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Retrospective Correction for T_1 -Weighting Bias in T_2 Values Obtained with Various Spectroscopic Spin-Echo Acquisition Schemes

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Abstract

Localized tissue transverse relaxation time (T_2) is obtained by fitting a decaying exponential to the signals from several spin-echo experiments at different echo-times (TE). Unfortunately, time constraints in MR spectroscopy (MRS) often mandate *in vivo* acquisition schemes at short repetition-times (TR), *i.e.*, comparable to the longitudinal relaxation constant (T_1). This leads to *different* T_1 -weighting of the signals at each TE . Unaccounted for, this varying weighting causes systematic *underestimation* of the T_2 s, sometimes by as much as 30%. In this paper we (i) analyze the phenomenon for common MRS spin-echo T_2 acquisitions schemes. (ii) Propose a general *post hoc* T_1 -bias correction for any (TR , TE) combination. (iii) Show that approximate knowledge of T_1 is sufficient, since a 20% uncertainty leads to under 3% bias in T_2 ; and consequently, (iv) efficient, precision-optimized short- TR spin-echo T_2 measurement protocols can be designed and used without risk of accuracy loss. Tables of correction for single-refocusing (conventional) spin-echo and double-refocusing, *e.g.*, PRESS acquisitions are provided.

Keywords

T_2 relaxation; Spin echo; T_1 -weighting; Tissue relaxation times

INTRODUCTION

Local transverse relaxation time (T_2) of tissue water and metabolites is needed for quantitative MRI and MR spectroscopy (MRS) (1–6). It is estimated by fitting a decaying exponential to the signals at different spin echo-times (TE) (2,4,7). In MRI, strong signals facilitates fast TrueFISP or CPMG spin-echo train acquisition (3,8,9). In MRS, however, where (i) the signals are much weaker, mandating signal averaging; (ii) longer sampling is required to realize the desired spectral resolution; and (iii) suppression of unwanted signals from outside the volume of interest (VOI) may be needed, variants of the double-refocusing (PRESS) sequences prevail (2,5,10–12).

The needs for at least two (different TE) acquisitions to obtain T_2 , of acceptable spatial resolution and duration, mandate acquisition strategies that yield the best signal-to-noise-ratio (SNR)/unit-time. If an Ernst or 90° flip-angle is used for that purpose, hundreds of millisecond preparation [PRESS, water and (often) outer volume suppression] and digitization time in MRS lead to an optimal recycle-time, $TR \approx T_1$ (13,14). As a result, the longitudinal magnetization

(M_Z) is at steady-state during the experiment and for either flip-angle choice experiences at the short TE_1 an “effective” $TR_{eff} \approx TR$ and at TE_2 a $TR_{eff} = TR - TE_2$ which can be significantly shorter. Consequently, in addition to the T_2 -weighting encoded by the different TE s, the signals also incur a *variable* T_1 -weighting that depends on the TR , TE and number of refocusing pulses per TR .

This weighting has been known for decades and strategies devised to address it include eliminating it entirely with long $TR \gg 5.T_1$ (15); or making it constant by saturating M_Z after each acquisition to provide equal TR_{eff} to all TE s (16). Since T_2 precision is determined by the SNR (17), however, and their protocols *in vivo* are already many minutes to an hour long (8, 9), either remedy is inefficient for MRS and invariably limits spatial resolution, precision and coverage. The third strategy, to apply T_1 corrections to the signals before T_2 is calculated (11,12), does not account for the effects the number of refocusing pulses *during* the TE has on the steady-state of M_Z . This is a shortcoming for three-dimensional (3D) MRS especially when interleaving several slabs (to increase spatial coverage) in each $TR \approx 1.2.T_1$ (14,18), since their spin-echo refocusing pulse(s) act on the whole VOI, modifying M_Z in ways not accounted for by simple T_1 corrections.

In this paper we propose a general procedure to retrospectively remove T_1 -weighting from metabolite T_2 s obtained with spin-echo MRS sequences at short $TR \approx T_1$. Without it, T_2 values in the literature may represent underestimates by as much as 30%, depending on the acquisition parameters, suggesting that their cited variations may be artificially large. When similar acquisition settings are used, the variance may appear (deceptively) smaller but the result may still be an underestimate. Although retrospective removal of this bias requires knowledge of T_1 , it is found that an approximate value is enough. Spin echo based MRS sequences can, therefore, be used at efficient $TR \approx T_1$ to limit acquisition duration without loss of T_2 accuracy. Sample T_1 -bias corrections for one and two refocusing pulses and their multi-slab implementation are provided.

THEORY

Single- or multi-slab implementations of spin-echo sequences consist of a 90° pulse followed by one or more refocusing pulses, a readout and gradient to crush any remaining transverse magnetization. In this sequence the longitudinal magnetization, M_Z , is nutated into the transverse plane by the 90° pulse and begins to recover immediately towards its thermal equilibrium value, M_0 . The recovery is hindered by repeated refocusing pulses that appear to M_Z as inversions. Changes to the RF pulse train timing by different TE s, therefore, will alter the steady state of M_Z .

In order to determine the T_1 -weighting we need to compute M_Z prior to the 90° pulse in the steady state. From the RF-pulse train perspective such sequence is identical to multiple inversion recoveries with data acquisition occurring after the last refocusing rather than after the 90° pulse. Calculation of M_Z in such instances may be simply adopted from Dixon *et al.* (19):

$$M_z = M_0 \left(1 - 2e^{-\frac{TI_1}{T_1}} + 2e^{-\frac{TI_2}{T_1}} - 2e^{-\frac{TI_3}{T_1}} + \dots \pm e^{-\frac{TR}{T_1}} \right), \quad [1]$$

where TI_1 TI_2 $TI_3 \dots$ are “inversion” times between the refocusing and the 90° pulses (see Fig. 1a) and TR is the duration of the entire RF pulse train. This equation is obtained by following the prescription of continuous sign alternation of the terms given beneath equation 10 of Dixon *et al.* (19). To illustrate its use we write it out explicitly for a simple (single-slab) spin-echo.

In this case the TI is the time by which the refocusing precedes the 90° pulse and is related to TE by $TI=TR-TE/2$. The full expression for the signal as a function of TE becomes:

$$S(TE)=M_0\left(1-2e^{-(TR-\frac{1}{2}TE)/T_1}+e^{-TR/T_1}\right)e^{-TE/T_2}. \quad [2]$$

For PRESS (10), referred here as a “single-slab” to distinguish it from the multi-slab case below, $TI_1=TR-\frac{3}{4}TE$, $TI_2=TR-\frac{1}{4}TE$ and the observed signal as a function of TE is given by:

$$S(TE)=M_0\left(1-2e^{-(TR-\frac{3}{4}TE)/T_1}+2e^{-(TR-\frac{1}{4}TE)/T_1}-e^{-TR/T_1}\right)e^{-TE/T_2}. \quad [3]$$

The two examples yield the known expressions and demonstrate that unless $TE \ll TR$ or $T_1 \ll TR$, TE variation induce different unwanted T_1 -weighting in addition to the expected T_2 decay (16).

Multi-slab multi-refocusing spin-echo sequences

We consider a sequence to be “multi-slab” in this context when consecutive 90° pulses select non-overlapping slabs in the VOI, but the refocusing pulses act the entire VOI. (In a “single-slab” the refocusing acts on the same region as the 90°). Multi-slab multi-refocusing sequences may be characterized by their cycle-time, TC , the interval between subsequent 90° pulses (see Fig. 1b) within which m refocusing pulses, a readout and gradient crushers are executed. To optimize the SNR and coverage efficiency TC is related to TR and the number of slabs, n , as $TR=n \cdot TC$ (14). Examples are multi-slab spin-echo with non-selective refocusing or the multi-slab PRESS (14).

The general expression for the longitudinal magnetization prior to the 90° pulse in the n -slab m -refocusing spin-echo sequence is shown in the Appendix to be given by,

$$M_z=M_0\left(\frac{1-(-1)^{mn}e^{-nTC/T_1}}{1-(-1)^me^{-TC/T_1}}\right)\left(1+2\sum_{k=1}^m(-1)^ke^{-TI_k/T_1}-(-1)^me^{-TC/T_1}\right) \quad [4]$$

with the echo time given by $TE=2\left(\sum_{k=1}^m(-1)^kTI_k\right)$ for even number of refocusing pulses within one cycle and $TE=2\left(\sum_{k=1}^m(-1)^kTI_k+TC\right)$ for odd.

The structure of Eq. [4] leads to three important observations. First, at $TR \approx T_1$ the different TE s needed to measure T_2 alter the TIs thereby changing the value of the rightmost term and introducing the unwanted TE dependence in T_1 -weighting. Since the other terms remain constant when TE is varied, the bias in T_2 is determined entirely by this rightmost term. Second, although the T_1 -weighting of the observed signal depends on the number of slabs, their number, n , does not affect the bias since it does not appear in the rightmost term. On the other hand, the number of refocusing pulses in the cycle does, therefore, the bias depends on m . Consequently, it is this, rightmost, term expressing the T_1 -weighting of the *single-slab* m -refocusing sequence with TR replaced by TC that will be of further interest. Third, for a given TC the magnetization in multi-slab experiments is larger (the middle term in Eq. [4] exceeds unity) than in a single-slab for even m and is smaller for odd. This reflects the fact that for odd number of refocusing

pulses magnetization that recovered along +Z during the TE is “inverted” to re-start from below the transverse plane. Consequently, a multi-slab PRESS sequence ($m=2$) will yield higher signal than single-slab, while multi-slab spin-echo ($m=1$) will yield lower signal than its single-slab version.

Bias in multi-slab single and double refocusing spin-echo sequences

Since the bias in T_2 is independent of the number of slabs, we calculate its correction for two cases of interest: multi-slab spin-echo ($m=1$) and PRESS ($m=2$) using the corresponding single-slab expressions, Eqs. [2] and [3] replacing TR with TC (see above). Furthermore, since the two-point protocol with appropriate TE s and number of averages at each is optimal for T_2 estimation (7), we restrict our calculation to it. (Correcting multi- TE protocols is outlined in the Discussion).

Both equations [2] and [3] (with TR replaced by TC , see above) have the form,

$$S(TE)=M_0f(TC/T_1, TE/TC)e^{-TE/T_2}. \quad [5]$$

with $f(TC/T_1, TE/TC)=1 - 2e^{-(TR-\frac{1}{2}TE)/T_1}+e^{-TR/T_1}$ for spin-echo (Eq. [2]) and $f(TC/T_1, TE/TC)=1 - 2e^{-(TR-\frac{3}{4}TE)/T_1}+2e^{-(TR-\frac{1}{4}TE)/T_1} - e^{-TR/T_1}$ for PRESS (Eq. [3]).

The apparent value of T_2 extracted from two acquisitions at TE_1 and TE_2 ($TE_2 > TE_1$) is obtained from

$$\frac{1}{T_2^{app}} = \frac{\ln S(TE_1) - \ln S(TE_2)}{TE_2 - TE_1}, \quad [6]$$

or, denoting $\Delta TE = TE_2 - TE_1$ and $f_{1,2} = f(TE_{1,2})$:

$$\frac{\Delta TE}{T_2^{app}} = \frac{\Delta TE}{T_2} + (\ln f_1 - \ln f_2). \quad [7]$$

Equation [7] prescribes how to obtain the true value of T_2 provided that the bias introduced by the $c = (1/f_1 - 1/f_2)$ term can be estimated. In general, it is a function of three variables: TE_1/T_1 , TE_2/T_1 and TC/T_1 all of which require knowledge of T_1 . Fortunately, c is only a weak function of T_1 (see below) therefore, in practice, an approximate value may suffice. In addition, since for the highest T_2 precision TE_1 is usually made as short as possible (7), $TE_1 \ll T_1$, then $TE_1 / T_1 \approx 0$ and its influence may be neglected. Then c becomes a function of two variables,

$$c(TC/T_1, \Delta TE/TC) = \ln f_1 - \ln f_2, \quad [8]$$

which may be presented graphically as shown for the spin-echo and PRESS sequences in Fig. 2 or tabulated (see Table 1).

METHODS

All experiments were done in a 3 T Magnetom Trio imager (Siemens AG, Erlangen, Germany) using a 25 cm diameter $\times$ 27 cm depth TEM3000 transmit-receive circularly-polarized head-coil (MRInstruments, Minneapolis, MN). The sample was a 2 L sphere of 12.5 mM *N*-acetylaspartate (NAA), 10.0 mM creatine (Cr) and 3.0 mM choline (Cho) in water doped with 2 cm³ Magnavist. The T_1 values of 605, 336 and 235 ms for the NAA, Cr and Cho were obtained using non-localizing multi-point inversion-recovery.

To demonstrate the effect of T_1 -bias on the metabolites' apparent T_2 (T_2^{app}) estimates through the choice of acquisition parameters (TR , TE , TC , n) we used our multi-slab PRESS sequence (14,20). It excited a 10 $\times$ 8 $\times$ 4 cm³ anterior-posterior (AP) $\times$ left-right (LR) $\times$ inferior-superior (IS) VOI in a 16 $\times$ 16 $\times$ 4 cm³ (AP $\times$ LR $\times$ IS) field-of-view (FOV). The FOV was encoded into 16 $\times$ 16 $\times$ 4 matrix using 2D chemical shift imaging hybrid (AP $\times$ LR) with either fourth-order Hadamard spectroscopic imaging (HSI) along IS ($n=1$, $m=2$) (21); or two interleaved second-order HSI slabs along IS ($n=2$, $m=2$) (14). Each used one of the five TR , TC and TE combinations in Table 2 to demonstrate their influence on T_2^{app} . Experiment number 5 may be considered a gold standard since its TC is 3 times longer than the longest T_1 .

The ¹H-MRS signals were acquired with 1024 complex points at a 500 μ s sampling rate for 2-Hz spectral resolution. The data were processed off-line using in-house software. Residual water signals were removed in the time domain (22), followed by Hadamard transform along the IS direction and Fourier transform in the time and the AP and RL dimensions.

RESULTS

Relative amounts of NAA, Cr and Cho in the phantom were estimated from their peak areas in each of the 320 voxels in the VOI using the FTT parametric spectral modeling and least-squares optimization package (23), and used to calculate the experimental T_2^{app} -values via Eq. [6]. Since the phantom is uniform, all T_2^{app} values for each metabolite were used to compute an average and standard deviation (SD) for each of the five experimental setups in Table 2. The resultant average values of T_2^{app} and their SD for the metabolites for each experiment are shown in Fig. 3a. Then, the bias correction, c , was calculated using Eq. [8] for each TC/T_1 and $\Delta TE/TC$ combination of Table 2 and applied to the T_2^{app} values to obtain the corrected T_2 's, shown in Fig. 3b.

Note that the correction greatly reduced the T_1 bias (T_2^{app} difference for the same metabolite for the different experimental setups of Table 2) but at the same time increased the SD of the average (error bars) for each. This phenomenon is discussed below. Also note that since the NAA has the longest T_1 (605 ms) and Cho the shortest (235 ms), the bias caused by the TE dependence of the T_1 -weighting is, as expected, most pronounced for the former and least for the latter.

DISCUSSION

The correction developed for the two-point method in Eq. [8] and plotted in Fig. 2 leads to four practical consequences. First, the correction is independent of the number of slabs. Second, it is always positive, *i.e.*, T_2^{app} , always underestimates the true T_2 , sometimes by as much as 50% for some of the TC and TE combinations considered. Indeed, while the existence of a T_1 bias and the importance of its correction is recognized, it is often ignored and rarely implemented properly (5,6,11,12,24). Third, the correction depends only weakly on the value of T_1 through the TC/T_1 term in Eq. [8]. Indeed, panels **c** and **d** of Fig. 2 show that a 20% position shift on the TC/T_1 axis (20% variation in T_1) leads to a correction change of only ~ 0.04 . Given that $\Delta TE/T_2 \approx 1.1$ to 1.35 in Eq. [7] (7), in the worst case scenario of short TC

and long ΔTE the systematic error will be reduced from ~50% to about $0.04/(1.1 \text{ to } 1.35) \times 100\% \approx 3\%$. Finally, in designing T_2 -measurements using the precision-per-unit-time optimized two-point method (7,17), it is preferable to “tune” the protocol to the apparent value, T_2^{app} given by Eq. [7].

For example, the T_1 -bias corrections to the T_2^{app} s at 3 T, reported by Zaaraoui *et al.* (5) using $n=1$ slab PRESS with $\Delta TE=250$ ms, $TC=1000$ ms and assuming metabolites T_1 s of 1.0 to 1.5 s (11,15), are 0.18 to 0.22. Retrospective application of this correction to remove the bias from the 258, 152 and 203 ms average T_2^{app} reported for NAA, Cr and Cho yields 328, 174 and 244 ms. Such a correction was already applied in two previous studies reporting T_2 s at 3 and 7 T (25,26).

Although the above discussion and examples focused on two-point T_2 estimation protocols, multi- TE acquisitions also suffer variable T_1 -weighting. Due to the sheer number of possibilities, however, the bias will need to be computed on a case by case basis (6,11,12,24). To illustrate this, we consider PRESS with $TC=T_1=1200$ ms and $TE=50, 100, 160, 220, 300$ ms, reported recently by Tsai *et al.* (6). Using these parameters, the natural logarithm of the observed signal at these five TE s (Eq. [3]) will be:

$$\begin{aligned}\ln S(TE_1) &= \ln M_0 - \frac{TE_1}{T_1} - 0.616 \\ \ln S(TE_2) &= \ln M_0 - \frac{TE_2}{T_2} - 0.600 \\ \ln S(TE_3) &= \ln M_0 - \frac{TE_3}{T_2} - 0.580 \\ \ln S(TE_4) &= \ln M_0 - \frac{TE_4}{T_2} - 0.558 \\ \ln S(TE_5) &= \ln M_0 - \frac{TE_5}{T_2} - 0.528\end{aligned}\quad [9]$$

The first two terms at each TE represent the usual linear dependence of the logarithm of the decaying signal with respect to echo time with the slope given by $(-1/T_2)$. However, the third term represents deviations due to T_1 bias: the numbers on the right hand side also fit a straight line but with an effective decay constant of 2800 ms. Since sum of two straight lines is again a straight line, the apparent slope $(-1/T_2^{app})$ extracted from this multi- TE experiment will be given (in milliseconds) by:

$$\frac{1}{T_2^{app}} = \frac{1}{T_2} + \frac{1}{2800}.$$
[10]

Hence, the reported T_2^{app} s of 262, 151 and 221 ms for NAA, Cr and Cho (6), after this retrospective T_1 bias removal become 290, 160 and 240 ms.

Throughout the presentation we assumed a separate run of the sequence for each echo time. Although multiple acquisitions within one multi-refocusing RF train are used to speed up the measurement, imperfect RF pulses lead to incomplete refocusing and therefore to shortening of the apparent T_2 's. Because of the absence of RF train timing modifications (data at several TE 's is collected in one run), the discussed shortening caused by varying T_1 -weighting does not apply. However, the signal sampling must be fast to complete within gaps of the RF train which may not be possible, especially in spectroscopic applications. Another disadvantage of multi-refocusing sequences is much higher power depositions especially at higher magnetic fields or when imaging nuclei with lower gyromagnetic ratios or when using adiabatic pulses to rectify refocusing. As mentioned in the introduction, another method that does not incur T_1 -weighting bias is to saturate after echo (16). However, it may suffer from imperfect saturation which in turn will still lead to T_1 weighting bias in T_2 values. The single saturation pulse can

be replaced by a train of saturation pulses driving the spins into a steady state, then, even if the saturation is incomplete, the magnetization recovery from it will not depend on TE . This, however, is time consuming making the acquisition inefficient.

Sensitivity of the longitudinal magnetization of the underlying spin-echo sequences to flip angle imperfections transforms somewhat to the proposed correction as well. While it can be shown with tedious and non-insightful algebra in a manner similar to that presented in the Appendix that when the angles deviate from their nominal values, the correction still does not dependent on the number of slabs, its value deviates from the ideal case presented in Fig. 2 and Table 1. Assuming that the actual pulses remain within $\pm 30\%$ of their nominal values, we performed simulation of the spin dynamics and found the maximum deviation incurred by the correction, which is presented in Fig. 4. It is seen that such a large variation in flip angles results in very small, less than ± 0.02 , change of the correction for PRESS acquisitions. Spin-echo is more sensitive to the imperfections, but if cycle time is not too small and ΔTE is not too large (to avoid top left corner of Fig. 4a) the deviation is still small. For comparison, we remind that the 20% uncertainty in T_1 causes ± 0.04 deviation in the correction and less than 3% bias in T_2 . Therefore, for many practical purposes, sensitivity of the correction to pulse imperfections can be ignored. While we do not know the extend of pulse imperfections in our experiments, the validation that we can offer is that the data presented, which no doubt suffered from the effect, is in good agreement with the theory.

The proposed correction is only as good as the original assumptions made by the experimenter. For example, if the sample's T_1 is unknown or deviates substantially from the value used in the correction or if tissues with very different T_1 and/or T_2 are mixed within one voxel, the corrected value will still be meaningless. While the correction provides certain robustness to the value of T_1 , we can only hope that, as always, the researchers are mindful about the (implicit) assumptions made.

While it is clear from Fig. 3 that the proposed correction removes the T_1 -bias, it also leads to larger error bars. This reflects random noise propagating from the measurement error in T_2^{app} into the calculation of T_2 . Indeed, applying error propagation rules to Eq. [7] establishes the relationship between the two relative errors (27):

$$\frac{\sigma(T_2)}{T_2} = \frac{T_2}{T_2^{app}} \frac{\sigma(T_2^{app})}{T_2^{app}}, \quad [11]$$

revealing that since T_2 / T_2^{app} is always larger than unity, the relative error of the corrected

value, $\frac{\sigma(T_2)}{T_2}$ always exceeds $\frac{\sigma(T_2^{app})}{T_2^{app}}$. Since Eqs. [7] and [10] are of similar form, the relative error will increase in the same manner in multi- TE acquisitions. The amount of the increase depends on T_2/T_2^{app} ratio, which in turn depends on the choice of the TE s and TC . The natural extension of this and prior work (7), therefore, is to find their optimal values for precise and accurate multi-slab T_2 measurements given the available imaging time, which is currently under investigation.

Finally, we note that while for experimental verification we utilized a spectroscopic multi-slab PRESS sequence available to us, the theory is general and independent of the type of signal encoding: Cartesian, spiral, radial, Fourier, Hadamard or any other type of imaging or spectroscopy. This is because encoding does not interfere with the spin excitation and relaxation history.

CONCLUSION

We presented a general paradigm for correcting systematic T_1 -weighting bias in T_2 measurements that can be applied retrospectively to values obtained with many existing spin-echo sequences of arbitrary TR and TE . Several examples demonstrate that depending on the T_1 and choice of TR and TE combinations, the correction may range from “negligible” to over 50%. Although knowledge of T_1 is needed, it is also shown that the systematic error caused by the uncertainty in its value is much lower than the original bias. The simplicity of the correction in conjunction with the optimal two-point protocol, therefore, opens the possibility to devise optimal acquisition schemes that will also reduce the duration of T_2 mapping protocols.

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APPENDIX A

To derive the general Eq. [4] we first consider the simplest case of the n -slab single-refocusing spin-echo sequence. It is clear that derivation of the expression for M_z amounts to setting $TI_k = (k - 1)TC + TI$ and $TR = nTC$ in Eq. [1], and once done we are to replace TI with $TC - TE / 2$. Substituting this into Eq. [1] yields:

$$M_z = M_0 \left(1 - 2e^{-TI/T_1} + 2e^{-(TC+TI)/T_1} - 2e^{-(2TC+TI)/T_1} + \dots - (-1)^n e^{-nTC/T_1} \right) \quad [12]$$

Let us now insert zeros in the form $0 = (+e^{-TC} - e^{-TC}) = (-e^{-2TC} + e^{-2TC}) = (+e^{-3TC} - e^{-3TC}) = \dots$ between the terms with factor 2, then group every three terms together and rearrange:

$$\begin{aligned}
M_z = & M_0 \left(\underbrace{1 - 2e^{-TI/T_1} + e^{-TC}}_{\text{Term 1}} - \underbrace{e^{-TC} + 2e^{-(TC+TI)/T_1} - e^{-2TC}}_{\text{Term 2}} \right. \\
& \left. + \underbrace{e^{-2TC} - 2e^{-(2TC+TI)/T_1} + e^{-3TC}}_{\text{Term 3}} - e^{-3TC} + \dots - (-1)^n e^{-nTC/T_1} \right) \\
= & M_0 (1 - 2e^{-TI/T_1} + e^{-TC}) (1 - e^{-TC} + e^{-2TC} - e^{-3TC} + \dots - (-1)^n e^{-(n-1)TC/T_1})
\end{aligned} \quad [13]$$

Then, finally, summing the geometric series we obtain:

$$M_z = M_0 \frac{1 - (-1)^n e^{-nTC/T_1}}{1 + e^{-TC/T_1}} (1 - 2e^{-TI/T_1} + e^{-TC/T_1}) \quad [14]$$

Replacing TI by $(TC - TE/2)$ we arrive at the final expression for the signal as a function of TE in the n -slab single-refocusing spin-echo sequence:

$$S(TE) = M_0 \frac{1 - (-1)^n e^{-nTC/T_1}}{1 + e^{-TC/T_1}} (1 - 2e^{-(TC-TE/2)/T_1} + e^{-TC/T_1}) e^{-TE/T_2} \quad [15]$$

Now, in the case of n -slab double-refocusing spin-echo sequence (multi-slab PRESS) we proceed in the similar manner starting from Eq. [1], where TI 's alternate between $(k-1)TC + TI_1$ and $(k-1)TC + TI_2$ (see Fig. 1b):

$$\begin{aligned}
M_z = & M_0 \left(1 - 2e^{-TI_1/T_1} + 2e^{-TI_2/T_1} - 2e^{-(TC+TI_1)/T_1} + 2e^{-(TC+TI_2)/T_1} \right. \\
& \left. - 2e^{-(2TC+TI_1)/T_1} + 2e^{-(2TC+TI_2)/T_1} - \dots + e^{-nTC/T_1} \right)
\end{aligned} \quad [16]$$

Inserting zeros in the form $0 = (+e^{-TC} - e^{-TC}) = (-e^{-2TC} + e^{-2TC}) = (+e^{-3TC} - e^{-3TC}) = \dots$ after the terms with TI_2 excluding the last one, then grouping every four terms together, re-arranging and summing the geometric series as before we obtain:

$$M_z = M_0 \frac{1 - e^{-nTC/T_1}}{1 - e^{-TC/T_1}} (1 - 2e^{-TI_1/T_1} + 2e^{-TI_2/T_1} - e^{-TC/T_1}) \quad [17]$$

Echo time of the PRESS sequence is double the interval between the refocusing pulses and is given by $TE = 2(TI_2 - TI_1)$, therefore the final expression for the signal as a function of TE in the n -slab double-refocusing spin-echo sequence is:

$$S(TE) = M_0 \frac{1 - e^{-nTC/T_1}}{1 - e^{-TC/T_1}} (1 - 2e^{-TI_1/T_1} + 2e^{-TI_2/T_1} - e^{-TC/T_1}) e^{-2(TI_2 - TI_1)/T_2} \quad [18]$$

Inspecting Eqs. [14] and [17] it is easy to infer the general expression for the longitudinal magnetization in an n -slab m -refocusing sequence:

$$\begin{aligned}
M_z = & M_0 \frac{1 - (-1)^m e^{-nTC/T_1}}{1 - (-1)^m e^{-TC/T_1}} \left(1 - 2e^{-TI_1/T_1} + 2e^{-TI_2/T_1} - \dots \right. \\
& \left. + 2(-1)^m e^{-TI_m/T_1} - (-1)^m e^{-TC/T_1} \right)
\end{aligned} \quad [19]$$

Or, in a more compact form:

$$M_z = M_0 \frac{1 - (-1)^m e^{-nTC/T_1}}{1 - (-1)^m e^{-TC/T_1}} \left(1 + 2 \sum_{k=1}^m (-1)^k e^{-TI_k/T_1} - (-1)^m e^{-TC/T_1} \right) \quad [20]$$

where TI_k , $k=1, \dots, m$ are times of m “inversions” within cycle time TC . It is easy to convince oneself that the echo time is given by $TE=2 \left(\sum_{k=1}^m (-1)^k TI_k \right)$ for even number of refocusing pulses within one cycle and $TE=2 \left(\sum_{k=1}^m (-1)^k TI_k + TC \right)$ for odd.

Fig. 1.

a: Schematic diagram of the RF pulse train in an m -refocusing spin-echo sequence. The duration of the train is TR after which it is repeated. Data acquisition followed by a crusher gradient is taking place somewhere within the TI_1 interval. **b:** Schematic diagram of the RF pulse train in an n -slab double-refocusing spin-echo sequence (multi-slab PRESS) (14,20). Vertical dashed lines represent excitations of slabs other than the one given by the 90° pulses marked by solid lines. Note that since the dashed 90° pulses do not affect the magnetization in the slab, then from the slab spins' point of view this is a special case of the multi-refocusing sequence (panel **a**) with a certain relationships between the “inversion” times. The refocusing pulses define the PRESS box in directions perpendicular to the slabs plane and thus, act on all

of them. The duration of the train is $TR = n TC$ after which it is repeated. Data acquisitions followed by crushers somewhere within the t_3 intervals. The echo time is given by $TE=2t_2$.

Fig. 2. Corrections $c(TC/T_1, \Delta TE/TC)$ for the spin-echo (a, c) and PRESS (b, d) sequences computed using Eq. [8]. Panels c and d plot the corrections as function of TC/T_1 for several TE 's and demonstrate low sensitivity of the correction to the value of T_1 which may not be known exactly. Correction does not depend on the number of slabs.

Fig. 3.

Top, **a**: Apparent values of T_2 (T_2^{app}) for three metabolites extracted from each of the five experiments whose settings are given in Table 2. Note that T_2^{app} of NAA varies strongly with experimental conditions while that of choline does not, because its T_1 is much shorter than the TCs used. Bottom, **b**: After the bias is removed, T_2 s of each metabolite become much more uniform, but the error bars increase.

Fig. 4.

Maximum deviation of the correction from its nominal value (Fig. 2) when the transmit RF field is varied within $\pm 30\%$ of its nominal for the spin-echo (**a**) and PRESS (**b**) sequences. The plots demonstrate that spin-echo acquisition is more prone to the pulse imperfections than PRESS. (Note different color scales.) Since the correction does not depend on the number of slabs, the same applies to multi-slab versions of the acquisitions.

Table 1

Tabulated T_1 -weighting bias correction (Eq. [8]) for spin-echo and PRESS. (Same as presented graphically in Fig. 2.) Correction does not depend on the number of slabs.

TC/T ₁	Spin-echo										PRESS									
	0.1					0.2					0.3					0.4				
	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.35	0.4	0.45	0.45
0.1	0.10	0.15	0.21	0.27	0.34	0.41	0.48	0.57	0.10	0.16	0.21	0.28	0.34	0.41	0.49	0.58	0.41	0.49	0.58	0.58
0.2	0.10	0.15	0.20	0.26	0.32	0.39	0.46	0.54	0.10	0.15	0.20	0.26	0.33	0.40	0.47	0.55	0.40	0.47	0.55	0.55
0.3	0.09	0.14	0.19	0.25	0.31	0.37	0.44	0.51	0.09	0.14	0.19	0.25	0.31	0.38	0.45	0.53	0.38	0.45	0.53	0.53
0.4	0.09	0.13	0.18	0.23	0.29	0.35	0.41	0.48	0.09	0.13	0.19	0.24	0.30	0.36	0.43	0.51	0.36	0.43	0.51	0.51
0.5	0.08	0.13	0.17	0.22	0.27	0.33	0.39	0.46	0.08	0.13	0.18	0.23	0.29	0.35	0.42	0.49	0.35	0.42	0.49	0.49
0.6	0.08	0.12	0.16	0.21	0.26	0.31	0.37	0.43	0.08	0.12	0.17	0.22	0.27	0.33	0.40	0.47	0.33	0.40	0.47	0.47
0.7	0.07	0.11	0.15	0.20	0.25	0.30	0.35	0.41	0.07	0.12	0.16	0.21	0.26	0.32	0.38	0.45	0.32	0.38	0.45	0.45
0.8	0.07	0.11	0.15	0.19	0.23	0.28	0.33	0.39	0.07	0.11	0.15	0.20	0.25	0.31	0.37	0.43	0.31	0.37	0.43	0.43
0.9	0.07	0.10	0.14	0.18	0.22	0.27	0.32	0.37	0.07	0.10	0.15	0.19	0.24	0.30	0.35	0.42	0.30	0.35	0.42	0.42
1.0	0.06	0.10	0.13	0.17	0.21	0.25	0.30	0.35	0.06	0.10	0.14	0.18	0.23	0.28	0.34	0.40	0.28	0.34	0.40	0.40
1.1	0.06	0.09	0.12	0.16	0.20	0.24	0.28	0.33	0.06	0.09	0.13	0.17	0.22	0.27	0.32	0.38	0.27	0.32	0.38	0.38
1.2	0.05	0.08	0.12	0.15	0.19	0.22	0.27	0.31	0.06	0.09	0.12	0.16	0.21	0.25	0.31	0.37	0.25	0.31	0.37	0.37
1.3	0.05	0.08	0.11	0.14	0.18	0.21	0.25	0.29	0.05	0.08	0.12	0.15	0.20	0.24	0.30	0.35	0.24	0.30	0.35	0.35
1.4	0.05	0.08	0.10	0.13	0.17	0.20	0.24	0.28	0.05	0.08	0.11	0.15	0.19	0.23	0.28	0.33	0.23	0.28	0.33	0.33
1.5	0.05	0.07	0.10	0.13	0.16	0.19	0.22	0.26	0.05	0.08	0.11	0.14	0.18	0.22	0.27	0.32	0.22	0.27	0.32	0.32
1.6	0.04	0.07	0.09	0.12	0.15	0.18	0.21	0.25	0.04	0.07	0.10	0.13	0.17	0.21	0.25	0.30	0.21	0.25	0.30	0.30
1.7	0.04	0.06	0.09	0.11	0.14	0.17	0.20	0.23	0.04	0.07	0.09	0.13	0.16	0.20	0.24	0.29	0.20	0.24	0.29	0.29
1.8	0.04	0.06	0.08	0.10	0.13	0.16	0.19	0.22	0.04	0.06	0.09	0.12	0.15	0.19	0.23	0.28	0.19	0.23	0.28	0.28
1.9	0.04	0.06	0.08	0.10	0.12	0.15	0.18	0.21	0.04	0.06	0.08	0.11	0.14	0.18	0.22	0.26	0.18	0.22	0.26	0.26
2.0	0.03	0.05	0.07	0.09	0.11	0.14	0.17	0.20	0.04	0.06	0.08	0.11	0.14	0.17	0.21	0.25	0.17	0.21	0.25	0.25

Table 2

Acquisition parameters of the conducted PRESS ($m=2$) experiments with different combinations of TC , TE and number of slabs.

Parameter	1	2	3	4	5
TC (ms)	630	650	1000	1260	1800
n (slabs)	2	2	1	1	2
TE_1 (ms)	35	35	35	35	35
TE_2 (ms)	260	285	285	260	260