

## Simultaneous EPI-based T1, T1, and T2' mapping

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**Introduction:** The partial Fourier and generalized autocalibrating partially parallel acquisition (GRAPPA) accelerated gradient-recalled echo, asymmetric spin-echo (GREASE-II) pulse sequence was developed to produce relaxivity maps with the same echo planer imaging (EPI) readouts used in functional studies (1). The GREASE-II sequence included six EPI readouts following a single excitation, and T<sub>1</sub>, T<sub>2</sub> and T<sub>2</sub><sup>\*</sup> voxel-wise relaxivity maps were calculated utilizing echo pairs. It has since been found that these echo pair calculations can lead to systematic errors due to lack of signal-to-noise ratio (SNR) for T<sub>2</sub> and T<sub>2</sub><sup>\*</sup> echo pairs and the inaccuracy of the flip angles. A new non-linear model was developed which greatly increase the accuracy of the relaxivity maps, while maintaining the ability to provide precise dynamic time series T<sub>2</sub> and T<sub>2</sub><sup>\*</sup> maps.

**Theory:** The modified GREASE-II sequence, described in Figure 1, produced five images with a single excitation. The five images were used to calculate T<sub>1</sub>, T<sub>2</sub> and T<sub>2</sub><sup>\*</sup> relaxivity maps. These maps were created through a Nelder-Mead simplex algorithm (2), which was utilized to fit a nonlinear recursive model of five repetitions of the GREASE-II sequence to the acquired data in MATLAB (MathWorks, Natick, MA). The magnitude portion of the image signal shown in Eq. [1] was modeled for the parameters T<sub>1</sub>(x,y), T<sub>2</sub>(x,y), T<sub>2</sub>'(x,y), and the product, a(x,y)ρ(x,y)

$$I(x,y) = a(x,y)\rho(x,y)\left(1 - e^{-TR/T_1(x,y)}\right)e^{-t/T_2(x,y)}e^{-\tau/T_2'(x,y)}e^{i\gamma\Delta B(x,y)\tau} \quad [1]$$

The nonlinear least-squares fit inherently gives higher weight to stronger amplitude observations, reducing the propagation of errors introduced by the later echoes with low SNRs. The echo pair fit, which was previously used to calculate the relaxivity maps were used as the initial seed required by the simplex algorithm.

To validate the GREASE-II acquired relaxivity maps, separate estimates of T<sub>2</sub>, T<sub>2</sub><sup>\*</sup>, and T<sub>1</sub> were made with EPI methods so that readout-specific artifacts, including geometric distortion, would be consistent across methods. To estimate transverse relaxation rates, a series of EPI spin-echo images was acquired with stepped echo times to estimate T<sub>2</sub>, and a series of EPI gradient-echo images was acquired with stepped echo times to estimate T<sub>2</sub><sup>\*</sup>. In each case, the echo time was stepped in intervals of 20 ms over a length of 80 ms. To attenuate contributions from T<sub>1</sub> to image contrast, repetition times of 10 s were used in the acquisition of 50 repetitions for each echo time. The signal for each echo time was modeled using the nonlinear least-squares Nelder-Mead algorithm for the signal equations:

$$I(x,y) = a(x,y)\rho(x,y)e^{-TE/T_2'(x,y)} \quad [2] \quad \& \quad I(x,y) = a(x,y)\rho(x,y)e^{-TE/T_2(x,y)} \quad [3]$$

for spin-echo and gradient-echo images. To estimate the longitudinal relaxation rate, a short series of echo-planar images was acquired such that the first image was excited from the fully relaxed. This series was collected with a repetition time of 2 s. Thus, the ratio of the relaxed image magnitude to the steady state image magnitude can be used to estimate T<sub>1</sub>(x,y), following the work of Bodurka et al. (3):

$$T_1(x,y) = \frac{TR}{\ln\left(\frac{M_1(x,y)/M_{ss}(x,y)}{(M_1(x,y)/M_{ss}(x,y))^{-1}}\right)} \quad [4]$$

**Methods:** A healthy human subject was imaged after informed consent was obtained. An 8-channel head receiver was utilized on a 3.0 T General Electric Signa LX scanner. The scanning parameters were TR = 2 s, TE = 11 ms, t<sub>1</sub> = 13 ms, t<sub>4</sub> = 26 ms, SE = 91.576 ms, acquisition matrix 96 x 96, field of view 19.2 cm, slice thickness 2 mm, and 5 repetitions. Acceleration was achieved using partial Fourier acquisition with 8 overscan lines and GRAPPA with an acceleration factor of 2 and 4 ACS lines. T<sub>2</sub><sup>\*</sup>, T<sub>2</sub>, and T<sub>1</sub> were calculated as described above.

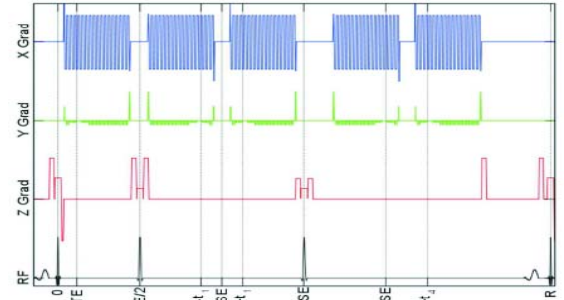
**Results:** In comparing the maps calculated from the GREASE-II sequence to the single echo method, very little difference can be seen between the two sets of relaxivity maps. It took ten seconds to obtain the GREASE-II relaxivity maps and 10-15 minutes to set up and collect three series of scans needed for the standard relaxivity maps.

There were some errors in the partial voluming of the CSF due to slight subject motion between acquisitions of GREASE-II and standard reference scans. This shift altered the partial volume fractions of CSF, white matter, and gray matter in voxels particularly along the sulci of the brain. This alteration in the partial volume fraction led to a systematic pattern of regions of large positive-percent difference and neighboring regions of large negative-percent difference. This systematic error caused by partial volume alterations shows the necessity of having a very fast relaxometry mapping technique such as GREASE-II.

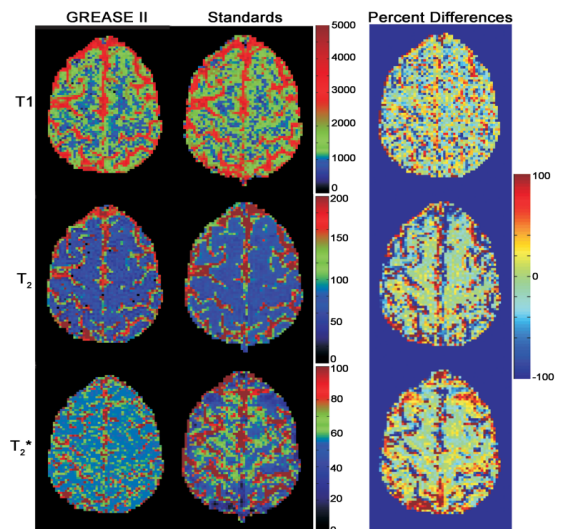
This work offers three benefits. First, the GREASE-II sequence permits collection of whole brain EPI relaxivity maps in as little as 90 seconds assuming 72 slices across the brain. Second, this sequence provides allows use of a moving window across a functional or resting data collection to produce dynamic relaxivity maps upon which fMRI or fcMRI analysis can be performed. Lastly, the relaxivity maps that are created by this sequence are acquired with the same imaging readout as used with functional imaging methods. Tissue segmentation based on this sequence enables more aggressive image masking to reduce both false positives. With this ability, more accurate fMRI and fcMRI studies can be conducted with 1-to-1 registration of the functional data to the underlying anatomy without the need for non-linear image registration.

### References

1. Shefchik et. al. *Proc. ISMRM*. 2011. 19:4510.
2. Lagarias JC, et. al. *SIAM Journal of Optimization* 1998;9:112-147.
3. Bodurka J, Ye F, Petridou N, Murphy K, Bandettini PA. *Neuroimage* 2007;34:542-549.



**Figure 1:** The GREASE-II sequence was modified to a 5 echo sequence, since the six echo in the original GREASE-II sequence was used to calculate the T<sub>1</sub> echo pair.



**Figure 2:** Column 1: The resulting relaxivity maps, which are obtained through the five echo sequence and enhanced nonlinear fit algorithm. Column 2: independently calculated, single-echo EPI parameter estimates Column 3: percent-difference of Column 1