LST-Based Optimization of Patient Specific Contrast Media Administration for CE-MRA: Validation Studies in Phantoms and Volunteers

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Introduction: Synchronizing the k-space acquisition with the intravascular enhancement after contrast media bolus administration is very crucial in contrast enhanced MRA (CE-MRA). So far, high temporal resolution, fluoroscopic triggering and test bolus injection have been proposed to achieve optimal vessel opacification, since the pharmacokinetic relationship between the intravenously injected contrast media and the resulting concentration time curve varies between each individual. Therefore, a forward approach -- as introduced last year -- uses a test bolus of contrast media to extract patient-specific physiological properties with the objective to compute an injection profile that results in a desired intravascular enhancement profile. The test bolus is followed by a saline flush, which turned out to be a very decisive component of the injection profile and especially important for the low contrast dosages used in MRI. In this study, 1) the implemented forward approach facilitated by a graphical user interface (GUI) was validated via phantom and volunteer studies, and 2) the influence of saline chaser on modulated injection profile was demonstrated. **Materials and Methods:** We validated our model by phantom experiments and volunteer studies on a 1.5T unit (GE Healthcare) using a dual piston power injector (2 phases per piston, Medrad). To measure exact concentration values without inflow effects a dynamic single-slice SR sequence (FOV=18 cm, 128x96, GRAPPA R=2, FA=90, TR =17.52 msec, TE =3.29 msec, Tsat= 12.22 msec, slice thickness =20 mm, BW= ±62.5 kHz, non-slice-selective saturation) with a temporal resolution of 0.88 s was prescribed[2]. The image acquisition was synchronized with the beginning of the injection and the images were then pushed from the scanner to a Laptop where the 'forward' approach was used to design and predict the target enhancement. For the phantom studies, the contrast agent was injected into a circular-flow phantom, simulating the human vascular system. Thereafter, a correction against non-linearity effects caused by high tracer concentrations was applied using a pre-acquired calibration curve[3]. With IRB approval and informed consent, our approach was also tested on two healthy male volunteers. The total amount of the contrast agent (0.5M Multihance, Bracco, Milano, Italy) per volunteer/experiment was limited by the body weight (0.1 mmol/kg) for the in vivo studies resulting in a maximum dose of 14mL for volunteer one and 15.4mL for volunteer two. Following recent suggestions[4], a higher administrable volume of diluted contrast agent permits a more flexible tailoring of the injection profile. Therefore, Gd-DTPA was diluted 1:1 with normal saline to form a 28 mL (volunteer one) and a 30.8mL (volunteer two) solution (0.25M). A test bolus of 12 mL followed by a 40 mL saline flush was injected into the cubital vein at 3 mL/s, whilst the remainder was used for tailoring the target injection. To show the effect of the saline flush on the tailored injection profile, a 50% higher saline flush flow rate compared to phase one of the biphasic injection profile was administered to volunteer two. **Results:** The phantom studies showed excellent agreement between the predicted and measured vascular enhancement (fig. 3). With the correction for non-linearity, a mean error norm$\|(TE_M\text{-}TE_P)\|$ = 0.15 was achieved over all 8 phantom experiments. One limitation of these phantom studies was the limited modeling/studying of intrinsic cardiovascular effects (e.g. recirculation time, variable heart rate during the scan). However, at least from the limited numbers of volunteers studied thus far an influence by any of these factors could not be observed. Specifically, our experiment on volunteer #1 showed a very good agreement between the predicted and the measured enhancement profile (error norm = 0.17, error norm during the 'plateu' = 0.05), (fig. 1). In this experiment a monophasic injection was used to test the convolution model. For volunteer 2 (fig. 2) the initially correct vascular response (when compared with the designed uptake function) deviated largely from the desired profile. This was caused by a saline flush that was administered at an injection rate that did not match the injection rate of the last phase of the Gd injection, which ultimately destroyed the designed vascular waveform profile and indicates how critical it is to choose the right parameters for the saline flush. However, flush speeds of greater or lower values than the contrast media injection rate can be appropriately integrated into our software to permit determination of an enhancement profile that matches well with the measured vascular uptake. **Conclusion:** The LST-based approach to optimize patient-specific contrast injections for individualized vascular enhancement profiles was validated on phantoms and volunteers. The measured time courses were in excellent agreement with the predicted waveforms and demonstrated the practical feasibility of this approach. To date, we could not observe that intrinsic cardiovascular effects cause much influence on the prediction. However, a more detailed investigation on a larger cohort of volunteers/patients is warranted to safely confirm this finding. Conversely, for the small Gd injection volumes used in CE-MRA it could be shown how a wrong choice of parameters for the saline flush can impair the desired vascular enhancement. The current version of the software allows one to use either a pre-defined desired enhancement profiles or the use of manually adjusted profiles to compute the patient specific injection profile in less than 30 seconds. **References**: [1]*D.Kopeinigg, et al.* ISMRM 2008; [2]*Stollberger R, et al.* ISMRM 2006; [3]*J.P. van Osch M, et* al., MRM 49:1067-76, 2003;[4]*Gerhard Laub*, AngioClub 2008; [5]Fleischmann D, Hittmair K, JCAT 23:474-84, 1999. **Acknowledgements:** The project is supported by NIH (1R01EB002771+S1, 1R21EB006860, P41RR09784), Lucas Foundation. The authors are grateful to Bracco Diagnostic for providing the contrast agent to support those experiments.

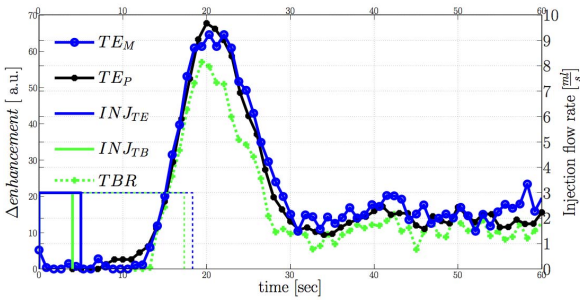

Figure 1 – Test bolus injection (INJ_{TB}) of 12ml@3ml/s (solid green) plus a 40ml@3ml/s flush (thin dotted green) yields a corresponding response in the vasculature (dashed green curve) from which the impulse response function can be derived. To verify the convolution approach, a monophasic injection profile INJ_{TE} = 16ml@3ml/s (solid blue), 40mL@3ml/s flush (thin dotted blue) was injected. The target enhancement observed in the vasculature (blue curve) agreed well with the predicted enhancement by our software (black).

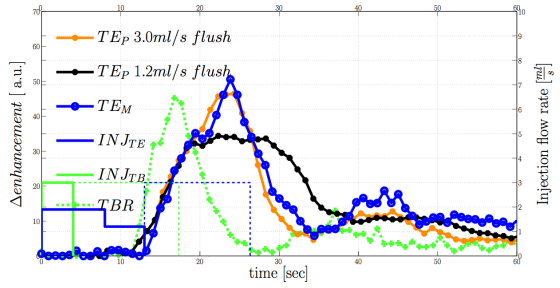

Figure 2 – Demonstration of the impact of the saline flush. Test bolus injection (solid green), saline flush (thin dotted green) and corresponding vascular response (dashed green). Biphasic bolus injection (solid blue) 15 mL at 1.9 mL/s plus 6 mL at 1.2 mL/s and corresponding vascular uptake (blue). The measured uptake curve initially agrees with the predicted curve (black) but then overshoots because the saline chaser (40mL) was administered with too high a flow rate, i.e. 3 mL/s (thin dotted blue) instead of 1.2mL/s. Predicted enhancement profile (orange) for a flush injection flow rate of 3ml/s.

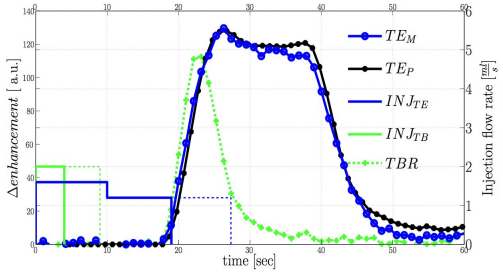

Figure 3 – Measured enhancement in the phantom (green curve) after a test bolus administration, INJ_{TB} = 8ml@2ml/s (solid green) plus 10mL@2mL/s flush (thin dotted green). Injection of the computed biphasic profile INJ_{TE} = 16mL@1.6mL/s + 11mL@1.2mL/s (solid blue) plus 10mL@1.2mL/s flush (thin dotted blue) results in the measured enhancement (blue curve), which shows very good agreement with the prediction from our software (black).