Specialty Area: Molecular Imaging

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Highlights

- Overview of state-of-the-art hyperpolarized (HP) pulse sequences
- Discussion of RF excitation, data acquisition, acceleration methods, acquisition timing and image contrast
- Comparison of tradeoffs between acquisition and reconstruction strategies

How to Detect HP Agents: Pulse Sequences

TARGET AUDIENCE: Scientists, engineers, and physicians interested in MRI with hyperpolarized agents.

OUTCOME/OBJECTIVES: To goal of this talk is to describe MR pulse sequence strategies that are specifically tailored to the unique physics, biochemical conversions, and in vivo behavior of hyperpolarized (HP) agents. Participants will be able to understand various pulse sequence strategies and tradeoffs between them in terms of SNR, acquisition time, and robustness.

PURPOSE: Hyperpolarized agents can provide unique information about tissue function by probing metabolism, perfusion, redox state, and more. The unique behavior of these agents, including unrecoverable T1 relaxation, conversion to other compounds with different chemical shifts, and bolus injection dynamics, necessitates specialized MR pulse sequences.

METHODS, RESULTS, & DISCUSSION: HP agent pulse sequences involve specialized strategies for **RF excitation, data acquisition**, and **acquisition timing**. These sequences benefit from **acceleration** and can be combined with specialized **image contrast**.

RF excitation strategies

1. *Variable flip angles*: To efficiently sample the limited, unrecoverable hyperpolarization available, variable flip angles are used to account for magnetization losses from previous RF pulses [1]. These can be designed considering T1 decay and metabolic conversion [2].
2. *Multiband excitation*: When attempting to observe a metabolic product, it is advantageous to minimally perturb the hyperpolarized substrate, particularly in dynamic imaging. Multiband excitation refers to applying different flip angles to different compounds using spectrally-selective RF pulses [3, 4, 5].

Acquisition strategies: (For agents that are not converted into other compounds, such as ^{13}C-urea, ^{13}C-HP001, ^{13}C-tert-butanol, conventional MRI acquisition strategies combined with HP RF excitation strategies are highly efficient.)

1. *MR spectroscopic imaging (MRSI)*: In MRSI, spectral and spatial dimensions are fully resolved. For HP agents, spectral-spatial readout gradients are used to accelerate the acquisition, including echo-planar spectroscopic imaging (EPSI) [6, 7], concentric rings [8, 9], radial spectroscopic imaging [10], and spiral CSI [11]. Of these three, EPSI is the slowest but most robust, rings are faster but still robust, while spiral CSI is the fastest but most sensitive to system imperfections. For the large spectral bandwidths found with some HP agents, an alternating band strategy maybe necessary [12]. Overall MRSI is generally the slowest acquisition strategy but is very flexible and provides the most spectral information.
2. *Chemical shift separation methods*: Images for compounds with known chemical shifts can be created from acquisitions at a few echo times (generally N+1 TEs for N different compounds) [13, 14]. This can be approximated using oversampled spiral trajectories

[15]. Different compound images can also be created by exploiting the chemical shift frequency or EPI phase encoding [16, 17, 18]. These methods are faster than MRSI, but are constrained by the chemical shifts present

3. *Metabolite-specific imaging*: Rapid imaging of compounds with sufficiently large chemical shifts can be performed by using a spectrally-selective excitation of a single compound followed by a fast imaging readout, such as spirals or EPI [19, 20, 21, 22]. This can also be accomplished using the steady-state free precession (SSFP) frequency response [23]. These methods are extremely fast and efficient, and work very well for pyruvate and its metabolic products. They may not be readily applicable to all HP agents, depending on the chemical shifts present.

Acquisition Timing: Data can be either as a dynamic time series or from a single time-point. Single time-point acquisition has an SNR advantage because all the available magnetization is devoted to one acquisition. Dynamic acquisitions allow for measurement of conversion and relaxation rates, monitoring perfusion, and are less sensitive to injection and acquisition timing, but have less SNR. [4, 5, 24, 25, 26, 27, 28] Another consideration in the acquisition timing is calibration. Rapid B1 mapping sequences have been applied to HP agents for calibration prior to imaging acquisition [29, 30].

Acceleration methods: HP pulse sequences benefit significantly from accelerated imaging methods. Unlike conventional MRI, there is no SNR penalty because the variable flip angles can be adjusted to redistribute the available magnetization. Furthermore, signal loss and blurring due to T1 relaxation, metabolic conversion, motion, and flow during the acquisition is reduced during a shorter acquisition.

1. *Parallel imaging* has been successfully applied for HP agents when appropriate coil arrays are available [31, 32, 33]. Autocalibrating methods such as GRAPPA are highly desirable because it is difficult to obtain non-proton sensitivity maps due to low natural abundance.
2. *Compressed sensing* has also been shown to be very effective taking advantage of sparsity in the HP agent spectrum as well as in the dynamics and spatial distribution [34, 35].

Contrast methods: Similar to conventional MRI, HP pulse sequences have been designed to provide novel contrast.

1. *T2-mapping* with multiple spin-echoes has shown promise for novel contrast [36, 37, 38].
2. *Diffusion-weighted* pulse sequences may provide additional information regarding HP agent compartmentalization and/or vascular suppression [38, 39, 40, 41, 42].
3. *2D NMR, saturation transfer, inversion recovery, and related methods* have promise for quantitative direction detection of HP agent exchange and metabolic conversion [5, 43, 44, 45, 46, 47]
4. *Selective spatial or spectral saturation* can be used to isolate the source of metabolites or reduce acquisition contraints [48].

CONCLUSION: Specialized pulse sequences must be designed for HP agents to account for unrecoverable signal decay, conversion between compounds, and in vivo dynamics. RF excitation should be done with variable flip angles for efficient magnetization usage. MRSI, chemical shift separation, and metabolite-specific imaging are all promising acquisition strategies, with MRSI the most flexible but slowest compared whereas metabolic-specific imaging is the fastest but most restrictive pulse sequence design. Dynamic imaging is less sensitive to injection timing but has generally less SNR that single time-point imaging. Parallel imaging and compressed sensing acceleration is very advantageous for HP agents. These can

all be combined with pulse sequence contrast strategies to be sensitive to agent compartmentalization and exchange/conversion.

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