# Which pulse sequence is optimal for myo-Inositol detection at 3T?

**I. Hancu**[1]
[1]GE Global Research Center, Niskayuna, NY, United States

## Introduction

Myo-inositol (mI) is a cyclic sugar alcohol found in the brain. Although its concentration is high (up to 8mM), repeatable measurements of its concentration are difficult. Multiple acquisition strategies were proposed in the past to increase the reproducibility of mI measurements. These strategies either selectively boost the mI signal (usually by reducing mI signal evolution under J coupling), or selectively reduce the overlapping, background resonances. While all such strategies have compelling arguments in their favor, they also have flaws. It is difficult to increase the mI signal without also increasing the signal of the overlapping resonances; it is also difficult to decrease the background signal without also decreasing the mI signal to low levels. It is therefore not immediately straightforward to decide which of the proposed approaches yields the most accurate and reproducible mI measurements. Monte Carlo simulations are presented here for a number of pulse sequences to decide which approach results in improved repeatability and accuracy of mI measurements. Pulse sequences considered include a TE=35ms PRESS pulse sequence (defined as the clinical standard), a very short TE PRESS pulse sequence [1], a Carr-Purcell echo train (CPRESS) [2], an optimized STEAM sequence [3], a zero quantum filter (ZQF) [4] and a single quantum filter (SQF) [5], whose timings were numerically optimized in this work for improved mI detection. Simulation results, validated *in vivo*, showed that a CPRESS sequence offers the most reliable mI measurements at 3T.

## Methods

The response of the 14 most important brain metabolites to a number of pulse sequences was individually computed using the GAMMA libraries. These 14 spectra, weighted according to their reported in vivo concentration, together with simulated residual water and macromolecule signals were added together to simulate a human brain. Noise was then added to the resulting "brain" signal, and the data was fit using LCModel. The process was repeated 1000 times for each pulse sequence, while using different noise seeds; the resulting fitted mI concentration was saved for each run. Two separate noise levels were considered in our simulations: one corresponding to a standard clinical acquisition (a 5 min acquisition from a 8cc voxel) and the second one corresponding to double the signal to noise (SNR) of the standard clinical acquisition.

## Results

Tables 1 and 2 present a measure of repeatability (the coefficient of variation expressed as a percentage, %CV) and accuracy (defined as the average measured concentration minus the known input concentration divided by the known input concentration) for (mI+Gly) and mI levels, for all ten pulse sequences considered at the clinical SNR level (Table 1) and twice the clinical SNR level (Table 2). CPRESS 2, 4 and 6 represent CPRESS pulse sequences with 2, 4 and 6 refocusing pulses. The Cramer Rao Lower Bounds (CRLB's) are also included the tables. N/A was displayed when insufficient SNR existed for proper spectral quantification. Consistent with previous literature reports, the two tables show that increased measurement repeatability is associated with increased SNR. These tables also show that the mI and Gly signals are not distinguishable from each other, unless a multiple quantum filter (MQF) is used to remove the Gly signal. The MQF's, however, reduce the undesired, background signals, but they also reduce the mI signal to low or very low levels. Among the variants, the optimized SQF appears the better choice for uncontaminated mI detection. Unless strong evidence exists that in a certain disease when mI signal is known to change, Gly is also changing, much more accurate detection of mI + Gly is possible. According to Tables 1 and 2, it was decided that, at a clinical SNR level, a CPRESS sequence offers the best compromise between measurement repeatability and accuracy, at least in the case when the compromise of measuring the (mI+Gly) levels is acceptable. The improvement in repeatability over a PRESS, TE=35ms sequence is statistically significant for CPRESS. This sequence, with 2 additional refocusing pulses (TE=45ms), was implemented in a 3T clinical scanner. Three volunteers were scanned 3 times each using this sequence. The average CRLB's from our small pool of measurement in human volunteers are 5% for the TE=45ms, CPRESS sequence, and 6.2% for the TE=35ms PRESS sequence, confirming the improvement in measurement repeatability predicted by our simulations.

| Pulse Sequence | % CV (mI+Gly) | CRLB's [%] | absolute error (mI+Gly) [%] | % CV mI | CRLB's [%] | absolute error mI [%] |
|---|---|---|---|---|---|---|
| **PRESS** | | | | | | |
| TE=35ms | 4.6% | 6.1% | -0.6% | 13.9% | 19.3% | -19.3% |
| TE=15ms | 4.2% | 5.1% | 1.2% | 8.3% | 10.9% | -4.6% |
| **Carr Purcell echo train** | | | | | | |
| CPRESS 2 (TE=45ms) | 3.3% | 4.3% | 2.8% | 8.4% | 11.7% | -3.2% |
| CPRESS 4 (TE=67ms) | 3.0% | 4.1% | 5.8% | 4.9% | 6.9% | 14.2% |
| CPRESS 6 (TE=89ms) | 3.8% | 5.1% | 4.5% | 5.8% | 8.4% | 12.8% |
| **STEAM** | | | | | | |
| TE/TM=5/5ms | 6.8% | 8.4% | 1.8% | 17.6% | 24.2% | -25.5% |
| TE/TM=180/40ms | N/A | N/A | N/A | N/A | N/A | N/A |
| **Zero Quantum Filter** | | | | | | |
| TE1/TE2/TE3=50/9/30ms (maximum mI signal) | | | | 8.5% | 8.9% | ~9% |
| TE1/TE2/TE3=75/9/30ms (optimized mI/background ratio) | | | | N/A | N/A | N/A |
| **Single Quantum Filter** | | | | | | |
| SQF, TE=90ms | | | | 6.9% | 7.5% | ~10% |

**Table 1:** Simulations results at the clinical SNR level.

| Pulse Sequence | % CV (mI+Gly) | CRLB's [%] | absolute error (mI+Gly) [%] | % CV mI | CRLB's [%] | absolute error mI [%] |
|---|---|---|---|---|---|---|
| **PRESS** | | | | | | |
| TE=35ms | 2.6% | 3.9% | 1.0% | 6.8% | 9.5% | -6.5% |
| TE=15ms | 2.2% | 3.1% | -3.7% | 4.1% | 6.4% | -2.1% |
| **Car Purcell echo train** | | | | | | |
| CPRESS2 (TE=45ms) | 1.9% | 3.0% | 1.8% | 4.6% | 6.9% | 6.1% |
| CPRESS4 (TE=67ms) | 1.9% | 2.6% | 4.4% | 2.7% | 4.0% | 13.7% |
| CPRESS6 (TE=89ms) | 2.3% | 3.0% | 3.8% | 3.2% | 4.5% | 13.1% |
| **STEAM** | | | | | | |
| TE/TM=5/5ms | 4.4% | 5.1% | -0.6% | 8.8% | 12.1% | -17.1% |
| TE/TM=180/40ms | 26.8% | 31.0% | -37.0% | N/A | N/A | N/A |
| **Zero Quantum Filter** | | | | | | |
| TE1/TE2/TE3=50/9/30ms (maximum mI signal) | | | | 4.4% | 5.0% | ~10% |
| TE1/TE2/TE3=75/9/30ms (optimized mI/background ratio) | | | | 11.5% | 12.1% | ~15% |
| **Single Quantum Filter** | | | | | | |
| SQ, TE=90ms | | | | 3.6% | 4.0% | ~10% |

**Table 2:** Simulation results at twice the clinical SNR level.

## Discussion and conclusions

Simulations are presented to decide which pulse sequence has the most significant advantage in terms of improving repeatability and accuracy of mI measurements at 3T. Five classes of pulse sequences, 4 previously suggested for optimized mI detection (a short TE PRESS, a CPRESS sequence, a STEAM sequence, and an optimized ZQF), and one optimized for mI detection in this work (a SQF) were compared to a standard PRESS TE=35ms pulse sequence. The results of the simulations, indicating more repeatable mI measurements with a Carr-Purcell sequence, were validated *in vivo*.

## References

**1.** Zhong et al, Magn Reson Med, 52:898 (2004); **2.** Hennig et al, Magn Reson Med, 37:816 (1997); **3.** Kim et al, Magn Reson Med, 53:760 (2005); **4.** Kim et al, Magn Reson Med, 51:263 (2004); **5.** Trabesinger et al, J Magn Reson, 145:237 (2000);