# The influence of cardiac frequency on the properties of the arterial input function (AIF) and computed DCE-MRI parameter values

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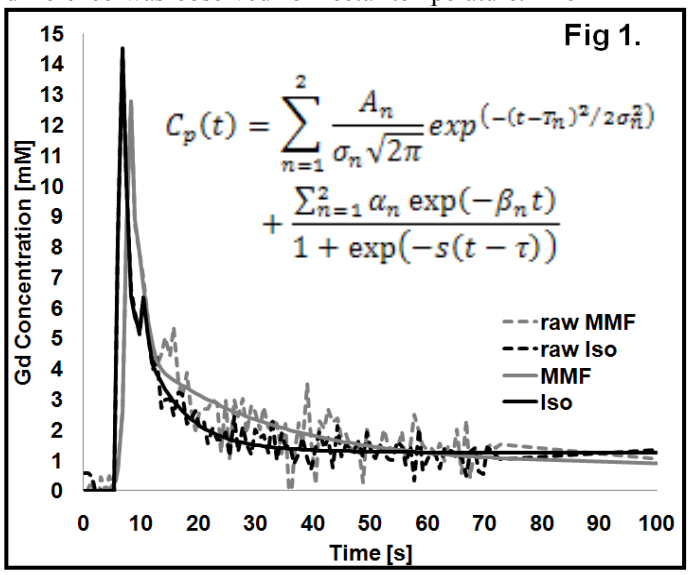
**Introduction:** Quantitative determination of tissue perfusion, permeability and blood volume fraction applying DCE-MRI requires knowledge of the arterial plasma concentration of the contrast agent (CA) in the vessels feeding the tissue of interest. This arterial input function (AIF) must be sampled with high temporal and spatial resolution to enable stable pharmacokinetic (PK) modeling [1]. With current MRI techniques it is difficult to achieve the temporal resolution needed for CA dynamics present in small animals. Partial volume and flow artifacts further complicate the situation. It was previously demonstrated that the use of dynamic computed tomography (CT) in combination with standard MR CA allows the determination of a population AIF (popAIF) in rats [2]. Applying this technique, we analyzed the impact of rat cardiac frequency on the AIF properties detected in the rat abdominal aorta and the accompanied changes in computed DCE-MRI parameter values.

**Methods**: All animal experiments were approved by the local ethics committee. 10 healthy Buffalo rats (10-13 weeks old) were imaged twice (separated by 19 days) by DCE-CT using a clinical CT scanner (Siemens Somatom, Erlangen, Germany). Different anesthesia was used to induce altered cardiac frequency. The first imaging session was performed with rats being anesthetized by gaseous infusion of isofluorane (*Iso*), whereas i.m. injection of a mixture of midazolam, medetomidine and fentanyl (*MMF*) was used for anesthesia in the second session. Rectal temperature and cardiac frequency of the rats was continuously monitored. Dynamic acquisition was performed with three axial slices (thickness = 4.8 mm, in-plane resolution = 0.3 mm$^2$, 40 mAs) centered over the upper abdomen. A double dose of Gd-DTPA (Magnevist®) was injected as bolus after 4.5 s. Bolus arrival and first pass was sampled every $\Delta t_1$ = 0.75s until 75s and then every $\Delta t_2$ = 38.5s until 380s. Corresponding plasma concentration time curves $C_p$ were derived as previously described [2] and averaged prior to modeling of the population AIF. A model similar to the one described in [3] with an additional exponential to account for slow clearance was used for AIF fitting. The resulting popAIFs were applied to one-compartment PK modeling and computation of $K^{trans}$ and $v_e$ [4] of previously measured DCE-MRI data of muscle, liver and hepatic tumor in 20 buffalo rats [5].

**Results:** The raw averaged and fitted AIF curves of the *Iso* and *MMF* session and the AIF model function are displayed in **Fig 1**. Corresponding individual and mean cardiac frequencies are listed in **Table 1**. A mean difference of 97.4 ± 22.9 bpm was detected. No difference was observed for rectal temperature. The *MMF* AIF exhibited a slower initial rise, broader bolus and later recirculation peak. The recirculation was successfully fitted only for the *Iso* AIF. AIF modeling parameters are listed in **Table 2**. The observed changes in AIF properties due to the different cardiac frequency resulted in significantly > 10% higher $K^{trans}$ values ($p < 0.0001$) for the *Iso* AIF (**Table 3**). For tumor and liver, ve had significantly higher values ($p < 0.05$) whereas for muscle ve showed significant lower values ($p < 0.001$).

Fig 1.




| Table 1 | |
|---|---|
| *Iso* | *MMF* |
| 370 | 225 |
| 367 | 295 |
| 365 | 262 |
| 351 | 240 |
| 384 | 260 |
| 360 | 280 |
| 370 | 280 |
| 368 | 260 |
| 388 | 265 |
| 363 | 265 |
| **368.6** | **263.2** |

| Table 2 | *Iso* | *MMF* |
|---|---|---|
| $A_1$ | 9.17 | 9.49 |
| $A_2$ | 2.34 | 14.66 |
| $T_1$ | 6.87 | 7.77 |
| $T_2$ | 10.81 | 8.98 |
| $\sigma_1$ | 0.50 | 0.55 |
| $\sigma_2$ | 0.22 | 1.59 |
| $\alpha_1$ | 16.58 | 5.50 |
| $\beta_1$ | 0.15 | 0.05 |
| $s$ | 66 | 68 |
| $\tau$ | 6 | 8 |
| $\alpha_2$ | 1.36 | 0.94 |
| $\beta_2$ | 0.0013 | 0.0013 |

| Table 3 | $\Delta K^{trans}$ [%] | Δve [%] |
|---|---|---|
| Tumor | 14.8 ± 10.8 | 8.9 ± 14.5 |
| Muscle | 36.7 ± 8.6 | -17.2 ± 13.4 |
| Liver | 10.6 ± 10.0 | 13.8 ± 5.9 |

**Discussion:** This study demonstrates the influence of changes in cardiac frequency on the properties of the arterial input function and the systematic errors hereby induced in quantitative DCE-MRI data. Especially in longitudinal studies, i.e. therapy response monitoring, where systemic changes, due to drug treatment or surgical intervention, are very likely to occur this phenomenon must thoroughly be considered. As presented, the population based AIF approach is unable to account for these changes. The simultaneous acquisition of CA dynamics in a reference tissue, indirectly reflecting the properties of the current AIF, may overcome this limitation and present a more robust approach in therapy response studies. The latter hypothesis was demonstrated in a separate parallel study.

**References:** 1. Cheng H. et al, JMRI 28:736-743 (2008); 2. Jonas S. et al, Proc 17th ISMRM 2009 (4368); 3. Parker et al, MRM 56:993-1000 (2006); 4. Tofts P. et al JMRI 10:223-232 (1999); 4. Steingoetter A. et al, Proc 17th ISMRM 2009 (2288).