Optimizing Simultaneously Acquired Single- and Triple-Quantum Imaging with Time Proportional Phase Increment for ^{23}Na and ^{35}Cl

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Target: Researchers interested in multi-quantum imaging techniques and/or ^{23}Na and ^{35}Cl NMR

Purpose: Multi-quantum filtered imaging methods utilize the spin-3/2 characteristic of ^{23}Na and ^{35}Cl to produce multi-quantum coherences. Such coherences reflect on the binding of the corresponding ions to macromolecules depending on molecular environments and metabolic processes. Conventional triple-quantum filtered sequences are restrained by low triple-quantum (TQ) signal due to the single-quantum (SQ) coherence being discarded. For the attempt to track disease progression on a molecular level, the combined information of the TQ/SQ progression is especially valuable and could lead to a deeper understanding of metabolic processes in healthy and diseased tissue.
One method to concurrently acquire SQ and TQ signal and without SQ filtration uses time proportional phase increments (TPPI). We combined the TPPI pulse train and density-adapted projection reconstruction (DA-PR) and developed the DA-PR-TPPI spectroscopic imaging sequence. The aim of this work was to establish and optimize the DA-PR-TPPI method for both ^{23}Na and ^{35}Cl.

Figure 1: Sequence diagram of DA-2DPR-TPPI

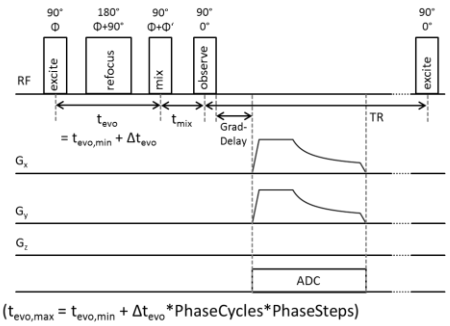

Figure 1: *Sequence diagram of DA-2DPR-TPPI with pseudo-2D readout. The t_{evo}-FID is sampled by incrementing t_{evo} with Δt_{evo}. Fourier Transform of t_{evo}-FID yields the spectrum containing SQ and TQ frequency.*

Materials/Methods: Experiments were performed on a 9.4 T preclinical MR system (BioSpec, Bruker, Germany). ^{23}Na experiments: A Bruker ^{1}H/^{23}Na volume coil was used to scan three 50 ml vials with 134.75 mM NaCl and 2/4/6 % agarose. ^{35}Cl experiments: A custom-made ^{35}Cl saddle surface coil was used to scan two 2 ml vials with 50 mM NaCl and 2/4 % agarose.
For all experiments, pseudo-2D readout (**Figure 1**) was used. SQ and TQ images were obtained by performing Fourier Transform along the SQ and TQ frequency of the spectrum, respectively. Two sets of experiments were conducted:
(I) ^{23}Na: To overcome low signal, t_{scan} has to be spent on either averaging t-FID in t-domain or finer sampling of t_{evo}-FID in t_{evo}-domain. The latter is realized by shorter Δt_{evo} and more phase cycles. Combinations of Δt_{evo} and phase cycles were tested in phantoms. The following parameters were set: TR = 150 ms, t_{scan} = 11 min - 4.5 h, averages = 1, bandwidth 25 kHz, t_{acq} = 8 ms, spokes = 70, resolution = (3x3) mm^2, GradDelay = 10 ms, phase steps = 8, Δt_{evo} = 150/300 µs, phase cycles = 4-64.
(II) ^{23}Na and ^{35}Cl: Binding times to macromolecules are widely distributed in vivo, and a proper choice of GradDelay (delay between the observation pulse and the start of the gradient) ensures that triple-quantum signal (TQS) is acquired in the right window. An optimal GradDelay to achieve overall high TQS while maintaining high TQS contrast among phantoms mimicking different binding environments was determined with the following parameters for ^{23}Na/^{35}Cl: TR = 100/80 ms, t_{scan} = 1.4/2 h, averages = 1/16, bandwidth 25/25 kHz, t_{acq} = 8/8 ms, spokes = 70/50, resolution = (3x3)/(2.5x2.5) mm^2, GradDelay = 1-19/1-25 ms, phase steps = 8, Δt_{evo} = 300/650 µs, phase cycles = 32/6.

Figure 2: Na SQ and TQ agarose phantom images

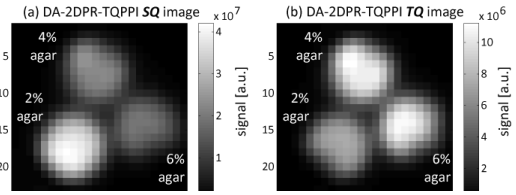

Figure 2: *^{23}Na (a) SQ and (b) TQ phantom image. TQS values are generally lower than SQS values. As expected, SQS decreases and TQS increases with increasing agarose concentration.*

Results/Discussion: ^{23}Na DA-2DPR-TPPI SQ and TQ phantom images (**Figure 2**) confirm that single-quantum signal (SQS) decreases and that TQS increases with increasing agarose concentration.
(I) ^{23}Na SQS and TQS (**Figure 3**) with different combinations of Δt_{evo} and number of phase cycles reveal that for the same $t_{evo,max}$, a 2-fold increase in sampling fineness (Δt_{evo}/2, PhaseCycles*2 and t_{scan}*2) results in a 2-fold SQS and TQS increase. Furthermore, incomplete t_{evo}-FID sampling (small $t_{evo,max}$) leads to signal loss.
(II) For both ^{23}Na (**Figure 4a**) and ^{35}Cl (**Figure 4b**), an increase in GradDelay is observed to be accompanied with an increase in SQS, while TQS reaches a maximum at a value depending on the agarose concentration and the nucleus. For ^{23}Na, evaluation yielded a GradDelay of 8-10 ms for high TQS and optimal contrast among different agarose environments. In agreement with expectation, TQS in phantoms with higher agarose concentration reaches its maximum at a smaller GradDelay. For ^{35}Cl, measurements were restricted by smaller vials and lower physical NMR sensitivity compared with ^{23}Na, resulting in a higher noise level. Nevertheless, Figure 4b confirms the tendency that TQS maximum is reached at a smaller GradDelay value for the phantom with higher agarose concentration. The optimal range of GradDelay (5-15 ms) for ^{35}Cl can be determined more accurately in future experiments.

Figure 3

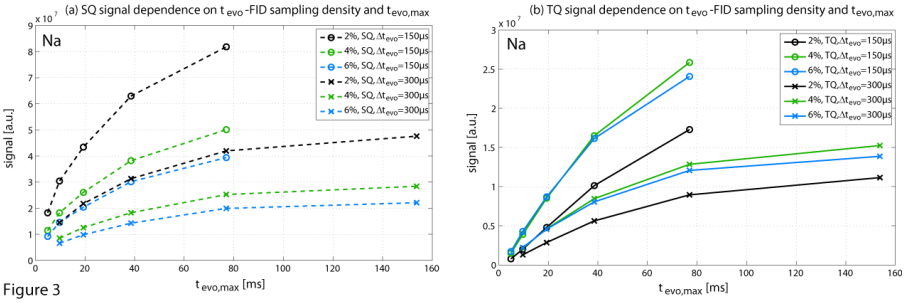

Figure 3: *Results of (I) with (a) SQ and (b) TQ signals with different combinations of Δt_{evo} and phase cylces over $t_{evo,max}$. Incomplete sampling of t_{evo}-FID results in SQS and TQS loss. For constant $t_{evo,max}$, sampling with finer Δt_{evo} and higher number of phase cycles leads to a signal increase by a factor proportional to t_{scan} increase.*

Figure 4

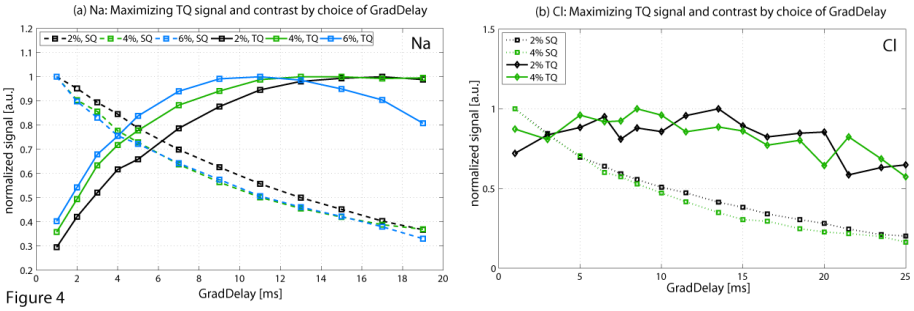

Figure 4: *Normalized (a) ^{23}Na and (b) ^{35}Cl signal courses of (II) with varying GradDelay was determined such that TQS contrast amongst different environments was maximized while keeping TQS as high as possible.*

Conclusion: A simultaneously acquired SQ and TQ spectroscopic imaging method with TPPI was successfully applied to ^{23}Na and ^{35}Cl phantom studies. The optimal delay between the observation pulse and signal acquisition to maximize TQS contrast among environments emulating different binding strength to macromolecules was determined. The sequence optimization undertaken in this study helps paving the road to in vivo studies using animals models, ultimately leading to a better understanding of the involvement of 3/2-spin nuclei in diseases on a physiological level.