for all methods using Spearman correlation. Imaging analysis was performed using *nordicICE* (NordicNeuroLab AS, Norway).

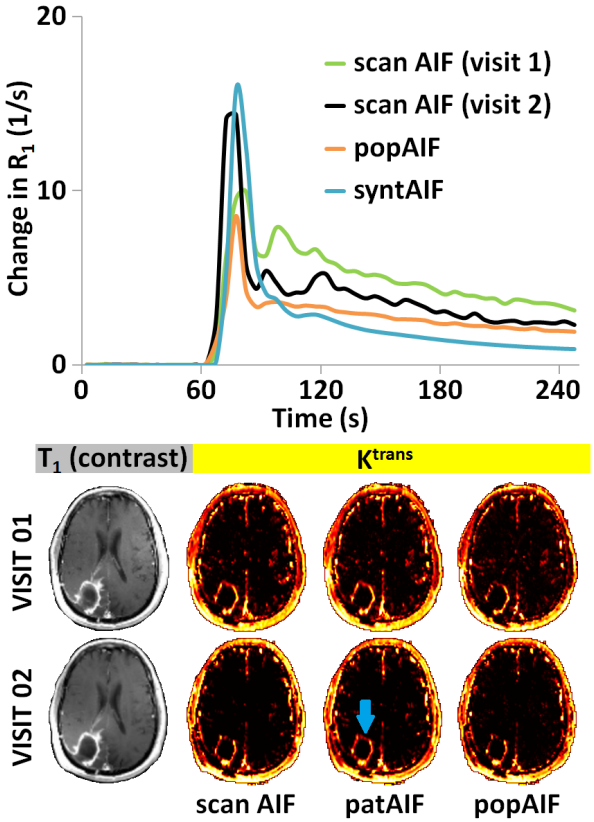

Figure 1. Top: Representative AIFs from a patient illustrating variations in AIF selections between visits 1 and 2. **Bottom**: Contrast-enhanced MRI and resulting K^{trans} showing regional variations (blue arrow) from different AIFs.

Table 1	K^{trans}	
	Correlation	R^2
scanAIF	0.56	0.12
patAIF	0.94	0.79
popAIF	0.78	0.66
syntAIF	0.77	0.64

RESULTS: Correlations between K^{trans} estimated at visit 1 and visit 2 using all four methods are shown in Table 1. The patAIF method yielded the highest interscan correlations of all methods (0.94; $P<0.001$) followed by popAIF (0.78; $P<0.001$). The lowest correlation value was observed for scanAIF (0.56; $P<0.01$). Furthermore, the highest R^2 value was observed for patAIF (Table 1). Figure 1 illustrates examples of AIFs using scanAIF, patAIF and popAIF, respectively, as well as corresponding regional variations in K^{trans} values.

DISCUSSION: In this study we demonstrate substantial improvements in reproducibility by revising the AIF search strategy. A re-use of the subject-specific AIF considerably outperformed a scan-specific AIF. In addition, a population or synthetic AIFs yields higher reproducibility than a scan-specific AIF with the added value of not having to manually select an AIF.

CONCLUSION: A re-use of subject-specific AIFs are warranted in longitudinal DCE-MRI.

REFERENCES: [1] Tofts PS et al, JMRI 1999;10(3):223-32, [2] Batchelor TT et al, Cancer Cell 2007;11(1):83-95, [3] Mouridsen K et al, proc ISMRM 2011 (p376), [4] Mouridsen K et al, MRM 2006;55(3):524-31, [5] Barboriak DP et al, JMRI 2008;27(6):1388-98