Targeted Contrast Enhancement Using Linear System Theory

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Introduction: The timing of the contrast bolus arrival in conjunction with the acquisition of k-space data has been always a critical part in contrast-enhanced MRA. Depending on the patients condition (e.g. cardiac output, heart rate, etc.) the contrast arrival time, peak concentration and mean transit time can largely vary. Thus far, fluoroscopic triggering, high temporal resolution, and test bolus injections have been proposed to achieve optimal vessel opacification when essential parts of k-space are acquired. From Fig. 1 it becomes evident that both the injection flow rate and the amount of contrast injected into the blood stream play important yet different roles for final vascular enhancement in the targeted vessel. Here, we propose a new approach based on linear system theory to derive an optimized contrast injection protocol to achieve desired enhancement profiles under special consideration of the physiological limits within each patient.

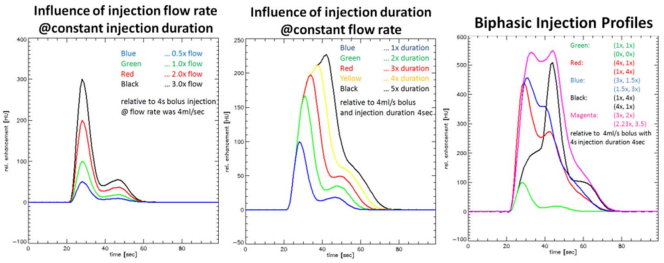

Figure 1 – Vascular enhancement as a function of flow rate (left), injection duration (middle), or both (right). The right figure considers a biphasic bolus injection with two different flow rates and injection durations, respectively. Note the flow rate determines how quickly peak enhancement is achieved (left), whilst injection duration determines when peak enhancement is achieved. Even when the amount of contrast material injected is doubled (single vs. double dose) the initial upslope does not change. When the injection duration exceeds the recirculation time the bolus starts to become degraded.

Materials and Methods: Assuming a linear relationship between contrast concentration and signal changes detected, the vascular enhancement following a test bolus injection can be characterized by the arterial impulse response function. Here, the vascular enhancement, $C_{vessel}(t)$, in the targeted vessel can be modeled as the convolution of the bolus injection function, $I(t)$, with the arterial impulse response, $AiF(t)$: $C_{vessel}(t) = AiF(t)*I(t)$, where "*" denotes convolution. From a test bolus injection $I_{test}(t)$, the $AiF(t)$ can be determined from the vascular enhancement response to the bolus, $C_{test}(t)$, by means of deconvolution ("$*^{-1}$"): $AiF(t) = C_{test}(t)*^{-1}I_{test}(t)$. Numerical deconvolution can be performed either in the Fourier domain or by truncated block-circulant SVD. Unlike previous attempts (that involved another deconvolution step), to determine the optimal bolus injection function, $I_{angio}(t)$ to achieve a desired enhancement profile, $C_{angio,\ desired}(t)$, we propose a forward modeling approach, that directly tries to minimize the error norm: $I_{angio}(t) = \texttt{argmin}\ \|AiF(t)* I_{angio}(t) - C_{angio,\ desired}(t)\|$. That is, the optimized injection protocol is not determined through computing a pseudo-inverse. In practice, however, several physiological constraints have to be considered, such as recirculation, maximum injection flow rate, or non-negative flow rates, to achieve a realistic model of the vascular response. By combining these constraints with a parameterized "forward" - approach in which $I_{angio}(t)$ is approximated by using a set of basis functions (i.e. a set of injection pulses of fixed length and flow rate), one can identify an injection profile that matches the desired injection profile in a minimum norm sense and which is also programmable into current power injectors that are not able to play out continuously varying flow rates over time. Do note that, most state-of-the art injectors have only a limited number of flow rates and injection durations to program in. Therefore, we used a set of 12 time shifted step functions as basis functions, for which the individual flow rates and injection durations were determined using a constrained optimization approach of the aforementioned cost function (Fig. 2). From Fig. 1 it becomes also evident that certain uptake rates or peak enhancements cannot be reached for physiological reasons. Moreover, total amount of contrast volume administered has to be also added as a constraint to the computational model. Currently, an exhaustive search method is used to determine these parameters under the aforementioned constraints. However, the processing time is still very short (<20sec).

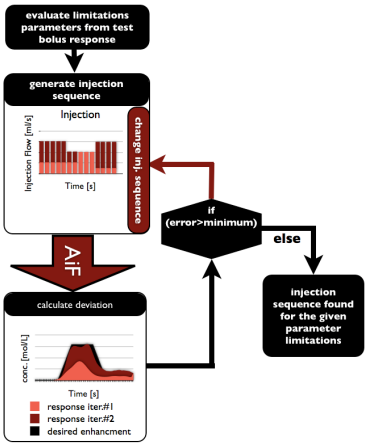

Figure 2 - The main method, which is shown here, computes the injection sequence for the target enhancement.

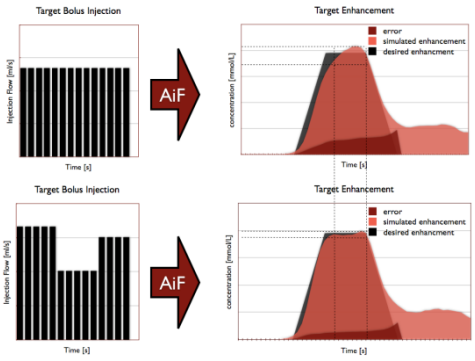

Figure 3 – Shows the difference between the injection sequences uniphasic (top) and multiphasic (bottom) and their relationship due the AiF and the resulting target enhancement.

Results & Conclusion: Optimal timing of the contrast arrival as well as an opacification profile that matches the k-space sampling trajectory is of great relevance in CE-MRA to minimize AV-overlay and unwanted k-space filtering effects. Realistic enhancement profiles can be achieved by considering physiological constraints (e.g. maximum rate of enhancement possible, total amount of contrast material injected, etc.) in the desired enhancement pattern. A program has been developed to predict the injection sequence - for a predefined target enhancement and currently supports uniphasic and multiphasic injections. The software also takes into consideration physiological and technical limitations. The parameterized "forward" technique more closely resembles desired enhancement profiles than previous work, which ran through a second deconvolution and then added constraints to this function (Hittmair *et al*). With the availability of more freely programmable power injectors also non-parameterized "forward" approaches would be possible which potentially could lead to ever further improvements of the achievable enhancement profile. An error analysis from measured data has shown that the norm of the difference between the simulated and the measured enhancement is 11.4% (Fig. 4).

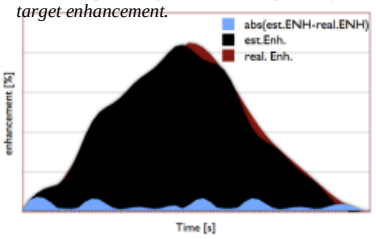

***Figure 4**–Shows the response of the estimated AiF and the real AiF. The absolute difference of those is also shown. The norm of both is 0.114 which is interpreted as a normilazed value and corresponds to a norm error of 11.4%.*

References: [1]Fleischmann D, Hittmair K, *JCAT* 23:474-84, 1999; [2]Fleischmann D, Rubin G, *et al. Radiology* 214: 363-71, 2000; [3]Stollberger R, *et al*. ISMRM 2006.

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