Saturation-Pulse Prepared Heart-Rate Independent Inversion-REcovery (SAPPHIRE) Biventricular T1 Mapping: Inter-Field Strength, Head-To-Head Comparison of Diastolic, Systolic And Dark-Blood Measurements

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Abstract

Purpose To assess the feasibility of SAPHIRE T_1 mapping *in vivo* across field strengths and compare results to those obtained by conventional Modified Look-Locker inversion recovery (MOLLI).

Methods 10 healthy volunteers underwent same-day non-contrast cardiovascular magnetic resonance at 1.5 Tesla (T) and 3T. Left and right ventricular (LV, RV) T_1 mapping was performed in the basal, mid and apical short axis using MOLLI and 4-variants of SAPHIRE: diastolic, systolic, 0th and 2nd order motion-sensitized dark blood (DB).

Results LV myocardial T_1 times differed significantly between MOLLI and each of the SAPHIRE variants (all $p < 0.005$). LV global myocardial T_1 (1.5T then 3T results) was significantly longer by diastolic SAPHIRE (1283±11|1600±17ms) than any of the other SAPHIRE variants: systolic (1239±9|1595±13ms), 0th order DB (1241±10|1596±12) and 2nd order DB (1251±11|1560±20ms, all $p < 0.05$). In the mid septum MOLLI and diastolic SAPHIRE exhibited significant T_1 signal contamination (longer T_1) at the blood-myocardial interface not seen with the other 3 SAPHIRE variants (all $p < 0.025$). Additionally, systolic, 0th order and 2nd order DB SAPHIRE showed narrower dispersion of myocardial T_1 times across the mid septum when compared to diastolic SAPHIRE (interquartile ranges respectively: 25ms, 71ms, 73ms vs 143ms, all $p < 0.05$). RV T_1 mapping was achievable using systolic, 0th and 2nd order DB SAPHIRE but not with MOLLI or diastolic SAPHIRE. All 4 SAPHIRE variants showed excellent re-read reproducibility (intraclass correlation coefficients 0.953 to 0.996).

Conclusion These preliminary data suggest that systolic and DB SAPHIRE approaches can reduce myocardial T_1 signal contamination by the adjacent bright blood pool at the blood-myocardial interface.

Introduction

The myocardial longitudinal relaxation time, T_1 is a sensitive imaging biomarker for heart muscle disease, linked to both functional capacity and mortality [1–5]. Native myocardial T_1 mapping, that is without the administration of gadolinium-based contrast agents (GBCA), measures this myocardial relaxation time making it a useful imaging biomarker for fibrosis.

The general principle for obtaining T_1 maps is to acquire multiple images each with a different T_1 weighting on a longitudinal magnetisation recovery curve. Various techniques have been proposed to quantify T_1 relaxation (Fig. 1), each with its own advantages and limitations. One of the main issues of commonly-used T_1 mapping techniques is the partial volume effect that can artifactually increase the myocardial T_1 times of voxels located at the myocardial-blood pool interface due to confounding by the higher native T_1 signal of the blood pool (consider that typical native myocardial T_1 is ~ 1000ms while native blood pool T_1 is ~ 1500ms at 1.5 Tesla (T)). This is most apparent in cross sectional imaging and its effects are especially detrimental to the study of thin-walled cardiac structures, notably the right

ventricular (RV) free wall, atrial walls and the thinned myocardium in dilated cardiomyopathy (DCM) [6, 7]. Partial volume effects are problematic because they reduce the accuracy and reproducibility of T_1 mapping. To overcome this problem in the right and left ventricles (LV), systolic readouts have been proposed [8, 9], as it was hypothesized that the increased myocardial wall thickness during systole would increase the abundance of myocardial voxels that were free from partial volume effects. It follows then that systolic T_1 mapping would measure lower myocardial T_1 values at the blood-myocardial interface compared to conventional diastolic T_1 mapping because of the reduced confounding from the high blood pool signal.

The modified Look-Locker inversion recovery (MOLLI) sequence is still the most commonly used T_1 mapping approach in clinical practice due to its widespread availability across vendors and superior precision and reproducibility when compared to most other sequences and prototypes [11]. Being an inversion recovery-based approach, it is vulnerable to the aforementioned partial volume effects, as well as to off-resonance artifacts, and confounding contributions by magnetisation transfer and T2 effects [12]. MOLLI and its derivative, shortened MOLLI (ShMOLLI), have higher precision than the saturation recovery-based T_1 mapping technique SATuration-recovery single-SHot Acquisition (SASHA) but are less accurate and prone to underestimate T_1 [13].

A T_1 mapping sequence that combines saturation recovery and inversion recovery approaches, termed SAPPHIRE–SATuration Pulse Prepared Heart-rate independent Inversion REcovery–has recently been shown to have potential advantages in arrhythmia [14]. A further refinement to SAPPHIRE that provides blood suppression resulting in dark-blood (DB) native myocardial T_1 mapping has shown additional promise at addressing the problem of myocardial signal contamination from the adjacent blood pool [7]. DB SAPPHIRE potentially measures more accurate T_1 than the conventional diastolic SAPPHIRE because of less contamination from the blood pool signal, but this is at the expense of precision.

Here we undertake a head-to-head comparison of MOLLI versus SAPPHIRE T_1 mapping across field strengths. We assess the performance of LV and RV SAPPHIRE T_1 mapping *in vivo* considering 4 of its variants: diastolic, systolic, 0th and 2nd order DB SAPPHIRE, and compare results to those obtained by conventional MOLLI across field strengths.

Materials And Methods

All subjects provided written informed consent. The study received ethical approval from the University College London (UCL) Research Ethics Committee (Project number 6782/001) and it conformed to the principles of the Helsinki Declaration.

Study population and data collection

In this prospective single-center observational study, 10 healthy volunteers underwent non-contrast CMRI scanning at both field strengths on the same day at the UCL Bloomsbury Center for Clinical Phenotyping

(London, UK). Volunteers had no prior cardiac history or known cardiac risk factors, were not on cardiovascular medications, had a normal resting electrocardiogram (ECG), and were free of conventional contra-indications for CMRI.

Cardiovascular magnetic resonance

CMRI studies were performed using two Siemens MR systems (Erlangen, Germany): MAGNETOM AERA 1.5 Tesla (T) (Serial Number 141303) operating VE11C-SP01 and MAGNETOM PRISMA 3T (Serial Number 166032) operating VE11C-SP01, with an 18-channel phased-array chest coil. The scan protocol was identical for the two field strengths and consisted of localizers, transaxial black blood HASTE anatomical stack, breath-held retrospectively ECG-gated balanced steady-state free precession (bSSFP) cines in standard long and short axis views[15], and then breath-held ECG-gated T_1 mapping in the basal, mid and apical LV short axis slices (co-registered with the cines) using MOLLI with motion correction (MOCO), bright-blood diastolic SAPHIRE, bright-blood systolic SAPHIRE, 0th order DB SAPHIRE and 2nd order DB SAPHIRE in random order per scan. To minimize off-resonance artifacts with higher field strengths, the 3T protocol additionally included frequency scouts and attention to volumetric shimming.

Typical imaging parameters for the sequences were as follows:

Cine bSSFP **1.5T**: Repetition time (TR, time between two consecutive excitations)/ echo time (TE) 35/1.14ms, flip angle (FA) 73°, matrix 168 x 208. **3T**: TR/TE 38.09/1.25ms, FA 43°, matrix 168 x 208.

MOLLI 5s(3s)3s **1.5T**: TR/TE 291.84/1.22ms, FA 35°, matrix 256 x 144, 125 phase-encoding steps, trigger delay (TD) 605ms, slice-thickness 8mm. **3T**: TR/TE 283.8/1.16ms, FA 20°, matrix 256 x 144, 125 phase-encoding steps, TD 780ms, slice-thickness 8mm.

Bright-blood diastolic SAPHIRE **1.5T**: TR/TE 830/1.12ms, FA 70°, matrix 256 x 192, inversion time (TI) 715ms; images acquired 10; breath-hold duration (@60bpm) 10s; slice-thickness 8mm. **3T**: TR/TE 856/1.12ms, FA 68°, matrix 256 x 192, TI 740ms; images acquired 10; breath-hold duration (@60bpm) 10s; slice-thickness 8mm.

Bright-blood systolic SAPHIRE **1.5T**: TR/TE 830/1.12ms, TD 315ms, FA 70°; matrix 256 x 192; images acquired 10; breath-hold duration (@60bpm) 10s; slice-thickness 8mm. **3T**: TR/TE 857/1.12ms, TD 392.5ms, FA 68°, matrix 256 x 192; images acquired 10; breath-hold duration (@60bpm) 10s; slice-thickness 8mm.

0th order DB SAPHIRE **1.5T**: TR/TE 800/1.28ms, TD 677.5ms, TI 670ms, FA 70°, matrix 256 x 192; images acquired 10; breath-hold duration (@60bpm) 10s; slice-thickness 8mm; MSDE gradient amplitude 20 mT/m with preparation duration 10ms. **3T**: TR/TE 857/1.12ms, TD 752.5ms, TI 740ms, FA 68°, matrix 256 x 192; images acquired 10; breath-hold duration (@60bpm) 10s; slice-thickness 8mm; MSDE gradient amplitude 20 mT/m with preparation duration 10ms.

2nd order DB SAPHIRE **1.5T**: TR/TE 800/1.28ms, TD 677.5ms, TI 670ms, FA 70°, matrix 256 x 192; images acquired 10; breath-hold duration (@60bpm) Xs; slice-thickness 8mm; MSDE gradient amplitude 20 mT/m with preparation duration 10ms. **3T**: TR/TE 857/1.12ms, TD 750ms, TI 740ms, FA 68°, matrix 256 x 192; images acquired 10; breath-hold duration (@60bpm) 10s; slice-thickness 8mm; MSDE gradient amplitude 20 mT/m with preparation duration 10ms.

Cardiovascular magnetic resonance analysis

All images were analysed using CVI42 software (Circle Cardiovascular Imaging Inc. v.5.10.1, Calgary, Canada). Measurements were performed by two readers (M.A., J.A.). LV volumes, LV ejection fraction (LVEF) and mass (papillary muscles included in the LV cavity) were determined according to standardized CMRI methods [16] using a semiautomated threshold-based technique and body surface area (BSA) indexation where appropriate. Atrial volumes, LV maximal wall thickness, and mitral and tricuspid annular plane systolic excursions were determined as previously described [17, 18, 19].

For native T_1 measurements in the LV, endo- and epicardial borders were manually drawn per segment according to the 16-segment American Heart Association model, in the 3 short axis slices (10% offset to avoid the blood-myocardial interface). Segmental T_1 values were averaged to obtain the mean slice T_1 and global (whole-heart) T_1 . The global T_1 was calculated as the mean of basal, mid and apical LV short axis slices.

As demonstrated in *Fig. 2* the RV ROI measurement were obtained from the RV inferior wall or free wall in the basal or mid short axis slices if wall thickness ≥ 5 mm.

The transeptal myocardial T_1 times for MOLLI and SAPHIRE variants were calculated using six-points evenly-spaced linear callipers transecting the mid-septal short axis slice on the T_1 maps of each healthy volunteer (measurements obtained using OsiriX MD).

Intra- (M.A. X 2) and inter-observer (M.A. and J.A.) re-read variability was determined for measurements of average mid slice T_1 , and mid septal region of interest (ROI) T_1 in 5 randomly chosen CMRI scans (2 at 1.5T and 3 at 3T). Intra-observer variability (M.A. X 2) was performed with one-month temporal interval between repeat analyses.

Native SAPHIRE T_1 mapping sequences

A. Diastolic SAPHIRE

Conventional diastolic SAPHIRE (without any attempt to suppress the blood signal, i.e. 'bright blood') consists of a combination of saturation and inversion pulses. A saturation pulse is applied immediately after the R wave followed by an inversion pulse inserted in the same heartbeat prior to image acquisition (*Fig. 3a*). The first image acquisition is done without magnetisation preparation.

B. Systolic SAPHIRE

Systolic SAPHIRE also consists of saturation and inversion recovery magnetisation preparation hybrid and 10-ECG triggered readouts but data is acquired during systole. Imaging in systole is challenging due to the short time window available between R waves resulting in a weak saturation recovery T_1 mapping signal. As a fix, saturation is performed in the preceding heart-beat directly following the imaging pulses played in the previous heart-beat. Similar to diastolic SAPHIRE, the first image is acquired without magnetisation preparation. The remaining images are obtained with an extra inversion pulse with variable delay following the R wave (Fig. 3b).

C. 0th and 2nd Order dark blood diastolic SAPHIRE

Dark blood T_1 mapping is achieved using a modified SAPHIRE technique [10]. For blood suppression, motion sensitized driven equilibrium (MSDE) preparation is inserted before the bSSFP imaging readout (Fig. 4a). The MSDE preparation consists of a 90° excitation tip-down pulse, a one or more 180° refocusing pulse, and a -90° flip-back pulse to encode the spin dephasing in the longitudinal magnetisation (Fig. 4a). Strong motion sensitising gradients are also sandwiched in between the radiofrequency pulses to induce dephasing. Two kinds of motion sensitising gradients are employed, with nulling the gradient moment up to the 0th and 2nd order respectively. To achieve 0th order gradient nulling, identical trapezoidal gradients are played before and after the refocusing pulse.

Additionally, in this study advanced motion sensitising gradients were introduced. As illustrated in Fig. 4b, reverse bipolar gradient blips are inserted to achieve 0th and 2nd moment nulling.

Data analysis and statistics

Statistical analysis was performed in R programming language (version 3.6.0, The R Foundation for Statistical Computing) and SPSS statistical software (version 26.0, IBM Corp., Armonk, NY, USA). Descriptive data are expressed as mean $\pm$ standard deviation except where otherwise stated. The distribution of data was evaluated by histograms and Shapiro-Wilk test. Parametric and nonparametric continuous variables pertaining to participants were compared using student t -test or Mann-Whitney U test as appropriate. Categorical variables were compared by χ^2 or Fisher's exact tests.

Linear mixed effect models were used to compare T_1 times across SAPHIRE techniques (fixed effects: e.g. systolic vs. diastolic, 1.5T vs. 3T, slice level) accounting for repeatedness (participant number). In addition, paired-samples t -test (parametric) or related-samples Wilcoxon signed rank test (non-parametric) were used for pairwise comparisons between MOLLI and SAPHIRE, and within SAPHIRE, across field strengths using Bonferroni correction.

Differences in transeptal T_1 mapping profiles between sequences were assessed using two samples Anderson-Darling test as it gives more weight to the tails of the distribution (that is close to the blood-myocardial interface which was of particular interest to us). Two-sided p -values < 0.05 were considered significant.

Intra- and inter-observer variability (absolute agreement) of T1 mapping values was assessed using two-way random, single measures intraclass correlation coefficient (ICC).

Results

Study population characteristics

Demographic and CMRI characteristics of the 10 healthy volunteers (8 females, age 36 ± 10 years) are presented in *Table 1*.

Feasibility in vivo

SAPPHIRE T₁ mapping using all 4 variants was completed successfully in all subjects (*Tables 2 & 3*). ROI placement for RV T1 mapping was not feasible using MOLLI or diastolic SAPPHIRE because of insufficient wall thickness, but it was possible using systolic, 0th order and 2nd order DB SAPPHIRE and results are reported in *Table 3*.

Inter-field strength differences

Healthy volunteer native myocardial T₁ values obtained by MOLLI and the 4 SAPPHIRE variants across field strengths are reported in *Table 2* and global LV T₁ times provided in *Fig. 5*. As expected T₁ values within sequences were consistently higher at 3T than at 1.5T (all $p < 0.005$, *Fig. 6*).

Differences between MOLLI and SAPPHIRE variants

Pairwise comparisons showed that at both field strengths MOLLI measured significantly lower LV global myocardial T₁ times than any of the other 4 SAPPHIRE variants (all $p < 0.005$, *Online Resource 1, Table 1*). These differences persisted after removing the apical slice data (*Online Resource 1, Table 2*, $p < 0.005$).

Differences between SAPPHIRE variants

Using linear mixed models to adjust for field strength, phase, slice location and subject, myocardial T₁ times by diastolic SAPPHIRE were significantly longer than with systolic, 0th order DB and 2nd order DB SAPPHIRE at 1.5T and significantly longer than with systolic and 2nd order DB SAPPHIRE at 3T (all $p < 0.05$, *Fig. 7a*). However, after excluding the apical slice the myocardial T₁ times by diastolic SAPPHIRE were significantly longer than with systolic, 0th order DB and 2nd order DB SAPPHIRE at both field strengths (all $p < 0.05$, *Fig. 7b*).

At 1.5T pairwise comparisons for LV global T₁ showed that diastolic SAPPHIRE measured significantly longer T₁ times than the 0th order DB SAPPHIRE ($p = 0.014$, *Online Resource 1, Table 1*) but not after excluding the apical slice data (*Online Resource 1, Table 2*). Pairwise comparisons of RV T₁ times showed no differences between DB SAPPHIRE variants (all $p > 0.005$, *Online Resource 1, Table 3*). At 3T

systolic SAPHIRE measured significantly longer RV T_1 times than the 0th order and 2nd order SAPHIRE ($p = 0.028$ and 0.001 , respectively) but no such differences were observed at 1.5T (all $p > 0.05$)

Transmural T_1 mapping profiles of MOLLI and SAPHIRE variants

Transmural T_1 times (Fig. 8b) in the mid septum immediately adjacent to the LV and RV blood pools were longer by MOLLI and diastolic SAPHIRE when compared to systolic, 0th order DB and 2nd order DB SAPHIRE. Contamination from the high T_1 of the blood pool appeared as an upsloping T_1 profile near the edges of the septal profile for both MOLLI and diastolic SAPHIRE sequences, but not for the other SAPHIRE variants. Indeed, the profile distributions of transmural myocardial T_1 times by the Anderson-Darling test differed significantly between MOLLI and all 4 SAPHIRE variants (diastolic $p = 0.0003$; systolic $p = 0.0003$; 0th order DB $p = 0.024$; 2nd order DB $p = 0.025$); between diastolic SAPHIRE and both DB variants (0th order DB $p = 0.0003$; 2nd order DB $p = 0.001$); and between systolic SAPHIRE and both DB variants (0th order DB $p = 0.0003$; 2nd order DB $p = 0.0005$). Furthermore, the dispersion of transmural T_1 times across the mid septum for systolic ($1233.3 \pm 21.6\text{ms}$; interquartile range [IQR] = 25.3ms) and DB SAPHIRE variants (0th order: $1205.8 \pm 46.1\text{ms}$; IQR = 71.0ms | 2nd order: $1177.5 \pm 51.9\text{ms}$; IQR = 72.9ms) was narrower when compared to diastolic SAPHIRE ($1263.3 \pm 85.6\text{ms}$; IQR = 142.8ms), and the dispersion for systolic SAPHIRE narrower than of MOLLI ($1054 \pm 42.2\text{ms}$; IQR = 56.4ms).

Re-read variability of T_1 mapping measurements

Intra- and interobserver variability of myocardial T_1 reads was excellent across all sequences tested with ICCs ranging from 0.953–0.996 (Table 4).

Discussion

This study sought to compare native myocardial T_1 mapping values of both ventricles by MOLLI against those obtained by diastolic, systolic and dark blood SAPHIRE variants, across field strengths. As expected MOLLI measured longer myocardial T_1 times than the conventional diastolic SAPHIRE sequence [13]. We found that native T_1 was significantly shorter by the systolic, 0th order DB and 2nd order DB SAPHIRE variants compared to diastolic SAPHIRE across field strengths. We go on to show that systolic and DB SAPHIRE variants reduce the dispersion of trans-myocardial T_1 times across the septum and abolish the artefactual T_1 lengthening in voxels located at the blood-myocardial/epicardial boundaries that remains a visible problem for both MOLLI and diastolic SAPHIRE. Combined, these data suggest that systolic and DB SAPHIRE approaches may help counteract the problem of partial volume effects. According to these data, the 0th and 2nd order DB SAPHIRE sequences appear to be equivalent at preventing myocardial T_1 signal contamination by the adjacent blood pool. Systolic SAPHIRE was the sequence that produced the narrowest dispersion of myocardial T_1 times across the mid septum (even narrower than MOLLI).

Previous work at 3T has suggested that native myocardial T_1 in health lengthens progressively from base to apex [20, 21] and we observed a similar trend by MOLLI at 3T but not at 1.5T, and not with the majority of SAPHIRE variants used in this study. The most likely explanation for the lengthening T_1 from base to apex is that partial volume effects are more prevalent in the thinner more apical segments, and exacerbated by the natural curvature of the apical cap.

Results from linear mixed model analysis showing that native myocardial T_1 by diastolic SAPHIRE was significantly longer than by systolic SAPHIRE at both field strengths, are in agreement with previous work [8, 12, 22–23]. It has been postulated that in systolic T_1 mapping these differences were due to reduced partial volume effects thanks to the increased LV wall thickness. The fact that 0th order and 2nd order DB SAPHIRE T_1 times were significantly shorter than diastolic SAPHIRE suggests that blood pool suppression is another potential solution for the problem of partial volume effects.

We observed that the RV free wall was visible and indeed analysable on the short axis cine slices by systolic and DB SAPHIRE approaches but hardly visible at all by conventional bright blood SAPHIRE or MOLLI. We found that RV T_1 was significantly longer than LV T_1 which might be due to residual partial voluming and/or the naturally higher collagen content of the RV [24].

The published literature provides conflicting data on the relationship between RV and LV T_1 , with groups reporting higher RV T_1 [25–27], lower RV T_1 [28] or equivalent RV/LV T_1 reads [29] in various cohorts, not all of which were healthy controls as in our case. Although we took care to draw precise ROIs in the RV myocardium, partial voluming and contamination of RV T_1 times from the inadvertent inclusion of voxels contaminated by blood pool or epicardial fat signals are plausible pitfalls that could have artefactually lengthened our native RV myocardial T_1 times.

Overall, the evidence presented in this study suggests that systolic and DB approaches are less prone to partial volume effects than MOLLI and diastolic SAPHIRE. The transeptal myocardial T_1 times immediately adjacent to LV/RV blood pools recorded for 0th and 2nd order DB SAPHIRE were significantly lower than those recorded for systolic SAPHIRE (Fig. 8b) suggesting that blood pool nulling achieved by the DB T_1 mapping approaches provides some additional benefit thanks to the reduced sensitivity to partial volume effects. Future work should explore the potential clinical utility of DB SAPHIRE T_1 mapping in the thin-walled hearts of patients with dilated or arrhythmogenic right ventricular cardiomyopathy.

We report excellent intra- and inter-observer re-read reproducibility for all the methods studied with all ICCs (> 0.90) being well in line with previous reports [7, 20, 22, 23, 30–33].

In this study we also demonstrate the use of higher order gradient moment nulling for dark blood T_1 mapping. In previous literature 0th order nulling was found to be susceptible to residual myocardial motion in some cases, necessitating fine tuning of the motion sensitising gradient moment. As the residual cardiac motion is less turbulent compared to blood flow, stronger motion sensitizing gradients

may be applied when nulling the gradient moment up to the 2nd order. Even though quantification results were comparable between 0th and 2nd order DB SAPHIRE in our experiments, 2nd order nulling may have the advantage of increased ease of use for clinical translation. Robustness of higher order gradient nulling for DB T_1 mapping, thus, warrants further investigation in a patient cohort.

Limitations

Study limitations include the small healthy volunteer cohort size and single-center, single-vendor study design. Comparison to other T_1 mapping sequences (such as ShMOLLI and SATuration recovery single-SHot Acquisition [SASHA]) was not undertaken and neither was post-GBCA T_1 mapping. Future work will need to examine the clinical utility of these SAPHIRE sequences in patients with arrhythmia, dilated cardiomyopathy and for the study of other thin-walled cardiac structures such as the atria. RV T_1 analysis was not possible on MOLLI or diastolic SAPHIRE due to the RV thickness limitation. MOCO was used for MOLLI sequences but not for the SAPHIRE T_1 mapping sequences. Future work should seek to assess the impact of heart rate variability on the spin dynamic in the systolic SAPHIRE sequence.

In conclusion these preliminary healthy volunteer data suggest that systolic and dark blood approaches can reduce myocardial T_1 signal contamination by the adjacent bright blood pool at the blood-myocardial interface—a problem which still hampers other widely-used conventional T_1 mapping approaches in clinical practice.

Declarations

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Competing interests

The authors declare that they have no competing interests

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable

Authors' contributions

M.A. analysed the data, performed the statistical analysis and wrote the manuscript. J.B.A., K.D.K. and G.C. collected the data. J.B.A., K.D.K., N.F., P.K.M. and S.W. contributed to data analysis and review of the manuscript. R.B., A.D.H. and J.C.M. provided expert review of the manuscript. G.C., S.W. and J.C.M. conceived of the project.

Ethics approval and consent to participate

The study received ethical approval from the University College London (UCL) Research Ethics Committee.

Consent for publication

All subjects provided written informed consent

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Tables

Table 1
Demographic and CMRI characteristics of the healthy volunteers.

Healthy Volunteers (n = 10)	
Demographics	
Age, years	36 ± 10
Female	8 (80%)
Height, cm	168.4 ± 8.7
Weight, kg	71.6 ± 13.3
BSA, m ²	1.8 ± 0.2
CMRI parameters	
LAVi, mL/m ²	11.0 ± 2.1
RAVi, mL/m ²	11.3 ± 1.3
LVEDVi, mL/m ²	74.6 ± 0.2
LVESVi, mL/m ²	27.6 ± 0.2
LVEF, %	63 ± 5.1
MAPSE, mm	15.3 ± 2.7
LV MWT, mm	7.8 ± 1.0
LVMi, g/m ²	48.3 ± 12.5
RVEDVi, mL/m ²	75.1 ± 9.0
RVESVi, mL/m ²	38.6 ± 9.9
RVEF, %	49 ± 10.2
RVMi, g/m ²	25.8 ± 4
TAPSE, mm	25.3 ± 3.1
<p>Data reported as mean ± 1SD or count (%) as appropriate. BSA, body surface area; CMRI, cardiovascular magnetic resonance imaging; LAVi, left atrial volume; LVEDVi, left ventricular end-diastolic volume indexed to body surface area; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume indexed to body surface area; LVMi, left ventricular mass; MAPSE, mitral annular plane systolic excursion; MWT, maximum wall thickness; RAVi, right atrial volume; RVEDVi, right ventricular end-diastolic volume indexed to body surface area; RVEF, right ventricular ejection fraction; RVESVi, right ventricular end-systolic volume indexed to body surface area; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.</p>	

Table 2

Summary of LV T₁ mapping data by MOLLI and the 4 SAPPHIRE variants across field strengths.

Sequence	Field Strength	Basal SAX	Mid SAX	Apical SAX	Mid Septal ROI	Global T ₁	Non-apical Global T ₁
MOLLI	1.5T	1032.1 ± 22.9	1028.8 ± 25.8	1029.6 ± 20.9	1037.3 ± 27.7	1034.1 ± 6.7	1031.3 ± 2.3
	3T	1297.2 ± 26.7	1296.7 ± 25.5	1310.7 ± 31.9	1309.9 ± 36.4	1298.2 ± 8.8	1295.4 ± 2.5
Diastolic SAPPHIRE	1.5T	1261.4 ± 45.2	1266.7 ± 33.3	1341.9 ± 59.9	1249.6 ± 79.4	1283.6 ± 10.5	1264.1 ± 3.1
	3T	1636.5 ± 83	1596.2 ± 48.4	1593.3 ± 70.1	1602.5 ± 52.7	1600.7 ± 17.3	1612.2 ± 5.7
Systolic SAPPHIRE	1.5T	1285.9 ± 51.1	1225.4 ± 21	1238.9 ± 18	1224.7 ± 41.8	1238.6 ± 8.9	1252.7 ± 4.9
	3T	1580.1 ± 40.5	1586.3 ± 44.2	1596.3 ± 43.4	1584.7 ± 47.6	1595.7 ± 12.9	1590.6 ± 4.2
DB 0th order SAPPHIRE	1.5T	1228.5 ± 57	1247.8 ± 29.7	1245.9 ± 54.7	1227.8 ± 78.2	1240.9 ± 9.7	1242.4 ± 2.9
	3T	1570.9 ± 68.6	1595.2 ± 45.5	1607.5 ± 42.3	1596.7 ± 73.9	1596.4 ± 11.9	1583.7 ± 4.7
DB 2nd order SAPPHIRE	1.5T	1234.6 ± 46.1	1225.3 ± 61	1297.7 ± 50.6	1220.1 ± 110.6	1251.2 ± 10.9	1237.2 ± 4.6
	3T	1549.6 ± 64.9	1554.6 ± 63.9	1569.1 ± 31.3	1503.2 ± 132.3	1560.6 ± 20.2	1560.5 ± 4.1
Values reported are mean ± 1SD. DB, Dark blood; MOLLI, Modified Look-Locker inversion recovery; ROI, region of interest; SAPPHIRE, SATuration Pulse Prepared Heart-rate independent Inversion REcovery; SAX, short axis; T, Tesla. Other abbreviations as in Table 1.							

Table 3

Summary of RV T₁ mapping values by MOLLI and the 4 SAPPHIRE variants across field strengths

Sequence	Field Strength	Basal SAX (inferior or free wall)	Mid SAX (inferior wall)	Mid SAX (free wall)	Global T1 ROI
MOLLI*	1.5T	NA	NA	NA	NA
	3T	NA	NA	NA	NA
Diastolic SAPPHIRE*	1.5T	NA	NA	NA	NA
	3T	NA	NA	NA	NA
Systolic SAPPHIRE	1.5T	1530.9 ± 93.9	1479.3 ± 97.9	1421.5 ± 57.5	1477.2 ± 83.1
	3T	1766.2 ± 14.0	1757.3 ± 51.4	1769.0 ± 31.2	1764.2 ± 32.2
DB 0th order SAPPHIRE	1.5T	1439.6 ± 67.3	1453.0 ± 122.7	1452.6 ± 104.4	1448.4 ± 98.1
	3T	1723.8 ± 37.1	1680.5 ± 43.0	1688.8 ± 49.0	1697.7 ± 43.0
DB 2nd order SAPPHIRE	1.5T	1523.9 ± 44.3	1416.9 ± 81.5	1452.4 ± 54.0	1464.4 ± 60.0
	3T	1684.0 ± 101.3	1666.8 ± 63.0	1657.9 ± 77.5	1669.5 ± 80.6
<p>Values reported are mean ± 1SD.</p> <p>* RV measurements were obtained only when the RV wall thickness ≥ 5 mm and this was not achievable with MOLLI or diastolic SAPPHIRE.</p> <p>DB, Dark blood; MOLLI, Modified Look-Locker inversion recovery; ROI, region of interest; RV, right ventricle; SAPPHIRE, SATuration Pulse Prepared Heart-rate independent Inversion REcovery; SAX, short axis; T, Tesla. Other abbreviations as in Table 1.</p>					

Table 4
Re-read variability of T₁ mapping measurements.

Sequence	Region	Intra-observer ICC (95% CI)	Inter-observer ICC (95% CI)
MOLLI	Average mid	0.989 (0.91–0.99)	0.968 (0.76–0.99)
	Septal ROI	0.978 (0.78–0.99)	0.950 (0.53–0.99)
Diastolic SAPPHIRE	Average mid	0.996 (0.45–0.99)	0.993 (0.82–0.99)
	Septal ROI	0.987 (0.89–0.99)	0.954 (0.52–0.99)
Systolic SAPPHIRE	Average mid	0.957 (0.64–0.99)	0.953 (0.54–0.99)
	Septal ROI	0.964 (0.66–0.99)	0.982 (0.87–0.99)
0th order DB SAPPHIRE	Average mid	0.994 (0.95–0.99)	0.984 (0.50–0.99)
	Septal ROI	0.991 (0.76–0.99)	0.986 (0.84–0.99)
2nd order DB SAPPHIRE	Average mid	0.973 (0.78–0.99)	0.967 (0.47–0.99)
	Septal ROI	0.994 (0.79–0.99)	0.992 (0.88–0.99)
<p>Agreement was considered excellent when ICC > 0.74, good when ICC = 0.60–0.74, fair when ICC = 0.40–0.59 and poor when ICC < 0.4</p> <p>CI, confidence interval; ICC, intraclass correlation coefficient. Other abbreviations as in Tables 1 and 2.</p>			

Figures

Figure 1

Basic overview of T1 mapping acquisition strategies. ANGIE, Accelerated and Navigator-Gated Look-Locker Imaging for Cardiac T1 Estimation; 3D-QALAS, three-dimensional-QuAntification using an interleaved Look-Locker Acquisition Sequence with T2 preparation pulse; MOLLI, Modified Look-Locker Inversion recovery; Prep, preparation; SAPPHIRE, Saturation Pulse Prepared Heart-Rate Independent Inversion REcovery Sequence; SASHA, saturation recovery single shot acquisition; SAT, saturation; Seg, segmented; ShMOLLI, shortened MOLLI; STONE, slice-interleaved T1 mapping sequence.

Figure 2

Right ventricular (RV) T1 times were determined by manually tracing regions of interest on the short axis slices as follows: (a) Basal short axis slice: RV inferior wall or RV free wall; (b) Mid short axis slice: RV inferior wall and RV free wall. Exemplar RV ROIs at 1.5T are shown for 3 study participants. Other abbreviations as in Figure 1.

Figure 3

Sequence diagrams of the SAPHIRE bright blood diastolic (a) and systolic (b) T1 mapping variants. ECG, Electrocardiogram; INV, Inversion pulse. Other abbreviations as in Figure 1.

Figure 4

Sequence diagrams of the SAPHIRE dark blood T 1 mapping variants with 0th (a) and 2nd (b) order flow sensizting gradients. MSDE, Motion-sensitized driven equilibrium. Other abbreviations as in Figures 1 and 3.

Figure 5

Profile plot displays the global T1 times obtained using the various SAPHIRE variants in all ten healthy volunteers in our study. Each dot represents an individual. DB, Dark blood. Other abbreviations as in Figure 1.

Figure 6

Bullseye plots illustrating the mean segmental T1 values of all healthy volunteers in three short-axis slices (B, basal; M, mid-ventricular; A, apical) according to SAPHIRE variant and field strength (1.5T blue, 3T red). Global T1 is reported in the center of the bullseye and slice-specific means in the bottom right boxes. T, Tesla. Other abbreviations as in Figures 1 and 5.

a) Global T1 values across sequences (including apical slice data).

b) Global T1 values across sequences (after excluding the apical slice)

Figure 7

Global T1 mapping values at 1.5T (left) and 3T (right) by diastolic, systolic, 0th order and 2nd order SAPHIRE sequences (a) including the apical slice (b) excluding the apical slice. Numbered lines above the bars represent p values for differences obtained using mixed effect models. Abbreviations as in Figures 1, 5 and 6.

Figure 8

(a) Exemplar mid left ventricular short axis slice native T1 maps from the same participant by MOLLI and the 4 SAPHIRE variants (diastolic, systolic, DB 0th and 2nd order) at 1.5T. (b) Averaged transmural 6-point linear profiles (from the RV to LV side of the mid septum) of myocardial T1 times for all participants. LV, left ventricle. Other abbreviations as in Figures 1 and 5.

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