Saturation pulse design for quantitative myocardial T$_1$ mapping

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Abstract

Background: Quantitative saturation-recovery based T$_1$ mapping sequences are less sensitive to systematic errors than the Modified Look-Locker Inversion recovery (MOLLI) technique but require high performance saturation pulses. We propose to optimize adiabatic and pulse train saturation pulses for quantitative T$_1$ mapping to have <1 % absolute residual longitudinal magnetization ($|M_Z/M_0|$) over ranges of $B_0$ and $B_1$ ($B_1$ scale factor) inhomogeneity found at 1.5 T and 3 T.

Methods: Design parameters for an adiabatic BIR4-90 pulse were optimized for improved performance within 1.5 T $B_0$ ($\pm$120 Hz) and $B_1$ (0.7–1.0) ranges. Flip angles in hard pulse trains of 3–6 pulses were optimized for 1.5 T and 3 T, with consideration of $T_1$ values, field inhomogeneities ($B_0 = \pm 240$ Hz and $B_1 = 0.4$–1.2 at 3 T), and maximum achievable $B_1$ field strength. Residual $M_Z/M_0$ was simulated and measured experimentally for current standard and optimized saturation pulses in phantoms and in-vivo human studies. $T_1$ maps were acquired at 3 T in human subjects and a swine using a SAuration recovery single-SHot Acquisition (SASHA) technique with a standard 90°-90°-90° and an optimized 6-pulse train.

Results: Measured residual $M_Z/M_0$ in phantoms had excellent agreement with simulations over a wide range of $B_0$ and $B_1$. The optimized BIR4-90 reduced the maximum residual $|M_Z/M_0|$ to <1 %, a 5.8× reduction compared to a reference BIR4-90. An optimized 3-pulse train achieved a maximum residual $|M_Z/M_0|$ < 1 % for the 1.5 T optimization range compared to 11.3 % for a standard 90°-90°-90° pulse train, while a 6-pulse train met this target for the wider 3 T ranges of $B_0$ and $B_1$. The 6-pulse train demonstrated more uniform saturation across both the myocardium and entire field of view than other saturation pulses in human studies. $T_1$ maps were more spatially homogeneous with 6-pulse train SASHA than the reference 90°-90°-90° SASHA in both human and animal studies.

Conclusions: Adiabatic and pulse train saturation pulses optimized for different constraints found at 1.5 T and 3 T achieved <1 % residual $|M_Z/M_0|$ in phantom experiments, enabling greater accuracy in quantitative saturation recovery $T_1$ imaging.

Keywords: Saturation pulses, Adiabatic pulses, $B_0$ inhomogeneity, $B_1$ inhomogeneity, $T_1$ mapping, Saturation recovery, SASHA

Background

Saturation pulses are commonly used in MRI pulse sequences to prepare longitudinal magnetization to a known zero state, independent of previous acquisitions, and generate spin–lattice ($T_1$) relaxation contrast. Several methods for $T_1$ quantification in the heart are based on multiple image acquisitions with variable saturation recovery times such as the saturation recovery turbo flash (SRTFL) [1], short acquisition period (SAP-T1) [2], and the recently proposed SAuration recovery single-SHot Acquisition (SASHA) [3] sequences. All of these techniques assume ideal saturation efficiency, and poor saturation performance results in errors in calculated $T_1$ values. The saturation efficiency can be quantified using residual longitudinal magnetization ($M_Z/M_0$), which can range from −1 (full inversion) to 1

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(no effect) and 0 for perfect saturation. In the standard three-parameter exponential model for SASHA T$_1$ data, saturation efficiency is a fitted parameter, but imperfect saturation may still result in errors in the calculated T$_1$ values due to residual magnetization remaining between heartbeats [3]. Two-parameter fitting of SASHA data assuming ideal saturation has been shown to substantially reduce variability of calculated T$_1$ values [4], but results in larger T$_1$ errors when imperfect saturation is present.

Composite saturation pulses consisting of trains of shaped RF pulses with numerically optimized flip angles have been designed for several different ranges of $B_0$ (off-resonance) and $B_1$ scale factors (ratio of actual radiofrequency field strength to nominal radiofrequency field strength). For example, enhanced water suppression has been achieved over narrow $B_0$ and $B_1$ ranges for spectroscopy applications at 1.5 T [5] and numerically optimized adiabatic pulses have been used for wide $B_0$/$B_1$ ranges at 7 T [6]. Hard RF pulse trains have also been proposed [7] and a train of 3 pulses with flip angles tailored for improved performance over $B_0$ and $B_1$ ranges expected at 3 T has been evaluated in-vivo [8]. However, the maximum residual $M_2/M_0$ of >8% of this design may be a significant source of error when used in quantitative imaging sequences.

Adiabatic BIR4-90 saturation pulses [9] and hybrid adiabatic-rectangular saturation pulses [10] have also been proposed, but the high $B_1$ field strength required to meet the adiabatic criteria may exceed the allowable specific absorption rate (SAR), particularly on larger subjects. On higher $B_0$ field strength magnets, lower $B_1$ scale factors may also reduce the effective $B_1$ field to below the adiabatic limit and result in poor performance [8, 11].

In this work, we expand upon existing literature regarding the design of saturation pulse trains and adiabatic saturation pulses with the primary goal of significantly improving performance to less than 1% residual $|M_2/M_0|$ over ranges of $B_0$ and $B_1$ values found at 1.5 T and 3 T, given the practical constraints of peak $B_1$ transmit field strength. The performance of the proposed saturation pulses are simulated, experimentally validated, and compared to current standard saturation pulses in phantom experiments and in-vivo human studies. The effect of saturation pulse performance on the two-parameter SASHA T$_1$ mapping technique is also characterized through simulations and in-vivo studies on humans and a swine.

**Methods**

**B$_1$ field strength limitations**

The maximum $B_1$ field strength is predominately limited by the achievable RF amplifier voltage for a given RF coil. These $B_1$ limitations reduce the off-resonance performance of both adiabatic pulses and hard pulse trains, imposing an additional constraint in their optimization. For the MRI systems used in this study, a reference voltage was calculated for each subject corresponding to the amplifier voltage required to achieve a $B_1$ field strength of 11.7 μT, equivalent to a 180° flip angle with a 1 ms rectangular pulse. The maximum achievable $B_1$ was calculated by multiplying 11.7 μT by the ratio of maximum voltage to the reference voltage. The maximum achievable $B_1$ field strength was calculated in this way for subjects on Siemens MAGNETOM 1.5 T Aera and 3 T Skyra systems over an approximate period of 6 months, with information collected as quality assurance data and analysis approved by the NIH Office of Human Subject Research.

**Spoiler gradient design**

Spoiler gradients in between RF pulses in a saturation pulse train were designed to minimize transverse magnetization. In contrast to previous pulse train designs where inter-pulse spoilers were polarity cycled along a single direction [7, 8, 10], inter-pulse spoilers in the proposed design were cycled along multiple gradient directions in order to dephase magnetization in all spatial directions and reduce the likelihood that spoiler gradients could be unwound during image readouts. Spoiler durations and total areas were also varied to minimize the potential formation of coherent stimulated echoes, with no two spoilers on the same axis having the same area. The implementation in this study uses a gradient strength of 24 mT/m per channel, which is achievable on most modern MRI scanners. At this strength, the minimum spoiler area in the 6-pulse train was 60 mT·ms/m, equivalent to 2π phase dispersion across 0.4 mm, with other spoiler areas and directions detailed in Fig. 1a. Spoiler designs for shorter pulse trains with $n$ pulses share the same design as the first $n$ spoiler gradients in the 6 pulse design, as shown for a 4-pulse train in Fig. 1b. The final trailing spoiler gradients are also of the same design, although its polarity is adjusted to maintain alternating polarity within that axis.

**Numerical pulse train design**

The residual $M_2/M_0$ following pulse train saturation is dependent on the flip angle order due to T$_1$ effects and thus direct gradient descent minimization of an ordered flip angle set may be trapped in local minima. Instead, an unordered set of flip angles was minimized using a standard Nelder-Mead algorithm [12], but in each iteration, all possible permutations of the flip angle set were evaluated and the lowest $|M_2/M_0|$ from all permutations was returned. A detailed description of the minimization algorithm can be found.
in Additional file 1 and MATLAB source code used is provided in Additional files 2, 3, 4, 5 and 6 and available online at https://bitbucket.org/kelvinc/pulsetrainopt.

Optimal flip angles were calculated for pulse trains ranging from 3 to 6 RF pulses. Pulse trains were optimized for 1.5 T using a $B_1$ range of 0.7–1.0 [13], a $B_0$...
range corresponding to ±120 Hz, and a maximum $B_1$ field strength of 26.9 μT. Pulse trains were also optimized for 3 T using a larger $B_1$ range of 0.4–1.2 [8, 14], a $B_0$ range corresponding to ±240 Hz, and a maximum $B_1$ of 14 μT. In all Bloch simulation optimizations, the $T_1$ range was 200–2000 ms and $T_2$ was 45 ms (native myocardium). $T_2$ dependence of optimized pulse trains was characterized through simulations using $T_2$ values from 5 ms to 250 ms.

Proposed saturation pulse trains were compared to a commonly used reference pulse train consisting of three 90° RF pulses, each with a fixed duration of 0.5 ms [7]. Spoiler durations for the reference pulse train were 1.00, 8.80, 5.86, and 1.55 ms, with a total time of 18.71 ms.

**BIR4-90 pulse optimization**

A BIR4-90 pulse was numerically optimized by a brute force optimization over adiabatic design parameters [15]. The pulse duration, amplitude, maximum frequency sweep, and parameters $\zeta$ and $\kappa$ which define the adiabatic half passage section of the BIR4-90 defined in Equations 4 and 6 in [15] were varied and the optimum pulse was selected which achieved the best saturation over the specified range of $B_1$ and off-resonance, i.e., best worst-case deviation. The frequency sweep parameter was varied from 4–20 kHz in 1 kHz steps, $\tan(\kappa)$ ranged from 8 to 22 in steps of 2, and $\zeta$ ranged from 8 to 30 in steps of 2. Bloch simulations assumed values for native myocardium of $T_1 = 1100$ ms and $T_2 = 45$ ms. Pulse durations between 4 and 10 ms were evaluated. The design range was ±120 Hz off-resonance and $B_1$ ranged from 0.7 to 1.0. The peak amplitude was limited to approximately 20 μT. The optimized BIR4-90 pulse was further characterized with simulations using $T_2$ values from 5 ms to 250 ms.

**RF power calculation**

Relative RF energy was calculated for each saturation pulse as $B_1^2$ integrated over time divided by the RF energy of the 90°-90°-90° pulse train. Relative peak RF power was calculated as the maximum $B_1^2$ for each saturation pulse, normalized to the maximum $B_1^2$ in the reference 90°-90°-90° pulse train.

**Phantom validation**

Saturation efficiency was experimentally assessed for five saturation pulses: the reference 90°-90°-90° pulse train, the 3 T optimized 6-pulse train (Fig. 1a), the 1.5 T optimized 4-pulse train (Fig. 1b), the reference BIR4-90 pulse, and the optimized BIR4-90 pulse (Fig. 1c). Performance for each pulse was assessed in a Siemens 2 L plastic bottle phantom (1.25 g NiSO$_4$⋅6H$_2$O + 5 g NaCl per 1000 g water). Imaging was performed on a Siemens 1.5 T MAGNETOM Aera MRI scanner (Siemens Healthcare; Erlangen, Germany) and the pulses in the 3 T 6-pulse train were limited to 14 μT to reflect the typical limitation at 3 T. The $T_1$ value was measured using an inversion recovery spin echo sequence with inversion times between 100 ms and 500 ms and a non-prepared image. $T_2$ was measured using spin echo repeated with echo times varied between 11 ms and 300 ms. All spin echo imaging was performed with a single k-space line acquired per excitation and a 10 s TR to ensure complete magnetization recovery between excitations.

A linear spatial gradient was applied along the long axis of the phantom to assess performance as a function of off-resonance. To calculate an off-resonance ($B_0$) map, gradient echo images were acquired with 5 echo times (TE) between 4 and 6 ms, 3000 ms repetition time (TR), 90° flip angle, 128 × 44 matrix size, 400 × 138 mm$^2$ field of view, and 8 mm slice thickness. The $B_0$ map was generated by fitting the equation $\phi = \Delta B_0 \cdot TE$ for every pixel, where $\phi$ is the phase of gradient echo images. To calculate an optimum $B_1$-field map for the phantom, gradient echo images were acquired with 45°, 60°, 90°, and 120° flip angles, 3.79 ms TE, and other parameters as above. The signal intensity as a function of flip angle was simulated using a Bloch equation simulation accounting for slice profile effects [16], and a $B_1$ map was generated by fitting the measured signal intensity to this simulated curve for every pixel.

Saturation pulse efficiency was calculated using a gradient echo sequence with 3.79 ms TE, 3000 ms TR, 90° flip angle, and other parameters as above. Images were acquired without a saturation pulse and with 4 saturation recovery times (TS = 10–40 ms) for each of the 5 saturation pulses, where TS is defined as the time from the end of the last RF pulse in the saturation and the middle of the imaging excitation RF pulse. A saturation efficiency map was generated by fitting acquired data to $\{\text{Signal} = A^*[1 - \eta \exp(-TS/T_1)]\}$, where $\eta$ is the saturation efficiency and residual (signed) $M_2/M_0$ is equal to 1- $\eta$. These acquisitions were repeated 9 times with the flip angles of the saturation RF pulses scaled by 40–120 % to emulate the effect of varied $B_1$ values.

For each pixel of the nine resulting residual $M_2/M_0$ maps, the $B_0$ and effective $B_1$ (equal to $B_1$ map multiplied by the flip angle scaling factor) could be determined, separately for each saturation pulse considered. Together, the intrinsic variation in $B_1$ over the phantom in combination with the 9 repeated experiments with flip angle scaling from 40 % to 120 % yielded a wide range of effective $B_1$ values. With the variation in $B_0$ provided by the linear gradient, the $M_2/M_0$ values were thus directly measured over a wide range of $B_0$ and $B_1$ values. The missing data within the $B_0$–$B_1$ space...
was calculated by fitting a surface over the scattered points with a modified ridge estimator using the gridfit function [17].

**SASHA sequence simulation**

Bloch equation simulations of the SASHA sequence were performed with a range of residual $M_2/M_0$ (−5% to 5%) and relaxation values emulating myocardium (native $T_1/T_2$: 1175/50 ms, post-contrast $T_1/T_2$: 725/50 ms) and blood (native $T_1/T_2$: 1650/240, post-contrast: 500/180 ms) at 1.5 T [3]. Typical in-vivo SASHA acquisition parameters were used: 1.3/2.6 ms TE/TR, 70° target flip angle, 70 phase encode lines, 60 bpm simulated heart rate, 10 images with maximum 775 ms saturation recovery time (TS) and a non-saturated image. Image readout flip angles were scaled using a variable flip angle (VFA) scheme to minimize $T_1$ error with two parameter fitting as previously described [18]. In this scheme, the prescribed flip angle of the first 45° RF pulses was scaled by $\sin(x)$ for $\pi/90 < x < \pi/2$. Simulations used actual RF pulse waveforms and the transverse magnetization ($M_{XY}$) at the centre k-space readout as the image signal intensity. $T_1$ values were calculated by fitting simulated data to a 2-parameter exponential recovery model with assumed ideal saturation.

**In vivo human study**

Saturation efficiency was assessed in 3 human volunteers on a Siemens 3 T MAGNETOM Skyra MRI scanner (Siemens Healthcare; Erlangen, Germany) using a single-shot centrically ordered gradient echo sequence. Volunteers provided written informed consent and the study was approved by the University of Virginia Health System Institutional Review Board. Typical sequence parameters were: 1.14/2.31 ms TE/TR, 10° flip angle, 128 × 90 matrix, 400 × 281 mm$^2$ field of view, and 10 mm slice thickness. Saturation recovery images were acquired for the 90°-90°-90°, 1.5 T 4-pulse, 3 T 6-pulse, reference BIR4-90, and optimized BIR4-90 saturation pulses with a 7.5 ms saturation recovery time, defined from the end of the last saturation RF pulse to the center of the first imaging RF pulse. A proton density image was acquired with the same pulse sequence parameters. All images were obtained in short-axis and 4-chamber orientations, acquired in diastasis with end-expiratory breath-holds.

Saturation recovery images were processed using a phase-sensitive reconstruction using the proton density image phase as a reference in order to avoid Rician noise bias. The residual $M_2/M_0$ was calculated as the ratio of the saturation recovery image to the proton density image.

$B_1^+$ maps were acquired using a free-breathing saturated double angle method [11] with single-shot echo planar imaging (EPI) readouts. Typical sequence parameters were: electrocardiogram (ECG) gated diastasis imaging, 45°/90° flip angles, 80 × 50 matrix, rate 2 parallel imaging (GRAPPA), 360 × 225 mm$^2$ field of view, 10 mm slice thickness, 2 saturation bands on the chest and back to reduce the field of view, and 15 repetitions per flip angle. All images were registered and a $B_1^+$ scale factor map was calculated as $B_1 = \cos^{-1}\left(\frac{I_{45°}}{I_{90°}}\right)/45°$, where $I_{45°}$ and $I_{90°}$ are the signal intensities from the 45° and 90° flip angle images respectively.

$T_1$ maps were collected using SASHA with 90°-90°-90°, optimized BIR4-90, and 6-pulse saturation and MOLLI with an optimized adiabatic inversion pulse [13] in diastasis with end-expiratory breath-holds. SASHA sequences used a 70° imaging flip angle with VFA modulation and 10 images with the longest TS time allowable by the heart rate [19] and MOLLI used a 35° imaging flip angle with a 5(3)3 sampling pattern.

**In vivo swine study**

Myocardial $T_1$ mapping was performed on a 66 kg swine on a Siemens 3 T Skyra MRI scanner using the SASHA and MOLLI [20] $T_1$ mapping sequences. SASHA was acquired using both 90°-90°-90° and 6-pulse saturation with a 45° imaging flip angle and VFA modulation. MOLLI used an optimized inversion pulse with a 20° imaging flip angle. A $B_1^+$ map was acquired using a saturated double angle method as described above. Swine were studied in accordance with a protocol approved by the Animal Care and Use Committee of the National Institutes of Health (protocol number H-0214).

**Results**

**$B_1$ field strength limitations**

The maximum $B_1$ field strength was calculated for 379 subjects on the Siemens MAGNETOM Skyra platform and 230 subjects on the Siemens MAGNETOM Aera platform. A maximum $B_1$ field strength of 14 μT was achievable on the 3 T Skyra platform in >98% of subjects, while 26.9 μT was achievable on the 1.5 T Aera platform in >99% of subjects. At a $B_1$ strength of 14 μT, a 90° rectangular pulse is 419 μs and the full width half maximum effective $B_1$ scaling is ±1334 Hz.

**BIR4-90 pulses**

The numerically optimized BIR4-90 design used a duration of 5.12 ms, maximum $B_1$ field of 20.6 μT, swept over ±7 kHz, with $\xi = 22$ and $\tan(\xi) = 18$. This design is longer and has a lower maximum $B_1$ compared to the reference BIR4-90 pulse that has a 4.00 ms duration and a maximum $B_1$ of 25.1 μT, resulting in lower relative peak RF energy and power (Table 1). The optimized BIR4-90 design had substantially improved performance with a maximum residual $|M_2/M_0|$ within the 1.5 T
optimization range 5.8× lower than the reference pulse. More detailed comparisons of the two BIR4-90 pulses are characterized in the phantom study below.

**Numerically optimized pulse trains**

Characteristics of the Bloch simulation numerically optimized pulse trains are summarized in Table 1 and their simulated performance is plotted in Fig. 2. The reference 90°-90°-90 pulse train has poor performance at the lower end of $B_1$ scale factors expected at 1.5 T, with a residual $M_Z/M_0$ of 10% at a $B_1$ of 0.7 while on-resonance and a 1000 ms $T_1$. For the 1.5 T optimization range, the optimized 3-pulse train (90°-107°-126°) achieved the target residual |$M_Z/M_0$| of <1%, while 6 pulses (115°-90°-125°-85°-176°-223°) were necessary to achieve this target for the 3 T optimization range due to the larger $B_1$ range of 0.4–1.2. For both $B_1$ optimization ranges, simulated residual |$M_Z/M_0$| increased rapidly outside of the optimization region. Minor off-resonance and $T_1$ effects were also observed, but did not have a consistent trend over the range (Fig. 2).

**Table 1 Summary of characteristics for Bloch simulation numerically optimized saturation pulses**

| Flip Angle [°] | Duration [ms] | Relative RF Energy | Relative Peak RF Power | Residual | $|M_Z/M_0| [%]$ mean±std (max) |
|----------------|--------------|--------------------|------------------------|----------|-------------------------------|
| Reference saturation pulses | 90°-90°-90° | 90-90-90 | 18.7 | 1.0 | 1.0 | 2.86±2.98 (11.31) |
| BIR4-90 | 25.1 μT (adiabatic) | 11.1 | 11.0 | 4.1 | 0.92±0.92 (5.32) |
| Optimized for 1.5T | BIR4-90 | 20.6 μT (adiabatic) | 12.2 | 10.0 | 2.9 | 0.30±0.14 (0.91) |
| $B_0 = ±120$ Hz | 3 pulse train | 90–107–126 | 19.5 | 2.7 | 5.2 | 0.40±0.21 (0.80) |
| $B_1 = 0.7$–1.0 | 4 pulse train | 96–91–127–124 | 23.6 | 3.7 | 5.2 | 0.11±0.07 (0.25) |
| $B_1$ field = 26.9 μT | 5 pulse train | 89–106–89–145–127 | 27.4 | 4.7 | 5.2 | 0.06±0.03 (0.11) |
| | 6 pulse train | 116–99–81–92–146–139 | 30.6 | 5.7 | 5.2 | 0.02±0.01 (0.04) |
| Optimized for 3T | 3 pulse train | 220–136–93 | 20.8 | 2.0 | 1.4 | 4.33±2.49 (8.70) |
| $B_0 = ±240$ Hz | 4 pulse train | 75–103–149–213 | 25.0 | 2.4 | 1.4 | 1.99±1.22 (4.17) |
| $B_1 = 0.4$–1.2 | 5 pulse train | 99–76–120–169–220 | 29.2 | 3.0 | 1.4 | 0.64±0.41 (1.58) |
| $B_1$ field = 14 μT | 6 pulse train | 115–90–125–85–176–223 | 32.8 | 3.6 | 1.4 | 0.27±0.19 (0.87) |

Total duration values include post-spoiler and pre-spoilers where applicable. Residual $M_Z/M_0$ values are simulated using Bloch equation simulations and the mean, standard deviation, and maximum are calculated over the entire optimization space, i.e., $B_0$, $B_1$, and $T_1$. Residual $M_Z/M_0$ for reference pulses was evaluated over the 1.5 T $B_1$ range. Relative RF energy and power are normalized to a reference 90°-90°-90° pulse train as described in the methods.

$T_1$ relaxation effects

Simulated residual $M_Z/M_0$ for selected saturation pulses are shown as a function of $B_1$ and $T_1$ in Fig. 3. A larger range of $B_1$ values (0.4 and 1.2) are shown only for the 6-pulse train, which is full range for the 3 T field strength. Performance is only weakly related to $T_1$ in the optimization range used for pulse design (200–2000 ms), but residual |$M_Z/M_0$| increases rapidly for $T_1$ values shorter than 25 ms for all pulse trains, with divergent behavior depending on the $B_1$ scale factor. The 90°-90°-90° train has poor performance with a $B_1$ scale factor of 0.7, with residual |$M_Z/M_0$| exceeding 15% for a 50 ms $T_1$. The 3 T 6-pulse train maintains |$M_Z/M_0$| < 1% for $T_1$ greater than 186 ms at ±240 Hz and for $T_1$ greater than 140 ms at ±120 Hz. The optimized BIR4-90 pulse had the best performance at short $T_1$ values, with 1.6% residual |$M_Z/M_0$| at 25 ms.

$T_2$ relaxation effects

The effects of $T_2$ relaxation on residual $M_Z/M_0$ are shown for the optimized 3 T 6-pulse train and BIR4-90 saturation pulses in Fig. 4. Saturation pulse trains were insensitive to $T_2$ relaxation and the optimized BIR4-90...
pulse had less than a 1% change in residual $M_z/M_0$ for $T_2$ values from 25 to 250 ms.

**Phantom validation**

The $T_1$ and $T_2$ of the bottle phantom was measured to be 316 ms and 274 ms respectively using spin echo experiments, and the intrinsic $B_1$ scaling factor across the image was found to range from 0.83 to 1.05. The applied linear magnetic field gradient resulted in off-resonance values from $-605$ to $697$ Hz across the phantom. The performance of each saturation pulse as a function of $B_0$ and $B_1$ scaling factor is plotted in the top row of Fig. 5, with the optimization range of $B_0$ and $B_1$ values demarcated with a white box.

Experimentally measured residual $M_z/M_0$ (middle row, Fig. 5) shows excellent agreement with simulations...
Fig. 3 Simulated residual $M_z/M_0$ for selected saturation pulses as a function of $T_1$ for different off-resonance ($B_0$) and $\beta_1$ values.
Saturation pulse trains are robust to off-resonance due to the short individual pulse durations, while the BIR4-90 pulses with an overall shorter duration have tighter off-resonance constraints and more complex relationships with $B_0$ and $B_1$. The reference 90°-90°-90° pulse train shows poor performance at low $B_1$ scaling factors, even in the relatively narrow range of 0.7–1.0 expected at 1.5 T. All proposed pulses show greatly improved performance within their respective optimization spaces (white dashed box) compared to the reference designs. The average measured residual $|M_Z/M_0|$ within these spaces was 0.24 ± 0.16 %, 0.11 ± 0.06 %, and 0.20 ± 0.18 % for the optimized BIR4-90, 4 pulse (1.5 T), and 6 pulse (3 T) trains respectively.

**SASHA sequence simulation**

Figure 6 shows the relationship between residual $M_Z/M_0$ and simulated $T_1$ errors in the SASHA sequence. SASHA $T_1$s are generally underestimated with incomplete saturation, with a 1.3–1.6 % increase in 2-parameter SASHA $T_1$ error for every 1 % change in residual $M_Z/M_0$. A higher heart rate of 100 bpm results in greater SASHA $T_1$ errors for native (pre-contrast) $T_1/T_2$ values compared to 60 bpm, with negligible effects for post-contrast values. Overall, 2-parameter model fitting results in greater $T_1$ error dependence on residual $M_Z/M_0$ than 3-parameter fitting, particularly for the lower post-contrast $T_1/T_2$ values.

**In vivo human study**

Subjects had an average heart rate of 63 ± 10 bpm with no mis-triggering. Representative $B_1$ and residual $M_Z/M_0$ maps from one subject are shown in Fig. 7. $B_1$ was decreased near the acute margin of the right ventricle and coincided with increased residual $M_Z/M_0$ values for the 90°-90°-90° and reference BIR4-90 pulses. A similar spatial pattern was observed in all subjects, although there was considerable variability in $B_1$ between subjects (Table 2). The optimized BIR4-90 pulse had lower residual $M_Z/M_0$ than the reference BIR4-90 pulse in the myocardium (2.8 ± 1.1 % vs 6.1 ± 3.1 %) as well as in the blood pool. The 6-pulse train had the lowest overall...
residual $M_Z/M_0$ in the myocardium (1.8 ± 0.3 %) and significantly more uniform saturation over the entire body (Fig. 7).

Calculated in-vivo $T_1$ values for the SASHA sequence with various saturation pulses and MOLLI are summarized in Table 3. The 6-pulse SASHA sequence had longer myocardial and blood $T_1$ values than the 90°-90°-90° and optimized BIR-4 variants and all SASHA $T_1$ values were longer than MOLLI $T_1$ values. Right ventricular blood $T_1$s were lower than left ventricular blood $T_1$s for all sequences, with the largest differences in the 90°-90°-90° SASHA and MOLLI data (193 ± 100 ms and 143 ± 83 ms respectively).

In vivo swine study

Parametric $T_1$ and $B_1$ maps acquired in a swine are shown in Fig. 8 and a profile is extracted along the left ventricle. Myocardial $T_1$ values from the 90°-90°-90° SASHA and MOLLI sequences show a >50 % artifactual decrease in the lateral wall, spatially coinciding with reduced $B_1$ values. $T_1$ values using the 6-pulse SASHA sequence were more spatially uniform across both the myocardium (1386 ± 70 ms along the profile) and the overall field of view.

Discussion

In this study, adiabatic BIR4-90 and pulse train saturation designs were optimized for 1.5 T and 3 T with the objective of achieving <1 % residual $|M_Z/M_0|$ for the wide ranges of $B_1$ and $B_0$ inhomogeneities expected at these field strengths, while imposing the typical peak $B_1$ field amplitude limitations measured on 1.5 T and 3 T scanners. New pulses were shown to have significantly improved saturation performance as compared to current standard pulses. Measured saturation performance in phantoms had excellent agreement with simulations and in-vivo experiments demonstrated the superior performance of the proposed 6-pulse train saturation pulse. $T_1$ maps calculated using SASHA with proposed 6-pulse train saturation showed greater spatial homogeneity than the reference pulse in both human and swine studies.

BIR4-90 pulse design

Experimental data in this study shows the reference BIR4-90 saturation pulse has relatively poor performance with low $B_1$ and high off-resonance within the range expected at 1.5 T. A new optimized BIR4-90 pulse was shown to have improved performance with <1 % residual $|M_Z/M_0|$ over the 1.5 T optimization range of $B_0$ and $B_1$ fields while reducing maximum $B_1$ field strength and resulting SAR. Although the required $B_1$ of 20.6 μT was achievable on the 1.5 T MRI systems used here, the 14 μT $B_1$ limit at 3 T reduces the effective flip angle and saturation performance. In the 3 T human study, the
optimized BIR4-90 SASHA had 1.6% shorter myocardial T1 values than 6-pulse SASHA, consistent with T1 underestimation from slightly larger residual MZ/M0.

**Pulse train design**

The ordering of flip angles in saturation pulse trains was found to be important, with a reduction in the maximum residual |MZ/M0| by a factor of 5.7× from

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**Fig. 6** Simulated T1 error for SASHA as a function of residual MZ/M0 for native (top) and post-contrast (bottom) myocardium (left) and blood (right) using 2 and 3 parameter models at 60 and 120 bpm. Input native relaxation times were T1/T2 = 1175/50 ms (myocardium) and T1/T2 = 1650/240 (blood) and post-contrast relaxation times were T1/T2 = 725/50 ms (myocardium) and T1/T2 = 500/180 ms (blood)
the best order permutation to the worst. The evaluation of all permutations of an unordered flip angle set in the minimization subroutine provided a straightforward means of considering flip angle ordering while avoiding trapping within local minima. This is likely to provide a more optimal solution than the previous minimization approach which considered ordering only in the final stage [8].

Pulse trains were designed for expected ranges of $\hat{B}_1$ values at both 1.5 T and 3 T, with excellent performance within those optimization ranges when a sufficient number of pulses are used. As performance decreases rapidly outside of the $\hat{B}_1$ optimization range for all pulse trains (Fig. 2), conservative estimates of $\hat{B}_1$ ranges were used in the design process. Experimentally measured residual $M_Z/M_0$ in a phantom closely matched simulations for both the adiabatic BIR4-90 pulses as well as all saturation pulse trains, confirming the validity of the Bloch equation simulations used in the design process.

For the $\hat{B}_1$ range of 0.7 to 1.0 expected for 1.5 T, the optimized 3-pulse train has the same number of pulses as the reference 90°-90°-90° pulse train and reduces the maximum residual $|M_Z/M_0|$ by 14×, meeting the target of <1 %. The 4-pulse train has even better performance with <0.25 % peak residual magnetization (0.11 % mean residual signal), with minimal additional time and SAR.

The design $\hat{B}_1$ range for 3 T was chosen to be 0.4–1.2 to encompass the widest range of in-vivo cardiac $\hat{B}_1$ values measured in a handful of small studies [8, 11, 14, 21]. The in-vivo $\hat{B}_1$ maps for the 3 human subjects in this study show a smaller range of $\hat{B}_1$ values than previous studies, but with a similar spatial pattern of variation primarily in the anteroposterior direction and larger $\hat{B}_1$ values in the lateral wall of the left ventricle [14]. This may be due to a difference in body coil design between scanner manufacturers, and further variations may exist between models with different bore sizes. However, $\hat{B}_1$ values less than 0.4 were observed in the swine model,

| $\hat{B}_1$ scale factor | 90°-90°-90° | 1.5 T 4-pulse train | 3 T 6-pulse train | Reference BIR4-90 | Optimized BIR4-90 |
|--------------------------|-------------|---------------------|------------------|-------------------|-------------------|
| LV myocardium            | 0.87 ± 0.21 | 3.5 ± 2.3           | 3.4 ± 0.5        | 1.8 ± 0.3         | 6.1 ± 3.1         | 2.8 ± 1.1         |
| LV blood pool            | 0.94 ± 0.19 | 0.5 ± 1.1           | 2.1 ± 1.7        | 0.6 ± 0.1         | 2.5 ± 2.3         | 0.8 ± 0.3         |
| RV blood pool            | 0.86 ± 0.12 | 7.5 ± 7.5           | 0.8 ± 0.5        | 0.6 ± 0.1         | 10.6 ± 7.5        | 2.3 ± 2.2         |

Fig. 7 $\hat{B}_1$ scale factor and residual $M_Z/M_0$ maps measured in a human volunteer for various saturation pulses. Air regions with low signal intensity are masked for visualization. A profile is extracted from the short axis images (black and white dashed line) across both the right and left ventricles.
Table 3 Measured $T_1$ values at 3 T in 3 human subjects

| Subject                | $T_1$ [ms] | SASHA $T_1$ [ms] | Optimized BIR4-90 | 3 T 6-pulse train | MOLLI $T_1$ [ms] |
|------------------------|------------|------------------|-------------------|-------------------|------------------|
| LV myocardium          | 1431 ± 55  | 1470 ± 47        | 1491 ± 30         | 1212 ± 11         |
| LV blood pool          | 1921 ± 132 | 1845 ± 97        | 2048 ± 69         | 1811 ± 81         |
| RV blood pool          | 1728 ± 229 | 1819 ± 113       | 1991 ± 57         | 1668 ± 162        |
| LV - RV blood pool     | 193 ± 100  | 26 ± 50          | 57 ± 13           | 143 ± 82          |

Fig. 8 A $B_1$ map (bottom left) and $T_1$ maps (top row) using SASHA with a reference 90°-90°-90° saturation pulse, SASHA with a proposed 6-pulse train, and MOLLI in a swine. Air regions with low signal intensities are masked for visualization. A profile of $T_1$ values along the left ventricular wall shows decreased $T_1$ values in the lateral wall coinciding with reduced $B_1$ values.
suggestions that the design $\tilde{B}_1$ range may need to be further widened for large animal model studies. Further work is needed to characterize the ranges of $\tilde{B}_1$ values in larger representative populations of both human and swine on different scanner platforms.

The 3 T 6-pulse train achieved <1% peak residual magnetization over the wide design range of $\tilde{B}_1$ values, with excellent performance (mean residual $|M_2/M_0|$ of 0.27%) and only 1.4× greater peak RF power compared to the 90°-90°-90° reference pulse train. The relatively short RF pulse durations used in the pulse trains resulted in a wide range of $B_0$ insensitivity for all pulse train designs, with a negligible drop in measured performance at ±450 Hz (Fig. 5). This is consistent with superior saturation of fat signals, which have a ~440 Hz shift in resonant frequency at 3 T, and more uniform saturation over the entire field of view compared to the BIR4-90 pulses (Fig. 7).

Further pulse train optimization

The saturation pulses presented in this study were optimized for myocardial $T_1$ mapping, but their excellent performance over a typical optimization range makes them suitable for other applications as well such as myocardial first-pass perfusion sequences or the saturated double angle method. In settings with much different criteria, such as $B_1$ amplitude limitations or $B_0$, $B_1$, and $T_1$ ranges, the supplied optimization code may be used to design more application-specific pulse trains.

For example, while relatively short RF pulses were selected to maximize the off-resonance performance, pulse lengths may be increased considerably to reduce peak $B_1$ amplitude and SAR. Additionally, while the maximum $B_1$ amplitude was characterized for 2 common MRI scanner models, other models and scanners by different vendors likely have different limitations. The inter-pulse spoiler durations could also be shortened to further reduce $T_1$ dependencies, which would improve performance for very short $T_1$ values encountered in contrast-enhanced first-pass myocardial perfusion imaging.

Saturation performance and SASHA $T_1$ mapping

Simulations of 2-parameter fitting with SASHA data show increased sensitivity to saturation pulse performance compared to 3-parameter fitting. In human studies, there was consistently lower $\tilde{B}_1$ in the right ventricle leading to increased residual longitudinal magnetization with the 90°-90°-90° saturation pulse, but not the 6-pulse train. Correspondingly, right ventricular $T_1$ values with 90°-90°-90° SASHA were substantially lower (193 ± 100 ms) than in the left ventricle, but the difference was much lower (57 ± 13 ms) with 6-pulse SASHA which had more spatially uniform saturation. This remaining difference between the left and right ventricular blood with 6-pulse SASHA is comparable to a difference of ~80 ms between atrial and venous blood with a 0.42 hematocrit previously reported at 3 T [22]. Shorter MOLLI $T_1$ values compared to SASHA are consistent with known influences of factors such as $T_2$, magnetization transfer, and off-resonance on the MOLLI sequence [4].

Substantially larger $\tilde{B}_1$ variations observed in the swine may be the result of the more cylindrical chest geometry compared to humans. These variations resulted in a >50% artifactual decrease in myocardial $T_1$ values for both the 90°-90°-90° SASHA and MOLLI sequences while 6-pulse SASHA had spatially homogenous $T_1$s. SASHA with a 6-pulse saturation may provide more reliable $T_1$ measurements in pre-clinical large animal studies at 3 T, but further study is needed to determine the impact on the quantification of myocardial fibrosis.

Study limitations

Gradient spoiler design and its effect on the possible formation of stimulated echoes were not studied in detail. The proposed spoiler design utilizes relatively large gradient areas played in multiple directions, with care taken to avoid duplicate gradient areas. While no stimulated echo artifacts were observed in our data, a more systematic study of stimulated echo formation is warranted.

Residual $M_2/M_0$ was measured in-vivo using images with a saturation recovery time of 7.5 ms, which was the minimal duration due to the length of post-saturation spoiler gradient for the reference BIR4-90 pulse. Calculated residual $M_2/M_0$ values are likely to have a small positive bias due to $T_1$ recovery during this duration. Although centricordering was used, $T_1$ recovery during the readout results in a further positive bias and may explain the larger residual $M_2/M_0$ in the LV myocardium compared to the blood pool it encloses.

In-vivo measurements in this study were limited to 3 human subjects and a single animal. However, the magnitude and spatial pattern of $\tilde{B}_1$ heterogeneity in the human subjects are consistent with existing literature [14] and $\tilde{B}_1$ variations in the swine were representative of the authors' previous experience.

Conclusions

This study has described the optimization of saturation pulses and validated their performance in both phantom experiments and in-vivo studies. While an optimized BIR4-90 design and a 3-pulse train were able to meet the design criteria of <1% residual $|M_2/M_0|$ at 1.5 T, only the optimized 6-pulse train met the criteria for $B_0$ and $\tilde{B}_1$ values expected at 3 T. The robust performance of optimized saturation pulse trains to a wide range of off-resonance, $T_1$ values, and $\tilde{B}_1$ scale factors can minimize these as sources
of errors in quantitative saturation-recovery based sequences such as SASHA or in other applications such as first pass perfusion imaging.

Additional files

**Additional file 1:** Numerical pulse train optimization algorithm. (DOCX 137 kb)

**Additional file 2:** Main optimization code (MATLAB), (TXT 5 kb)

**Additional file 3:** Additional optimization code (MATLAB), (TXT 2 kb)

**Additional file 4:** Additional optimization code (MATLAB), (TXT 2 kb)

**Additional file 5:** Additional optimization code (MATLAB), (TXT 2 kb)

**Additional file 6:** Additional optimization code (MATLAB), (TIF 4449 kb)

**Additional file 7:** Saturation Pulse Performance with Flip Angle Permutations (3 T 6-pulse train), (TXT 8 kb)

**Abbreviations**

ECCG: Electrocardiogram; GRAPPA: Generalized auto-calibrating partially parallel acquisition; LV: Left ventricle; MOLLI: Modified Look-Locker inversion recovery; RF: Radiofrequency; RR: Right ventricle; SAR: Specific absorption rate; SASHA: Saturation recovery single-shot acquisition; TE: Echo time; TR: Repetition time; TS: Saturation recovery time; VFA: Variable flip angle.

**Competing interests**

Dr. Spottiswoode is employed by Siemens Medical Solutions USA, Inc. Dr. Arai is a principal investigator on a US government Cooperative Research And Development Agreement (CRADA) with Siemens Medical Solutions (HL-CR-05-004).

**Authors’ contributions**

KC, PK, and RBT contributed to study design and saturation pulse optimization and BSS assisted in pulse sequence implementation. KC performed pulse train simulations, phantom experiments and all data analysis. SNV and AEA were responsible for swine imaging and the B1 mapping sequence and MS assisted in human imaging. All authors contributed to and approved the final manuscript.

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