Feasibility of myelin water fraction quantification using multi-component gradient echo sampling of spin echoes

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Introduction: Multi-component T2 imaging has been used to investigate the pathophysiology of white matter in various disorders such as multiple sclerosis (1). The metric of interest is principally the myelin water fraction (MWF) which is the proportion of the T2 signal arising from water trapped within layers of the myelin sheath surrounding myelinated axons. The most established method used to obtain the MWF involves the acquisition of 32 or more spin echoes to sample the T2 signal decay. The inability to perform a multi-slice acquisition and the high specific absorption rate (SAR) of this method are drawbacks that have motivated the development of alternate acquisition schemes to obtain the MWF. These include mcDESPOT (2) and mcT2*(3) which can both obtain whole-brain MWF data but still present some disadvantages such as a complicated model which is computationally intensive to evaluate (mcDESPOT) and the inability to evaluate data near sources of susceptibility induced gradients (mcT2*). We propose a new acquisition scheme which consists of symmetrically sampling, using gradient echoes, the rephrasing and subsequent dephasing parts of multiple spin echos, termed multi-component gradient echo sampling of spin echoes (mcGESSE). The purpose of this study was to evaluate the theoretical ability of this method to calculate the MWF in a two-component model using simulated data and realistic temporal signal to noise (SNR) profiles.

Methods: The approach is based on the work of Yablonskiy and Haacke (4) which takes advantage of the refocusing nature of the 180° refocusing pulse to disregard the irreversible component of the transverse relaxation (T2′, where 1/T2* = 1/T2 + 1/T2′). The signal is sampled at equal intervals using gradient echoes placed symmetrically about a spin echo while it rephases and subsequently dephases. Extending the approach to a two component model with a bi-exponential signal decay, a ratio of the signal before and after the spin echo can be obtained which depends on $T2_{short}$, $T2_{long}$ and the MWF (Eq. 1).

Three logarithmically spaced spin echoes were chosen based on preliminary simulations with TEs of 16, 50 and 150 ms, respectively flanked by 8, 18 and 40 pairs of gradient echoes spaced 1 ms apart. Using Matlab, data was generated based on these parameters according to Eq. 1 with $T2_{short}$ = 25ms and $T2_{long}$ = 80ms and a MWF values of 0, 0.10 and 0.20. T2* dependent temporal SNR profiles were also generated for initial SNR levels of 120, 100 and 95 for the case of zero static dephasing (T2=T2*) and for a pair of $T2^*_{short}$ and $T2^*_{long}$ values chosen to reflect realistic expectations at 3T from a previously acquired gradient echo dataset. To this end, T2′ was calculated in the ventral region of the frontal lobe, close to the frontal sinuses to establish a worst case scenario for T2* shortening. To calculate the MWF from these simulated signal data, a least squares fit was performed using Matlab's trust-region-reflective algorithm, based on the interior-reflective Newton method. For each analysis, 200 sets of simulated noisy data were generated and fit.

$$\frac{S(TE-n\Delta t)}{S(TE+n\Delta t} = \frac{MWF\cdot exp(\frac{n\Delta t-TE}{T2_{short}})+(1-MWF)\cdot exp(\frac{n\Delta t-TE}{T2_{long}})}{MWF\cdot exp(\frac{-n\Delta t-TE}{T2_{short}})+(1-MWF)\cdot exp(\frac{-n\Delta t-TE}{T2_{long}})} \quad [1]$$

Results: Table 1 summarizes the MWF calculated for the case of no static dephasing for which the signal equation and sampling is depicted in Figure 1. Figure 2 shows a representative histogram of MWF values calculated for SNR=100 and MWF=0.10. Our inspection of the gradient echo dataset yielded a T2′ value of ~25ms, yielding worst case scenario values of $T2^*_{short}$= 12.5 ms and $T2^*_{long}$= 19 ms. Table 2 summarizes the MWF obtained for this case and the signal equation and sampling is shown in Figure 3.

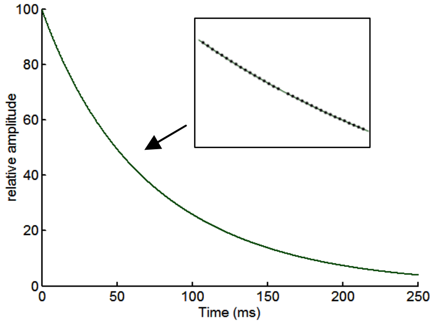

Fig. 1 – Simulated signal for the case of no static dephasing (T2*=T2)

MWF	SNR =120	SNR=100	SNR=95
0.00	0.012(0.017)	0.017(0.023)	0.015(0.023)
0.10	0.113(0.032)	0.114(0.034)	0.118(0.037)
0.20	0.203(0.028)	0.213(0.033)	0.212(0.037)

Table 1 – MWF values obtained for T2*=T2. Data presented as mean(standard deviation)

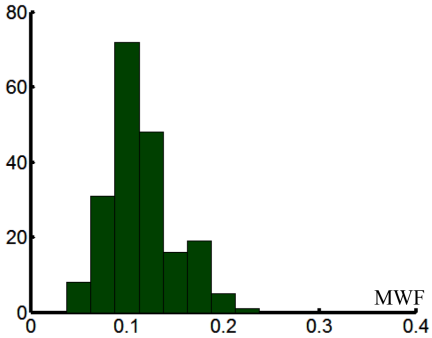

Fig. 2 – Histogram representing MWF obtained with SNR=100, MWF=0.10, T2*=T2

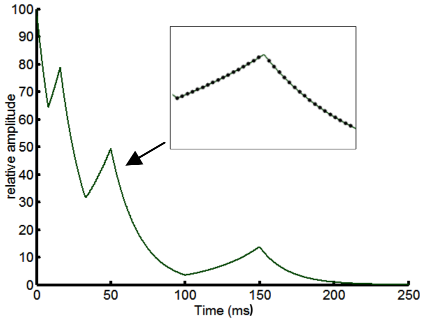

Fig. 3 – Simulated signal for a worst case scenario of static dephasing with $T2^*_{short}$=12.5ms, $T2^*_{long}$=19ms.

MWF	SNR =120	SNR=100	SNR=95
0.00	0.024(0.033)	0.029(0.042)	0.029(0.040)
0.10	0.117(0.052)	0.122(0.057)	0.122(0.062)
0.20	0.214(0.050)	0.225(0.063)	0.218(0.068)

Table 2 – MWF values obtained for $T2^*_{short}$=12.5ms and $T2^*_{long}$=19ms. Data presented as mean(standard deviation)

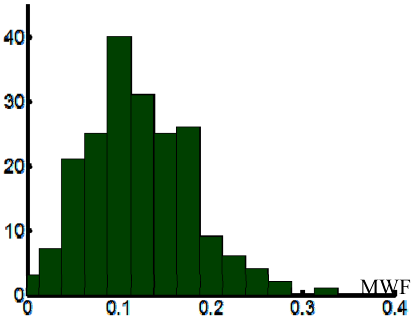

Fig. 4 – Histogram representing MWF obtained with SNR=100, MWF=0.10, $T2^*_{short}$=12.5ms, $T2^*_{long}$=19ms

Discussion: The presented data demonstrate the ability of this acquisition scheme and simple model to evaluate the contribution of a short T2 component despite a systemic overestimation of the MWF. For the case of zero static dephasing, the standard deviation is similar to those of other reported methods (2,3). When considering a worst case scenario representative of signal loss caused by static field dephasing, the standard deviation almost doubles, but the distribution of the MWF remains well behaved. Two considerations which may improve this issue are immediately apparent. First, the model could be revised to include currently unsampled data from the initial free induction decay as well as at each spin echo time. Second, more advanced data fittings could be applied to the revised model where the expected misfit could be taken into account to avoid attributing noise to either component. For the practical implementation of this technique in-vivo, the performance of the 180° pulse across the selected slice would be crucial. Further, including three echoes in the same acquisition creates the potential for stimulated echoes. This could be remedied by completing two acquisitions with two pairs of echoes each, where the repeated echo could be the currently least sampled first echo.

Conclusion: The feasibility of a new technique for whole-brain mapping of the MWF was demonstrated on theoretical grounds based on the gradient echo sampling of three spin echoes. Implementation of this sequence would allow for whole-brain MWF data in a clinically relevant scan time of approximately 10 to 20 minutes.

References:
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