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B_0 inhomogeneity-insensitive triple-quantum-filtered sodium imaging using a 12-step phase-cycling scheme

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Abstract

Triple-quantum-filtered (TQF) sodium MRI can be used to separate sodium NMR signals from different physiological compartments. Although three-pulse triple-quantum filtering has been demonstrated to be better suited for *in vivo* imaging, the absence of the refocusing pulse in the filter increases its sensitivity to magnetic field inhomogeneities. Therefore, several TQF cycles have been developed previously to correct image distortions caused by B_0 inhomogeneities. In this paper, we present a new 12-step phase-cycling TQF scheme based on three radiofrequency pulses which allows the compensation of B_0 variations both with and without ancillary B_0 map information. The method offers 40% higher signal-to-noise-ratio efficiency compared with the previously developed B_0 -correcting phase-cycling schemes.

Keywords

multiple quantum filter; sodium imaging; coherence; inhomogeneity

INTRODUCTION

Several studies (1-6) have demonstrated the potential of triple-quantum techniques for imaging sodium nuclei for which the correlation time is longer than the Larmor period *in vivo*. The conventional implementation of a triple-quantum-filter (TQF) [see, for example, refs. (7,8)] relies on three hard pulses with one additional hard refocusing pulse between the first two (see Fig. 1a). If appropriate phase-cycling procedures (7,8) are performed, the four coherence transfer pathways, contributing to the TQF signal, would add up to produce the highest possible signal-to-noise ratio (SNR). However, the high efficiency of this method may not be achievable in *in vivo* applications at high fields because of the specific absorption rate (SAR) limitations counteracting the gains offered by high signal levels at such fields. In addition, in such implementations of the TQF, transmitted B_1 field inhomogeneities introduce strong modulation in the images obtained which are difficult to correct in post-processing (5,9). Therefore, a three-pulse TQF was used by Hancu *et al.* (5) which does not employ the refocusing pulse (see Fig. 1b). This technique offers a simple B_1

correction in post-processing and reduces significantly the energy deposits in the body/sample associated with filter use, making it an appealing candidate for *in vivo* applications. A disadvantage of this sequence design, however, is its increased sensitivity to B_0 inhomogeneities (8,10,11). The phenomenon manifests itself as a signal loss which arises as a result of destructive interference between the different pathways contributing to the TQ coherence signal in areas with B_0 offsets.

As modern clinical MRI systems cannot provide B_0 homogeneity significantly better than approximately 0.5 p.p.m. *in vivo*, B_0 -correcting methods of TQF sodium imaging are of great interest. One such technique was proposed by Wimperis *et al.* (12) in which only two of four contributing pathways are selected. The method employs three hard radiofrequency (RF) pulses, phase cycling and gradients (see Fig. 1c) for coherence pathway selection. This reduces significantly the sensitivity of the method with respect to B_0 offsets, but also reduces the measured signal and SNR efficiency by a factor of two. A different method to resolve the problem was proposed by Tanase and Boada (11). Their approach is based on the concurrent acquisition of all four signal constituents contributing to the TQ signal and their appropriate recombination in post-processing with an ancillary B_0 map (11). Because 24 steps are needed to complete the TQF phase cycle, the SNR efficiency of this technique is also one-half of that of the conventional method.

The purpose of this work was to introduce a new, high-efficiency, three-RF-pulse, 12-step, phase-cycling method which allows the reconstruction of B_0 -corrected TQF images. The idea behind the new method is to provide the combination of the advantages of the two techniques (11,12). Indeed, most of the damage to the TQF signal as a result of possible B_0 offset occurs during the creation time between the first and second excitation pulses. The method of Wimperis *et al.* (12) solves this problem by dephasing two of the four contributing pathways using a gradient pulse, whereas the technique of Tanase and Boada (11) extracts all four contributing signals and corrects for B_0 in post-processing. Both of these approaches lead to a loss of SNR efficiency. In our method, the signal is split into two pairs of two coherence transfer pathways, and the corresponding B_0 correction is applied to each pair separately. This increases the TQF SNR efficiency by a factor of $\sqrt{2}$ relative to refs. (11,12). In addition, if the SNR is relatively high ($\text{SNR} \gtrsim 10$), the method can produce accurate B_0 -corrected TQF images even without additional B_0 map information.

THEORY

TQF overview

Consider the TQF sequence (5) which consists of three excitation pulses of the same flip angle θ and corresponding phases ϕ_1 , ϕ_2 and ϕ_3 (see Fig. 2) followed by a readout. The delays τ_1 and τ_2 after the first and second pulses allow the creation of higher order coherences and their propagation. The recorded signal consists of contributions from all allowed coherence pathways; therefore, the task of a TQF is to discard the undesired signal components. As every pathway must end at a coherence level of -1 to be observable, each pathway is completely characterised by two numbers p_1 and p_2 representing the levels of coherence after the first two excitations, respectively. Formally, the received signal is [see, for example, refs. (11,14)]:

$$S_{\Omega}(\phi_1, \phi_2, \phi_3, t) = \sum_{p_1=-1}^1 \sum_{p_2=-1}^1 e^{-i(p_1\phi_1 + (p_2-p_1)\phi_2 - (1+p_2)\phi_3)} B_{p_1 p_2} \quad [1]$$

$$B_{p_1 p_2} = e^{-i(p_1 \tau_1 + p_2 \tau_2) \Omega} e^{i \Omega t} A_{p_1 p_2} \quad [2]$$

where $A_{p_1 p_2} = A_{p_1 p_2}(\tau_1, \tau_2, \theta, t)$ is the amplitude of the specified coherence pathway and is a function of the delays τ_1 and τ_2 , flip angle θ and measurement time t . The presence of magnetic field inhomogeneity Ω is described by deviation of the Larmor frequency $\omega_0 = \gamma B_0$ from the frequency of the RF field ω :

$$\Omega = \omega_0 - \omega \quad [3]$$

The maximum signal caused by the presence of order 3 coherence is the sum of $A_{\pm 1 \pm 3}$:

$$S^{\text{TQ}} = A_{+1-3} - A_{-1-3} - A_{-1+3} + A_{+1+3} \quad [4]$$

In the absence of magnetic field inhomogeneities, $\Omega=0$, the maximum signal can be obtained from eqn [1] by a six-step=phase cycle (7,8):

$$\begin{aligned} S^{\text{TQ}} &= \frac{i}{6} \sum_{k=0}^5 (-1)^k S_{\Omega}(\phi_{1;k}, \phi_{2;k}, \phi_{3;k}, t), \\ \phi_{1;k} &= \frac{\pi}{6} + \frac{\pi k}{3}, \quad \phi_{2;k} = \frac{2\pi}{3} + \frac{\pi k}{3}, \quad \phi_{3;k} = 0, \quad k=0, 1, \dots, 5 \end{aligned} \quad [5]$$

Application of the classical filter (7,8) in the presence of magnetic field inhomogeneities, $\Omega \neq 0$, may result in severe signal dropouts. Indeed, substitution of eqn [1] into eqn [5] yields:

$$S_{\Omega; \text{Cl}}^{\text{TQ}} = ([A_{+1-3} - A_{-1-3}] e^{+i3\tau_2 \Omega} + [A_{+1+3} - A_{-1+3}] e^{-i3\tau_2 \Omega}) e^{i \Omega t} \quad [6]$$

and the different terms may annihilate each other when the frequency offset Ω approaches $\pi/6\tau_2 + \pi/3\tau_2 n$, $n = 0, \pm 1, \pm 2, \dots$. In practical terms, this dephasing will not lead to significant signal loss if $\Omega \ll 160$ Hz and $\tau_2 < 500$ μs . These conditions are often satisfied in various applications. It should be noted that these conditions also apply to the modified six-step cycle of Wimperis *et al.* (12) even though contributions from the $-1-2$ (A_{-1-3} term) and $-1+4$ (A_{-1+3} term) pathways have been suppressed.

In contrast, the six-step cycle of Hancu *et al.* (5) is more sensitive to B_0 inhomogeneities (11):

$$\begin{aligned} S_{\Omega}^{\text{TQ}} &= B_{+1-3} - B_{-1-3} - B_{-1+3} + B_{+1+3} = \\ &= (A_{+1-3} e^{-i(\tau_1 - 3\tau_2) \Omega} - A_{-1-3} e^{+i(\tau_1 + 3\tau_2) \Omega} - A_{-1+3} e^{+i(\tau_1 - 3\tau_2) \Omega} + A_{+1+3} e^{-i(\tau_1 + 3\tau_2) \Omega}) e^{i \Omega t} \end{aligned} \quad [7]$$

For example, as has been shown in ref. (11), a combination of $\tau_1 \approx 5$ ms, $\tau_2 \approx 0$ ms and $\Omega \approx 50$ Hz leads to total signal annihilation. Such B_0 sensitivity is not acceptable and a way to rectify this problem was developed in ref. (11). According to the method, the amplitudes $B_{\pm 1 \pm 3}$ are extracted from the measured data (11), phase corrected using a B_0 map, and recombined into eqn [4]:

$$S^{TQ} = (B_{+1-3}e^{+i(\tau_1-3\tau_2)\Omega} - B_{-1-3}e^{-i(\tau_1+3\tau_2)\Omega} - B_{-1+3}e^{-i(\tau_1-3\tau_2)\Omega} + B_{+1+3}e^{+i(\tau_1+3\tau_2)\Omega})e^{-i\Omega t} \quad [8]$$

This method provides the B_0 -corrected TQF signal, but at reduced SNR efficiency (see below).

In the next section, we develop a new B_0 -correcting phase-cycling sequence which offers a $\sqrt{2}$ higher SNR efficiency.

The 12-step cycle

As mentioned earlier, possible dephasing between the coherence pathways as a result of B_0 offset in the conventional TQF (7,8) and modified filter (12) may be considered negligible. This is because, in many practical situations, it is possible to arrange that $\Omega\tau_2 \ll 1$ by setting τ_2 as small as possible. Under these conditions, the expression for the TQF signal of eqn [8] simplifies to:

$$\begin{aligned} S^{TQ} &\approx ([B_{+1-3} + B_{+1+3}]e^{+i\Omega\tau_1} - [B_{-1-3} + B_{-1+3}]e^{-i\Omega\tau_1})e^{-i\Omega t} \\ &= e^{-i\Omega t} \sum_{p_1=\pm 1} p_1 [B_{p_1-3} + B_{p_1+3}]e^{+ip_1\Omega\tau_1} \\ &= \sum_{p_1=\pm 1} p_1 [A_{p_1-3}e^{3i\Omega\tau_2} + A_{p_1+3}e^{-3i\Omega\tau_2}] \end{aligned} \quad [9]$$

Thus, the task of phase cycling is to select the needed combinations ($B_{+1-3} + B_{+1+3}$) and ($B_{-1-3} + B_{-1+3}$). After the selection has been performed, the B_0 correction can be applied to remove destructive interference between the different coherence pathways contributing to the signal. Indeed, this can be achieved in just 12 phase-cycling steps. To demonstrate this, let us introduce a more convenient notation:

$$\xi_1 = (\phi_1 - \phi_2), \quad \xi_2 = (\phi_2 - \phi_3) \quad [10]$$

set $\phi_3 = 0$ and rearrange the terms in eqn [1], so that it becomes:

$$S(\phi_1, \phi_2, \phi_3) = S(\xi_1, \xi_2) = \sum_{p_1=-1}^1 \sum_{p_2=-3}^3 e^{-i(p_1\xi_1 + p_2\xi_2)} B_{p_1 p_2} \quad [11]$$

From eqn [11], it is clear that, by cycling the phases ξ_1 and ξ_2 , the target amplitude combinations ($B_{p_1-3} + B_{p_1+3}$) of eqn [9] can be extracted. A six-step cycle in ξ_2 according to

$\xi_{2,k} = \frac{2\pi k}{6}, k = 0, 1, \dots, 5$, followed by an inverse Fourier transform applied to the collected signals along the cycle index k (13), leads to:

$$C_m(\xi_1) = \frac{1}{6} \sum_{k=0}^5 S(\xi_1, \xi_{2,k}) e^{i\frac{2\pi mk}{6}}, \quad m=0, 1, \dots, 5 \quad [12]$$

The amplitude $C_3(\xi_1)$ is of particular interest and is given by:

$$C_3(\xi_1) = \sum_{p_1=\pm 1} e^{-i\xi_1 p_1} [B_{p_1+3} + B_{p_1-3}] \quad [13]$$

Finally, by cycling the phase ζ_1 according to $\zeta_{1;1} = 0$ and $\zeta_{1;2} = \pi/2$, using eqn [13], it is possible to recover ($B_{+1+3} + B_{+1-3}$) combinations:

$$\begin{aligned} B_{+1+3} + B_{+1-3} &= \frac{1}{2} (C_3(0) + iC_3(\pi/2)) \\ B_{-1+3} + B_{-1-3} &= \frac{1}{2} (C_3(0) - iC_3(\pi/2)) \end{aligned} \quad [14]$$

In summary, all amplitude combinations $B_{\pm 1 \pm 3}$ contributing to the TQF signal can be measured using the above 12-step cycling scheme. After application of the B_0 correction, the appropriate TQF signal can be recovered using eqn [9].

Consequently, the acquisition of B_0 -corrected TQF data would consist of a B_0 mapping acquisition followed by a 12-step phase cycle. The cycle would consist of 2×6 nested acquisitions with the following phase-cycling rules:

1. Acquire signals with $\phi_{1;k} = 0 + \frac{2\pi k}{6}$, $\phi_{2;k} = \frac{2\pi k}{6}$, $\phi_{3;k} = 0$ for $k = 0, 1, \dots, 5$.
2. Acquire signals with $\phi_{1;k} = \frac{\pi}{2} + \frac{2\pi k}{6}$, $\phi_{2;k} = \frac{2\pi k}{6}$, $\phi_{3;k} = 0$ for $k = 0, 1, \dots, 5$.

The processing of the acquired data would consist of the application of one-dimensional Fourier transformation to the 2×6 dataset along the larger phase-cycle index and appropriate recombination of the amplitudes obtained (9,14).

Validity of the approximation

Comparing eqns [6] and [9], it becomes apparent that the sensitivity of the 12-step TQF cycle developed above to the B_0 inhomogeneities is identical to that of the classical SAR-intensive six-step TQF cycle with the 180° refocusing pulse (7,8) and that of the modified less SNR-efficient cycle (12). To investigate the validity of the $\Omega\tau_2 \ll 1$ approximation used in eqns [6] and [9], we recall that, up to a normalisation constant, the amplitudes $A_{\pm 1 \pm 3}$ are given by [see, for example, ref. (11)]:

$$\begin{pmatrix} A_{-1-3} \\ A_{-1+3} \\ A_{+1-3} \\ A_{+1+3} \end{pmatrix} = \left(e^{-t/T_s} - e^{-t/T_f} \right) \left(e^{-\tau_1/T_s} - e^{-\tau_1/T_f} \right) e^{-\tau_2/T_s} \times \sin^5(\theta) \cdot \begin{pmatrix} -\sin^2(\theta/2) \cos^2(\theta/2) \\ -\sin^2(\theta/2) \cos^2(\theta/2) \\ \cos^4(\theta/2) \\ \sin^4(\theta/2) \end{pmatrix} \quad [15]$$

where T_f and T_s are the fast and slow relaxation times. Therefore, up to a normalisation constant, the true TQF signal of eqn [4] is:

$$S^{\text{TQ}} = \left(e^{-t/T_s} - e^{-t/T_f} \right) \left(e^{-\tau_1/T_s} - e^{-\tau_1/T_f} \right) e^{-\tau_2/T_s} \cdot \sin^5(\theta) \quad [16]$$

Instead, from eqns (15), (2) and (9), the approximate TQF signal becomes:

$$\begin{aligned}
S^{\text{TQ}} &\approx e^{-i\Omega t} \sum_{p_1=\pm 1} p_1 \left[B_{p_1-3} + B_{p_1+3} \right] e^{+ip_1\Omega\tau_1} \\
&= \left(e^{-t/T_s} - e^{-t/T_i} \right) \left(e^{-\tau_1/T_s} - e^{-\tau_1/T_i} \right) e^{-\tau_2/T_s} \times \sin^5(\theta) \cdot (\cos(3\Omega\tau_2) + i \cos(\theta) \sin(3\Omega\tau_2))
\end{aligned} \quad [17]$$

It can be seen from eqns [16] and [17] that, under the condition of $\Omega\tau_2 \ll 1$, the approximated signal is virtually identical to the true signal. More specifically, appreciable deviation of the approximated signal from the true signal will occur only when the flip angle θ approaches $\pi/2$ and the frequency offset Ω approaches $\pi/6\tau_2$ simultaneously. In practical terms, neglecting the signal evolution under frequency offset Ω during the evolution time τ_2 will not lead to significant signal loss if $\Omega \ll 160$ Hz and $\tau_2 < 500$ μ s. It should be noted that these conditions are much more favourable relative to $\Omega < 50$ Hz needed for correct operation of the six-step cycle (5) [see eqn [7] and the discussion after it]. This possible partial dephasing between the coherence pathways is not unique to the proposed method. As mentioned earlier, the same dephasing occurs in the conventional TQF (7,8) and in the modified filter (12) as a result of the absence of B_0 stabilisation during the propagation time τ_2 . Because $\Omega\tau_2 \ll 1$ can be arranged in many practical situations, this possible dephasing is ignored.

B_0 correction without an ancillary B_0 map

Although, in spectroscopic applications, it is important to keep the signal in a complex form, MRI mostly relies on magnitude reconstruction. It is feasible to perform magnitude reconstruction directly by replacing the TQF image created from equations [2], [4] and [9] with:

$$\begin{aligned}
|S^{\text{TQ}}| &= |A_{+1-3} - A_{-1-3} - A_{-1+3} + A_{+1+3}| \\
&= |A_{+1-3} + A_{+1+3}| + |A_{-1-3} + A_{-1+3}| \\
&\approx |B_{+1-3} + B_{+1+3}| + |B_{-1-3} + B_{-1+3}|
\end{aligned} \quad [18]$$

and dependence of the TQF signal on the magnetic field offset Ω vanishes. Here, we have used the fact that amplitudes $A_{+1\pm 3}$ are real-valued and positive, whereas amplitudes $A_{-1\pm 3}$ are real-valued and negative [see eqn [15]], and enter into the signal equation with opposite signs [see, for example, ref. (11)]. The approximation in eqn [18] is due to eqn [9].

Therefore, it is evident that B_0 -corrected magnitude TQF images can be reconstructed correctly in the presence of B_0 inhomogeneities without a knowledge of the B_0 distribution.

SNR analysis

As eqn [9] is relatively simple, and as noise in the NMR receiver may be considered Gaussian with a standard deviation σ_0 (15,16), SNR analysis can be performed analytically. As shown in the Appendix, the SNR in such a measurement is:

$$\text{SNR}_{12} = \frac{S^{\text{TQ}}}{\sigma_0} \sqrt{6}$$

For comparison with other TQF techniques, it is convenient to introduce the SNR efficiency or SNR per unit time $\varepsilon = \text{SNR} \sqrt{N}$, where N is the number of phase-cycle steps (17). As the described method requires 12 steps, the SNR efficiency is:

$$\epsilon_{12} = \frac{\text{SNR}_{12}}{\sqrt{12}} = \frac{S^{\text{TQ}}}{\sigma_0 \sqrt{2}}$$

A similar analysis can be performed for the 24-step TQF acquisition scheme. From eqn [27] of ref. (11), it can be seen that

$$\text{SNR}_{24} = \frac{S^{\text{TQ}}}{\sigma_0} \sqrt{6}$$

and the SNR efficiency for this method is:

$$\epsilon_{24} = \frac{\text{SNR}_{24}}{\sqrt{24}} = \frac{S^{\text{TQ}}}{2\sigma_0}$$

The assessment of the SNR efficiency ϵ_6 of the six-step cycle described in ref. (12) reveals that this technique has the same SNR efficiency as the 24-step cycle of Tanase and Boada (11). The rationale for this SNR penalty is that the signal from two of the four contributing pathways is rejected by the pathway selection rules (12).

Thus, the method developed here provides a $\sqrt{2}$ higher SNR efficiency compared with the previously described methods (11,12). It is important to note that this SNR improvement is independent of the B_0 offset only within the limits of applicability of the approximation used. For high magnetic field offsets, destructive interference between contributing pathways will reduce the achievable SNR, as shown in eqn [17].

Experimental verification of the SNR efficiency differences between the 12-step and 24-step TQF methods can be performed by studying the noise in the image backgrounds, as the mean value in the image background outside of the object is proportional to the noise level (15,16). Therefore, the ratio of these means, corrected for acquisition duration, will provide the ratio of the SNR efficiencies of the two methods. In other words, if η_{24} and η_{12} are the mean noise levels observed in the 24- and 12-step cycles, respectively, the experimental ratio of the efficiencies $\epsilon_{12}/\epsilon_{24}$ is:

$$\frac{\epsilon_{12}}{\epsilon_{24}} = \frac{\eta_{24}}{\eta_{12}} \sqrt{\frac{24N_{24}}{12N_{12}}} \quad [19]$$

where N_{24} and N_{12} are the number of averages used for 24- and 12-step cycles, respectively.

Considering that η_{24} and η_{12} are subject to measurement noise themselves, the SNR efficiency ratio [eqn [19]] may differ from the theoretically predicted value of $\sqrt{2}$ by chance. This random deviation can be evaluated by comparing the SNR efficiency ratios from different slices in the three-dimensional volume. In practical terms, the single-quantum images can be used to select regions outside of the imaged object on the TQF images, and the mean noise levels in the TQF data can be evaluated in each slice independently. As there are no slice-to-slice noise correlations in Fourier-encoded data, noise measurements from each slice may be treated as noise measurements from independent experiments, providing the TQF noise level error estimate.

A special remark should be made about the noise level in the magnitude reconstruction of eqn [18]. Because each of the measured quantities B_{p1p2} is subject to random Gaussian noise with $\sigma = \sigma_0 / \sqrt{12}$, the magnitudes $|B_{p1p2}|$ come from a Rician distribution with parameters B_{p1p2} and $\sigma_0 / \sqrt{12}$ [see, for example, refs. (15,16)]. Hence, a loss of precision and accuracy may occur in the areas of small SNR (such as regions outside of the imaged sample). Fortunately, the Rician distribution approaches the Gaussian distribution quite rapidly when SNR in the data increases. As shown in refs. (15,16), the difference between the Rician and Gaussian distributions can be neglected for SNR levels above about 10. Thus, the B_0 -corrected magnitude TQF image can be reconstructed without any knowledge of the B_0 distribution and without loss in accuracy and precision when $\text{SNR} \gtrsim 10$.

EXPERIMENTAL

The MRI experiments were performed on a whole-body MAGNETOM 3T Tim Trio scanner (Siemens AG, Erlangen, Germany) with a custom-built, dual-tuned, transmit-receive proton-sodium head coil (Stark Contrast, Erlangen, Germany) and a modified gradient echo sequence (see Fig. 2). The RF excitation train comprised three nonselective pulses, each of 500 μs in duration.

For the purposes of B_0 mapping, two single-quantum gradient echo images with a TE difference of 2.0 ms were acquired without changes in other acquisition parameters. The offset frequency Ω was obtained from the phase difference of the two images on a voxel-by-voxel basis. Phase unwrapping was not necessary because frequency offsets were smaller than the 500 Hz bandwidth of this measurement.

To demonstrate the utility of the method, three cylindrical phantoms were used. The larger 2 L bottle was filled with 90 mmol/L saline. The two smaller 250 mL bottles were filled with 4% agar gel and contained 100 and 140 mmol/L sodium concentrations. It is known that third-order coherences are produced in such gels (18,19).

Acquisition parameters for TQF imaging were as follows: $240 \times 240 \times 240 \text{ mm}^3$ field of view with $16 \times 16 \times 16$ encoding matrix, TR = 165 ms, TE = 6.6 ms, flip angle, 90° ; $\tau_1 = 5.5 \text{ ms}$; $\tau_2 = 150 \mu\text{s}$. The acquisition parameters were optimised to produce the highest TQF signal. The images were acquired both with a 24-step cycle of ref. (11) and with the 12-step phase cycle as described here without averaging. The experiments took about 25 min providing an SNR of about 20.

B_0 mapping was performed with single-quantum sodium imaging at TE = 6.6 ms and TE = 8.6 ms, TR = 61 ms using the same field of view and spatial resolution.

RESULTS

Figure 3a depicts a single-quantum sodium image of the phantom arrangement, and Fig. 3b presents the B_0 field distribution in the same slice. The large bottle contains saline, whereas the two small bottles contain agar gel with sodium. TQF images of the same slice are presented in Fig. 4. Images in Fig. 4a and 4b demonstrate TQF reconstruction with the use of the B_0 map and the magnitude-based correction, respectively. Both of these images are quite similar and are robust against existing B_0 inhomogeneities (see Fig. 3b). For comparison, a B_0 -uncorrected TQF image is shown in Fig. 4c, revealing strong signal dropouts in the areas of magnetic field offset. Based on the acquisition parameters (see Theory and Experimental sections), the areas with field offsets of $\Omega \approx 45 + 91n \text{ (Hz)}$, $n = 0, 1, 2, \dots$ should show significant signal loss, whereas areas with $\Omega \approx 0 + 91n \text{ (Hz)}$, $n = 0, \pm 1, \pm 2, \dots$ should not show any effect. This theoretical result is confirmed by comparing the

TQF images of Fig. 4 with the B_0 map of Fig. 3b. Signal dropouts caused by B_0 offset are clearly visible, and the image artefacts caused by B_0 inhomogeneities and offsets are largely removed after B_0 correction has been applied. Finally, in Fig. 4d, the same slice acquired with a B_0 -corrected, 24-step phase cycle is shown. In Fig. 5, one-dimensional sections through the centres of the agar gel phantoms are superposed to illustrate the differences between the B_0 correction methods. It should be noted that, even though the two gel phantoms were prepared with a 1.4 ratio in sodium concentrations, the single-quantum images (see Fig. 3a) show only a 1.27 ± 0.06 ratio. This approximately 10% deviation from the nominal value could be attributed to spatial B_0 and B_1 variations. In addition, as the two agar gels were produced independently, different amounts of air microbubbles could have formed in the two phantoms causing additional differences in the phantom image intensities via different T_2^* properties. Such effects may also be responsible for spurious image intensity inhomogeneities observed in single- and triple-quantum images. Regardless of the cause of the effect, properly reconstructed TQF images should show the same signal ratio as the single-quantum images. Indeed, B_0 -corrected 12-step TQF images reveal a 1.21 ± 0.08 ratio between the signals from the two gel phantoms (see Figs 4 and 5), and confirm quantitatively that appropriate scaling in the TQF images is preserved. The measured SNR efficiency ratio between the 12-step and 24-step methods (19) was $\varepsilon_{12}/\varepsilon_{24} = 1.47 \pm 0.08$, which is in good agreement with the theoretically predicted value of $\sqrt{2}$.

DISCUSSION

Because modern clinical scanners cannot provide B_0 homogeneity significantly better than several decahertz, some steps need to be taken to counteract the dephasing between the TQF pathways. There are several known ways to achieve this goal. The conventional-type TQF [see, for example, refs. (7,8)] employs a 180° refocusing pulse which significantly increases SAR requirements and may not be acceptable in clinical settings. For example, in our system, as a result of SAR constraints, the TQF with the refocusing pulse would require a minimum TR of 385 ms, whereas the three-pulse filter was operated at TR = 165 ms (see Experimental). In addition, a nonideal refocusing pulse may produce undesired higher order coherences (5,20) necessitating phase cycling of the refocusing pulse in order to select the desired pathways. This can be accomplished using, for example, an ‘exorcycle’ (21), but it would further increase the required time per volume. Selection of a single pathway using, for example, phase-cycling (13), cogwheel phase-cycling (22,23) or pulsed-gradient (24,25) methods would resolve the problem completely. Although these methods offer effective protection against B_0 inhomogeneities, they generally are associated with low SNR efficiency and/or a long imaging time.

The matter is further complicated by the fact that the B_0 stability of the method may depend on the selected acquisition parameters. The optimal choice of parameters is often governed by the tissue properties (26), providing unwelcome coupling between the tissue and the robustness of the technique against B_0 inhomogeneities. In other words, generally, one may not arbitrarily set the creation time τ_1 to a small value in an attempt to improve the B_0 stability of the method without severe SNR penalty.

The new TQF imaging method developed here is robust against B_0 inhomogeneities and removes the undesired interaction between the tissue properties and B_0 sensitivity. We showed that the stability of the new method against B_0 inhomogeneities is the same as that of the classical SAR-intense TQF with a refocusing pulse (7,8) and that of the modified less SNR-efficient cycle (12). In addition, the technique offers a $\sqrt{2}$ increase in SNR efficiency compared with the previous B_0 correction methods (11,12). This is an important improvement, as the 12-step cycle allows two-fold shorter acquisition of the B_0 -corrected TQF images with the same SNR as the 24-step cycle.

CONCLUSIONS

We have described a new 12-step phase-cycling scheme which allows the acquisition and reconstruction of the TQ coherences in the presence of magnetic field inhomogeneities. We have compared the performance of the proposed method with the currently available techniques theoretically and experimentally. We have shown that this method offers an increase in SNR efficiency by 40% compared with the previous methods (11,12). If SNR is relatively high ($\text{SNR} \gtrsim 10$), accurate B_0 -corrected magnitude images can be produced without a B_0 map and without any loss in precision.

NOTE ADDED IN REVIEW

During the review of the manuscript, a paper by Matthies *et al.* (27) on the same subject appeared in the *Journal of Magnetic Resonance*. Compared with this reference, our approach is more general, as it outlines the advantages of the method theoretically and offers the analysis of the approximations used. In addition, both complex and magnitude reconstructions are described with their advantages and disadvantages. An analysis of the signal and the approximation quality on the flip angle is also provided in this work.

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APPENDIX

Noise calculation

For noise analysis, it is convenient to simplify the expression for the recovered TQF signal [eqn [9]]. For this purpose, we combine the expressions in eqns [12] and [14] into:

$$B_{p_1+3} + B_{p_1-3} = \frac{1}{12} \sum_{k=0}^5 (-1)^k [S(0, \xi_{2,k}) + ip_1 S(\pi/2, \xi_{2,k})], p_1 \pm 1 \quad [20]$$

Then, eqn [9] becomes:

$$S^{\text{TQ}} = \frac{1}{12} e^{-i\Omega\tau} \sum_{k=0}^5 \sum_{p_1=\pm 1} (-1)^k [p_1 S(0, \xi_{2,k}) + iS(\pi/2, \xi_{2,k})] e^{ip_1\Omega\tau_1} \quad [21]$$

And, after summation over p_1 , we obtain:

$$S^{\text{TQ}} = \frac{i}{6} e^{-i\Omega\tau} \sum_{k=0}^5 (-1)^k \{S(\pi/2, \xi_{2,k}) \cos(\Omega\tau_1) + S(0, \xi_{2,k}) \sin(\Omega\tau_1)\} \quad [22]$$

As all measurements $S(\xi_1, \xi_2)$ are subject to measurement noise with standard deviation σ_0 , following the propagation of errors technique (28), we obtain an estimate of noise in the TQF signal (9,22):

$$\begin{aligned} \sigma^2(S^{\text{TQ}}) &= \frac{1}{36} \sum_{k=0}^5 \{\sigma_0^2 \cos^2(\Omega\tau_1) + \sigma_0^2 \sin^2(\Omega\tau_1)\} = \\ &= \frac{1}{6} \sigma_0^2 \end{aligned} \quad [23]$$

Because the normalisation factors have been tracked throughout the calculation, direct substitution of the signal from eqn [1] into eqn [22] will lead to eqn [4] without any extra normalisation needed. This greatly simplifies the SNR analysis, and the SNR in the recorded TQF signal (9,23) is:

$$\text{SNR}_{12} = \frac{S^{\text{TQ}}}{\sigma_0} \sqrt{6} \quad [24]$$

Abbreviations used

RF	radiofrequency
SAR	specific absorption rate
SNR	signal-to-noise ratio
TQF	triple-quantum-filtered/filter

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Figure 1.

Pulse sequences and coherence transfer pathway diagrams (13) for triple-quantum filtration. (a) Version of the triple-quantum-filtered (TQF) technique of refs. (7,8). The sequence employs a 180° refocusing pulse which provides B_0 stability at a cost of increased specific absorption rate (SAR) requirements. The TQF (b) of refs. (5,11) does not have a refocusing pulse and the B_0 stability is provided by special phase-cycling and post-processing (11). The TQF method (c) of ref. (12) provides B_0 stability by dephasing two of the four contributing pathways with a gradient pulse.

Figure 2.

Schematic diagram of the triple-quantum-filter (TQF) excitation block superposed with TQF signal evolution and imaging readout. As a result of delayed peak formation and slow signal decay, a Cartesian gradient echo readout is well suited for sodium TQF imaging.

Figure 3.

(a) A single-quantum sodium image of an axial section of the phantom set-up. Small bottles contain 4% agar gel with sodium, and the large bottle contains saline. (b) B_0 map of the same slice. The field gradients cause minor intravoxel dephasing on single-quantum images, but major signal dropout on triple-quantum images (see Fig. 4).

Figure 4.

Triple-quantum-filtered (TQF) image produced by the 12-step cycle after B_0 correction (a) and after magnitude B_0 correction (b). B_0 -uncorrected TQF image (c) reveals signal dropouts in the areas of magnetic field offsets. For comparison, the TQF image produced with a 24-step cycle is presented in (d).

Figure 5. One-dimensional profile through the centre of the agar phantoms for 12-step triple-quantum-filtered (TQF) images (a) and comparison between 12-step and 24-step methods (b).