

Cross-over: Measuring the arterial input function in DCE- and DSC-MRI

Anders Garpebring, PhD

Department of Radiation Sciences, Umeå University, Umeå, Sweden

Objective: The main objective of this lecture is to give answers to the questions:

- When and why is a measured AIF important?
- What are the challenges in obtaining an accurate AIF?
- What methods to measure the AIF exist and what are their strengths and weaknesses?

Background: The analysis of DCE- and DSC-MRI data consists primarily of identifying, from contrast agent (CA) uptake curves, the impulse response of a linear systems. However, the signal observed in each voxel is merely the output of the linear system and unless the input is known very little can be inferred about underlying physiology. This input is referred to as the arterial input function (AIF) and is the blood plasma CA concentration in the arterial blood that oxygenates the tissue of interest. Since the size and shape of the AIF depends on factors such as patient blood volume, heart rate, injection rate and much more, it should ideally be measured to reduce uncertainties in estimated physiological quantities. Measuring the AIF is very challenging and unless a great deal of care is taken the measurement itself may introduce as much or even more errors than an assumed AIF [1].

The challenge: Table 1 summarizes some of the demands a sequence should fulfill to yield high quality tissue uptake curves and AIFs. These demands are clearly in conflict, e.g., high CA sensitivity and fast imaging. This is the case even if one focusses on only measuring either the tissue uptake curves or the AIF, and the situation gets more complex if both types of data are acquired simultaneously. There is no obvious solution that gives the “best” compromise and consequently many methods have been introduced to obtain simultaneous tissue uptake curves and AIFs.

Available methods: The most obvious approach to acquire an AIF is to use the magnitude signal curve from a large artery within the imaged volume. Although this is very reasonable, it is not unproblematic, since suitable vessels may not be available and factors such as partial volume effects (PVEs), B_1 -inhomogeneity, unknown flow-rate [2], [3] and unknown relaxivity [4] may affect the signal intensity. If the signal phase is used instead, one gets a simple relationship between phase and CA concentration [5] and corrections for PVEs can be performed [6]. To this date the phase-based approach has not gained widespread use likely due to problems in isolating the phase changes due to the CA from phase changes due to other sources [7]. By using a prebolus injection one can separate the tissue uptake curve measurement and the AIF measurement and get more flexibility in AIF measurement site [8], however at the expense of longer imaging time. A final method that will be discussed is to completely remove the need to measure the AIF by inferring it from the tissue uptake curves using reference region or blind estimator methods [9–12].

Table 1: Sequence requirements

Requirements	Tissue CA uptake curves	AIF
Volume coverage	Large	Small
Spatial resolution	Low to high	High
Temporal resolution	Medium to high	High to very high
CA sensitivity	High	Medium
CA measurement range	Small	Large
Handle confounding effects	Water exchange, unknown relaxivity. T1 and T2* effects in DSC and DCE-MRI, respectively.	Signal dropout and signal displacement in DSC-MRI. Inflow and T2* effects in DCE-MRI.

References:

- [1] G. J. M. Parker et al., "Experimentally-derived functional form for a population-averaged high-temporal-resolution arterial input function for dynamic contrast-enhanced MRI," *Magnetic Resonance in Medicine*, vol. 56, no. 5, pp. 993–1000, Nov. 2006.
- [2] H.-L. M. Cheng, "T1 measurement of flowing blood and arterial input function determination for quantitative 3dt1-Weighted dce-Mri," *Journal of Magnetic Resonance Imaging*, vol. 25, no. 5, pp. 1073–1078, May 2007.
- [3] A. Garpebring, R. Wirestam, N. Ostlund, and M. Karlsson, "Effects of inflow and radiofrequency spoiling on the arterial input function in dynamic contrast-enhanced MRI: a combined phantom and simulation study.," *Magnetic Resonance in Medicine*, vol. 65, no. 6, pp. 1670–9, Jun. 2011.
- [4] G. J. Stanisz and R. M. Henkelman, "Gd-DTPA Relaxivity Depends on Macromolecular Content," *Magnetic Resonance in Medicine*, vol. 44, no. July, pp. 665– 667, 2000.
- [5] E. Akbudak and T. E. Conturo, "Arterial input functions from MR phase imaging," *Magnetic Resonance in Medicine*, vol. 36, no. 6, pp. 809–815, 1996.
- [6] M. J. p. Van Osch, E. P. A. Vonken, C. J. G. Bakker, and M. A. Viergever, "Correcting Partial Volume Artifacts of the Arterial Input Function in Quantitative Cerebral Perfusion MRI," *Magnetic Resonance in Medicine*, vol. 485, no. 3, pp. 477– 485, 2001.
- [7] A. Garpebring, R. Wirestam, J. Yu, T. Asklund, and M. Karlsson, "Phase-based arterial input functions in humans applied to dynamic contrast-enhanced MRI: potential usefulness and limitations.," *Magma (New York, N.Y.)*, May 2011.
- [8] L. E. Kershaw and H.-L. M. Cheng, "A general dual-bolus approach for quantitative DCE-MRI.," *Magnetic resonance imaging*, vol. 29, no. 2, pp. 160–6, Feb. 2011.
- [9] T. Yankeelov et al., "Quantitative pharmacokinetic analysis of DCE-MRI data without an arterial input function: a reference region model," *Magnetic Resonance Imaging*, vol. 23, no. 4, pp. 519–29, May 2005.
- [10] C. Yang, G. S. Karczmar, M. Medved, and W. M. Stadler, "Multiple reference tissue method for contrast agent arterial input function estimation.," *Magnetic Resonance in Medicine*, vol. 58, no. 6, pp. 1266–75, 2007.
- [11] M. C. Schabel, J. U. Fluckiger, and E. V. R. DiBella, "A model-constrained Monte Carlo method for blind arterial input function estimation in dynamic contrast-enhanced MRI: I. Simulations.," *Physics in Medicine and Biology*, vol. 55, no. 16, pp. 4783–806, Aug. 2010.
- [12] M. C. Schabel, E. V. R. DiBella, R. L. Jensen, and K. L. Salzman, "A model-constrained Monte Carlo method for blind arterial input function estimation in dynamic contrast-enhanced MRI: II. In vivo results.," *Physics in Medicine and Biology*, vol. 55, no. 16, pp. 4807–23, Aug. 2010.