R2/R2* estimation errors in combined gradient- and spin-echo EPI sequences due to slice-profile differences between RF pulses

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Introduction There is increased interest in a combined acquisition of gradient-echo (GE) and spin-echo (SE) signals for applications in DSC-PWI and fMRI. One of the main reasons is the different sensitivity of GEs and SEs to different compartments of the underlying microvasculature. While GEs are sensitive to both static and dynamic dephasing of spins, SEs are sensitive to dynamic spin dephasing only. The net difference is that GEs have generally a higher sensitivity, which increases further with vessel size, while SEs are mostly sensitive to the small vessel range [1]. The simultaneous acquisition of SE and GE signals allows one to perform PWI and fMRI with two different contrast mechanisms and to calculate vessel size indices [2,3]. Particular problems with combined GE/SE acquisitions in EPI sequences are poor slice profiles, specifically caused by spectral-spatial pulses that often excite slices that are too wide. RF pulses with better slice profiles are seldom feasible due to timing constraints. Here, we describe a potential problem in quantification of R_2 and R_2^* that can be attributed to mismatched slice profiles in combined GE/SE-EPI (cf. Fig.1).

Theory A multi-echo GE/SE-EPI pulse sequence allows one to measure multiple EPI trains with T_2^* or T_2 contrast. This facilitates T_1-independent calculations of $R_2^* = R_2 + R_2'$ and R_2 by least-squares fitting of the characteristic system of signal equations [5]:

$$S(t)^I = S_0^I \cdot e^{-t\cdot(R2+R2')} \qquad 0 < t < TE/2$$
$$S(t)^{II} = S_0^{II} \cdot e^{-TE\cdot R2'} \cdot e^{-t\cdot(R2-R2')} \qquad TE/2 < t \le TE.$$

In practice, the assumption that S_0 before and after the refocusing pulse is identical does not generally hold for combined GE/SE-EPI measurements. This can be attributed to differences between the excitation and refocusing pulse profiles and requires careful attention. One potential remedy is to introduce an additional correction term δ that relates S_0^I prior to the refocusing pulse to the equilibrium signal after the 180° pulse by $S_0^I = \delta \cdot S_0^{II}$, so that the equations account for the differences in the excitation profiles. Here, δ can be estimated by adding it as a 4th unknown to the parameter estimation, or it can be calculated from the effective slice profiles (not the FT) – $p_1(z)$ and $p_2(z)$ – of the two RF pulses. Thus,

$$S_0^I = S_0 \cdot \int_{-\varepsilon}^{\varepsilon} p_1(z)\,dz \qquad S_0^{II} = S_0^I \cdot \int_{-\varepsilon}^{\varepsilon} p_2(z)\,dz \qquad \delta = \frac{\int_{-\varepsilon}^{\varepsilon} p_1(z)dz}{S_0^I \int_{-\varepsilon}^{\varepsilon} p_1(z)dz}\,.$$

Methods On our system (1.5T GE Signa Excite 14.0, gradients: 50 mT/m, 150 T/m/s), the measured FWHM slice thickness was ~1.4x larger than the nominal slice thickness for the standard spectral-spatial (SPSP) excitation pulse provided by the vendor for their EPI-sequences, whereas the subsequent refocusing pulse affected only a smaller portion of the previously excited spins and effectively reduced the effective slice profile to the nominal width (cf.Fig.2A). Thus, EPI readout trains occurring before the refocusing pulse produced a higher signal than those occurring after the refocusing pulse. To test our hypotheses, we acquired phantom data with a 7-echo version of the SAGE-EPI pulse sequence (Fig.1), and solved the characteristic system of equations with and without adding δ. In a 2nd experiment, the slice profiles of the two pulses were matched (by widening the slice thickness of the refocusing pulse, cf. Fig.2B), so that everything previously excited was refocused, and the data were compared to the non-matched measurements. To verify R_2 (without considering diffusion effects), we acquired SE-EPI measurements with varying TE=30–105ms, R_2^* was calculated with a GE-EPI sequence with TE=10.4–84.9ms.

Results Fig.3 shows the measured signal over an ROI in a phantom experiments (black dots) superimposed on the signal characteristics using fitted values for R_2, R_2', S_0^I and S_0^{II}. In case of mismatched slice profiles, the non-corrected signal equations induced large overestimations of R_2/R_2^* (RMS fit error = 659.1, cf. Fig.3A, Table 1). By adding δ to the fitting function, the measured signal closely followed the fitted model (RMS error = 49.8). With minimal slice-profile mismatches (Fig.3B/D), results with both models were similar with a smaller RMS error in case of δ-correction (if the slice profiles were truly identical, the 2 models would yield the same results). Table 1 provides a summary:

	Mismatch	*δ-Correction*	$R_2\ s^{-1}$	$R_2^*\ s^{-1}$	S_0^I	S_0^{II}	δ	*RMS error*
(A)	Yes	No	12.70	27.48	23746	-	-	659.1
(B)	No	No	5.25	19.08	20231	-	-	112.8
(C)	Yes	Yes	6.85	19.68	20481	14659	1.40	49.8
(D)	No	Yes	5.83	19.85	20527	21218	0.97	75.5
Reference data			5.44	19.46	-	-	-	-

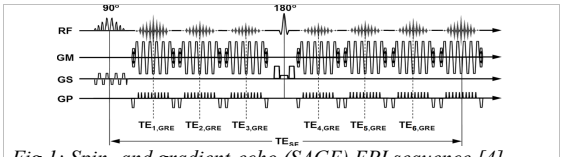

Fig.1: Spin- and gradient-echo (SAGE) EPI sequence [4]

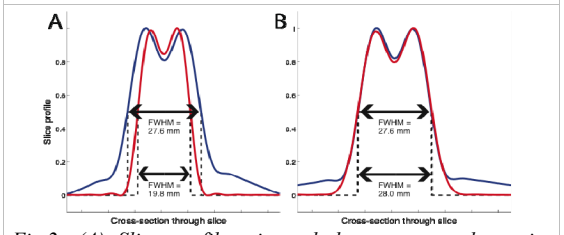

*Fig.2: **(A)** Slice profile mismatch between an echo train acquired prior to the 180° pulse (blue) and an echo train acquired after the 180° pulse (red). The slice profiles shown here were experimentally determined with a 2-echo version of the SAGE-EPI pulse sequence (Fig.1), except that all gradients on the slice-selective axis were moved to the readout axis. Nominal slice thickness = 20 mm. **(B)** Identical acquisition with matched pulse profiles.*

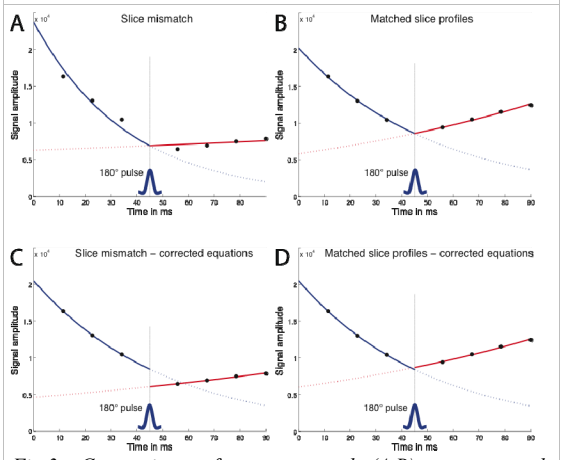

Fig.3: Comparison of non-corrected (A,B) to corrected method (C,D) for mismatched slice profiles (A,C) and matched profiles (B,D). The blue line shows the fitted signal decay before the 180° pulse ($S(t)^I$), while the red line shows the signal propagation after the refocusing pulse ($S(t)^{II}$). Note that the corrected signal characteristics have a sudden step at the location of the 180° pulse that is proportional to δ. This step accounts for the mismatched slice profiles. It approaches 0 if the slice profiles of the pulses are nearly matched (D).

Discussion EPI requires fat suppression or SPSP excitation to suppress chemical-shift artifacts. However, SPSP pulses often are too long or suffer from poor slice profiles. The introduction of a factor δ to correct for discordances in slice profiles between excitation and refocusing pulses mitigated errors in the estimation of R_2 and R_2^* in a pulse sequence that simultaneously measures GEs and SEs. In combined GE/SE-EPI measurements, it is highly advisable to assure matched slice profiles to minimize R_2/R_2^* estimation errors or to include a correction factor δ in the characteristic eq. to improve R_2/R_2^* estimation.

References [1] Boxerman *et al.* MRM 34:555-566 (1995), [2] Troprès *et al.* MRM 45, 397–408 (2001), [3] Kiselev et al. MRM 53: 553-563 (2005), [4] Newbould *et al.* Proc. ISMRM 2007, #1451, [5] MA *et al.* J MR B 111:61-69 (1996) – **Acknowledgements** Supported by NIH (1R01EB008706, 5R01EB002711, 1R01EB006526, 1R21EB006860), Center of Advanced MR Technology at Stanford (P41RR09784), Lucas & Oak Foundations