Black blood myocardial T₂ mapping

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Purpose: To develop a black blood heart-rate adaptive T₂-prepared balanced steady-state free-precession (BEATS) sequence for myocardial T₂ mapping.

Methods: In BEATS, blood suppression is achieved by using a combination of pre-excitation and double inversion recovery pulses. The timing and flip angles of the preexcitation pulse are auto-calculated in each patient based on heart rate. Numerical simulations, phantom studies, and in vivo studies were conducted to evaluate the performance of BEATS. BEATS T₂ maps were acquired in 36 patients referred for clinical cardiac MRI and in 1 swine with recent myocardial infarction. Two readers assessed all images acquired in patients to identify the presence of artifacts associated with slow blood flow.

Results: Phantom experiments showed that the BEATS sequence provided accurate T₂ values over a wide range of simulated heart rates. Black blood myocardial T₂ maps were successfully obtained in all subjects. No significant difference was found between the average T₂ measurements obtained from the BEATS and conventional bright-blood T₂; however, there was a decrease in precision using the BEATS sequence. A suppression of the blood pool resulted in sharper definition of the blood–myocardium border and reduced partial voluming effect. The subjective assessment showed that 16% (18 out of 108) of short-axis slices have residual blood artifacts (12 in the apical slice, 4 in the midventricular slice, and 2 in the basal slice).

Conclusion: The BEATS sequence yields dark blood myocardial T₂ maps with better definition of the blood–myocardium border. Further studies are warranted to evaluate diagnostic accuracy of black blood T₂ mapping.

KEYWORDS
black blood, double inversion recovery, myocardial edema, myocardial T₂ mapping, partial volume effect

INTRODUCTION

Inflammatory processes underlie a broad spectrum of conditions that injure the myocardium and cause both structural
and functional deficits.¹ In the presence of inflammation or edema, myocardial T₂ increases and can be detected using T₂-weighted MRI.³,⁵ Myocardial T₂ mapping is a quantitative technique that has emerged as a reproducible method to accurately measure T₂ relaxation times.⁴,⁵ Compared to conventional T₂-weighted imaging, myocardial T₂ mapping reduces the intersubject and interstudy variability. T₂ mapping has proven advantageous for visualizing myocardial edema in acute myocardial infarction (MI) cases with both high sensitivity and specificity, yielding improved diagnostic accuracy compared to T₂-weighted dark-blood imaging.

T₂ mapping can be performed using a single-shot turbo spin-echo (SE) sequence with multiple echoes.⁶ However, the turbo SE sequence is limited by cardiac motion artifacts due to a long acquisition window, which greatly affects the accuracy of T₂ measurements. An alternate method used for myocardial T₂ mapping is T₂-preparation (T₂prep)⁷ with balanced steady-state free precession (bSSFP) imaging or gradient echo.⁴,¹⁰,¹¹ A combination of spin echo excitations with gradient echo readouts was also recently proposed as part of this method.¹² T₂prep-bSSFP-based T₂ mapping sequence provides very reproducible T₂ measurements¹³ and has replaced the turbo SE-based approach on clinical recommendation.¹⁴ In this sequence, T₂prep pulses with different TEs are used to create T₂-decays of the magnetization for the given duration of the TE. A set of images are acquired with different TEs and used to generate a T₂ map through voxel-wise curve-fitting using either a 2-parameter or 3-parameter exponential model.¹⁵ However, T₂ quantification in areas bordering the myocardium and the blood pool is challenging due to partial volume errors that cause T₂ measurement errors. Although motion correction can improve measurement reproducibility,¹⁶ it cannot completely resolve the partial voluming error. One approach to resolve this limitation is to suppress the blood pool in myocardial T₂ mapping. Doing so would effectively reduce the partial volume effects to improve the image contrast at the blood–myocardium boundaries, allowing for improved image registration and motion correction. However, blood suppression in myocardial T₂ mapping is challenging, and there currently is no available sequence for black blood T₂ mapping.

There are numerous blood suppression preparation sequences in cardiac and vascular imaging.¹⁷–²⁵ Double inversion recovery (DIR)¹⁸–²⁵ sequencing is the most widely used technique; a nonselective 180° inversion pulse is followed by a slice-selective 180° inversion pulse to invert the blood signal outside the imaging plane.²⁵ Spatial saturation pulses²⁶,²⁷ in which a volume upstream from the slice is pre-excited and dephased have also been used in cardiac imaging. A motion-sensitizing magnetization preparation technique²⁸–³⁰ can also suppress the blood pool by dephasing all moving blood spins. However, these preparation sequences are not directly applicable to myocardial T₂ mapping. DIR sequence suffers from the problem of insufficient recovery time for T₂ mapping within a single R-R interval (the interval time between two R waves). Spatial saturation pulses cannot robustly suppress the blood chamber due to complex blood motion. DIR preparation also suffers from slow blood flow. Furthermore, motion-sensitized techniques cause additional signal suppression in the myocardium that impact T₂ measurements. Therefore, there is an unmet clinical need for developing a robust black blood T₂ mapping sequence.

In this study, we sought to develop a black blood myocardial T₂ mapping sequence. Numerical simulation and phantom experiments were used to evaluate the proposed sequence. In vivo studies in healthy subjects, patients, and an animal model were used to investigate the efficacy of the sequence to suppress the blood pool in myocardial T₂ mapping.

## 2 METHODS

All the scans were performed on a 1.5T MR system (Philips Achieva, Philips Healthcare, Best, The Netherlands), with maximum amplitude of 40 mT/m and a slew rate of 150 mT/m/ms. A 32-channel cardiac coil was used for signal reception.

### 2.1 Pulse sequence design

We propose a “Black blood hEart-rate Adaptive T₂-prepared bSSFP (BEATS)” sequence (Figure 1A) for myocardial T₂ mapping. The pulse sequence consists of 3 preparation pulses: 1) a preexcitation nonselective RF pulse with a flip angle of β, 2) DIR pulses, and 3) T₂prep pulses. Imaging was performed using bSSFP readouts, similar to a conventional bright blood T₂ mapping sequence.¹⁵

A DIR pulse is combined with T₂ preparation pulses to obtain T₂ mapping with blood suppression. However, blood suppression by DIR preparation pulses requires a long delay time for blood magnetization recovery (due to the long blood T₁ relaxation time), which is not feasible within a single R-R interval. Therefore, we propose to insert a preexcitation pulse with an adaptive flip angle prior to the DIR pulse (Figure 1A). The preexcitation pulse is implemented as a nonselective RF pulse followed by dephasing gradients. The flip angle of this preexcitation pulse is adaptively selected based on the patient’s heart rate to ensure that the blood signal is fully suppressed within an R-R interval. After the preexcitation pulse, DIR pulses are performed subsequently with a pair of inversion pulses: a nonselective 180° inversion pulse followed immediately by a slice-selective 180° inversion pulse. The width of the selective inversion pulse is 3 times that of the imaging slice thickness. Subsequently, T₂prep pulses, including an initial 90°, pulse, followed by 2
composite 180° pulses and a final 90°-x flipback pulse,7,15 are applied to generate T2 weighting with variable TE. Finally, black blood T2-weighted images are acquired with single-shot bSSFP readouts. A rest period of 3 heart beats is used following each image acquisition to ensure sufficient magnetization recovery.

The longitudinal signal changes during the BEATS sequence are shown in Figure 1B. After the preexcitation pulse, the longitudinal magnetizations (M_z) are reduced to \( \cos(\beta) \) of the initial magnetization \( M_0 \), and then recovered according to the T1 relaxation times:

\[
M_z(TD_b) = M_0 + M_0 \left( \cos(\beta) - 1 \right) \cdot e^{-TD_b/T_1},
\]

where \( M_0 \) is the initial longitudinal magnetization; \( \beta \) is the flip angle of the preexcitation pulse; and \( TD_b \) is the duration between the preexcitation pulse and the nonselective 180° pulse in DIR. After the application of DIR pulses, the blood signal is immediately inverted while the myocardial signal remains. During the TI time (i.e., the time between the nonselective 180° pulse and the start of T2prep pulses), blood and myocardial signals recover as follows:

\[
M_{z\text{blood}}(TI) = M_{0,\text{blood}} - \left( M_{0,\text{blood}} - M_{z\text{blood}}(TD_b) \right) \cdot e^{-TI/T_1}. 
\]

According to Equation 2, if \( TI \) is selected as \( T_1 \cdot \ln((M_0 + M_{z\text{blood}}(TD_b))/M_0) \), the blood signal can be fully nulled before the T2prep pulses. However, because the heart rate varies among different patients, it is difficult to fix the timing of TI. Therefore, we propose an adaptive timing design in which \( TI \) and \( \beta \) are automatically calculated based on the patient heart rate. The \( TI \) is set to \( T_{\text{dia}}-TD_b-T_{\text{TE2prep}} \) to acquire the data during the diastolic rest phase, for which \( T_{\text{dia}} \) is the trigger delay time and \( T_{\text{TE2prep}} \) is the TE of the T2 preparation pulse. The \( \beta \) is then calculated according to Equations 1 and 2, and given by:

\[
\beta = \arccos \left( 1 + e^{-TD_b/T_{\text{blood}}} \cdot \left( e^{-T_{\text{dia}}-TD_b-T_{\text{TE2prep}}/T_{\text{blood}}} - 2 \right) \right). 
\]

TI and \( \beta \) are adaptive to different heart rates in the BEATS sequence (Figure 1C), with \( T_{\text{dia}} \) equal to 1600 ms.30 A preexcitation pulse duration (\(~0.2 ms\) ), dephasing gradients (3.1 ms), a nonselective 180° inversion pulse (6.1 ms), and a \( TD_b \) of 20 ms (fixed empirically) were applied in this study.

### 2.2 Numerical simulations

Bloch simulation was performed to investigate the influence of heart rate (beats per minute [bpm]) and tissue T1 times
both on the efficiency of blood suppression and on the recovery of the myocardial signal in the BEATS sequence. The heart rates were simulated from 40 bpm to 130 bpm, whereas the blood and myocardial T1 values were simulated ranging from 1200 ms to 2000 ms and from 600 ms to 1600 ms, respectively. The value of \( \beta \) was calculated according to Equation (4), assuming a fixed arbitrary value for \( TD_β \) (20 ms) and \( T1_{\text{blood}} \) (=1600 ms). \( TI \) was estimated as a function of heart rate (HR):

\[
TI \approx 60(s)/HR \cdot T_{\text{rest}},
\]

where \( T_{\text{rest}} \) was the remaining time (ms) in each R-R interval (assumed to be 250 ms), including the acquisition window, trigger delay time, and pulse durations; and HR is heart rate. The blood and myocardium suppression were evaluated by calculating \( S1_{\text{blood}}/S1_{\text{blood},0} \) and \( S1_{\text{myo}}/S1_{\text{myo},0} \) in which \( S1_{\text{blood}} \) (or \( S1_{\text{myo}} \)) was the residual blood (or myocardium) signal intensity (SI) after the inversion recovery and \( S1_{\text{blood},0} \) (or \( S1_{\text{myo},0} \) ) represented the initial blood (or myocardium) signal intensity before suppression.

### 2.3 Phantom study

To evaluate the performance of the BEATS sequence, phantom scans were performed on 6 NiCl2 doped agarose vials, with similar \( T2 \) values as the myocardial \( T2 \) (~40 ms) but different \( T1 \) values.\(^{31}\) Both BEATS and conventional bright blood \( T2 \) mapping were performed on the phantom. The scanning parameters of the phantom were as follows: FOV = 320 × 320 mm\(^2\), in-plane resolution = 2 × 2 mm\(^2\), slice number = 1, slice thickness = 8 mm, SENSE factor = 2.5, bSSFP readout with TR/TE = 2.8/1.4 ms, flip angle = 60°, 10 linear ramp-up pulses, linear k-space ordering, and acquisition window = 150 ms. A total of 9 different \( T2_{\text{prep}} \) TEs were used, including \( T2_{\text{prep}} = 0, T2_{\text{prep}} = \infty, \) and \( T2_{\text{prep}} \) values ranging from 25 ms to 95 ms with linear steps of 10 ms.\(^{15}\) The \( T2_{\text{prep}} \) of \( \infty \) was representative of the long \( T2_{\text{prep}} \) TE achieved by applying a saturation pulse prior to image acquisition. Heart rates of 60 bpm were simulated for the conventional bright blood \( T2 \) mapping. For the BEATS scans, heart rates of 60, 70, 80, 90, 110, and 130 bpm were simulated to test whether they affected \( T2 \) measurement accuracy. To evaluate the repeatability of the \( T2 \) measurements, the BEATS sequence scan was repeated 3 times with 10 min between scans.

Reference \( T2 \) relaxation times were obtained using a SE sequence of 32 echoes. The scanning parameters were as follows: FOV = 320 × 320 mm\(^2\), in-plane resolution = 2 × 2 mm\(^2\), slice thickness = 8 mm, flip angle = 90°, TR = 10 s, TEs from 10 ms to 320 ms with gaps of 10 ms, and number of signal averages = 4. Reference \( T1 \) relaxation times were acquired using the SE sequence with 16 inversion times of 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1250, 1500, 1750, 2000, and 3000 ms. The other imaging parameters were: FOV = 320 × 320 mm\(^2\), in-plane resolution = 2 × 2 mm\(^2\), slice thickness = 8 mm, flip angle = 90°, TR/TE = 10 s/10 ms, and number of signal averages = 4. Both \( T1 \) and \( T2 \) values from the SE images were calculated using a 3-parameter fit model.\(^{32,33}\)

### 2.4 In vivo human study

This study was approved by our local institutional review board, and written informed consents were obtained from all participants. In vivo human studies were performed on 8 healthy adult subjects (26.0 ± 4.7 years, range: 21–35 years, 2 males) and 36 patients (55.1 ± 16.6 years, range: 20–82 years, 20 males) who were referred for clinical cardiac MR examinations. The patient population consisted of patients with suspected or known hypertrophic cardiomyopathy (\( N = 5 \)), nonischemic cardiomyopathy (\( N = 9 \)), suspected or confirmed ischemic cardiomyopathy (\( N = 4 \)), arrhythmias (\( N = 8 \)), valvular heart disease (\( N = 2 \)), left ventricular hypertrophy (\( N = 3 \)), lipomatous atrial septal hypertrophy (\( N = 1 \)), athletic cardiomyopathy (\( N = 1 \)), suspected or confirmed myo- or pericarditis (\( N = 2 \)), and cardioxic cardiomyopathy (\( N = 1 \)). For each subject, localizer scout images were first acquired to define the midventricular short-axis slice. For both BEATS and conventional bright blood \( T2_{\text{prep}} \)-bSSFP imaging, free-breathing ECG-triggered single-shot bSSFP readout was used for data acquisition. Sequence parameters were as follows: FOV = 320 × 320 mm\(^2\); in-plane resolution = 2 × 2 mm\(^2\); slice number = 3; slice thickness/gap = 8/4 mm; SENSE factor = 2.5; TR/TE = 2.8/1.4 ms; flip angle = 60°; and 9 \( T2_{\text{prep}} \) TEs, including \( T2_{\text{prep}} = 0, 25, 35, 45, 55, 65, 75, 85, 95, \) and \( \infty \) ms. A 2D spiral-beam navigator was placed at the lung–liver interface of the right hemidiaphragm and was used for gating with a window of 5 mm. The typical scan time for each slice was ~40 sec. To assess the scan repeatability of black blood \( T2 \) imaging using the BEATS sequence, each scan was repeated 3 times, 10 min apart, in only healthy adult subjects. Because recruited patients included those referred for clinical cardiac MR examinations, there was not sufficient time to assess repeatability in patients.

### 2.5 Animal study

The protocol was approved by The Beth Israel Deaconess Medical Center Institutional Animal Care and Use Committee and conformed to the position of the American Heart Association on Research Animal Use and the Declaration of Helsinki. Ischemia–reperfusion mediated MI was induced in 1 Yorkshire swine (35 kg), as previously described.\(^{34,35}\) Under fluoroscopic guidance, an angioplasty balloon was inflated in the mid-left anterior descending for 180 minutes.
The balloon was then deflated and withdrawn to create an ischemia–reperfusion mediated MI. The animal was imaged 1 week after infarct creation using an imaging protocol, which included both conventional bright blood T2 mapping and the BEATS sequence with similar imaging parameters, as described above in our human study.

2.6 Data analysis

T2 maps were reconstructed offline using a custom-written program on MatLab (MathWorks, Natick, Massachusetts). A 3-parameter fitting model was applied for pixel-wise T2 quantification:

\[ S_{\text{myo}}(T_{E_{T2\text{prep}}}) = A \cdot e^{-\frac{T_{E_{T2\text{prep}}}}{T_2}} + B, \]

where \( T_{E_{T2\text{prep}}} \) is the TE; \( A \) is a function of the signal at full recovery; \( T_2 \) is the myocardial T2 relaxation time; and \( B \) characterizes the effect of the bSSFP imaging pulses that were played until the acquisition of the central k-space line. Given a set of images acquired at different (known) TEs, the model in Equation 6 is used to fit the intensities at each voxel to estimate the parameter \( T_2 \).

In the phantom experiments, region-of-interest (ROI) analysis was performed for each vial, for which the mean value and SD were recorded. Identical ROIs were used in all the T2 maps with different simulated heart rates. SNR was calculated in the source images at \( T_{E_{T2\text{prep}}} = 0 \) ms as the average signal in the phantom divided by the SD of the noise region. ROI for the noise measurement was selected from a background area free of image artifacts.

For the in vivo study, the acquired images were coregistered using an affine coregistration algorithm before T2 fitting. Voxel-wise curve fitting was then performed on both black blood and conventional bright blood T2prep-bSSFP images according to Equation (5). To avoid fitting for the residual blood signal in black blood T2prep-bSSFP images, a threshold processing was performed. The threshold was selected empirically as 20% of the myocardial signal intensity in the black blood T2prep-bSSFP image, with \( T_{E_{T2\text{prep}}} = 0 \). Regions with signal intensities below this threshold were avoided by the T2 fitting. The myocardium was manually traced by drawing the epicardial and endocardial contours. T2 profiles of a cross section of the midventricular slice were obtained on black blood and conventional bright blood T2 maps. To evaluate the effectiveness of blood suppression, the blood-to-myocardial signal ratio was measured for each subject.

Furthermore, a segment-based analysis was performed to investigate the regional T2 variations. Six segments were used in the midventricular slice, in accordance with the American Heart Association segmentation guidelines. In each segment, the mean T2 value and its SD were calculated.

In clinical patients, interobserver agreement for T2 quantification was assessed by using intraclass correlation coefficient analysis from 10 randomly selected patients.

A subjective analysis was conducted by 2 experienced readers (U.N. and R.N.) in consensus to assess artifacts due to blood flow from DIR pulses in BEATS. Readers evaluated the T2 maps (reconstructed without performing any thresholding of signaling, as described above) and original T2-weighted images to identify slices with artifacts associated with incomplete suppression of the blood pool. The number of slices impacted by the artifacts are reported for apical, midventricular, and basal slices. Furthermore, for patients with flow artifacts, readers indicated whether the presence of flow artifact impacted their confidence in reliably measuring myocardial T2 values.

2.7 Statistical analysis

Data were reported as median (25th percentile; 75th percentile). The accuracy of the BEATS T2 measurement was assessed as the difference between the black blood T2 maps and reference T2 maps acquired with the standard SE sequence. Precision was assessed as the SD within the ROIs for the given T2 map. A higher SD indicates lower precision. Repeatability was defined as the SD over the 3 repeated scans of the spatial average T2 values in each subject. The accuracy, precision, and repeatability of the values were measured in each segment of the myocardium. The Wilcoxon signed-rank test was conducted to compare the T2 measurements with different methods. A \( P \) value of less than 0.05 was considered statistically significant.

3 RESULTS

3.1 Numerical simulation

In the numerical simulation, both heart rate and blood T1 relaxation time influence blood suppression (Figure 2A). The remaining blood signal dropped as the simulated heart rate increased due to limited T1 decay time. However, the residual blood signal after inversion recovery was maintained within 22.7% of the original blood signal for a wide range of simulated blood T1 values ranging from 1200 to 2000 ms.

Myocardial signal recovery was influenced by the heart rate and the myocardial T1 relaxation time (Figure 2B). As expected, the heart rate showed a strong influence on the myocardial signal intensity. For example, at \( T_1 = 1200 \) ms, the relative myocardial signal dropped as the simulated heart rate increased (1.00, 0.91, 0.79, 0.68, 0.58, 0.51, 0.44, 0.38, and 0.33 for simulated heart rates of 40, 50, 60, 70, 80, 90, 100, 110, and 120 bpm, respectively) due to reduced TI. In general, for \( T_1 < 1200 \) ms and heart rate < 85 bpm, more than 69.3% of the myocardial signal was preserved.
3.2 | Phantom

T₂ maps generated from the SE, conventional bright blood, and BEATS sequences are shown in Figure 3. The T₂ measurements of the phantoms using conventional bright blood and the BEATS sequence with different simulated heart rates are shown in Supporting Information Figure S1. Compared to T₂ measured from conventional bright blood T₂ mapping, the average T₂ measurements in BEATS T₂ maps were not affected with increased heart rates within a range of 60 to 110 bpm; however, higher heart rates decreased measurement precision (observed as increased SD). The SNR within the different vials decreased as the heart rate increased (Figure 4A) due to insufficient time for signal recovery. Good repeatability was achieved for the BEATS T₂ mapping, as measured by the SDs over repeated scans (0.29 ms, 0.35 ms, 0.29 ms, and 0.42 ms for heart rate of 60, 70, 80, 90, and 100 bpm, respectively). The phantom experiment confirmed the accuracy of the BEATS T₂ mapping (Figure 4B). As expected, T₂prep and heart rate had no impact on the accuracy of T₂ measurements in a range of 60 to 110 bpm but did have an impact at heart rates higher than 130 bpm. There was no difference in T₂ values in vials measured using the BEATS or conventional bright blood T₂ mapping sequences over heart rates of 60 to 130 bpm.

3.3 | In vivo human study

Black blood myocardial T₂ images were successfully obtained in all subjects using the BEATS sequence. The average heart rate was 67 ± 5 bpm (range: 55–75 bpm) for healthy subjects and 66 ± 11 bpm (range: 49–96 bpm) for patients. The blood-to-myocardial signal ratio was reduced from 3.03 (2.56; 3.72) to 0.15 (0.13; 0.17) (P = 0.01) in healthy subjects. T₂-weighted images with TET₂prep = 0, 25, and 55 ms, as well as fitted T₂ maps acquired by BEATS and conventional bright-blood T₂ mapping sequences, are shown in 2 healthy subjects with different heart rates: 70 bpm (subject 1) and 55 bpm (subject 2) (Figure 5). In both cases, the BEATS sequence produced T₂-weighted images without any visual artifact. Both images demonstrate a relatively high contrast between the myocardium and the blood pool, with defined borders. The partial volume effect was significantly reduced with the suppression of intraventricular blood signals.
Compared to conventional bright blood T2 mapping, BEATS T2 mapping successfully reduced the blood signal, leading to better depiction of the myocardial structures. Signal intensity profiles were drawn in the T2 maps across the myocardium (Figure 6, red lines). The T2 profiles have a much sharper transition between blood and myocardium compared to those in conventional bright blood T2 maps, suggesting a decrease in the partial volume effect of myocardial T2. Segment-based measurements show comparable T2 values calculated from BEATS and bright blood T2 mapping sequences (Figure 6). Example T2 maps from our patients are presented in Figure 7 and show good image quality and maps. The original T2-weighted images are included in Supporting Information Videos S1 and S2. Myocardial edema was visually present in only 1 patient with a recent history of MI (Figure 8). Arrows show areas of higher T2 values (59–63 ms) located at areas with recent infarct. A signal difference in this region can also be seen on original black blood T2 weighted images.

No significant difference was found between the average T2 measurements obtained from the BEATS and conventional bright-blood T2 maps (48.8 ms [48.2; 50.0] vs. 48.7 ms [48.0; 49.9], \( P = 0.67 \) in healthy subjects and 48.9 ms [47.1; 51.7] vs. 50.4 ms [48.7; 51.8], \( P = 0.05 \) in patients) (Figure 9). The interobserver agreement for both T2 maps was strong, with an
**FIGURE 6**  Examples of $T_2$ mappings obtained from conventional bright-blood $T_2$-prep-bSSFP and BEATS sequences and the $T_2$ profiles (drawn with interpolation). Segment-based $T_2$ measurements of both cases are also shown in the bullseye. The red lines in the $T_2$ mappings indicate where the $T_2$ profiles are generated. $T_2$ profiles through the $T_2$ maps indicate substantially steeper myocardial–blood transitions in the BEATS $T_2$ maps.

**FIGURE 7**  Examples of $T_2$-weighted images (TE = 0, 55, 95 ms) and $T_2$ maps acquired with BEATS from 2 patients with heart rates of 60 bpm (upper) and 70 bpm (lower). Both $T_2$-weighted images and $T_2$ maps show good image quality.
intraclass correlation coefficient of 0.74 (95% confidence interval [CI]: 0.29–0.93) for BEATS, and intraclass correlation coefficient of 0.93 (95% CI: 0.75–0.98) for the bright-blood T2 map. Homogeneous T2 maps, as quantified by precision, were observed throughout the myocardium using both techniques, with a decrease in precision for the BEATS sequence due to loss of signal associated with the DIR pulse (healthy subjects: 6.87 ms [6.2; 7.3] vs. 4.9 ms [4.7; 6.6] P = 0.01, patients: 8.4 ms [7.3; 11.1] vs. 6.7 ms [5.7; 7.8], P < 0.001). Repeatability analysis in healthy subjects shows that the variability of T2 measurements was low and thus comparable between the 2 techniques (BEATS, 2.0 ms [1.6; 2.5]; bright-blood T2, 1.95 ms [1.6; 2.2], P = 0.58).

The subjective assessment showed that 16% (18 of 108) of short-axis slices have artifacts due to a residual blood signal from the DIR pulse in BEATS (12 in the apical slice, 4 in the midventricular slice, and 2 in the basal slice). However, the slow-flowing blood artifact only impacted measurements in 10 slices (6 at the apex, 3 at the midventricle, and 1 at the base). The flow artifacts often resulted in large T2

**FIGURE 8** Posterior left ventricular wall edema after a myocardial infarct. The patient presented with new onset chest pain and electrocardiographic findings consistent with a posterior myocardial infarction (A, ST-segment depression and inverted T waves in V2–3; arrows). On coronary angiogram, a large obtuse marginal branch was occluded (B; arrow), and flow was reestablished with complete filling of the artery (C; arrow). On day 4 postinfarct, comparison of the myocardial T2 mappings obtained from conventional bright blood T2prep-bSSFP and BEATS sequences (D) showed left ventricular subendocardial edema (red arrows). Segment-based T2 measurements were also shown in the bullseye. ST-segment, the segment of the ECG between the end of the S wave and the beginning of the T wave
values or noisy areas with random values that could be identified by reviewing original T2 weighted images. The location of artifacts was random and varied among different patients, including the middle of the left ventricular cavity, the subendocardial region, and around the papillary muscle where blood is trapped between the papillary muscle and the myocardium (Supporting Information Figure S2). There was no correlation between the presence of flow-related artifacts and heart rate (Spearman’s rho 5 0.19, P 5 0.27), and artifacts were present in patients with both low and high heart rates (Supporting Information Figure S3) (Supporting Information Video S3 shows images of a patient with a heart rate of 96 bpm). In 1 patient, there was a large subendocardial enhancement in BEATS T2 maps, consistent with the patient’s clinical history; however, readers (U.N. and R.N.) could not confirm with confidence if the increased T2 was due to presence of edema or slow blood flow (Supporting Information Figure S4) (Supporting Information Video S4).

3.4 | Animal study

T2-weighted images and corresponding T2 maps in swine confirms the presence of edema (red arrows) in the anterior septum, consistent with the location of the infarct in our animal model (Figure 10). The measured T2 in an ROI within the edematous region was 82 ms for conventional bright blood T2 mapping and 81 ms for BEATS T2 mapping. The extent of edema was better depicted in the BEATS T2 map due to the suppression of the blood signal. Furthermore, the T2 weighted images with the suppressed blood pool in the BEATS sequence yielded improved depiction of myocardial edema in the anterior septum (red arrows), further confirming the presence of edema.

4 | DISCUSSION

In this study, we present a black blood myocardial T2 mapping sequence to reduce the partial voluming effect present in conventional bright blood T2 mapping by suppressing the blood signal using a combination of preexcitations and DIR pulses. The performance of the BEATS T2 mapping sequence was evaluated by numerical simulations, phantom studies, and in vivo studies. The results of our study demonstrated that the BEATS sequence yields images with suppressed blood pool signal, resulting in better definition of the blood–myocardium border and improved visualization of edema/inflammation.

In the BEATS sequence, selection of appropriate timings of the preexcitations and DIR pulses are essential for blood suppression and the minimization of SNR loss. These parameters should be adaptively selected based on an individual heart rate to achieve blood suppression. A lower flip angle of the preexcitation pulse will minimize the myocardial signal loss and improve SNR, but longer TI will be required. In the BEATS sequence, we proposed an adaptive parameter design according to the patient’s heart rate. TI and flip angle of the preexcitation pulse are autocalculated in the sequence to achieve optimal blood suppression with minimal myocardial signal loss. In our study, we applied a 3-parameter fitting model to 9 T2-weighted images, with an additional saturated image acquired during free-breathing to estimate the T2 maps. However, T2 maps can be estimated with as low as 4 images within a single breath-hold, albeit with lower precision.

One of the challenges of the DIR preparation pulse in black blood T2 mapping is the limitation of the number of slices that can be acquired per scan. There have been recent advances in myocardial T2 mapping to increase coverage and data acquisition efficiency using either whole heart or slice-interleaved acquisition. Our current implementation of BEATS limits the acquisition to a single slice per acquisition. Improved DIR for multi-slice imaging has been previously demonstrated and could potentially be adopted for BEATS T2 mapping and warrant further investigation.
Inflammation or edema could also occur in the thin wall of the left atrium (LA) or right ventricle. For example, radiofrequency ablation for treatment of atrial fibrillation causes LA edema, which can be detected with $T_2$ weighted imaging\cite{44-46}; however, $T_2$ weighted imaging in LA or right ventricle is challenging and interpretation is subjective. Conventional bright blood $T_2$ maps do not allow accurate measurement of LA $T_2$ due to partial voluming. The proposed black blood $T_2$ mapping could potentially be used to measure LA/right ventricle $T_2$; however, it will require higher spatial resolution. Further validation and technical improvements are necessary to develop high-resolution black blood $T_2$ mapping for LA/right ventricle.

We used a combination of a preexcitation pulses with DIR to suppress the blood pool in BEATS. We only acquired $T_2$ maps in the short-axis view because DIR does not effectively null the blood signal if blood flows within the imaging plane (Supporting Information Figure S5). One main problem with DIR could be slow-moving blood along the myocardial border. This is a well-known problem in myocardial regions affected by disease (e.g., dyskinetic myocardium following MI), overall contractile motion anomalies as observed in myocarditis, or significant trabeculations. In such cases, the stagnant blood can appear bright in each individual $T_2$-prep-SSFP image. However, blood will experience different preparation pulses in subsequent data acquisitions, and the signal may not follow a simple $T_2$ decay. Therefore, the region may either appear noisy in the estimated $T_2$ maps or with very high $T_2$ values. Our preliminary data shows these types of artifacts could occur in different slices and in patients with different heart rates. A combination of postprocessing to account for blood flow may be used to mitigate the issue. Further studies are needed to minimize artifact in the proposed black blood $T_2$ mapping sequence.

Our study has limitations. We used a predetermined fixed $T_1$ and did not measure $T_1$ values of the blood to optimize the imaging parameters. A patient-specific blood $T_1$ can be acquired using the $T_1$ mapping sequence, but this was not studied. For high heart rates $>100$ bpm, the myocardial signal will decrease, which could impact measurement accuracy and precision. For patients with high heart rates, DIR pulses and imaging readouts can be applied in 2 subsequent heartbeats; however, this will make the sequence sensitive to heart rate variability. The sample size of our patient data was small, and the majority of patients did not have edema or inflammation. Therefore, we cannot assess the diagnostic accuracy of BEATS; doing so requires a rigorous animal study with histological validation, which is not within the scope of our study. There is no gold standard noninvasive imaging modality with sufficient spatial resolution that can be used to assess sensitivity or specificity of black blood $T_2$ 

**FIGURE 10** Example of short-axis midventricular $T_2$ maps obtained from conventional bright-blood $T_2$-prep-bSSFP and BEATS sequences in an animal model with prior myocardial infarction. Edema was observed in anterior septum (red arrows) in both maps (bright-blood: 82 ms, BEATS: 81 ms). Signal intensity profiles drawn across the myocardium in edema (yellow lines) in BEATS show sharper transition between blood and myocardium.
mapping sequencing for identifying subendocardial inflammation in patients.

5 | CONCLUSION

The proposed black blood myocardial $T_2$ mapping sequence efficiently suppresses the blood signal, resulting in better definition of the blood–myocardium border by reducing the impact of the partial volume effect that is present in conventional bright-blood $T_2$ mapping. The residual blood flow associated with DIR is a limitation of the proposed technique.

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REFERENCES


**SUPPORTING INFORMATION**

Additional supporting information may be found in the online version of this article.

**FIGURE S1** T2 measurements of phantoms using conventional bright-blood T2prep-bSSFP (simulated heart rates of 60 bpm) and BEATS sequences with different simulated heart rates ranging from 60 bpm to 110 bpm. T1 values of each vial are shown on the left-top, denoted as Reference T1. All measurements are displayed with average T2 (top number) and standard deviation (bottom number), except for the reference T1 and T2 values.

**FIGURE S2** Example slices from 4 different patients with different degrees of blood flow related artifacts (red arrows). The residual artifacts could occur on different locations; however, it often has a different signal level and recovery curve compared to the myocardium. Images at the apex show more artifacts at the mid-LV blood cavity (bottom right case).

**FIGURE S3** Example of T2*-weighted images and BEATS T2 maps in apical, mid-ventricular, and basal slices from a...
patient with a heart rate of 96 bpm. Arrows show areas of blood-related artifact.

**FIGURE S4** Stunned myocardium after a non-ST segment elevation myocardial infarction (NSTEMI) affecting the left anterior descending artery territory. The patient was admitted with chest pain, a small troponin rise (Troponin I 0.12 ng/ml) and unspecific electrocardiographic changes (A). A coronary angiogram showed sequential severe stenosis in the left anterior descending artery (B, arrows). A cardiac MRI (C) on day 5 post NSTEMI showed improving left ventricular systolic function (LV ejection fraction of 59% vs. 35% on day 1 echocardiogram) with apical and mid-septal hypo- to dyskinesis. As the left ventricular function fully recovered 2 months later, the subendocardial to transmural late gadolinium enhancement (C, arrows) likely reflects cardiac edema secondary to stunned myocardium. In this context, septal subendocardial signal intensity appeared increased on short axis T2-weighted images by BEATS (TE = 0, 25, 55 ms; D-F) with the slice location and orientation depicted by green and orange lines (D). Comparison of T2 maps obtained from conventional bright blood T2prep-bSSFP (G) and BEATS (H) showed different results. This could potentially reflect on improved delineation of the subendocardial region on BEATS, blood flow, related artifacts, or both.

**FIGURE S5** Example of T2-weighted images and BEATS T2 maps acquired in short axis (SHAX), 4-chamber (4CH), horizontal long axis (HLA), and 2-chamber (2CH) views. In the imaging plane where the blood flows within the plane such as the 4CH, HLA, and 2CH views, DIR does not effectively null the blood signal.

**VIDEO S1** Examples of original T2-weighted images acquired with BEATS from one patient with heart rates of 60 bpm.

**VIDEO S2** Examples of original T2-weighted images acquired with BEATS from one patient with heart rates of 70 bpm.

**VIDEO S3** Example of original T2-weighted images in apical, mid-ventricular, and basal slices from a patient with a heart rate of 96 bpm.

**VIDEO S4** Example of original T2-weighted images in a patient with suspected large subendocardial enhancement in BEATS T2 maps.