Comparison of kinetic parameters estimated with unmeasured, partially measured, or fully measured input functions.

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Introduction: Time series of images obtained after injecting gadolinium (Gd) contrast in the blood can be characterized by kinetic parameters and modeled mathematically. In order to estimate quantitative kinetic parameters, the arterial input function (AIF) has to be estimated or measured. The AIF can be measured using various techniques either directly from the images, or by a population based approach [1]. The estimates are often inaccurate due to flow effects and a nonlinear response to Gd or variations in individuals. Hence a non-invasive approach such as 'blind estimation' has been proposed. In this approach, the same AIF is assumed to be the input to different tissues of interest. Systems of equations are constructed and the kinetic parameters along with the AIFs are solved in the regions of interest (ROI). This blind estimation method originated in telecommunication-related problems where multiple channels with unknown impulse responses are driven by the same input. Yankeelov et.al used a reference region model approach to estimate the kinetic parameters without actually measuring the AIF [2]. Others have explored different algorithms and experimented with the use of reference tissues [3, 4, 5]. We have compared several blind estimation methods using simulated noisy data, and found that an iterative alternating minimization method performed the best [6], but still was sensitive to noise. By using the alternating minimization method here and providing parts of the AIF measured from the images, it is hypothesized that the parameter estimates will be improved and will be correctly scaled.

Methods: The concentration of Gd in the tissue at any time can be represented by the convolution of the AIF and the tissue response. Mathematically this is written as: $X^{(i)}(n)=(h^{(i)}\otimes b)(n)+e^{(i)}(n)$, where X is the tracer concentration function, h is the tissue response, b is the AIF, and e is the noise in each region, i. From [6], the above equation can be written in terms of vectors as: $\mathbf{X}=\mathbf{Hb}+\mathbf{e}$. The parameters can be estimated by minimizing the cost function, R, which is given by $R=\|\mathbf{X}-\mathbf{Hb}\|_2$, where $\mathbf{H}$ is the tissue response, built from the current estimates of the washin and washout parameters and $\mathbf{b}$ is the estimated AIF. The input function $\mathbf{b}$ is solved from $\mathbf{b}\mathbf{H}^T\mathbf{H}=\mathbf{H}^T\mathbf{X}$ with a conjugate gradient method. $\mathbf{h}$ was assumed to follow a compartment model [7].
Dynamic perfusion images were acquired in five subjects using a saturation-recovery Turbo FLASH pulse sequence on a Siemens Avanto 1.5T or Trio 3T MRI scanner. During imaging, each patient was given a low-dose (0.02±0.001 mmol/kg) injection of Gd-DTPA (Gd). Low dose acquisitions were used to ensure changes in signal intensity (SI) varied linearly with [Gd] so that a standard analysis with the measured AIF could be assumed to represent "truth". Offline, the images were manually registered and the left ventricular myocardium was segmented to obtain 6-8 tissue enhancement curves from each of 3 short-axis slices in each subject.
Two variations of the method were studied. The first method (Complete Blind) estimates the AIF completely, which is then used to estimate the kinetic parameters. The second method (Partial Blind) estimates only the peak of the AIF. Often at the peak of the AIF bolus, the [Gd] is non-linearly proportional to changes in SI, while at lower doses, [Gd] varies linearly. All points on the measured blood curve whose magnitude was greater than an empirically determined threshold required blind estimation. The mean of the last ten points of the actual blood curve multiplied by 2.5 was chosen as the threshold.

Results and Discussion: Figures 1 and 2 show the true and estimated AIFs from partial blind estimation. The asterisks (not lying on the curve) are the points to be estimated and circles in green are the estimated points. Figure 3 shows the correlation plot between washin parameters from complete blind estimation and truth. Figure 4 shows the plot between washin parameters from Partial Blind estimation and truth. The washin parameters obtained from partial blind method have a higher correlation (r=0.94) than those obtained from complete blind estimation (r=0.48). Lines of best fit were also obtained and are shown in the figures. Correlation values and lines of best fit for the washout parameters and the ratio of washin parameters were also obtained and are shown in Table 1.

Parameters	Equation of line (Complete Blind)	Equation of line (Partial Blind)	Correlation (r) (Complete Blind)	Correlation (r) (Partial Blind)
Washouts	0.63*x+10.53	1.20*x+0.39	0.60	0.93
Ratio of washin parameters	1.36*x-0.36	1.08*x-0.08	0.70	0.98

Table 1: Table showing the equations of line and correlation coefficients for washout parameters and the ratio of washin parameters.

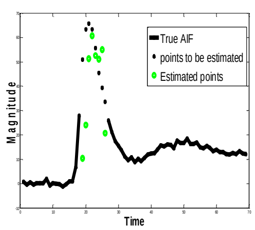

Figure 1: Plot of True and Estimated AIF

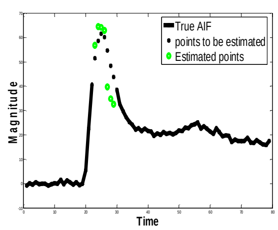

Figure 2: Plot of True and Estimated AIF.

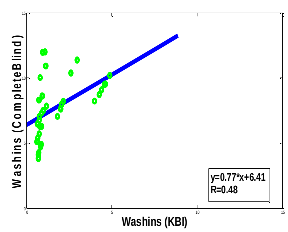

Figure 3: Correlation plot of Washin parameters (Complete Blind).

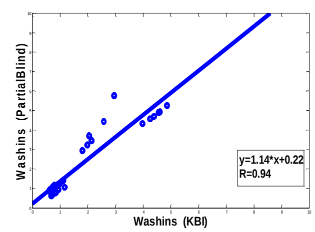

Figure 4: Correlation plot of Washin Parameters (Partial Blind)

Conclusion: In this paper, we have compared two blind estimation methods namely complete blind estimation and partial blind estimation. The partial blind estimation method performed better than the complete blind estimation method when estimating the kinetic parameters. For the threshold chosen, washin parameters obtained from partial blind estimation had a higher correlation(r=0.94) with the truth than those obtained from complete Blind estimation (r=0.48). If the threshold chosen was too high, fewer points on the AIF required blind estimation and we get a good estimate of the washin parameters. However there are chances, where the signal may be in the non-linear range below the threshold and the estimate of the kinetic parameters may not be very accurate. On the other hand, if the threshold chosen was too low, there may not be signal saturation, but the number of points requiring blind estimation increases and the estimates maybe inaccurate. Hence a threshold that is not too high or too low should be chosen to get a good estimate of the kinetic parameters.

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