Effect of Reduced Encoding Dynamic Data Size on Permeability-Surface Area Estimation

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Synopsis: We are testing the hypothesis that dynamic reference sets in reduced-encoding techniques have spatial resolution limits for accurate quantitative tumor typing based on volume normalized contrast agent transfer rates between tumor plasma and extravascular extracellular space (EES), $K_{p\leftrightarrow t}/V_T$, obtained from dynamic contrast enhanced (DCE) MRI. Specifically, we compared $K_{p\leftrightarrow t}/V_T$ "hot spot" values of ten infiltrating ductal carcinomas, obtained with fully reconstructed FFT to those obtained from Keyhole, reduced-encoding imaging by generalized-series reconstruction (RIGR), and two-reference RIGR (TRIGR), using dynamic data of decreasing size, PE_{DYN} = 128, 64, 32, 24, 16, and 4. Preliminary data suggests that TRIGR has lower resolution limits on dynamic data for obtaining accurate $K_{p\leftrightarrow t}/V_T$ "hot spots" than Keyhole or RIGR.

Introduction: Diagnostically accurate DCE MRI must have both high spatial and temporal resolution. High temporal resolution, or short acquisition time, is essential for accurate detection of the changes in image contrast due to physiological distribution of the injected contrast agent. In histopathology, only a narrow window of microscope fields of view between 0.152 mm^2 (390. μm diameter) and 0.740 mm^2 (860. μm diameter) can distinguish benign from malignant tumors(1). Therefore high spatial resolution is necessary to observe diagnostically important regions of greater $K_{p\leftrightarrow t}/V_T$ value, or $K_{p\leftrightarrow t}/V_T$ "hot spots", due to regions of pathologically relevant high capillary density. In general, increasing spatial resolution decreases temporal resolution. One possible solution to this undesirable trade-off is using reduced encoding techniques, such as Keyhole(2), RIGR(3), and TRIGR(4).

Methods: Thirty-six 30-day old female Sprague-Dawley rats were injected with n-ethyl-n-nitrosourea(5). Ten of these animals with infiltrating ductal carcinomas were analyzed in this study. Imaging was performed on a SISCO 4.7 T / 33 cm bore system by a rapid T_1-weighted GEMS (FOV = RO 24 cm / 512 × PE 6 cm / 128; averages = 2; TR = 63 msec; TE = 4.3 msec; thk = 2 mm; #slices = 7, TA = 18 sec, #acq = 112). Rats were anesthetized (1 mL/kg Ket/Xyl/Ace IM) and injected with Gd-DTPA (0.3 mmoles/kg IV).

Dynamic data were created from k-space subsets of the obtained high-resolution data, RO_{DYN} = 512 and PE_{DYN} = 128, 64, 32, 24, 16, and 4. In this application, both RIGR and TRIGR used a regularization of 0.2, phase information, and extrapolation of baseline data. The active reference used for TRIGR was during the rise in tumor contrast agent concentration.

To calculate $K_{p\leftrightarrow t}/V_T$, GEMS image signal intensities were converted to contrast agent concentration by a standard curve(6) and fit to a two-compartment model(7):

$$\left[CA_1(t)\right] = Da_1\left(v_p + \frac{v_e}{1-\frac{v_e V_T \alpha}{K_{p\leftrightarrow t}}}\right)e^{-\alpha t} + Da_2\left(v_p + \frac{v_e}{1-\frac{v_e V_T \beta}{K_{p\leftrightarrow t}}}\right)e^{-\beta t} - D\left(\frac{a_1 v_e}{1-\frac{v_e V_T \alpha}{K_{p\leftrightarrow t}}} + \frac{a_2 v_e}{1-\frac{v_e V_T \beta}{K_{p\leftrightarrow t}}}\right)e^{-\frac{K_{p\leftrightarrow t}}{v_e V_T}t}$$

where D ($mmol \cdot kg^{-1}$) is the injected contrast agent dose, $a_{1,2}$ ($kg \cdot L^{-1}$) are the normalized concentration amplitudes for unit dose, α (min^{-1}) is the distribution rate constant, β (min^{-1}) is the excretion rate constant v_p is the tumor plasma volume fraction, and v_e is the tumor EES volume fraction. The parameters $a_{1,2}$, α and β are obtained by fitting the contrast agent concentration's time-dependent biexponential decay obtained from slices through the heart. The parameters, v_e, v_p and $K_{p\leftrightarrow t}/V_T$, are fitted by a nonlinear least squares fitting by the Gauss-Newton method on a voxel-by-voxel basis. Each mapped point has an F-test for p values and r^2. The mapped points are filtered: mapped points that (1) did not converge, (2) were physiologically unrealistic, that is, the fitted values must be $0 \le v_e < 1$, $0 \le v_p < 1$, and $0 \le K_{p\leftrightarrow t}/V_T$, or (3) were poorly fit ($r^2 \le 0.5$), are dropped (set to zero). All data analysis was performed with MATLAB, (The Mathworks, Inc., Natick, MA).

Results and Discussion: In this study, at a 95% confidence interval, the top five $K_{p\leftrightarrow t}/V_T$ "hot spots" from fully reconstructed FFT and Keyhole are statistically the same only at PE_{DYN} = 128 and 64, while for RIGR they are statistically the same as FFT for all PE_{DYN}. Top five $K_{p\leftrightarrow t}/V_T$ "hot spots" from TRIGR and FFT are the same at PE_{DYN} = 128, 64, 32, and 24 (**Table 1**). At PE_{DYN} = 128, the FFT and reduced encoding techniques agree as the dynamic data is the full data. However, as PE_{DYN} decreases the generalized-series techniques are better able to accurately estimate image data and hence provide more accurate quantitative dynamic contrast information than Keyhole. Although RIGR agrees with FFT at all PE_{DYN} and appears statistically superior to TRIGR, RIGR has unrealistic outlier $K_{p\leftrightarrow t}/V_T$ "hot spots" and large standard deviations at lower PE_{DYN} not seen with TRIGR (**Tables 1** and **2**). Thus, Keyhole has the most limited dynamic data threshold and TRIGR more accurately obtains clinical low-resolution dynamic data, PE_{DYN} = 64, 32, and 24, than both Keyhole and RIGR. This implies that one can gain at least a fourfold improvement in spatial resolution without sacrificing the necessary temporal resolution.

PE_{DYN}	FFT	RIGR	TRIGR
128	1.0	1.0	1.0
64	0.58	0.23	0.38
32	0.043	0.33	0.69
24	0.0094	0.31	0.26
16	0.000016	0.44	0.0
4	0	0.19	0.0

Table 1: The p-value of the two-tailed t-test for Keyhole, RIGR, and TRIGR reconstructed with PE_{DYN} = 128, 64, 32, 24, 16, and 4 compared to fully reconstructed FFT (PE = 128) (n = 10).

PE_{DYN}	FFT		Keyhole		RIGR		TRIGR	
	Mean	STD	Mean	STD	Mean	STD	Mean	STD
128	0.059	0.025	0.059	0.025	0.059	0.025	0.059	0.025
64			0.056	0.028	0.065	0.023	0.055	0.020
32			0.050	0.020	0.064	0.023	0.057	0.022
24			0.047	0.020	0.30	1.6	0.054	0.019
16			0.039	0.020	0.055	0.029	0.046	0.020
4			0.017	0.009	0.15	0.50	0.036	0.019

Table 2: The mean and standard deviation of the top five $K_{p\leftrightarrow t}/V_T$ "hot spots" for fully reconstructed FFT (PE = 128), Keyhole, RIGR and TRIGR reconstructed with PE_{DYN} = 128, 64, 32, 24, 16, and 4 (n = 10).

References

1. Weidner, N. (1995) *Am J Pathol* **147,** 9-19.
2. Hu, X. (1994) *J Magn Reson Imaging* **4,** 231.
3. Webb, A., Liang, Z., Magin, R. & Lauterbur, P. (1993) *J Magn Reson Imaging* **3,** 925-928.
4. Hanson, J. M., Liang, Z.-P., Wiener, E. C. & Lauterbur, P. C. (1996) *Magn Reson Med* **36,** 172-175.
5. Stoica, G., Koestner, A. & Capen, C. C. (1984) *Anticancer Res* **4,** 5-12.
6. Aref, M., Brechbiel, M. & Wiener, E. C. (2002) *Investigative Radiology* **37,** 178-192.
7. Tofts, P. S. (1997) *J Magn Reson Imaging* **7,** 91-101.

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