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