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Optimizing MRF-ASL Scan Design towards Precise Quantification of Hemodynamic Properties in Cerebrovascular Disorders

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Synopsis

We investigate an optimization method to make fast, precise quantification of hemodynamic and tissue properties from an MRF ASL scan more robust to their respective feasible ranges, particularly when conditions pertaining to cerebrovascular disorders are included in consideration. We further validate our methods on synthetic and healthy human subject data.

Purpose

Multiparametric hemodynamic estimates obtained by combining ASL and MR Fingerprinting can be helpful in the comprehensive diagnosis and treatment planning of several cerebrovascular disorders^[1,2]. However, this requires precise quantifiability over a wide parameter range.

In previous work^[3], we focused on optimizing ASL scan designs for fast, precise estimation at a single parameter value representative of normative function. Here, we: (i) extend our optimization towards precise quantification over a wide range of parameter values that includes a number of pathological conditions while maintaining constraints on total scan time, and (ii) use separate neural networks for regression based estimation of individual parameters.

Methods

In our scan optimization approach, the cost function uses the Cramer-Rao Bound, which is the inverse of the Fisher information matrix defined as follows:

$$\mathbf{F}(\underline{\lambda}; \underline{s}) = \frac{1}{2} \cdot [\nabla_{\underline{\lambda}} \underline{s}]^T [\nabla_{\underline{\lambda}} \underline{s}], \quad (1)$$

where, $\underline{s}(\cdot) \in \mathbb{R}^{N \times 1}$ is the signal generated from our model, $\underline{\lambda} \in \mathbb{R}^{K \times 1}$ represents a single set of hemodynamic parameters, $\underline{\lambda} \in \mathbb{R}^{P \times 1}$ are the scan parameter(s) and σ^2 is the i.i.d. Gaussian noise variance.

In our previous work^[3], we optimized the scan parameters' $\underline{\lambda}$, namely the sequence of labeling durations of the ASL scan, by minimizing a weighted trace of \mathbf{F}^{-1} for a fixed vector \underline{s} . Here we optimize the scan timing parameters by considering a representative collection of true parameter values, Θ , spread uniformly over a comprehensive range by minimizing the following cost function:

$$\hat{\lambda} = \arg \min_{\lambda \in \Lambda} \frac{1}{|\Theta|} \sum_{\underline{\lambda} \in \Theta} \text{Tr} \left(\mathbf{W} \cdot \frac{|\mathbf{F}^{-1}(\underline{\lambda}; \underline{s})|^{0.5}}{\mathbf{N}(\underline{\lambda})} \cdot \mathbf{W} \right), \quad (2)$$

where \mathbf{W} is a diagonal weighting matrix assigning priority to each hemodynamic parameter in the cost function and $\mathbf{N}(\underline{\lambda}) = (\underline{\lambda}^{0.5}) (\underline{\lambda}^{0.5})^T$ is a normalization matrix that is divided element-wise into the inverse Fisher information matrix.

Since, given a signal model, the Cramer-Rao Bound predicts the lowest possible variance in parameter estimates from an unbiased estimator, using exhaustive search to minimize the design cost function eqn. (2) ensures that our optimized scan yields precise estimates.

The set of candidate labeling timing schedules is described using a linear interpolation of 5 equidistant points in the 'labeling space' (Fig 1).

We train individual neural networks^[3,4,5] for estimating each parameter using training data generated by this optimized scan design and the model in **Figure 2**. Namely, these parameters are Bolus Arrival Time (BAT), Perfusion (CBF), Magnetization Transfer Rate (MTR), Cerebral Blood Volume (CBV), Tissue T1, and Flip Angles. Using individual networks alleviates the need for relative weighing of targets during training, significantly reducing the need for parameter tuning.

The trained estimators are then used on synthetically generated anthropomorphic phantoms with built-in regions that capture tissue properties prevalent in cerebrovascular diseases like stroke (very low flows), tumor (higher flows), Moyamoya disease (high BATs) etc.

We also test our methods on data acquired from two healthy human subjects on a 3T MRI scanner with a 32 channel coil (MR750, GE, Waukesha, WI).

Results

Figure 1 depicts the optimized schedule for 700 frames and a 600s scan duration, as well as the predicted average normalized standard deviation of parameter estimates over a pathological range. It is clear that linear interpolation allows us to explore the 'label space' effectively.

Figure 3 shows predicted as well as ground truth maps for the synthetic 'pathological phantoms'. Regions of particular pathological interest are highlighted in the ground truth maps. Clearly, there is high fidelity between the maps even in regions with anomalies that are difficult to quantify.

Moreover, **Figure 4** shows estimated parameter maps from two healthy human subjects. The maps look plausible and the predictions are in line with values typically found in literature, but they are noticeably 'noisy' for certain hemodynamic properties. Coupled with the impressive results on synthetic data, this observation suggests imperfections in our modeling.

Conclusions

Combining CRB based optimization with regressional neural networks in MRF ASL enables fast, precise estimates of hemodynamic parameters and tissue properties in the presence of anomalies that are difficult to characterize. Our results on synthetic and healthy subject data hint at realizing the clinical potential of MRF ASL in diagnostics and treatment planning of multiple disorders.

Future work will involve more extensive testing and validation of our methods on patients with cerebrovascular disorders, as well as investigating more accurate signal modeling.

Acknowledgements

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Figures

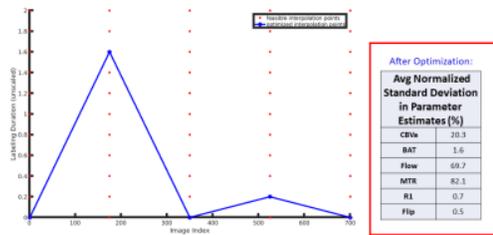


Figure 1 (Left) Red points denote the candidate interpolation points in designing the labeling schedule, while the blue ones are the ones selected by the optimization. It should be noted that each candidate schedule is scaled appropriately before evaluating the optimization cost to ensure that the scan duration is 600s. (Right) Average Normalized Standard Deviation of Parameter Estimates for the optimized scan, evaluated over 50 points spread uniformly over a large pathological range.

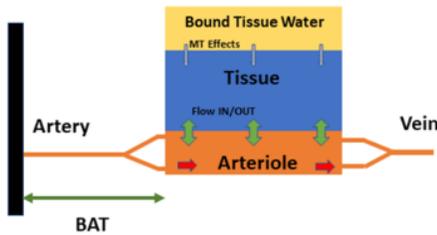


Figure 2 Depicted is the simple two compartment model used to model the ASL MRF signal in both optimization and estimation. It consists of a 'Tissue' compartment, where blood perfuses in from and out to the second compartment called 'Arteriole'. There is also an additional compartment to include the effects of Magnetization Transfer.

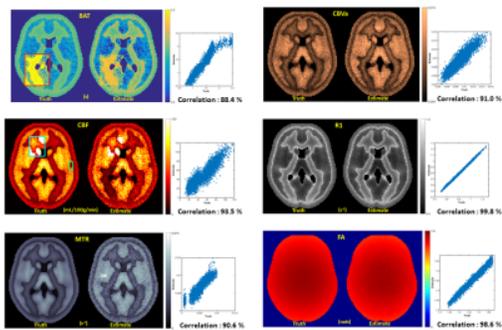


Figure 3 Comparison of ground truth vs estimated anthropomorphic brain maps from our methods for synthetically generated noisy data (AWGN std. deviation: 0.01) spread over a large range of parameter values. Regions of tentative pathological interest are highlighted using colored rectangular boxes. It is evident from the scatter plots and the correlation coefficients that our methods perform well for the assumed model, in terms of precise estimation.

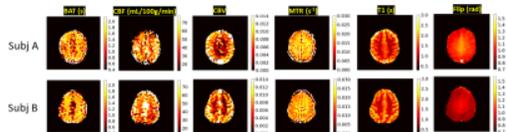


Figure 4 Predicted parameter maps for two healthy human subjects obtained from data acquired using our optimized scan design along with parameter-individualized neural networks. Each (64x64) parameter map requires about 1.5 - 2s to generate.