Clinical implementation of the Linear Reference Region Model for Dynamic Contrast-Enhanced MRI

Adam Bernstein[1], Phillip H Kuo[2], Mark D. Pagel[3], and Julio Cardenas-Rodriguez[3]

[1]Department of Biomedical Engineering, University of Arizona, Tucson, AZ, United States, [2]Department of Medical Imaging, University of Arizona, Tucson, AZ, United States, [3]Department of Biomedical Engineering and Arizona Cancer Center, University of Arizona, Tucson, AZ, United States

INTRODUCTION: The Reference Region Model (RRM) can analyze Dynamic Contrast-Enhanced (DCE) MRI results without requiring an Arterial Input Function (AIF).[1,2] This method relies on a non-linear least square-fitting algorithm (NLRRM) to estimate its parameters. A new version of this model based on linear Algebra was recently reported.[3] This new version of the RRM, deemed the linear reference region model (LRRM), relaxes three of the most stringent requirements to use the NLRRM: 1) High Temporal Resolution (TR), 2) High signal-to-noise ratio (SNR), and 3) Curve fitting speed. Based on simulations and *in vivo* data of a mouse model of breast cancer, it was determined that the LRRR is precise and accurate at a TR of 1-2 minutes and SNR ≥ 35. For instance, a 128X128 image can be processed in only 16 seconds using the LRRM. However, the LRRM has not been tested using clinical DCE MRI data. The application of the NLRRM in the clinical setting has been limited due to SNR and TR requirements. In this work we analyzed retrospectively clinical MRI of 17 patients, whom required DCE MRI as part of their standard of care.

METHODS: **Simulations:** Matlab (Mathworks, Inc.) was used to study the effect of temporal resolution and SNR on the time needed to process DCE MRI data with the LRRM and NLRRM. These simulations are based on methods previously reported [3]. **Clinical Protocol:** DCE MRI and standard MRI were performed in accordance with local institutional review board regulations. The dynamic series portion consisted of 7-8 3D-GRE images, which afforded a temporal resolution of 50–61 seconds in the DCE MRI series. Typical parameters for the 3D-GRE imaging were 140 slices reconstructed to a matrix size of 256×368, slice thickness=2.2 mm, FOV=25.6X36.8 cm, TR=5.5 ms, TE=2.5 ms, NEX=1, and α=15°. After 1–2 pre-contrast images had been acquired, gadolinium contrast was injected (0.1 mmol/kg). All data was processed using Matlab as described previously [3]. The following parameters were estimated using the LRRM and the NLRRM: R^{Ktrans} ($K^{trans,TOI}$ / $K^{trans,RI}$), kep_{TOI}, and kep_{RR}. Where ROI= region of interest and RR= reference region.

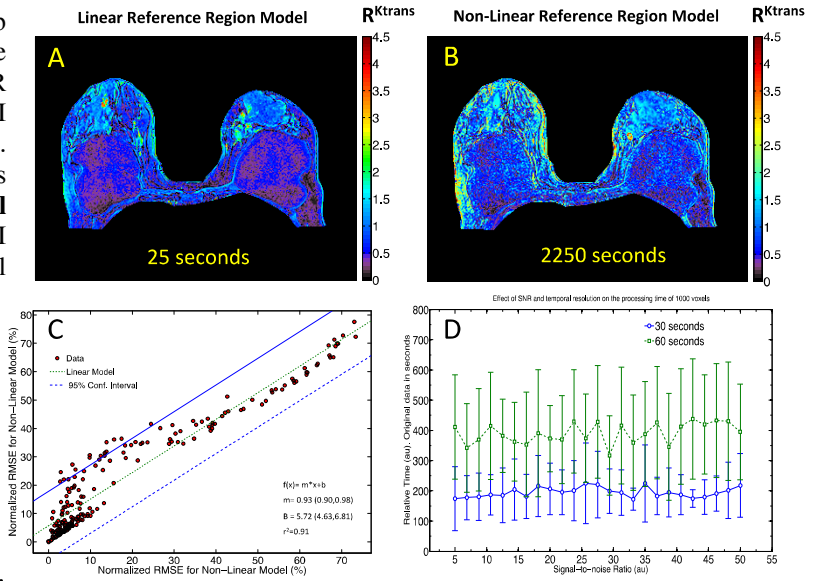

Figure 1. Comparison of the LRRM and NRRM for clinical DCE MRI. A) Representative R^{Ktrans} map using the LRRM, processed in 24 seconds. B) Representative R^{Ktrans} map using the NLRRM, processed in 37 minutes. C) Root-mean-square error (RMSE) for the curve fitting using the LRRM and NRRM. All points are normalized to the lowest RMSE with the LRRM. D) Simulation of the relative processing time (LRRM / NLRRM) as a function of temporal resolution.

RESULTS AND DISCUSSION: Clinical DCE MRI can be processed 90-400 times faster with the LRRM than with the NLRRM using a MacBook Pro under OSX 10.8.5 and a processor running at 2.4 GHz and 86G of RAM. This difference is highly dependent on the SNR and temporal resolution (**Figure 1A,1B and 1D**). The goodness of fit was evaluated using the root-mean-square error (RMSE). The RMSE was systematically higher for the NLRRM compared to the LRRM (Figure 1C). Figure 1 shows representative data for one subject in section A-C. This same trend was observed in all 17 DCE MRI. The results for kep_{TOI} and kep_{RR} *are not* shown due to space constraints but they are similar to R^{Ktrans}. These results suggest that the LRRM is more reliable than the NLRRM when data with low SNR and temporal resolution is available. Also, the LRRM offers the possibility of processing DCE MRI data in real time due to its speed.

REFERENCES: 1. Tofts P., et al. J Magn Reson Imaging 1999, 10:223. **2)** Yankeelov TE, et al. Magn Reson Imaging 2005, 23:519. **3)** Cárdenas-Rodríguez et al. Mag Reson Imaging 2013, 497:507.