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Functional LGE Imaging: Cardiac Phase-Resolved Assessment of Focal Fibrosis

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Abstract

Cardiac Magnetic Resonance Imaging (CMR) is a central tool for diagnosis of various ischemic and non-ischemic cardiomyopathies. CMR protocols commonly comprise assessment of functional properties using cardiac phase-resolved CINE MRI and characterization of myocardial viability using late gadolinium enhancement (LGE) imaging. Conventional LGE imaging requires inversion recovery preparation with a specific inversion time to null the healthy myocardium, which restricts the acquisition to a single cardiac phase. In turn, this necessitates separate scans for cardiac function and viability. In this work, we develop a new method for functional LGE imaging in a single breath-hold using a three-step approach: 1) ECG-triggered multi-contrast data is acquired for each cardiac phase, 2) semi-quantitative relaxation maps are generated, 3) LGE imaging contrast is synthesized based on the semi-quantitative maps. The proposed functional LGE method is evaluated in four healthy subject and 20 patients at 1.5T and 3T. Thorough suppression of the healthy myocardium, as well as 40–80ms temporal resolution are achieved, with no visually apparent temporal blurring at tissue interfaces. Functional LGE in patients with focal scar demonstrates robust hyperenhancement in the scar area throughout all cardiac phases, allowing for visual assessment of scar motility. The proposed technique bears the potential to simplify and speed-up common cardiac imaging protocols, while enabling improved data fusion of functional and viability information for improved evaluation of CMR.

I. INTRODUCTION

Cardiovascular magnetic resonance imaging (CMR) has been established as a central tool for diagnosis, prognosis and staging of numerous pathologies in the cardiovascular system [1]. CMR provides excellent soft-tissue contrast without exposing the patient to ionizing radiation. Key roles of CMR in the clinic include the reproducible assessment of cardiac function with CINE MRI, and non-invasive assessment of cardiac viability using late gadolinium enhancement (LGE) imaging. In CINE MRI, imaging data is collected throughout the cardiac cycle, and prospectively or retrospectively assigned to different cardiac phases in order to enable accurate visualization of the cardiac motion throughout the cardiac cycle [2]. CINE MRI is used in the assessment of key markers of cardiac function, including ejection fractions and stroke volume, as well as visual depiction of wall motion abnormalities. In LGE imaging, a T_1 -weighted inversion recovery sequence is used for imaging 10-to-20 minutes after the injection of an extracellular gadolinium-based contrast agent. The acquisition window of the cardiac cycle, during which data is sampled, is pre-defined before the scan and commonly set during the end-diastolic quiescence. The inversion time is adjusted to suppress the signal of the healthy myocardium and depict scar as bright hyperenhancement [3], [4]. According to the relevant clinical guidelines, most cardiac MRI protocols require assessment of wall motion abnormality by CINE MRI and scar presence in the myocardium using LGE [5], [6], [7]. For instance, when revascularization is considered only the joint assessment of both modalities is considered to provide comprehensive information on the myocardial viability [8].

Several studies have indicated the clinical benefit of assessing viability information at different cardiac phases [9], [10], [11], potentially revealing concealed scarification [12], [13]. However, the use of inversion-recovery and the necessity for a specific inversion time commonly restricts the acquisition to a single cardiac phase only. Conventionally this is incompatible with CINE acquisitions, which require sampling of multiple cardiac phases at a steady-state magnetization. Hence, even though CINE and LGE imaging are routinely evaluated alongside each other, to date the data still needs to be acquired in separate acquisitions for comprehensive characterization. This prolongs the duration of CMR examinations and increases the patient burden. More importantly, this substantially hampers fusion of functional and viability information. Finally, single-phase LGE imaging does not allow for cross-validation of the scar information throughout the cardiac cycle or any direct assessment of scar motility.

Synthetic LGE has been previously proposed to mitigate some of the short-comings of conventional LGE imaging, by generating LGE imaging contrast retrospectively [14], [15], [16] from quantitative or semi-quantitative T_1 relaxation information [17], [18]. This alleviates sensitivity to the correct choice of the pre-defined inversion time and allows visualization with varying contrasts [19].

In this study, we sought to develop and evaluate a technique for functional LGE imaging that facilitates joint assessment of functional and viability information in a single-scan. To overcome the confinement of conventional inversion recovery to a single cardiac phase we pursue a three step approach. First, multiple different T_1 -weighted images are acquired for

each cardiac phase. Second, semi-quantitative phase-resolved maps are generated by curve fitting to the acquired multi-contrast CINE data. Finally, the desired LGE imaging contrast, where the healthy myocardium is nulled, is obtained for each cardiac phase by contrast synthetization with a retrospectively chosen inversion time to enable depiction of the scar information in a CINE view. For the acquisition of the phase-resolved, multi-contrast baseline data we extend on our recently proposed sequence for Temporally-resolved assessment of Z-magnetization recovery (TOPAZ) technique [20]. Functional LGE imaging is evaluated in healthy volunteers and patients at 1.5T and 3T.

II. METHODS

A. Sequence

The proposed method is based on the recently developed TOPAZ technique [20]. The sequence consists of multiple triggered Look-Locker experiments with continuous FLASH imaging pulses throughout the entire cardiac cycle (Figure 1). Each Look-Locker experiment starts with a magnetization inversion from the pulsed-steady state. In order for the magnetization to re-reach pulsed steady-state with contiguous FLASH pulses, multiple heart-beats are required. This facilitates acquisition of multiple inversion times for each cardiac phase. The k-space information is collected in a segmented manner, similar to a CINE sequence. Thus, the Look-Locker experiments are repeated several times until the k-space is filled. Finally the Look-Locker blocks are repeated with varying position of the inversion pulse relative to the R-wave to allow denser sampling of the post-contrast inversion recovery curve. To allow uniform recovery in the presence of R-R variability, dummy excitations with no corresponding image readout are performed at the end of the cardiac cycle, after the pre-defined prospectively triggered imaging window and before detection of the subsequent R-wave.

As compared to TOPAZ T_1 mapping, no B_1^+ compensated absolute quantification is required. Hence, magnetization inversion in the functional LGE sequence is performed using an adiabatic full-passage pulse. Details of the post-processing pipeline are depicted in Figure 2. For each cardiac phase, the multiple samples on the inversion-recovery curve are subsequently fit to a two-parameter model with complete inversion efficiency. This leads to improved precision for semi-quantitative T_1^* maps compared to absolute quantification. Synthetic LGE images are then generated using a virtual inversion-time T_{inv} on a voxel wise basis, by calculating the image intensities as

$$S(T_{inv}) = M_0 \left(1 - 2 \exp\left(-\frac{T_{inv}}{T_1^*}\right) \right). \quad (1)$$

A single virtual inversion time is used for all cardiac phases in order to provide constant LGE contrast suited for cross comparison among the phases.

B. Imaging Experiments

The imaging protocol was approved by the respective local institutional review boards, and written informed consent was obtained from each subject prior to examination. Four healthy

subject (3 males, 39 ± 17 years) were imaged on the 3T Siemens Magnetom Prisma (Siemens Healthineers, Erlangen, Germany). Additionally 20 patients (13 males, 7 females, 50 ± 16 years) were scanned on a clinical 1.5T Siemens Avanto Fit (Siemens Healthineers, Erlangen, Germany). Due to decreased SNR and gradient strength, as well as different relaxation times in the heart at 1.5T compared with 3T [21] scans were performed with adapted sequence parameters. Full parameters for 1.5T and 3T are given in Table I. At 1.5T, clinical standard LGE imaging was performed as reference with matching resolution using an inversion recovery GRE imaging sequence with the following image parameters: TR/TE = 10ms/4.93ms, flip-angle = 30° , in-plane resolution = $2.1 \times 2.1 \text{ mm}^2$, slice thickness = 10.0mm, phase-sensitive inversion recovery [22].

III. RESULTS

A. Imaging Experiments

Figure 3 shows representative images acquired in two healthy subjects at 3T with a temporal resolution of 40 ms. The images depict thorough suppression of the healthy myocardial tissue and provide a clear delineation against the blood pool. This high-quality LGE contrast is maintained throughout the entire cardiac cycle. Figure 4 depicts results from patient imaging at 1.5T. Both patients were LGE-negative in the reference LGE scans. The proposed sequence displays thorough nulling of the healthy myocardial tissue, in agreement with the clinical reference. Even with a temporal resolution of 80 ms, clear separation of diastolic and systolic phases is achieved with minimal temporal blurring at the blood-myocardium interface. However, imaging resolution is reduced and noise variability is increased compared to 3T imaging, which has inherently higher signal-to-noise ratio.

Figure 5 shows images of a patient with a known history of coronary artery disease and myocarditis. Scar is clearly depicted in the antero-lateral segment with both the reference scan and the proposed functional LGE sequence. It remains clearly visible against a thoroughly nulled healthy myocardial background throughout the cardiac cycle in the proposed approach. Furthermore, as opposed to the reference LGE image, retrospective inversion time allows to optimize scar myocardial contrast, benefiting the depiction.

Figure 6 shows another example of patient images acquired at 1.5T and 80 ms temporal resolution. The patient suffered from coronary artery disease, and a scar in the lateral segment is clearly depicted. Functional LGE provides good visualization of the scarred tissue, while further enabling the assessment of scar motility and displacement as a function of the cardiac phase.

IV. DISCUSSION AND CONCLUSIONS

In this study we proposed a technique for integrated assessment of cardiac function and viability. Semi-quantitative cardiac phase-resolved assessment of the longitudinal relaxation time allowed synthetic generation of LGE contrast at all cardiac phases. In-vivo images at 3T and 1.5T demonstrate clear depiction of scar tissue with a temporal resolution of up to 40 ms.

Depiction of scarred myocardium in a phase-resolved manner allows cross-comparison of enhancement throughout the cardiac cycle. This may ease delineation of ambiguous enhancement areas against fatty tissue or inadvertent enhancement from the right ventricular blood pool. This is particularly advantageous, when thin myocardial walls hamper assessment in a single diastolic phase, and require alternative techniques [23], [24], [25]. Conventional LGE imaging is performed with a temporal resolution of 100–200 ms. In order to accommodate this imaging window without causing pronounced temporal blurring, careful placement at the diastolic quiescence is usually required. This remains a non-automated process that is potentially susceptible to operator errors. Furthermore, this procedure and the temporal resolution might not be suited for accurate visualization of highly mobile structures or for patients with high heart-rates [26], [27]. Functional LGE imaging was performed with temporal resolutions between 40–80 ms, inherently alleviating the problem of temporal blurring. Additionally the acquisition throughout the entire cardiac cycle eliminates the need to determine the start and duration of the cardiac quiescence, facilitating the scan setup.

LGE images are commonly evaluated jointly with CINE MRI in order to assess the amount of residual tissue viability and scar transmural. Acquisition in two separate scans hampers this data fusion, allowing only for a subjective alignment and cross-validation. Functional LGE imaging on the other hand provides the means to assess motility of the scar and the area surrounding it in an integrated manner. Furthermore, scar transmural can be assessed in multiple cardiac phases, including peak-systole, which was previously reported to be beneficial for accurate assessment [13], [12].

This study and the proposed technique have several limitations. First, in addition to the healthy subjects only a general patient-cohort was evaluated in order to demonstrate feasibility of the proposed sequence and to provide representative image quality that can be expected in clinical practice. The evaluation of diagnostic and prognostic value with respect to conventional LGE imaging is warranted in specific patient cohorts. Smaller imaging FOV were chosen in this study to provide adequate spatial resolution. While fold-over issues were avoided by careful planning of the oblique short-axis plane, other applications or imaging of larger patients may require increased matrix sizes to provide sufficient spatial coverage at adequate resolutions. Advanced image acceleration techniques explicitly taking the interdependence among the images are subjects of ongoing research [28], [29], [30], and they may prove valuable in providing a reasonable trade-off between spatio-temporal resolution and coverage in the proposed technique for clinical settings.

V. CONCLUSIONS

Functional LGE imaging allows clear depiction of myocardial scar and can be performed at temporal resolutions of up to 40 ms. This technique may allow the integration of functional and viability information, potentially depicting scar motility, while enabling time and cost efficient scan protocols.

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Fig. 1.

Sequence diagram of the proposed functional LGE sequence. Initially FLASH pulses are played to drive the magnetization to pulsed steady-state. After an adiabatic inversion pulse is played, continuous FLASH excitations are used to read out the magnetization recovery to the pulsed steady-state. Due to the segmented acquisition multiple inversion pulses are required to fill k-space. Finally, this Look-Locker experiment is repeated multiple times while varying the position of the inversion pulse with respect to the R-wave in order to provide a denser sampling of the recovery curve. These data points are used to fit a semi-quantitative T_1 recovery model, which are then used to synthesize LGE contrast, where the healthy myocardial tissue is nulled.

Fig. 2.

Illustration of the post-processing pipeline of the functional LGE technique. The proposed technique acquires multiple images with varying T_1 -weighted contrast for each cardiac phase. A semi-quantitative 2-parameter fit yields T_1^* maps. These are used to synthesize LGE image contrast in a voxel-wise manner for all cardiac phases with a retrospectively chosen virtual inversion time.

Fig. 3. Representative images illustrating the image quality of functional LGE imaging in two healthy subjects at 3T at 40 ms temporal resolution. For both subjects, thorough suppression of the healthy myocardium is achieved for all cardiac phases, while maintaining a sharp delineation against the blood pools.

Patient 1 **Patient 2** **Fig. 4.**

Representative images illustrating the image quality of functional LGE imaging in two LGE-negative patients at 1.5T at 80 ms temporal resolution. Thorough suppression of the healthy myocardium is achieved, albeit visually increased noise in the 1.5T images compared to 3T. Wall motion abnormality is readily visible in patient 2, despite the reduced temporal resolution.

Fig. 5.

Functional LGE images acquired in a patient suffering from coronary artery disease and displaying scar in the lateral segment (green arrows). Clear depiction of the scar is provided at all cardiac phases, which is in agreement with the reference scan for the matching phase. Furthermore, the proposed sequence provides information on scar displacement.

Fig. 6.

Functional LGE images acquired in a patient with a known history of coronary artery disease and myocarditis in comparison to a reference LGE acquisition. The patient displays a large antero-lateral scar (green arrows), which is clearly visualized with the proposed technique throughout all cardiac phases. Retrospective choice of the inversion time enables optimization of the scar contrast, providing very clear delineation against the myocardium.

TABLE I

Sequence parameters of the proposed functional LGE sequence at 1.5T and 3T.

	1.5T	3T
TE (ms)	3.2	2.6
TR (ms)	6.7	5.0
Flip angle	6°	3°
GRAPPA	2	2
In-plane Resolution (mm ²)	2.1 × 2.1	1.9 × 1.9
Slice Thickness (mm)	10.0	10.0
Temporal Resolution (ms)	80	40 – 60
Breath-hold Duration (s)	15 – 18	17 – 19