Whole-heart High-resolution Late Gadolinium Enhancement in Clinical Routine

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Introduction

Over the past two decades, late gadolinium enhancement (LGE) has become the preferred imaging technique for detecting myocardial infarction and fibrosis in various non-ischemic diseases [1–3]. LGE relies on a T1-weighted inversion-recovery gradient-echo pulse sequence acquired at least 10 minutes after gadolinium injection. The acquisition is performed during breath-hold with a conventional in-plane spatial resolution of 1.4–1.8 mm and a slice thickness of 6–8 mm [4]. Nowadays, several variants of LGE pulse sequences co-exist in clinical routine with different excitation pulses (2D or 3D), read-out schemes (FLASH or TrueFISP), acquisition strategies (segmented or single-shot), and motion compensation approaches (breath-hold or free breathing). In any case, the spatial resolution remains limited by scan time constraint, in other words by the breath-hold duration, which must stay below ~13 seconds to be acceptable in clinical routine.

A 38-year-old female patient presented with typical angina and mildly elevated troponin levels. Coronary angiography showed no significant coronary artery stenosis. During the CMR exam, T2-weighted STIR (1A) and conventional LGE (1B, C) were considered negative. HR-LGE (1D, E) revealed focal subendocardial enhancement on the inferolateral segment, consistent with microinfarction (orange arrowheads).
Whole-heart high-resolution LGE (HR-LGE) was initially introduced to assess fibrosis in the left atrial (LA) wall, which is five times thinner than the left ventricular (LV) wall. To achieve much higher spatial resolution, breath-hold had to be replaced by free breathing with navigator gating, resulting in an extended scan time. HR-LGE gained significant momentum with the DECAAF study (Delayed-Enhancement MRI Determinant of Successful Radiofrequency Catheter Ablation of Atrial Fibrillation), which demonstrated a significant association between atrial fibrosis and arrhythmia recurrence after ablation in 15 clinical centers using Siemens Healthineers MR systems [5]. The DECAAF study extensively validated a whole-heart LGE protocol with an improved spatial resolution of 1.25 × 1.25 × 2.5 mm at 1.5T and 3T.

As DECAAF study investigators, our group has been performing HR-LGE for more than a decade and we have found clear evidence of its clinical value in both the atria and the ventricles. In this article, we share when and how we perform HR-LGE imaging daily, and how we identify patients who are likely to benefit the most from it.

Why perform whole-heart high-resolution LGE?

Firstly, HR-LGE does not have to be performed in every patient, especially when conventional LGE is sufficient to make a diagnosis. However, HR-LGE can be instrumental for several diagnoses, which we present below.

Myocardial infarction with non-obstructive coronary arteries (MINOCA)

MINOCA is a ‘working diagnosis’ for patients who present with acute coronary syndromes and in whom the diagnosis of myocardial infarction remains uncertain after coronary angiography. In 2020, guidelines from the European Society of Cardiology (ESC) recommend performing cardiovascular MRI (CMR) in all MINOCA patients without an obvious underlying cause [6]. Indeed, the presence and topography of LGE assessed by CMR plays a key role for the differential diagnosis of Takotsubo syndrome, myocarditis, or true myocardial infarction without obstructive coronary artery disease. However, CMR imaging is normal or inconclusive in about 25% of patients with MINOCA, creating a problem for decision-makers [7, 8]. Our group recently investigated the diagnostic value of HR-LGE in these cases [9]. After studying 172 patients with MINOCA, we showed

![Image 1](https://siemens-healthineers.com/magnetom-world)

A 21-year-old female patient presented with atypical chest pain and elevated troponin levels. T2-weighted STIR (2A) and conventional LGE (2B, C) were considered negative. HR-LGE (2D, E) revealed focal subepicardial enhancement on the inferolateral segment, consistent with myocarditis (orange arrowheads).
that HR-LGE is particularly valuable when conventional LGE is negative or compatible with several diagnoses. Interestingly, it led to a change in the final diagnosis in 26% of the patients. Given that one third of these patients initially had a negative conventional LGE, these findings suggest that higher spatial resolution is of great interest. Examples of diagnoses made thanks to the addition of HR-LGE are shown in Figures 1 and 2. Improving the etiological diagnosis of MINOCA has a major impact on patient management, as it directly influences drug therapy and could motivate additional diagnostic tests to detect occult causes of myocardial infarction. This further supports the systematic use of HR-LGE in patients with MINOCA when conventional LGE is negative or inconclusive.

### Diagnosis and prognosis in ventricular arrhythmia

Ventricular arrhythmias are an extremely common phenomenon. Most arrhythmias are not sustained, and therefore do not expose the patient to an increased risk of sudden death. These ‘benign’ ventricular arrhythmias are due to an ectopic focus most often confined to the right ventricular outflow tract. They occur in structurally normal hearts and can usually be recognized from clinical presentation and 12-lead ECG characteristics. In many cases, though, the presentation is atypical and potentially suggests a structural substrate, which can either be ruled out or diagnosed on CMR. Myocardial scars detected on LGE CMR are known to facilitate arrhythmia sustenance and therefore play a major role in arrhythmia malignancy. Besides this prognostic role, CMR is also key to establishing the diagnosis of the underlying structural heart disease.

Our group investigated the value of using HR-LGE to improve the detection of focal arrhythmogenic substrates. After studying a series of 157 patients with ventricular arrhythmias, we showed that the detection rate of structural abnormalities improved two-fold with HR-LGE compared to conventional CMR methods [10]. This includes the detection of small scars on the left ventricle suggestive of occult ischemic and non-ischemic diseases, as well as the detection of right ventricular (RV) fibrosis, which can be key to diagnosing arrhythmogenic right ventricular cardiomyopathy. Indeed, although RV LGE is not part of the 2010 Task Force Criteria for the diagnosis of arrhythmogenic right ventricular cardiomyopathy, our experience suggests that in cases of borderline regional RV wall motion abnormalities, the presence of RV fibrosis on high-resolution LGE might help to confirm this challenging diagnosis (Fig. 3).

### Catheter ablation guidance in scar-related ventricular arrhythmias

In patients presenting with ventricular arrhythmias, HR-LGE is also useful for guiding catheter ablation by providing precise visualization of arrhythmogenic sites [11]. Indeed, channels of surviving fibers within scar are the substrate on which scar-related re-entrant tachycardia can occur. This can be recognized on LGE images as areas of intermediate signal intensity, the so-called ‘gray zones’. HR-LGE is crucial in this indication for detecting gray-zone channels on thinned walls and for appropriately rendering their 3D architecture. As shown in Figure 4, a 3D reconstruction of the different types of tissue (normal, dense scar, and gray-zone channels) can be processed from HR-LGE images using commercially available solutions. This pre-procedural analysis of the scar architecture can then be displayed in 3D electroanatomical mapping systems during the procedure, allowing the electrophysiologist to identify the best ablation strategy. It is important to mention here that in this indication, as most patients undergoing catheter ablation carry implantable cardioverter defibrillators (ICDs), the HR-LGE images acquired pre-operatively can be significantly hampered by susceptibility artifacts. Unfortunately, although wideband methods have been specifically developed to address this problem, they do not fully alleviate the image-quality issues. Our institution therefore routinely performs CMR including whole-heart high-resolution LGE before ICD implantation. This is justified by the need for accurate measurements of left ventricular ejection fraction to select patients eligible for implantation of a primary prevention ICD, and by the need to obtain detailed and

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**Figure 3**

A 45-year-old male patient was referred for evaluation due to a recent family history of sudden cardiac death. CMR showed right ventricular dilatation and borderline wall motion abnormality in the right ventricular outflow tract (3A, yellow arrow). HR-LGE showed focal fibrosis in the outflow tract (3B, orange arrowheads). The finding of focal LGE on an area of borderline wall motion was instrumental in retaining the diagnosis of arrhythmogenic right ventricular cardiomyopathy.
High-resolution 3D whole-heart LGE: how we do it

Sequence parameters and positioning
The sequence parameters are presented in Table 1. HR-LGE is a 3D inversion-recovery spoiled gradient-echo (FLASH) pulse sequence. The voxel size is 1.25 × 1.25 × 2.5 mm³, reconstructed to 0.63 × 0.63 × 1.25 mm³. All desired views can be reconstructed from the 3D volume, which is of particular interest compared to conventional breath-hold LGE. For that reason, the interpolation allows a better image quality for multi-planar reconstructions. Spectral fat saturation is used to remove epicardial fat signal and to facilitate the visualization of epicardial LGE. The volume is strictly transversal and positioned on free-breathing localizer images (Fig. 5). A margin is kept in head-feet direction to avoid cropping the ventricle. While this may at first seem counter-intuitive, the phase-encoding direction is set in left-right direction in order to minimize residual artifacts caused by breathing. To reduce the fold-over artifact from the arms, two saturation bands are positioned over the arms (see Fig. 5). A third band is positioned over the chest to also reduce ghosting artifacts and subcutaneous fat signal.

Table 1: High-resolution 3D whole-heart LGE sequence parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Sequence type</td>
<td>3D spoiled gradient-echo</td>
</tr>
<tr>
<td>Motion compensation</td>
<td>Diaphragmatic navigator gating</td>
</tr>
<tr>
<td></td>
<td>(acceptance window: 3 mm)</td>
</tr>
<tr>
<td>TR/TE</td>
<td>5.2/2.50 ms</td>
</tr>
<tr>
<td>Field of view</td>
<td>360 x 360 x 120 mm</td>
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<tr>
<td>Matrix</td>
<td>288 x 288 pixels</td>
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<td>Acquired voxel size</td>
<td>1.25 x 1.25 x 2.5 mm</td>
</tr>
<tr>
<td>Reconstructed voxel size</td>
<td>0.63 x 0.63 x 1.25 mm</td>
</tr>
<tr>
<td>Flip angle</td>
<td>19°</td>
</tr>
<tr>
<td>Bandwidth</td>
<td>255 Hz/pixel</td>
</tr>
<tr>
<td>Fat suppression</td>
<td>Spectral fat saturation</td>
</tr>
<tr>
<td>Phase encoding direction</td>
<td>Right-left</td>
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<td>Phase oversampling</td>
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<tr>
<td>Slice oversampling</td>
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</tr>
<tr>
<td>Acceleration method</td>
<td>Parallel imaging (GRAPPA)</td>
</tr>
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<td>Acceleration factor</td>
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</tr>
<tr>
<td>Number of heartbeats</td>
<td>295</td>
</tr>
<tr>
<td>Number of segments per heartbeat</td>
<td>35</td>
</tr>
<tr>
<td>Acquisition window</td>
<td>156 ms</td>
</tr>
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</table>

HR-LGE is segmented based on the signal intensity (4A–D) to reconstruct the complex scar architecture of this patient (4E): violet (normal tissue), blue-green-yellow (gray zone), and red (dense scar). A conducting channel (4D, white arrowhead; and 4E, white arrow) could be identified inside the dense scar area. This 3D rendering was useful for guiding the ventricular tachycardia ablation by integrating the image into electroanatomical systems.
**Sequence positioning on the MR console:** The volume (yellow box) is positioned in strict transversal orientation to cover the ventricles on free-breathing localizers: sagittal (5A), coronal (5B), and transversal (5C). The intersection of the crossed pair of the navigator is positioned on the liver dome (blue boxes). Three saturation bands are positioned on the patient’s chest (1) and arms (2 and 3) to reduce fold-over artifacts in the right-left direction (phase encoding direction, depicted by the yellow arrow).

**Navigator settings:** The sequence is first run with ‘Scout Mode’ selected (6A, orange rectangle) so that the navigator data is displayed in the ‘Online Display’ window (6B). This window shows the navigator line through the lung (hyposignal) and the liver (hypersignal). The expiratory phase is automatically detected and indicated as ‘Mode’ (6B, orange rectangle). The green box represents the acceptance window of ± 3 mm, in which data will be accepted. The scan efficiency is shown as a percentage next to ‘Accept’. The ‘Mode’ value has to be entered manually into the ‘Search Position (red)’ field (6C) to center both the green and red boxes on this position. ‘Scout Mode’ is then deselected to run the real scan (6C). During the scan, the navigator is displayed in the ‘Inline Display’ window, so that it can be checked by the technologist (6D). The remaining data to be acquired is indicated as a percentage to the right of ‘Ima’, and the scan efficiency is still indicated as ‘Accept’. As ‘Resp. Motion Adaptation’ is selected (6C), the acceptance position (green box) will be dynamically adapted over time to account for breathing drift.
Gadolinium injection and timing
HR-LGE is acquired 15 to 30 minutes after injection of gadolinium-based contrast agent (double dose) [12]. The inversion time (TI) must be set to null the normal myocardium signal. An off-set of 20–30 ms at 1.5 T and of 50–80 ms at 3 T must be added to account for gadolinium wash-out during the scan. This off-set must be determined empirically by each center and depending on their habits.

Navigator positioning and setting
A spectrally selective crossed-pair navigator is used to dynamically track the respiratory motion. The cross section of the two planes must be positioned on the liver dome at the interface between the lung and the diaphragm (Fig. 5). The navigator should not cross any anatomy of interest. The sequence is first run for ~20 seconds to check the quality of the navigator and enter the expiratory phase position (in mm). For this, ‘Scout Mode’ is selected in the ‘Physio/PACE’ section of the sequence settings (Fig. 6A). The navigator data will be displayed over time in the ‘Inline Display’ window as a line through the liver (hypersignal) and the lung (hyposignal) (Fig. 6B). The green box shows the positions in which data acquisition is permitted. In our protocol, the acceptance window (green-box thickness) is set to ± 3 mm. The ideal accepted position is automatically detected by the system and indicated as ‘Mode’. This value must be entered manually in the ‘Search Position (red)’ field, so that both red and green boxes are centered on this position (Fig. 6C). Scout Mode should be unchecked before validating the sequence. During the scan, the navigator data is displayed in the ‘Inline Display’ window (Fig. 6D). The scan efficiency is indicated as a percentage (“Accept 33%” in the example in Fig. 6). This value should remain above 30% to maintain a reasonable scan time. To ensure good scan efficiency, the patient should have the shallowest breathing pattern, which is not always easy to obtain. The ‘Respiratory Motion Adaptation’ feature allows the position of the green box to be dynamically adapted in case of breathing drift during the scan. However, if the drift is too severe, the scan efficiency will be preserved, but the image quality might be impaired. Note that the ‘Search Position (red)’ box is not updated during the scan.

ECG triggering
HR-LGE is electrocardiogram (ECG)-triggered in the end-diastolic phase every heartbeat. The number of segments determines the number of acquired lines per heartbeat, and therefore the total acquisition time. The longer the cardiac cycle, the longer the diastolic resting phase. With this in mind, we adapt the number of segments to the patient’s heart rate, following Table 2. That way, the scan time is less dependent on the patient’s heart rate. The repetition time (TR) is set below the cardiac cycle (e.g., TR = 680 ms for RR = 800 ms) to allow for potential changes in heart rate during the scan. In patients with arrhythmia, the TR is decreased to the shortest cardiac cycle encountered in the patient.

Future technical developments of high-resolution LGE
Despite promising results, the main problem with HR-LGE is the scan time, which is not compatible with all clinical workflows. Efforts are currently underway to accelerate this sequence, either by improving the navigator efficiency or by further under-sampling k-space data.

Data acquisition is currently restricted to an acceptance window of ± 3 mm at end expiration, resulting in a limited scan efficiency of 30–60%. This efficiency can further decrease in the case of irregular breathing and lead to long and unpredictable scan times. In addition, the complex motion of the heart is not taken into account, as a simplified linear correlation with the diaphragm is used. Novel image-based navigators (iNAV) have recently been introduced to directly track the heart and compensate for non-rigid motion during image reconstruction. This improves scan efficiency to 95–100%, reduces the scan time, and makes it predictable. The technique has shown promising results for whole-heart HR-LGE [13, 14].

k-space under-sampling is another way of accelerating HR-LGE by acquiring less data. Conventional HR-LGE is usually under-sampled by a factor of two using parallel imaging with generalized autocalibrating partially parallel acquisitions (GRAPPA). Higher acceleration rates are hindered by the inherent loss of signal-to-noise ratio and by parallel-imaging artifacts. As an alternative, compressed-sensing acceleration has been proposed to further accelerate whole-heart LGE sequences using incoherent k-space under-sampling followed by iterative non-linear reconstruction. Initial implementations showed scan time acceleration without compromising image quality in the atria and the ventricles [15–17]. However, iterative recon-

<table>
<thead>
<tr>
<th>Heart rhythm (beats per minute)</th>
<th>Cardiac cycle (ms)</th>
<th>Number of segments</th>
<th>TR (ms)</th>
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<tbody>
<tr>
<td>120</td>
<td>500</td>
<td>18</td>
<td>440</td>
</tr>
<tr>
<td>100</td>
<td>600</td>
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<tr>
<td>67</td>
<td>900</td>
<td>33</td>
<td>760</td>
</tr>
<tr>
<td>55</td>
<td>1000</td>
<td>37</td>
<td>840</td>
</tr>
</tbody>
</table>

Table 2: Physio settings for high-resolution 3D whole-heart LGE
struction is time-consuming and requires powerful reconstruction systems equipped with graphics processing units (GPU). Hence, artificial intelligence with fast deep-learning reconstruction might play a role in further developing the clinical availability of HR-LGE in the future [18].

Conclusion

High-resolution 3D whole-heart LGE improves the sensitivity of CMR for the detection and characterization of structural heart diseases. Preliminary experience, particularly in the context of MINOCA and ventricular arrhythmias, indicates that HR-LGE goes far beyond the current state-of-the-art breath-hold LGE imaging. Knowing the diagnostic and prognostic value of LGE, the method has the potential to significantly impact clinical decision-making in many domains of cardiology. Although the extended scan time remains a significant limitation, the combination of under-sampling and better scan efficiency might soon bring HR-LGE closer to widespread clinical use.

References


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