Journal of Visualized Experiments

Cardiac Magnetic Resonance Imaging at 7 Tesla

--Manuscript Draft--

Article Type:	Invited Methods Article - Author Produced Video
Manuscript Number:	JoVE55853R2
Full Title:	Cardiac Magnetic Resonance Imaging at 7 Tesla
Keywords:	Cardiac, MRI, CINE, Cardiac Function, High Resolution, 7 Tesla, Ultrahigh field, Parallel Imaging, 32 channel coil, Shimming
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Additional Information:	
Question	**Response**
Please indicate whether this article will be Standard Access or Open Access.	Standard Access (US$1200)

TITLE:
Cardiac Magnetic Resonance Imaging at 7 Tesla

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KEYWORDS:

Cardiac, MRI, CINE, Cardiac Function, High Resolution, 7 Tesla, Ultrahigh field, Parallel Imaging, 32 channel coil, Shimming

SHORT ABSTRACT:
The sensitivity gain inherent to ultrahigh field magnetic resonance holds promise for high spatial resolution imaging of the heart. Here, we describe a protocol customized for functional cardiovascular magnetic resonance (CMR) at 7 Tesla using an advanced multi-channel radio-frequency coil, magnetic field shimming and a triggering concept.

LONG ABSTRACT:
CMR at an ultra-high field (magnetic field strength $B_0 \geq 7$ Tesla) benefits from the signal-to-noise ratio (SNR) advantage inherent at higher magnetic field strengths and potentially provides improved signal contrast and spatial resolution. While promising results have been achieved, ultra-high field CMR is challenging due to energy deposition constraints and physical phenomena such as transmission field non-uniformities and magnetic field inhomogeneities. In addition, the magneto-hydrodynamic effect renders the synchronization of the data acquisition with the cardiac motion difficult. The challenges are currently addressed by explorations into novel magnetic resonance technology. If all impediments can be overcome, ultra-high field CMR may generate new opportunities for functional CMR, myocardial tissue characterization, microstructure imaging or metabolic imaging. Recognizing this potential, we show that multi-channel radio frequency (RF) coil technology tailored for CMR at 7 Tesla together with higher order B_0 shimming and a backup signal for cardiac triggering facilitates high fidelity functional CMR. With the proposed setup, cardiac chamber quantification can be accomplished in examination times similar to those achieved at lower field strengths. To share this experience and to support the dissemination of this expertise, this work describes our setup and protocol tailored for functional CMR at 7 Tesla.

INTRODUCTION:
Cardiovascular magnetic resonance (CMR) is of proven clinical value with a growing range of clinical indications[1, 2]. In particular, the evaluation of cardiac morphology and function is of major relevance and typically realized by tracking and visualizing the heart motion throughout the entire cardiac cycle using segmented breath-held two-dimensional (2D) cinematograpic (CINE) imaging techniques. While a high spatio-temporal resolution, high blood-myocardium contrast and high signal-to-noise ratio (SNR) are required, the data acquisition is highly constrained by the cardiac and respiratory motion and the use of multiple breath-holds as well as the need for whole heart or left-ventricular coverage often leads to extensive scan times. Parallel imaging, simultaneous multi-slice imaging or other acceleration techniques help to address the motion related constraints[3–6].

Moreover, to benefit from the inherent SNR gain at higher magnetic fields, high field systems with $B_0 = 3$ Tesla are increasingly employed in clinical routine[7,8]. The development has also encouraged investigations into ultra-high field ($B_0 \geq 7$ Tesla, $f \geq 298$ MHz) CMR[9–14]. The gain in SNR and blood-myocardium contrast inherent to the higher field strength holds the promise to be transferrable into enhanced functional CMR using a spatial resolution that exceeds today's

limits[15–17]. In turn, new possibilities for magnetic resonance (MR) based myocardial tissue characterization, metabolic imaging and microstructure imaging are expected[13]. So far, several groups have demonstrated the feasibility of CMR at 7 Tesla and specifically tailored ultra-high field technology has been introduced[17–22]. Regarding these promising developments, the potential of ultra-high field CMR can be considered to be yet untapped[13]. At the same time, physical phenomena and practical obstacles such as magnetic field inhomogeneities, radio frequency (RF) excitation field non-uniformities, off-resonance artifacts, dielectric effects, localized tissue heating and field strength independent RF power deposition constraints make imaging at ultra-high field challenging[10,17]. The latter are employed to control RF induced tissue heating and to ensure safe operation. Moreover, electrocardiogram (ECG) based triggering can be significantly impacted by the magneto-hydrodynamic (MHD) effect[19,23,24]. To address the challenges induced by the short wavelength in tissue, many-element transceiver RF coil arrays tailored for CMR at 7 Tesla were proposed[21,25–27]. Parallel RF transmission provides means for transmission field shaping, also known as B_1+ shimming, which allows to reduce the magnetic field inhomogeneities and susceptibility artefacts[18,28]. While at the current stage, some of these measures might increase the experimental complexity, the concepts have proven helpful and may be translated to the clinical field strengths of CMR 1.5 T or 3 T.

Currently, 2D balanced steady state free precession (bSSFP) CINE imaging is the standard of reference for clinical functional CMR at 1.5 T and 3 T[1]. Recently, the sequence was successfully employed at 7 Tesla, but a large number of challenges remain[19]. Patient specific B_1^+ shimming and extra RF coil adjustments were applied to manage RF power deposition constraints and careful B_0 shimming was performed to control the sequence typical banding artifacts. With an average scan time of 93 minutes for left-ventricular (LV) function assessment, the efforts prolonged the examination times beyond clinically acceptable limits. Here, spoiled gradient echo sequences provide a viable alternative. At 7 Tesla, total examination times of (29 ± 5) min for LV function assessment were reported, which corresponds well to clinical imaging protocols at lower field strengths[21]. Thereby, spoiled gradient echo based CMR benefits from the prolonged T_1 relaxation times at ultra-high field that result in an enhanced blood-myocardium contrast superior to gradient echo imaging at 1.5 T. This renders subtle anatomic structures such as the pericardium, the mitral and tricuspid valves as well as the papillary muscles well identifiable. Congruously, spoiled gradient echo based cardiac chamber quantification at 7 Tesla agrees closely with LV parameters derived from 2D bSSFP CINE imaging at 1.5 T[20]. Apart from that, accurate right-ventricular (RV) chamber quantification was recently demonstrated feasible using a high resolution spoiled gradient echo sequence at 7 Tesla[29].

Recognizing the challenges and opportunities of CMR at ultra-high field, this work presents a setup and protocol customized for functional CMR acquisitions on an investigational 7 Tesla research scanner. The protocol outlines the technical underpinnings, shows how impediments can be overcome, and provides practical considerations that help to keep the extra experimental overhead at a minimum. The proposed imaging protocol constitutes a four-fold improvement in the spatial resolution *versus* today's clinical practice. It is meant to provide a guideline for clinical adaptors, physician scientists, translational researchers, application experts, MR radiographers, technologists and new entrants into the field.

PROTOCOL:

The study is approved by the ethics committee of the University of Queensland, Queensland, Australia and informed consent has been obtained from all subjects included in the study.

1. Subjects

1.1) Recruit volunteer subjects over 18 years of age internally at the University of Queensland.

1.2) Informed consent

1.2.1) Inform each subject about potential risks of undergoing the examination before entering the magnetic resonance imaging (MRI) safety zone. Specifically, discuss the ultra-high magnetic field exposure and possible contraindications for undergoing an MRI examination. Inform the subject that participating in the examination is voluntary and that at all times he/she may abort the examination. Obtain informed consent in writing.

1.2.2) Explain the procedure to the participant. Since imaging is performed during breath hold at end expiration and consistent breath holding is integral to image quality, coach the subject on breathing technique prior to scanning.

1.2.3) Perform MR safety screening on all subjects before entering the MRI safety zone in writing and again before entering the scanner room. Exclude subjects with contraindications for undergoing an MRI examination (*e.g.*, pacemakers, implanted defibrillators, other unsafe medical implants or claustrophobia).

1.3) Ask the subject to change into scrubs before entering the scanner room.

2. Preparation

2.1) Set up the additional hardware required to operate the dedicated 32 channel ^{1}H cardiac transceiver (Tx/Rx) RF coil[26] on the patient table as outlined in **Figure 1a** and b. Apart from a small power splitter box (**Figure 1c**), the auxiliary coil equipment comprises one power splitter box and phase shifter box (**Figure 1d**) and one Tx/Rx interface box (**Figure 1e**) for each of the two RF coil sections that will be placed below and on top of the subject. The greater part it accommodates the local transmit electronics, which is required for signal excitation at 7 Tesla, since traditional birdcage body coils as commonly employed at 1.5 T and 3.0 T are not available.

2.2) Place the additional RF coil hardware at the top end of the patient table as outlined in **Figure 1b** and link the individual boxes together with the Bayonet Neill–Concelman (BNC) cables. Since the distance that the patient table can be driven into the MRI bore is limited,

ensure to leave sufficient space on the patient table for the coil infrastructure to guarantee that the subject's heart can be positioned with the center of the coil at the isocenter of the magnet.

2.3) Connect the Tx/Rx interface boxes to the four coil plugs on the patient table.

2.4) Place the center of the posterior coil array 147 cm away from top end of the patient table (**Figure 1b**). This spot defines where the posterior coil array has to be placed to ensure that the subject's heart is at the isocenter of the magnet if the patient table is maximally driven into the bore. The placement on the predefined coil spot is crucial, to ensure optimal operation. Determine the optimal position of the posterior coil array as well as the positioning of the auxiliary equipment in preliminary tests including several volunteers of different body height.

2.5) Connect the four cables of the posterior coil array into the appropriate sockets of the Tx/Rx interface box for the posterior array.

2.6) Connect the four modules of the anterior coil array are with the Tx/Rx interface box for the top array and flip the array over the auxiliary coil equipment to allow for subject positioning.

2.7) Attach the three ECG electrodes to the body of the subject. Follow the vendor guidelines for electrode placement to ensure optimal operation of the system's trigger algorithm.

2.8) Position the subject on the patient table (**Figure 1f**). Critically, make sure that the subject's heart is positioned central to the posterior coil in order to guarantee scanning within the isocenter of the magnet. As, depending on the subject's height, the head will have to be placed on top of the coil/interface box connectors, place the cables carefully and use appropriate cushioning to ensure the subject's comfort and compliance.

2.9) Connect the trigger device to the ECG electrodes.

2.10) Attach the pulse trigger device to the subject's index finger. Use this second device for triggering in the event of severe distortions of the ECG signal introduced by the MHD effect.

2.11) Hand the safety squeeze ball to the subjects.

2.12) Equip the subject with headphones and earbuds to reduce the noise exposure and to allow communication with the subject.

2.13) Place the anterior coil on the subject's chest, such that the cables that connect to the plugs E-F and G-H are located to the right and left of the subject's head, respectively.

2.14) Drive the subject into the scanner bore. Perform the driving operation manually and ensure that the speed button of the table controls is in the off-position to guarantee the

subject's safety during the driving process. Do not use the automatic mode as the variable table speed in this mode is optimized for neuro imaging and the distance the table can be driven automatically into the bore is limited by the scanner hardware.

2.15) Check if communication to the subject through the intercom is possible and if the subject is feeling well.

2.16) MR imaging

2.16.1) Run basic localizer (scout) scans along the three physical gradient axes for slice planning and B0-shimming.

2.16.2) Use an ECG-triggered fast low angle shot (FLASH) sequence with the following acquisition parameters: field of view (FOV) = 400 mm, matrix = 192 x 144, slices per gradient axis = 1, thickness = 8 mm, echo time (TE) = 1.24, repetition time (TR) = 298 ms, flip angle = 10°.

2.16.3) Apply parallel MRI with acceleration factor = 2, reference lines = 24 and generalized autocalibrating partially parallel acquisitions (GRAPPA) reconstruction.

2.16.4) Use the localizer images to verify that the subject's heart is positioned in the isocenter of the magnet. Reposition the subject if necessary.

2.17) 3rd order B0-shimming

2.17.1) Open the 3rd order shim tool (**Figure 2a**) and reset all 3rd order shim currents (**Figure 2b**).

2.17.2) Prescribe the shim volume for proper shimming over a region covering the heart (**Figure 2c**).

2.17.3) Run a non-triggered advanced flow compensated 2D multi-echo FLASH shim sequence for the calculation of the 3rd order shim currents. Use the following parameters: FOV = 400 x 400 mm, matrix = 80 x 80, slices = 64, thickness = 5.0 mm, TE1 = 3.06, TE2 = 5.10, TR = 7 ms, flip angle = 20 °, parallel MRI (GRAPPA), acceleration factor = 2, reference lines = 24.

2.17.4) To calculate and apply the 3rd order shim currents, open the next protocol and copy the above-mentioned shim volume. Execute the **SetShim** program in the start menu (**Figure 2a**). Next, open the **Manual Adjustments** window in the **Options** menu (**Figure 2d**). In the **3D Shim** tab, click **Calculate** | **Apply** to set the shim currents for the 2nd order (**Figure 2e**). Finally, set the shim currents by clicking **Set Shim_3rd** in the 3rd order shim tool (**Figure 2b**).

2.17.5) Close the **Manual Adjustments** window. Keep the shim volume and the shim currents fixed throughout the remainder of the examination. Note that the shimming procedure can be highly system specific.

2.18) Acquire further localizers to support double-oblique slice planning. Unless stated otherwise, use a breath held and ECG-triggered 2D FLASH sequence with the following parameters for all localizer measurements: FOV = 360 x 290 mm, matrix = 256 x 206, thickness = 6.0 mm, TE = 1.57, TR = 3.9 ms, flip angle = 35 °, parallel MRI (GRAPPA), acceleration factor: 2, reference lines: 24. Advise the patient to hold the breath in expiration. Employ high flip angles or use a segmented cine protocol (see below) to achieve improved contrast.

2.18.1) Acquire the 2 chamber localizer (1 slice), planned perpendicular on the axial scout parallel to the septal wall (**Figure 3a**).

2.18.2) Acquire the 4 chamber localizer (1 slice), planned perpendicular on the 2 chamber localizer slice through the mitral valve and the apex of the left ventricle (**Figure 3b**).

2.18.3) Acquire the short axis localizer (7 slices, FOV = 360 x 330 mm), planned perpendicular on the 4 chamber localizer parallel to the mitral valve and perpendicular to the septal wall (**Figure 3c**).

2.19) Perform the CINE acquisitions. Use a high resolution breath held ECG-triggered segmented 2D FLASH sequence with the following parameters: FOV = 360 x 270 mm, matrix = 256 x 192/264 x 352, thickness = 4.0 mm, TE = 3.14, TR = 6.3 ms, flip angle = 35-55 °, segments = 7, parallel MRI (GRAPPA), acceleration factor = 2/3, temporal resolution = 42.6/44.3 ms.
2.19.1) Start with the left ventricular 4 chamber view (horizontal long axis, HLA) slices. Plan the central slice through the center of the mitral and tricuspid valves and the apex of the left ventricle (**Figure 3d**). Acquire each slice within an individual breath hold in expiration.

2.19.2) Next, acquire the left ventricular short axis slices. Plan them perpendicular to the HLA and parallel to the mitral valve so that it covers the whole left ventricle from the base to the apex (**Figure 3e**). To ensure accurate function testing, position the first slice accurately at the mitral valve leaflet insertions, so that the center of the slice is within the ventricle. Again, acquire each slice within an individual breath hold in expiration.

REPRESENTATIVE RESULTS:

Representative results of cardiac CINE examinations derived from volunteers are depicted in **Figure 4**. Shown are diastolic and systolic time-frames of short axis and a four-chamber long axis views of the human heart. The significantly higher spatial resolution for the short axis views (**Figures 4a, 4b, 4e, 4f**) compared to the long axis views (**Figures 4c**, **4d**, **4g, 4h**) is clearly visible. In both short and long axis slices, the images provide ample signal-to-noise and blood-myocardium contrast to clearly delineate the myocardial walls, even when employing a slice thickness as thin as 4 millimeters. The employed parallel imaging acceleration scheme reconstructed the images with high image quality and without conspicuous noise enhancement.

Due to R-wave recognition failure of the ECG, pulse oximetry-based triggering was utilized for the image acquisitions on the right (**Figures 4e**-**4h**). The jitter in the pulse oximetry signal peak induced minor motion artifacts which were pronounced during periods of cardiac contraction and relaxation as highlighted in the long axis view shown in **Figure 4h** (red arrow). Signal voids due to destructive interferences in the transmission field are marked by yellow arrows.

Typical ECG signals obtained in one channel of the trigger device in one healthy subject are depicted in **Figure 5**. When comparing the ECG signal acquired outside of the magnet bore (**Figure 5a**) to the one obtained with the subject positioned at the isocenter of the magnet (**Figure 5b**), significant differences become evident. Within the ultra-high magnetic field, the ECG signal is severely corrupted by the MHD effect. The adverse phenomenon arises from the interaction between the conductive fluid blood with the external magnetic field. It induces a distorting electric field superimposing the heart's own depolarization fields and thus corrupts the signal picked up by ECG electrodes on the subject's skin. The MHD effect scales with B0 and is particularly pronounced during cardiac phases of systolic aortic flow, which is why mainly the S-T segment of the ECG signal is affected. Although the R-wave of the ECG signal is typically not directly affected, it can impair the R-wave recognition and cardiac synchronization. It is noteworthy that, due to the ECG signal distortions, ECG signals obtained in the presence of high magnetic fields cannot be used as a patient emergency condition indicator. A representative pulse signal obtained inside of the magnet bore is displayed in **Figure 5c**. The pulse signal is not affected by the magnetic field. The delay of the pulse wave to the R-wave at 0 ms, which can introduce artifacts, is clearly visible.

Figure Legends:

Figure 1: Experimental setup and elements of the 32 channel cardiac Tx/Rx coil and coil hardware. (a, b) The auxiliary hardware consisting of 7 hardware boxes and connecting BNC cables is placed at the top end of the patient table in order provide as much space as possible for subject positioning. The posterior and anterior coil elements are connected with eight cables to the interface boxes. For the system at hand, the posterior coil array is placed no further than 1470 mm from the top end of the table, to ensure positioning of the heart at the isocenter of the magnet. (c) small power splitter box. (d) one power splitter and phase shifter box each for the posterior and anterior coil array. (e) Tx/Rx interface boxes for the anterior (top) and posterior (bottom) coil array. Orange and black dotted arrows indicate transmit (Tx) and receive (Rx) signal pathways. (f) Subject positioned on the posterior coil array. The head rests on a cushion on the 8 coil connectors. The predefined coil spot is marked with a red label.

Figure 2: 3rd order shimming using the systems adjustment and shim tools. (a) Start menu with buttons for the "3rd order shim" tool and "set shim" program. (b) "3rd order shim" tool. (c) Positioning of the adjustment region over the heart. (d) Starting the "Adjustments" tool from the "Options" menu. (e) "Adjustments" tool with buttons to calculate and apply the 2nd order shim currents in the "3D shim" tab.

Figure 3: Slice planning for cardiac CINE imaging. (a) planning of 2-chamber localizer perpendicular on basic localizer. (b) planning of 4 chamber localizer perpendicular on 2 chamber localizer (c) planning of short axis localizer on 2 chamber localizer (left) and perpendicular on 4 chamber localizer (right). (d) planning of left ventricular 4 chamber view perpendicular on short axis localizer (left) and on 2 chamber localizer (right). (e) planning of left ventricular short axis slices on left ventricular 4 chamber view (left) and 2 chamber localizer (right).

Figure 4: Representative results of high resolution cardiac CINE imaging in two subjects using ECG triggering (a-d) and pulse triggering (e-h). (a, e) End-diastolic time frames of a mid-ventricular short axis slice acquired with a spatial resolution of 1.0 x 1.0 x 4 mm^3. (b, f) Corresponding end-systolic time frames. (c, g) End-diastolic time frames of a horizontal long axis slice. (d, h) Corresponding end-systolic time frames. Signal dropouts caused by RF field non-uniformities are marked by yellow arrows. Slight trigger errors caused by the latency of the pulse wave are depicted in the long axis view of the pulse-triggered scan (red arrow).

Figure 5: Representative ECG signals obtained outside and inside of the magnet bore at 7 Tesla. (a) ECG signal obtained in the two channels (red, blue) of the ECG trigger device outside of the magnet bore. The R-wave can be clearly distinguished. Trigger events are demarcated in green. (b) ECG signal obtained at the isocenter of the 7 Tesla magnet bore. The MHD effect clearly affects the ECG signal and particularly the S-T element of the ECG signal. The strong signal fluctuations can lead to mis-triggering. (c) Representative pulse signal obtained at the isocenter of the 7 Tesla magnet bore for comparison. The pulse signal is not affected by the magnetic field. Note that the pulse wave is delayed with respect to the ECG R-wave.

DISCUSSION:

Functional CMR examinations could be conducted successfully at 7 Tesla. Based on the field strength driven SNR gain, CINE images of the human heart could be acquired with significantly higher spatial resolution compared to 1.5 or 3 T. While a slice thickness of 6 to 8 mm and in-plane voxel edge lengths of 1.2 to 2.0 mm are commonly used at lower clinical field strengths[1,30], the measurements at 7 Tesla could be conducted with a slice thickness of 4 mm and an isotropic in-plane resolution of 1.0 mm.

The results obtained at 7 Tesla are promising. The image quality is comparable to that obtained at 1.5 T or 3 T although B_1+ shimming was not conducted and the experimental overhead was kept to a minimum to facilitate clinically acceptable examination times for cardiac chamber quantification. Occasionally image quality was slightly impaired by signal voids caused by focal RF field non-uniformities. In these cases, the use of B_1+ shimming, which is available through parallel transmission techniques might be beneficial. While this approach is tempting and looming on the horizon of clinical applications it requires further considerations on signal absorption rate (SAR) management.

On the triggering side, the ECG signal was occasionally severely corrupted by the MHD effect so that synchronization of image acquisition with the cardiac activity needed to be conducted

using the pulse triggering approach. When using the pulse trigger, slight impairment of the CINE image quality may occur. This impairment is caused by the time the pulse trigger is delayed with respect the R-wave of the ECG. Variations and jitter in the pulse trigger signal can range up to 60 milliseconds. This phenomenon may lead to mis-triggering and may risk introducing cardiac motion induced blurring in the reconstructed images. As recently demonstrated, accurate cardiac synchronization at 7 Tesla can be achieved by fully exploiting the technical capabilities of available trigger devices and by using state-of-the art trigger algorithms[19,24]. Besides this, the use of alternative triggering solutions[31–33] may also provide a good basis for synchronized imaging.

Scanning at ultra-high-field comes along with a significantly increased demand of hardware. In particular the scan preparations are more complex *versus* lower field strengths. This can be attributed to the use of auxiliary RF coil equipment due to the absence of a body coil that is integrated in clinical scanners. Subject positioning requires more care *versus* the routine clinical setup at lower field strengths, since not only the subject comfort but also the position of the coil with respect to the table has to be taken into account. This limitation is related to the design and the capabilities of today's patient tables for 7 Tesla MRI but is expected to be fixed with the ongoing move to the next generation of 7 Tesla MRI systems. Only recently, the first 7 Tesla MRI system was approved for clinical use for specific applications in the USA and Europe. Experimental overhead is also introduced by the MHD effect that can severely impair the R-wave recognition. To ensure a good cardiac synchronization, a careful subject preparation, an accurate ECG electrode placement in addition to an accurate calibration of the ECG trigger algorithm are required[24]. In some cases, repositioning of the ECG electrodes after moving the subject into the bore might become necessary. Also, to ensure the continuation of the examination in the presence of severe ECG trigger impairments, it is advisable to attach the pulse trigger device to the subject. As an alternative to ECG triggering, acoustic triggering[31] might be utilized, which is immune to MHD effects and has been shown to be superior to pulse triggering. If these considerations and measures are carefully included into functional CMR examinations at 7 Tesla, the workflow and duration of cardiac CINE measurements at ultra-high fields is similar to that at clinical field strengths.

The increasing use of ultra-high field systems in translational research will advance the capabilities of CMR for the assessment of cardiovascular diseases. Technological advances such as improved RF coil technology or multi-transmit MR systems will help to reduce the current experimental overhead and streamline additional scan preparations and shimming operations. Within this context, a careful validation of the novel ultra-high field CMR applications against the well-established CMR applications at 1.5 T or 3 T will be essential.

This study demonstrates, that functional CMR examinations can be successfully conducted at 7 Tesla. The field strength driven SNR gain at ultra-high field allows for CINE acquisitions with very high spatial resolutions. Compared to the clinical field strengths of 1.5 or 3 Tesla, the spatial resolution can be increased by a factor of 3 to 4. The experimental overhead required to tackle the various technical challenges can be kept to a minimum. These results as well as future technological developments will provide the basis for explorations into more advanced

applications such as myocardial tissue characterization, metabolic imaging or microstructure imaging.

ACKNOWLEDGMENTS:

The authors acknowledge the facilities, and the scientific and technical assistance of the National Imaging Facility at the Centre for Advanced Imaging, University of Queensland. We would also like to thank Graham Galloway and Ian Brereton for their help to obtain a CAESIE grant for Thoralf Niendorf.

DISCLOSURES:

Kieran O'Brien and Jonathan Richer are employed by Siemens Ltd. Australia. Jan Rieger and Thoralf Niendorf are founders of MRI.TOOLS GmbH, Berlin, Germany. Jan Rieger was CTO and an employee of MRI.TOOLS GmbH. Thoralf Niendorf is CEO of MRI.TOOLS GmbH.

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Figure 1

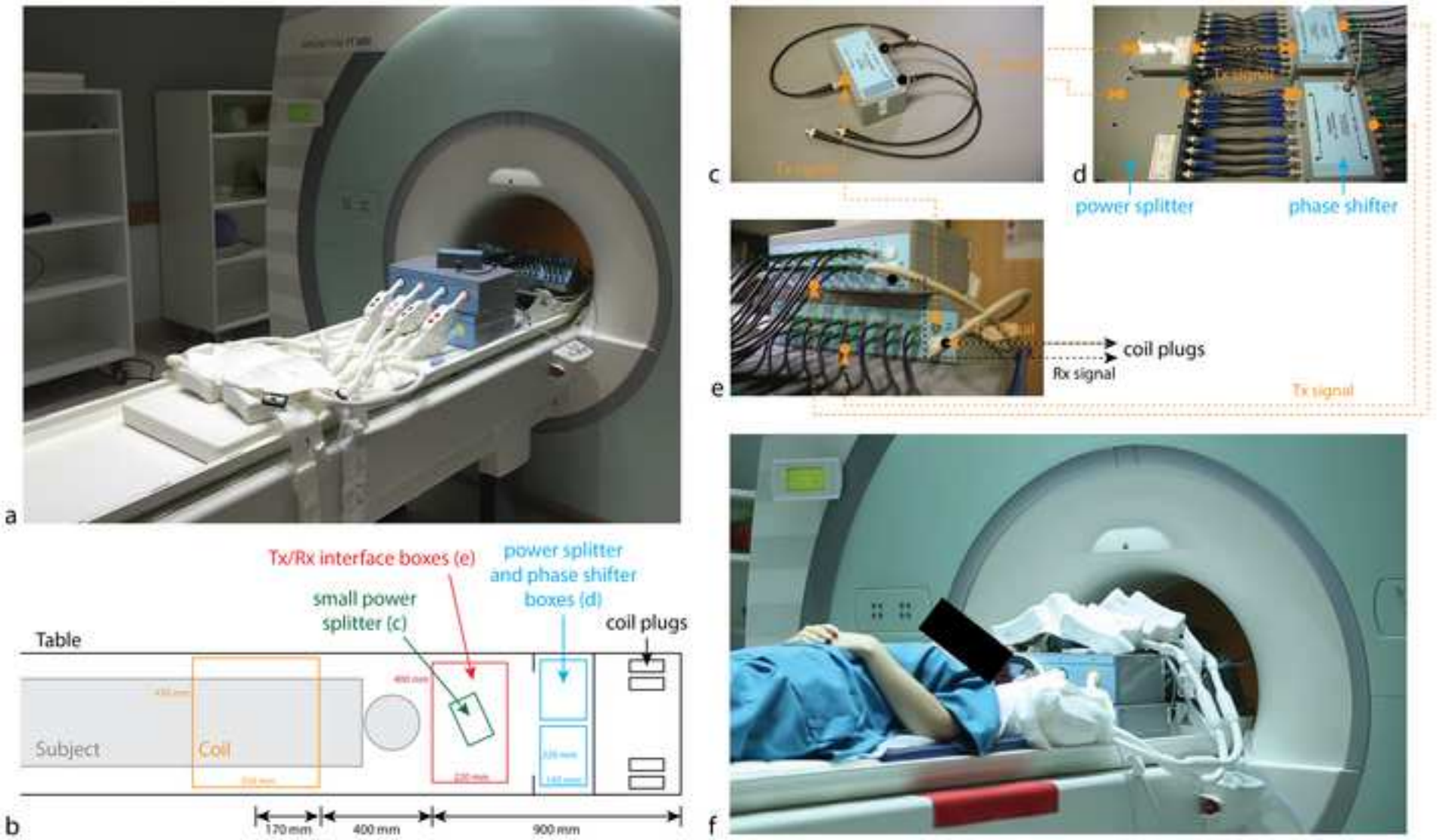

Figure 2

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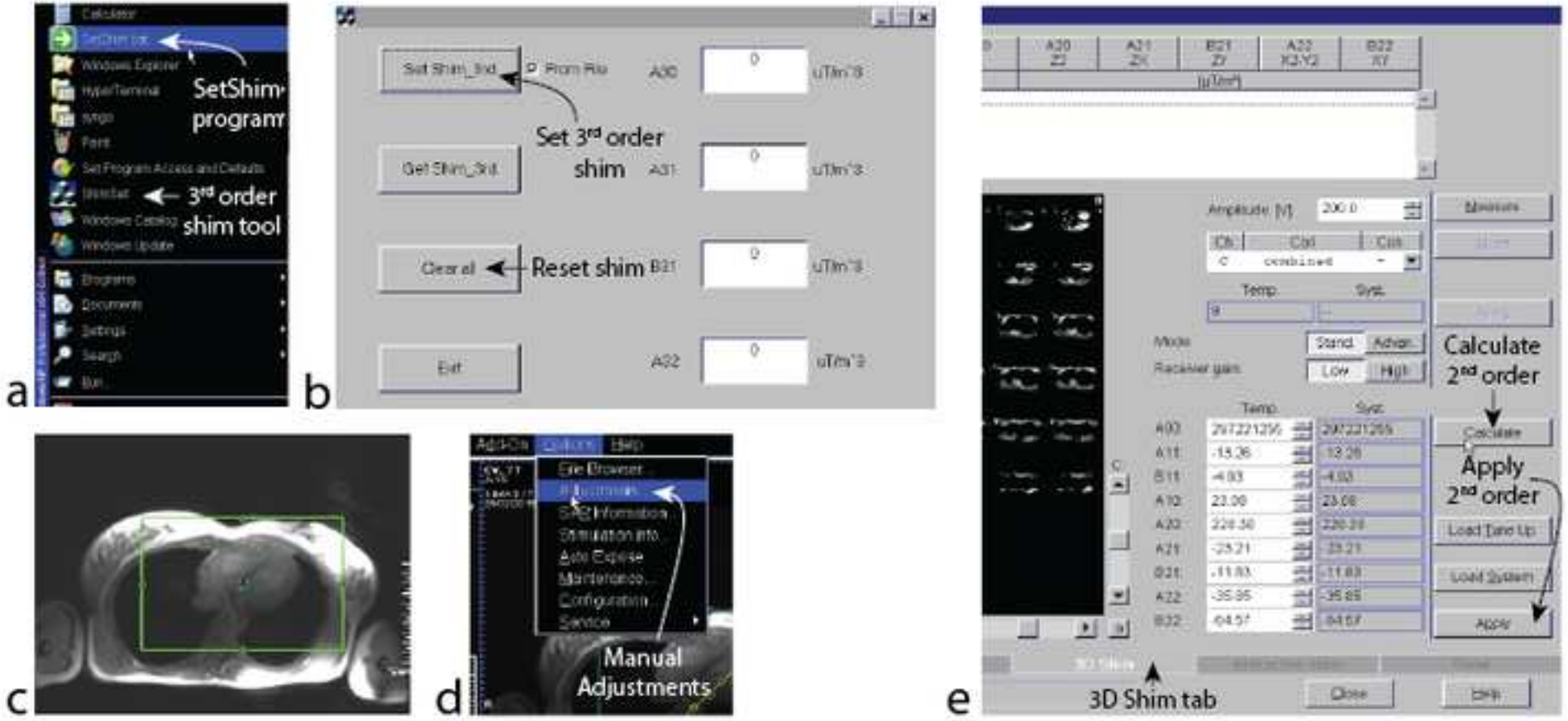

Figure 3

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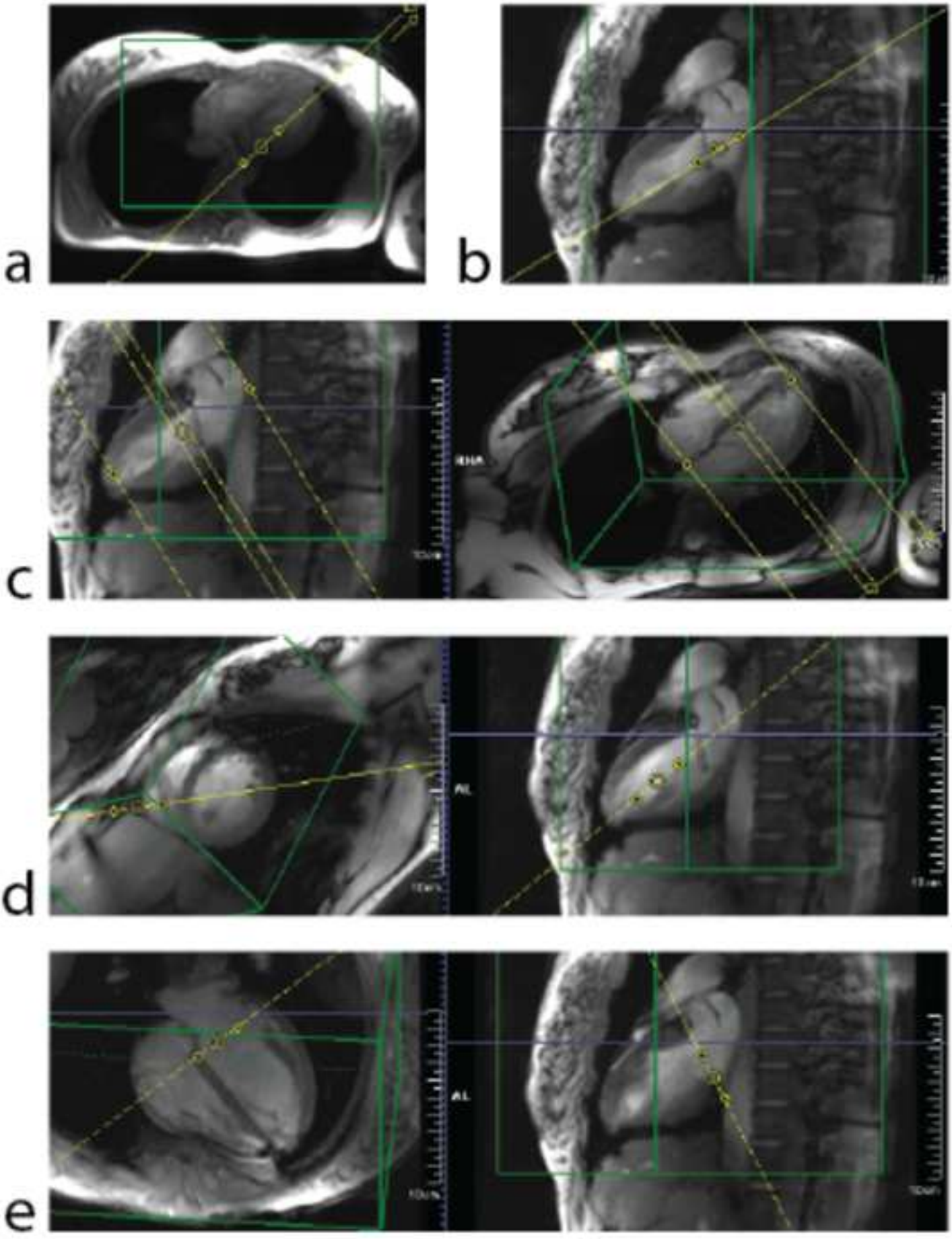

Figure 4

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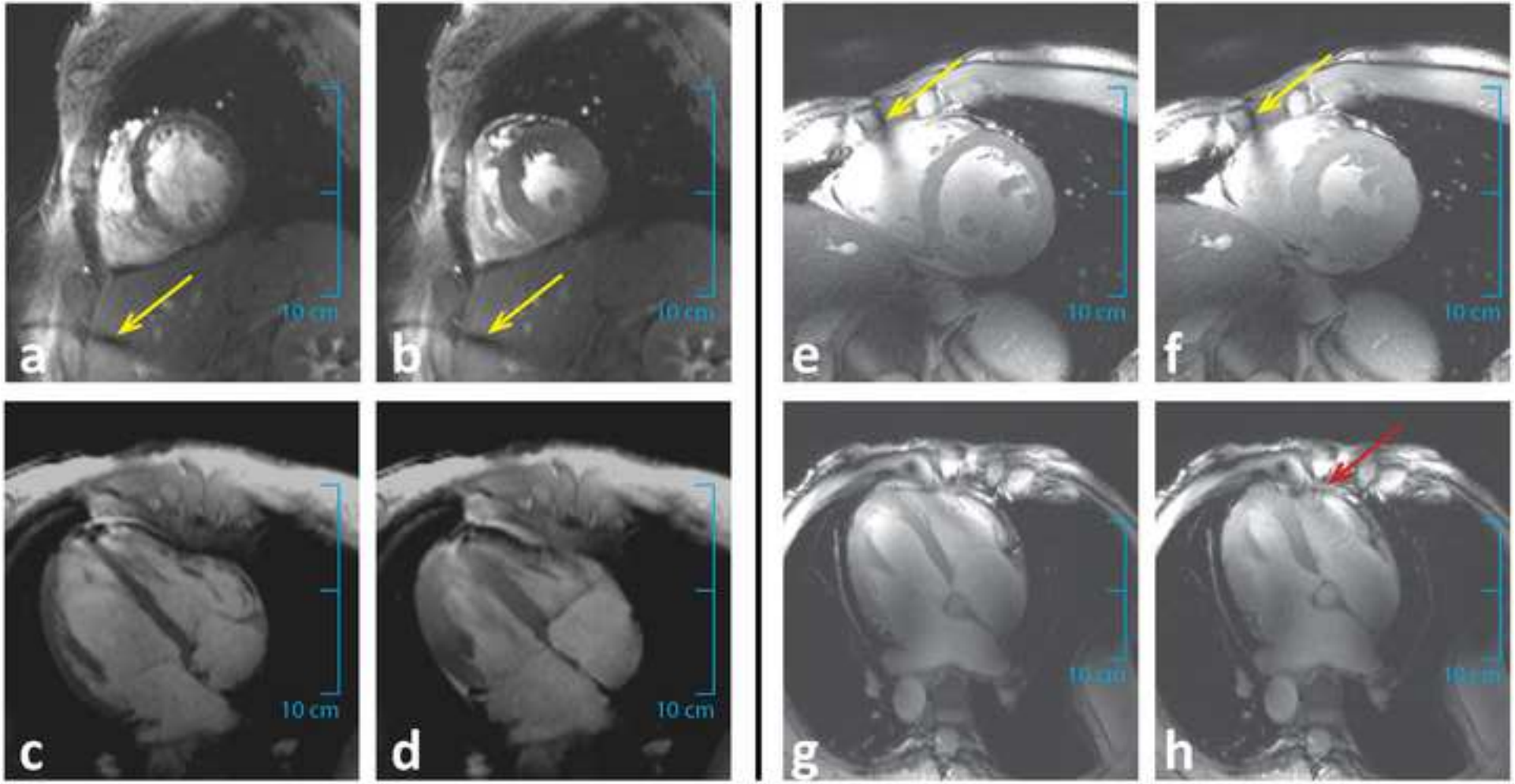

Figure 5

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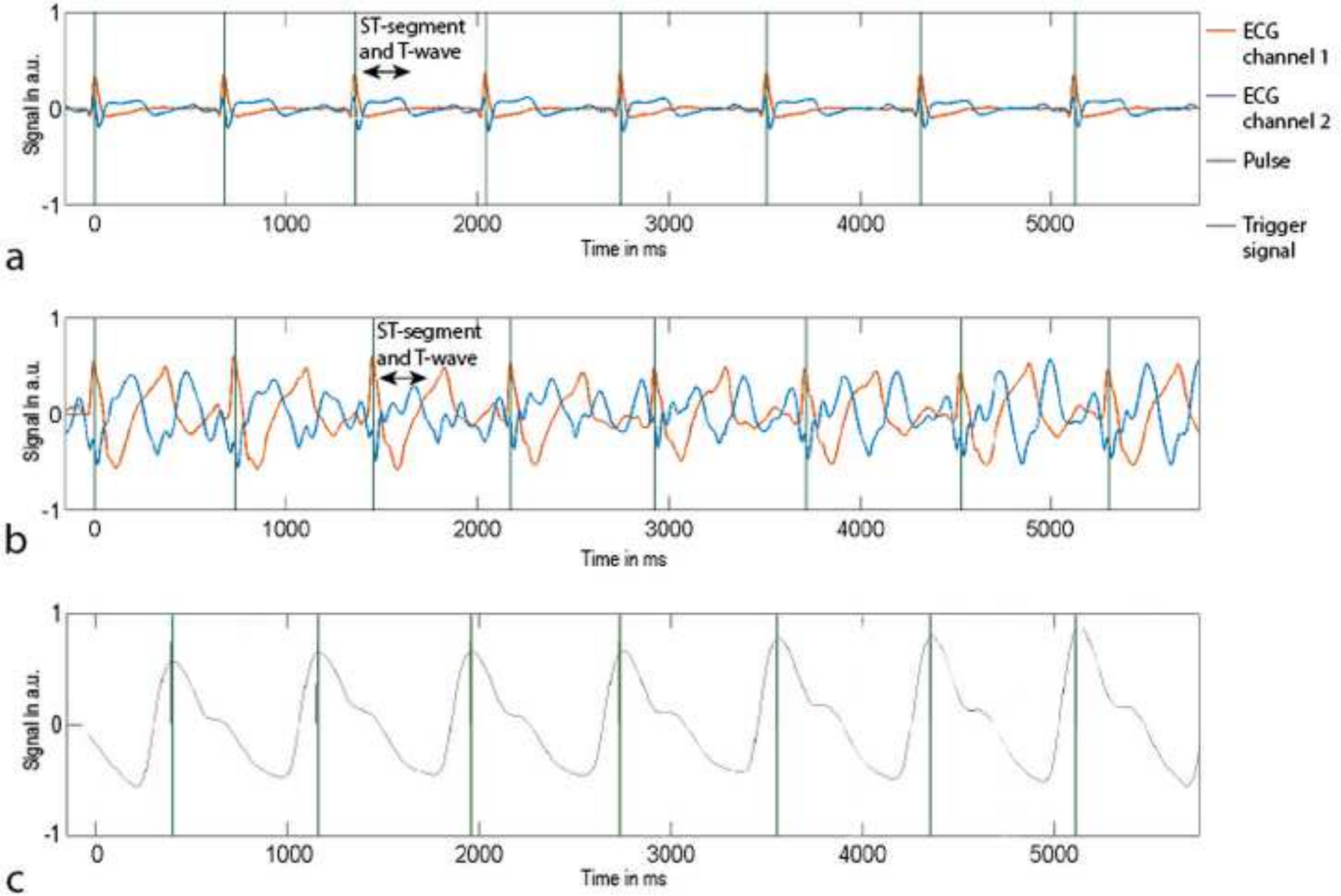

Table of Materials

Click here to download Table of Materials JoVE55853_cardiac7t_sub2_materials.xls

Name of Material/ Equipment	Company	Catalog Number	Comments/Description
7 Tesla MRI system	Siemens		Investigational Device
32-Channel -1H-Cardiac Coil	MRI.Tools GmbH		Transmit/Receive RF Coil for MR Imaging and Spectroscopy at 7.0 Te
ECG Trigger Device	Siemens		
Pulse Trigger Device	Siemens		

:sla

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Article Title:	Functional Cardiac Magnetic Resonance Imaging at 7 Tesla
Signature:	
Date:	11 June 2015

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MS # (internal use):

Editorial and production comments:

Changes to be made by the Author(s) regarding the manuscript:

E1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.

As suggested, we have revised the manuscript.

E2. Please abbreviate all journal titles.

As suggested, we have revised the list of references.

E3. Please revise the table of the essential supplies, reagents, and equipment. The table should include the name, company, and catalog number of all relevant materials in separate columns in an xls/xlsx file.

As suggested, we have reviewed the table of essential supplies.

E4. Figure 1: Please blur the Siemens name.

As suggested, we have blurred the Siemens name in Fig. 1

E5. Figure 2: Please provide scale bars to indicate the sizes here.

As suggested, we have revised the figure (now Fig. 4) and included scale bars.

E6. Figure 3: Please provide more information in the Figure to indicate what the Figure shows. It is not clear what the arrows represent.

We have modified Fig 3 and included significantly improved ECG signal curves. All labels are now fully labelled and explained in the caption.

E7. Please include an ethics statement before the numbered protocol steps, indicating that the protocol follows the guidelines of your institution's human research ethics committee.

As suggested, we have included an ethics statement before the numbered protocol steps.

E8. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note." However, notes should be concise and used sparingly. Please include all safety procedures and use of hoods, etc.

As suggested, we have modified the text in the protocol section to appear in the imperative tense.

E9. The Protocol should contain only action items that direct the reader to do something. Please move the discussion about the protocol to the Discussion.

We modified the protocol such that only directions are given to the reader.

E10. Please add more details to your protocol steps. Please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action.

As suggested, we have added more details to the protocol steps, e.g. for device setup, slice panning and shimming. We also added references where applicable.

E11. 2.1: How is the patient table prepared?

We have clarified item 2.1 and modified the text according to E8.

E12. Please provide specific values for the "sufficient space" and the predefined coil spots. We need specific values for the publication.

As suggested, we have extended Fig. 1 and have added specific values for the "sufficient space" and the predefined coil spots.

E13. 2.6: Where are the ECG electrodes placed on the body? How many?

We have added the number of electrodes (three). Regarding the electrode placement, we refer the reader to the system vendor's guidelines, as these are highly system specific and adhering to these guidelines is important to ensure optimal operation.

E14. 2.12: What orientation?

In general, there is only one possible orientation. We have clarified the text as follows:

"Place the anterior coil on the subject's chest, such that the cables that connect to the plugs E-F and G-H are located to the right and left of the subject's head, respectively."

E15. 2.14: Checked for what?

We have clarified this protocol step as follows:

"Check if communication to the subject through the intercom is possible and if the subject is feeling well."

E16. What are the MRI parameters used? How are the localizers examined?

We have added the specific parameters and clarified the text as given below:

"Run basic localizer (scout) scans along the three physical gradient axes for slice planning and B0-shimming. Use the following acquisition parameters: [...]. Use the localizer images to verify that the subject's heart is positioned in the isocenter of the magnet. Reposition the subject if necessary."

E17. Please provide all experimental parameters used throughout so others may replicate the protocol.

As suggested, we have included all acquisition parameters in the protocol.

Changes to be made by the Author(s) regarding the video:

E18. The voiceover narration should be peaking around -6dB. It may be that the audio level needs to be raised.

As suggested, we have adjusted the voiceover narration.

E19. The volume of the music should be lowered by at least 6dB, so that it competes less with the narration.

As suggested, we have adjusted the music volume.

Editing issues

E20. 1:12 - In the edit here, there is a frame or two of blank space. This seems like a mistake. It should be replaced by a fade.

As suggested, the blank space has been replaced by a fade.

Graphics/screen capture issues

E21. 4:35-6:59 - When the video is scaled to our webplayer's size, the details of the screen capture are very difficult to see. All text is illegible. If there are details in the screen capture that are important for the viewer to see, the areas of interest on the screen should be zoomed in on. For context, the authors can see what their video looks like on our website here: www.jove.com/video/55853

To account for parts in the video where text may be illegible, we have included detailed views and guides for the important parts of the imaging process in the manuscript.

E22. Once the video has been revised, please upload a high resolution video here: https://www.jove.com/account/file-uploader?src=17035213

Reviewers' comments:

Reviewer #1:

Manuscript Summary:

This manuscript describes how to conduct cardiac functional imaging at 7T using a dedicated coil. While the manuscript is clear and well written, it lacks the necessary amount of details for a Jove methodology paper. Furthermore, only 2 views used to evaluate LV function (short axis and 4CH) are described. I would advise to modify the manuscript as follows: 1) describe the general setup that is common to any cardiac examination; 2) focus on describing the imaging protocol for one specific functional evaluation, for example LV function (this change could/should be reflected in the title), and describe this examination in details (including images for each step); 3) describe and report results also for the standard analysis procedure, and compare results to the literature.

Major Concerns:

R1.1. a description of the 32 elements cardiac transceiver would be welcome

As suggested, we have extended Figure 1 to include more details about the 32 channel Tx/Rx array. We have also added a reference to a publication that provides deep technical insight into the coil array.

R1.2. vendor and model of the 7T scanner should be mentioned in the text

As suggested, we have included the vendors of the MRI system and coil in the text. A proper model for the system doesn't exist, as it is an investigational device. We also included this.

R1.3. several acronyms are not explained in the manuscript

We have reviewed the text and added explanations for the used acronyms

R1.4. all the information related to coil and relative patient positioning on the MRI table are indeed relevant for this specific experiment but most can only be better understood if a more detailed description of the coil array is provided. An expanded figure 1 to show patient and coil positioning would also be welcome. The authors should also make the point that this information will change and would need to be recalculated depending on the specific coil used.

As suggested, we have included additional picture material in Figure 1. We also included a schematic overview of the layout of the patient table. We also added a comment that the information is coil specific.

R1.5. In the spirit of providing a description of the experiments that can be easily replicated by other researchers, the MR imaging protocol description should be described in much more details. For example, images for each one of the planning steps, starting from localizers, should be provided. A more detailed description of the shimming procedure is also important: this step is crucial in being able to obtain good images and should be therefore described in details.

As suggested, we included images for the shimming steps (new Fig. 2) and individual protocol steps (new Fig. 3). We also extended the description on the shimming process and added a note that this may be highly system specific.

R1.6. The title of the article generally refers to the evaluation of cardiac functional MRI at 7T. However, steps to image only the left ventricle are described. I suggest this is reflected in the article.
Regardless, even if focusing on the left ventricle only, the paper only focuses on the acquisition of short axis and 4CH views. The authors should focus on one example of cardiac function evaluation, and describe it in details.

Given the limited amount of time available for the JOVE video we have decided not to include further details of a LV or RV chamber quantification procedure. The latter would itself consume a lot of time, so that the 7 Tesla specifics would become underrepresented. In fact, the quantitative evaluation at 7 Tesla does not differ from a quantitative evaluation at 1.5 or 3 Tesla. If not yet available, a demonstration of the quantification would certainly be interesting as a separate video, but it is beyond the scope of this work. To reflect this, we have included more details on setup and shimming (see other comments) and adjusted the manuscript title to be less function and more 7 Tesla specific:

"Cardiac Magnetic Resonance Imaging at 7 Tesla".

R1.7. An example and description of image analysis to calculate left ventricle cardiac parameters (if this is what the authors choose to describe), and comparison with literature values at 1.5 and 3 T should also be provided.

Please see comment R1.6. We consider the function evaluation beyond the scope of this work. In the introduction, the reader is referred to literature, which demonstrates cardiac chamber quantification at 7 Tesla:

"At 7 Tesla, total examination times of (29 ± 5) min for LV function assessment were reported, which corresponds well to clinical imaging protocols at lower field strengths[21]. Thereby, spoiled gradient echo based CMR benefits from the prolonged T_1 relaxation times at ultra-high field that result in an enhanced blood-myocardium contrast superior to gradient echo imaging at 1.5 T. This renders subtle anatomic structures such as the pericardium, the mitral and tricuspid valves as well as the papillary muscles well identifiable. Congruously, spoiled gradient echo based cardiac chamber quantification at 7 Tesla agrees closely with LV parameters derived from 2D bSSFP CINE imaging at 1.5 T[20]. Apart from that, accurate right-ventricular (RV) chamber quantification was recently demonstrated feasible using a high resolution spoiled gradient echo sequence at 7 Tesla[29]"

Reviewer #2:

Manuscript Summary:

This work presents a setup and protocol for functional CMR at ultrahigh field of 7 Tesla, and provides steps to perform the experiment in a minimum time. I believe this protocol can be published in JoVE after revision.

Some major concerns:

R2.1. The advantage of using ultrahigh field is the increase of signal to noise ratio. However, that also creates other side effects. One of my concerns is the change of the body temperature, why that is not being checked? Can this technique be used for a patient having fever?

Although the utilized system is an investigational device, safety measures similar to a standard clinical device are in place. Tissue heating due to RF exposure is a critical topic in MRI and measuring the body temperature wouldn't be accurate enough to ensure safety. The power deposition into the body is currently regulated with field strength independent limits and strictly controlled by the MRI system to ensure safe operation (like in other clinical systems). We have added a comment in the introduction section. In general, the safety precautions for ultra-high field imaging are similar to clinical imaging at lower field strengths.

R2.2. In addition, as authors indicated, the high magnetic field also may interfere with heart activity and changes ECG signal, so can it be used for patient with particular heart problems without any danger? If not, then I guess it should be indicated clearly in a warning section before starting the protocol.

Patients with cardiac disease are often examined using MRI systems and there is no specific danger of MRI related to cardiac disease. This also is the case for the investigational ultra-high field device, as the only difference is the field strength. There are general contraindications such as implants and pacemakers and such patients are typically excluded from research

studies. In diagnostic imaging, decisions are made on a case by case basis depending on the specifications of the implant.
The magnetic field does not interfere with the cardiac activity itself. The MHD effect only alters the signal that is picked up by the ECG electrodes. However, as indicated in the discussion section, the ECG signal obtained in high field environments is not suitable for patient monitoring.

R2.3. In my opinion, using the software program is also an important part of the protocol, although that is explained well in the video, however, it would be very useful to clearly describe it in the protocol text using some figures and snapshots.

As suggested, we have included additional figures with snapshots on the shimming and slice planning procedure.

Some minor concerns:

R2.4. Although some abbreviations are frequently used in any field of research, however, in a scientific publication, all abbreviations should be defined before use, e.g, RF and FOV have not defined in the text.

We have revised the text as suggested and included explanations of the used abbreviations and acronyms.

R2.5. More descriptions on the functional CMR would be useful since it is also appeared in the title.

Please see comment R1.6.

R2.6. It would be useful if the critical steps of the protocol, including the subject position, device setup etc., explained with figures and snapshots.

We have extended figure 1 to include additional information on subject placement and device setup.

Reviewer #3:

Manuscript Summary:

Functional Cardiac Magnetic Resonance Imaging at 7 Tesla

Major Concerns:

R3.1. A brief description and a schematic of the local transceiver RF coil array must be added. Was this previously published? If so, please also add reference to these previous works.

We have added a reference to the publication that explains the utilized RF coil in detail

R3.2. You claim a 4 fold improvement in spatial resolution compared to current clinical practice. How was this evaluated and quantified? Please also be a little more specific about what "current clinical practice" means in this context. Do you simply mean in comparison to 1.5 T machines?

Current clinical practice refers to protocols that are used by major cardiac service providers and clinical research studies. These protocols typically have an in-plane resolution of about 1.5 mm and a slice thickness of 8 mm. These protocols vary slightly from site to site but are typically close to the recommendations by the Board of Trustees Task Force on Standardized

Protocols of the Society for Cardiovascular Magnetic Resonance (SCMR). We have included corresponding reference in the text:

"While a slice thickness of 6 to 8 mm and in-plane voxel edge lengths of 1.2 to 2.0 mm are commonly used at lower clinical field strengths[1, 30], the measurements at 7 Tesla could be conducted with a slice thickness of 4 mm and an isotropic in-plane resolution of 1.0 mm."

R3.3. The protocol should be described in the form of stepwise actions rather than the passive-voice description you have provided.

We have modified the protocol as suggested.

R3.4. Please add all the results presented in the video into the manuscript and describe them there as well. The manuscript should serve as a standalone paper.

As suggested, we have added results. In particular, we have significantly improved the ECG figure and added images of an ECG triggered scan.

R3.5. Any comments on the status of clinical approvals of 7 T MRI in patients will be useful to a reader.

The status with respect to the clinical approval of 7T MRI in patients has recently changed. We added the following comment in the discussion section.

"Only recently, the first 7 Tesla MRI system was approved for clinical use within the USA."

Results:

R3.6. On Line 255: Why does R wave recognition fail? Since you eventually triggered acquisition using the pulse oximetry signal, please provide a figure to show these trigger signals. How does the ultrahigh magnetic field affect the signal acquired here?

It is unfortunately not possible to exactly pinpoint the reason, why the ECG trigger algorithm fails as we don't have access to the ECG trigger algorithm. In essence, the trigger algorithm aims at identifying the R-wave. While this works generally perfect outside of the magnetic field, this can be difficult in presence of the magnetohydrodynamic (MHD) effect. The reason for this is that the MHD effect is highly subject specific, so the ECG signal can be influenced in different ways for each subject. In some cases, the signal is altered such that the algorithm is not able to properly identify the R-wave. As a consequence, a large number of false positive and negative trigger events are generated.
We have amended the figure (now Fig. 5) to provide a clearer view of the ECG signals inside and outside of the magnetic field. As suggested, we have included a representative pulse signal from inside the field. The pulse signal is not affected by the static magnetic field and hence is distortion-free.

R3.7. Fig 1: A panel showing the device schematic will help here.

As suggested, we have revised Fig. 1 and included a schematic of the device and coil.

R3.8. Fig 3: For clarity, please mark R, S-T portions on both A and B.

As suggested, we have included labels of the R wave and S-T interval in the figure (now Fig. 5).

Discussion:

R3.9. Line 299 (and 354): As you do not present a direct comparison with 1.5 or 3 T systems, I do not think you can make this claim, unless you can add the comparison results here or have a published reference that can be added here.

Please see our comment on R3.2. We have clarified the resolution improvement. Indeed, we do not provide a direct comparison to 1.5 or 3 Tesla systems. Thus, we have removed the image quality claim in line 299 and 354, as suggested.

R3.10. Title: "Functional" MRI was not really presented here.

We have adjusted the manuscript title:

"Cardiac Magnetic Resonance Imaging at 7 Tesla".

Minor Concerns:

R3.11. Line 111: Please check the order of citations. This should be changed to 21,25-17

As suggested, we modified the order of citations.

R3.12. Line 125: "corresponds well to clinical imaging protocols at lower field" needs a reference.

As suggested, we have moved the corresponding reference to include this part of the sentence.

R3.13. Line 167-173: The protocol you present is too vague about the specifics of the RF coil array used. A schematic of the commercial device will be useful here.

We have extended Fig. 1 to include additional pictures and a schematic layout of the coil hardware. Technical details about the coils have been published elsewhere. We have added the reference.

R3.14. Fig 2 needs scale references.

We have included scales in the former Fig. 2, which is now Fig. 4.

R3.15. Fig 3 needs axis labels and axis ticks for reference.

We have completely revised the figure (now Fig. 5) and included adequate labelling.

Video:

R3.16. Text on software screen capture cannot be read, this is okay for portions showing set up and general actions but it is a bit hard to keep following this in the later portions around 5:10 timepoint on where specific software steps are being described. It will be useful if software screenshots are provided to match steps 3.3-3.4 (in the protocol).

As suggested, we added additional figures in the manuscript.

R3.17. The background music is a bit distracting.

We have adjusted the music to avoid distraction