Dark-blood late gadolinium enhancement cardiovascular magnetic resonance for improved detection of subendocardial scar: a review of current techniques

Robert J. Holtackers1,2,3*, Caroline M. Van De Heyning4, Amedeo Chiribiri3, Joachim E. Wildberger1,2, René M. Botnar3,5 and M. Eline Kooi1,2

Abstract
For almost 20 years, late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) has been the reference standard for the non-invasive assessment of myocardial viability. Since the blood pool often appears equally bright as the enhanced scar regions, detection of subendocardial scar patterns can be challenging. Various novel LGE methods have been proposed that null or suppress the blood signal by employing additional magnetization preparation mechanisms. This review aims to provide a comprehensive overview of these dark-blood LGE methods, discussing the magnetization preparation schemes and findings in phantom, preclinical, and clinical studies. Finally, conclusions on the current evidence and limitations are drawn and new avenues for future research are discussed. Dark-blood LGE methods are a promising new tool for non-invasive assessment of myocardial viability. For a mainstream adoption of dark-blood LGE, however, clinical availability and ease of use are crucial.

Keywords: Cardiovascular diseases, Myocardial infarction, Magnetic resonance imaging, Late gadolinium enhancement, Myocardial scar

Introduction
Late gadolinium enhancement (LGE), also sometimes referred to as late enhancement (LE) or delayed enhancement (DE), is a widely used cardiovascular magnetic resonance (CMR) technique to distinguish macroscopic scarring and myocardial infarction (MI) from normal myocardium. Since its initial validation against histology approximately two decades ago [1, 2], LGE has gained wide acceptance and is now considered the reference standard for the non-invasive assessment of myocardial viability. The clinical need for accurate scar detection was emphasized in the landmark study by Kwong et al. [3]. This study showed that using LGE, even small regions of scar tissue of only 2% of the mean left ventricular (LV) mass could be identified that were linked with a seven-fold increase in major cardiac events. Furthermore, the assessment of scar transmurality plays a major role in the prediction of the likelihood of regional functional recovery after revascularization [4], making LGE an important tool for image guided diagnosis, prognosis, and treatment planning.

The standard inversion-recovery (IR) LGE sequence with the inversion time (TI) set for myocardium nulling, however, has its limitations. Due to the often bright signal of the blood pool, blood may appear equally enhanced as adjacent subendocardial scar regions. As a result, these regions can be falsely interpreted as being...
part of the blood pool and therefore significantly reduce, or even completely obscure, the apparent scar volume. Scar tissue can also be mimicked by the blood pool signal in proximity of the subendocardium, resulting in false positive observations. Even though performing LGE at 20 min instead of 10 min post-injection intrinsically boosts scar-to-blood contrast due to contrast washout, this inefficient workaround is often not suitable for daily clinical practice.

Over the last 15 years, various novel “dark-blood” LGE approaches have been proposed to increase scar-to-blood contrast and improve subendocardial scar conspicuity. Most of these methods use additional magnetization preparation mechanisms to either suppress the blood pool signal partly (gray-blood techniques) or null the signal completely (black-blood techniques). These mechanisms include T2 preparation, magnetization transfer, and spin-locking in concert with the standard inversion pulse, and utilization of multiple inversion pulses. Similar effects, however, have also been achieved without using any additional magnetization preparation. As each approach utilizes a different contrast mechanism, a great variety in contrast between the normal myocardium, blood pool, and areas of myocardial enhancement can be achieved. This review aims to provide a comprehensive overview of current dark-blood LGE methods. For each method, the employed contrast mechanism and corresponding magnetization preparation scheme are illustrated, followed by a discussion on the findings in phantom, preclinical, and clinical studies. Finally, conclusions on the current evidence and limitations are drawn and new avenues for future research are discussed.

**Blood pool suppression techniques for LGE**

**T2 preparation**

T2 preparation can add additional contrast to the conventional heavily T1-weighted image based on the difference in T2 relaxation times of the normal myocardium and blood. Such a T2 preparation module starts with a 90° radiofrequency (RF) pulse that tips the longitudinal magnetization (M_l) into the transverse plane (Fig. 1, top panel). For each tissue, the created transverse magnetization (M_xy) will then start decaying with a rate given by the corresponding T2 relaxation time of that tissue, leading to significant signal loss in tissues with shorter T2 relaxation times, such as normal myocardium and areas of scarring (Fig. 1, bottom panel). One or more 180° refocusing RF pulses are applied to reduce dephasing caused by magnetic field inhomogeneities and to preserve M_xy of tissues with longer T2 relaxation times, such as the blood pool.

After a specific time, called the effective echo time (T_Eeff), a -90° ‘tip up’ RF pulse tips the remaining M_xy back towards the longitudinal axis where the magnetization is stored again for subsequent imaging. The longer T_Eeff, the more T2 weighting was added to the available signal. As the blood pool has a significant longer T2 relaxation time than normal myocardium, blood magnetization will be higher than that of normal myocardium directly after T2 preparation (shown in white rectangle).

In 2005, Kellman et al. proposed their ‘multi contrast delayed enhancement’ (MCODE) approach that combined a two-beat phase-sensitive inversion-recovery (PSIR) LGE sequence with the acquisition of a T2*-weighted image in the following third heartbeat [5]. Later in 2012, MCODE was validated in a cohort of 73 patients [6]. The extra T2*-weighted image was able to separate the blood pool from both normal and infarcted myocardium, and thereby improving the detection of scar regions on the T1-weighted images (where both blood pool and scar areas appear bright).

Instead of acquiring an additional T2*-weighted image, T2 preparation can also be incorporated into the LGE sequence itself to either suppress or completely null the blood pool signal. Two different forms can be distinguished based on the order of the T2 preparation module: those with T2 preparation before (T2 prep-IR) and those with T2 preparation after (IR-T2 prep) the inversion pulse.

**T2 preparation before the inversion pulse**

In case of T2 prep-IR, the almost unaffected magnetization level of the blood pool after T2 preparation leads to a more negative magnetization level for blood after the inversion RF pulse compared to normal myocardium and scar tissue (Fig. 2). Although blood and scar have similar T1 relaxation times and recover almost equally fast, blood now starts from a more negative magnetization level than scar tissue, leading to increased scar-to-blood contrast compared to conventional LGE where both start from a similar magnetization level after the inversion RF pulse. Since blood has a much shorter T1 relaxation time than normal myocardium, blood recovers faster and can therefore catch up with the normal myocardium, allowing for simultaneous nulling of both tissues. By adjusting the T_Eeff and TI, the blood pool appearance can range from being slightly suppressed to completely nulled.

In 2008, Liu et al. introduced their T2 prep-IR approach in a standard single-beat IR sequence [7]. Simulations for various combinations of T_Eeff and TI were performed followed by an evaluation in five healthy subjects and nine patients with known MI. Contrast-to-noise ratio (CNR) measurements showed a 32% increase in scar-to-blood contrast compared to conventional LGE. While T2 prep-IR may be a valuable tool for improved detection and assessment of subendocardial scar tissue, it was
mentioned that the per-patient optimization of $T_{E_{\text{eff}}}$ and TI is a potential pitfall.

**$T_2$ preparation after the inversion pulse**

In contrast to $T_2$ prep-IR, $T_2$ preparation can also be performed after the inversion pulse (IR-$T_2$ prep, Fig. 3). The magnetization levels are then inverted first, after which they recover by $T_1$ relaxation until $T_2$ preparation starts. $T_2$ preparation will then indirectly affect the rate at which the magnetization is recovering. Since normal myocardium and scar tissue have a relatively short $T_2$ relaxation time compared to blood, their increased signal loss during $T_2$ preparation will lead to a lower (negative) magnetization level after $T_2$ preparation than it would have without $T_2$ preparation. The recovery of normal myocardium and scar tissue have therefore effectively been accelerated during $T_2$ relaxation. In contrast, the relatively long $T_2$ relaxation time of blood results in far less signal loss during $T_2$ preparation, leading to a largely maintained negative magnetization level after $T_2$ preparation.

As a result, the magnetization levels of blood and normal myocardium will cross each other during $T_2$ preparation. Following $T_2$ relaxation, both tissues will further recover based on their individual $T_1$ relaxation times again. As blood recovers faster, the magnetization levels of blood and normal myocardium will cross again later. Instead of a single TI, two delay times have to be defined now: one between the inversion pulse and the $T_2$ preparation module ($TD_1$), and one between the $T_2$ preparation module and image acquisition ($TD_2$). By adjusting the two delay times and the $T_{E_{\text{eff}}}$, simultaneous nulling of the blood and normal myocardium can be achieved.

In 2016, Kellman et al. presented their IR-$T_2$ prep method in a free-breathing PSIR sequence and combined it with respiratory motion-corrected averaging [8]. Simulations were performed to obtain LGE images with various degrees of blood pool suppression. Subsequently, their approach was evaluated in a cohort of 61 patients which showed that subendocardial MI was observed best when nulling the blood pool completely.
Their CNR measurements, performed on a subset of 30 patients, showed increased scar-to-blood contrast compared to conventional LGE, however, at the cost of scar-to-myocardium contrast. Before image acquisition, a \( T_1 \) map was required to obtain actual \( T_1 \) relaxation times of both normal myocardium and the blood pool. After providing these times to the system, a custom ‘delta’ parameter is chosen which determines whether normal myocardium signal should be above or below that of the blood pool. The system then calculates \( T_D1, T_D2, \) and \( T_{E_{\text{eff}}} \) using a strategy that sought to achieve the desired blood suppression while keeping \( T_{E_{\text{eff}}} \) as short as possible to minimize signal loss.

In 2017, the same group compared this IR-\( T_2 \) prep approach to conventional bright-blood LGE in a larger cohort of 172 patients [9]. The IR-\( T_2 \) prep approach found significantly more segments that exhibited LGE and allowed for increased confidence with regard to scar detection when nulling the blood pool. Additionally, 18 patients with no enhancement on bright-blood LGE images were found to have LGE on dark-blood images, 15 of whom had no known history of MI. However, no histological confirmation was available.

In 2018, Basha et al. proposed their IR-\( T_2 \) prep approach for a free-breathing 3D acquisition without a PSIR reconstruction to reduce scan time [10]. Simulations and phantom experiments were performed showing the ability to simultaneously null the blood pool and normal myocardium. Based on the numerical simulations and phantom study, a contrast scout scan was developed that was used for all in-vivo imaging. For this scan, \( T_{E_{\text{eff}}} \) and \( T_D2 \) were kept constant (at 35 and 150 ms, respectively), while \( T_D1 \) was sampled between 15 and 115 ms with 5 ms increments, yielding 21 images with different tissue contrast. This scan was performed prior in-vivo LGE imaging, analogous to a Look-Locker scan. Their IR-\( T_2 \) prep approach was evaluated in nine infarcted swine and 42 patients. For both IR-\( T_2 \) prep and conventional LGE, 22 out of 42 patients were found showing myocardial enhancement. Quantitative analysis in a subset of 17 patients and all swine showed increased scar/blood signal ratios for IR-\( T_2 \) prep LGE compared to conventional LGE.
Also in 2018, the same group exploited the flexibility of their IR-T2 prep LGE approach by acquiring a suppressed (gray-blood) rather than a completely nulled blood pool (black-blood) using another set of parameter values [11]. Simulations were performed and a comparison between conventional LGE, black-blood IR-T2 prep LGE, and gray-blood IR-T2 prep LGE was carried out in 45 patients and five swine. Similar to the IR-T2 prep approach of Kellman et al., a T1 map was acquired prior LGE imaging to calculate the optimal imaging parameters. CNR measurements showed that although the black-blood approach outperformed gray-blood and conventional bright-blood LGE in terms of scar-to-blood contrast, scar-to-myocardium, and myocardium-to-blood contrast both decreased. In contrast, only gray-blood IR-T2 prep LGE achieved both increased scar-to-blood contrast and scar-to-myocardium contrast compared to conventional LGE. Furthermore, gray-blood LGE detected more scars compared to black-blood and conventional LGE. Subjective scores of the ability for localizing left-ventricular scar tissue and detecting papillary muscle scar was significantly improved for dark-blood LGE compared to both black-blood LGE and conventional LGE.

Although T2 preparation can be performed before or after the inversion pulse, both options have their pros and cons. By performing T2 preparation after the inversion pulse, an additional delay is created between the inversion pulse and T2 preparation module (Fig. 3). As a result, an additional third parameter, aside the T2 preparation duration (TEeff) and standard TI delay in T2 prep-IR, is available for IR-T2 prep to optimize contrast. On the other hand, however, the optimization process for the two delay parameters and TEeff is more demanding. Additionally, performing the preparation after the inversion pulse limits the shortest inversion that can be set. Hence, such techniques may not work soon after contrast administration.

**Magnetization transfer preparation**

Another contrast mechanism that can be used for increasing scar-to-blood contrast in LGE is magnetization transfer (MT): a process in which magnetization...
is exchanged between protons existing in two different pools, the detectable 'free' pool and the 'bound' pool [12]. During MT preparation, the 'invisible' bound pool is selectively saturated using a train of high flip-angle (500–800º) off-resonance (600–800 Hz offset) RF pulses followed by a spoiler gradient, leading to a loss of net magnetization for the bound pool (Fig. 4). However, as the bound and free pool are in continuous exchange with each other, magnetization will be transferred from the free to the bound pool, leading to a magnetization decrease in the free pool and thus in the detectable CMR signal. When looking at the heart, blood primarily consists of a large free pool and negligible bound pool, resulting in a minimal signal drop during MT preparation. In contrast, normal myocardium and scar tissue consist of a sizeable bound pool, causing a significant signal drop during MT preparation. When performing MT preparation before the inversion pulse (MT-IR), the almost unaffected magnetization level of blood after MT preparation is inverted to a more negative magnetization level compared to the normal myocardium and scar areas (Fig. 5). Although blood and scar tissue have similar $T_1$ relaxation times and recover almost equally fast, blood now starts from a more negative magnetization level than scar tissue, resulting in increased scar-to-blood contrast.

In 2015, Kim et al. proposed the 'flow-independent dark-blood delayed enhancement' (FIDDLE) method [13], designed as a modular approach to accommodate different magnetization preparation modules before the inversion pulse in a PSIR LGE sequence. In 2018, the performance of a FIDDLE variant, where MT was performed before the inversion pulse (MT-IR), was evaluated. [14]. First, a pilot study was performed in eight canines with induced MI to investigate the effects of MT preparation on the magnetization levels of both normal and infarcted myocardium, and blood pool. Using FIDDLE, the blood magnetization level was found below that of both normal and infarcted myocardium over a wide range of inversion times, therefore appearing black in the PSIR image (Fig. 5). The diagnostic performance of FIDDLE was assessed in 22 canines with histopathology as the reference standard, showing
that the shape and contour of hyperenhanced regions on FIDDLE closely resembled those observed by histopathology (−0.1% bias). FIDDLE also showed increased sensitivity (96 vs 85%) and accuracy (95 vs 87%) for the detection of MI compared to conventional LGE. The clinical performance of FIDDLE was further evaluated in 31 patients, of which 20 had MI. FIDDLE was able to resolve cases with ambiguous conventional LGE images, clearly distinguishing between patients with and without hyperenhanced areas, with no differences between 1.5 T and 3 T. Although scar-to-blood contrast increased using FIDDLE, CNR measurements in 11 additional patients showed a 14% and 10% loss in scar-to-myocardium contrast on 1.5 T and 3 T, respectively, compared to conventional LGE. As the characteristics for MT preparation were optimized in the preceding pilot study, only the TI needed to be chosen using a Look-Locker sequence, which was set as long as possible while still fulfilling the prerequisite that the blood pool signal was below that of normal myocardium.

A T2 preparation variant of FIDDLE (T2 prep-IR), similar to the T2 prep-IR approach introduced by Liu et al. in 2008, was also exploited. However, T2 preparation was found to be inferior compared to MT preparation because of image artefacts (due to B0 and B1 sensitivity) and different levels of blood pool suppression in the right ventricle (RV) and LV (due to different T2 relaxation times) [15].

**Spin-lock preparation**

Besides T2 and MT preparation, a third contrast mechanism known as ‘T1-rho relaxation’ (T1 relaxation in the rotating frame) can be used to improve scar-to-blood contrast. In T1-rho CMR, a series of RF pulses are used to create a situation called ‘spin-lock’ (Fig. 6) [16]. Although T1 and T2 relaxation are still taking place, the magnetization is continuously disturbed by the RF pulse and cannot return to its equilibrium. Instead, the transverse magnetization now decays due to T1-rho relaxation, which relaxation times are longer than that of regular T2 relaxation times. In contrast to conventional T1 relaxation, the...
interactions between water and other molecules (such as the exchange and rotational correlation times) now have to be near the spin-lock frequency, instead of the Larmor frequency, for relaxation to occur. Since macromolecules, such as collagen, have rotational correlation times at the order of the spin-lock frequency of ~ 500 Hz, the T1-rho relaxation mechanism is highly sensitive to their interaction with water. Animal studies showed that infarct regions, which contained higher collagen fractions on histology, had significantly higher T1-rho relaxation times compared to normal myocardium [17]. Although T1-rho relaxation CMR on its own may be of interest as an endogenous contrast method, the use of spin-locking after contrast administration as additional preparation module for LGE has also been evaluated recently.

In 2017, Muscogiuri et al. presented an LGE approach called ‘T(rho) and magnetization transfer and inversion recovery-prepared imaging’ (TRAMINER), where both spin-locking (SL) and MT are applied before the inversion pulse (SL/MT-IR) [18]. While a train of off-resonance MT pulses (typically 15–20) creates a ‘clean’ MT contrast in the MT-IR approach, TRAMINER uses three consecutive adiabatic B1-insensitive rotation-4 (BIR-4) pulses leading to a mixture of T1-rho and MT contrast (Fig. 7). These BIR-4 pulses led to attenuation of tissue magnetization while only minimally affecting the blood pool. Interestingly, in contrast to most other PSIR LGE techniques, TRAMINER uses an additional heartbeat for magnetization recovery in between the heartbeat with the image readout and the heartbeat with the PSIR reference readout (three heartbeats in total).

TRAMINER was evaluated in 40 patients with known or suspected prior MI [18]. TRAMINER showed an improved scar-to-blood signal intensity ratio and a maintained scar-to-myocardium signal intensity ratio, while the myocardium-to-blood contrast was slightly compromised. Although TRAMINER detected two patients with enhanced scar regions that were missed by conventional LGE, no significant difference in the transmural extent of enhanced myocardial segments was found. Additionally,
TRAMINER showed non-uniform blood suppression between the RV and LV chambers due to the presence of some $T_2$ effects in the used preparation pulses. More recently, the image quality and reliability of TRAMINER was evaluated [19]. In terms of tissue contrast, both subjective and quantitative analysis showed similar results as in their previous 2017 paper. In contrast with previous findings, it was found that scar transmurality was underestimated using TRAMINER. Additionally, it was reported that a possible underestimation of microvascular obstructions may occur when using TRAMINER.

**Preparation with multiple inversion pulses**

Instead of using an additional preparatory module before or after the standard inversion pulse, repetitive inversion pulses can be used to simultaneously null multiple tissues after contrast administration. These inversion pulses can be applied either selectively, where only tissues within the imaging slice are affected, or non-selectively, where the entire volume (including the blood pool) is affected.

In 2011, Farrelly et al. proposed an LGE approach that uses two subsequent inversion pulses to simultaneously suppress both normal myocardium and the blood pool [20]. By first applying a selective inversion pulse, both the normal myocardium and area of infarction are inverted while the blood pool remains unaffected due to the inflow of fresh blood (Fig. 8). After a specific delay time (TD1), a non-selective inversion pulse follows, inverting not only the normal myocardium and area of infarction again, but now also the entire blood pool. After another delay (TD), signal acquisition will take place. Due to the extra selective inversion-recovery (SIR) preparation, we will refer to this approach as SIR-IR.

The SIR-IR approach was first validated in three swine with induced MI, followed by an evaluation in 26 patients with MI [20]. Instead of providing a single TI (as in conventional LGE), the operator had to provide the system with two TIs obtained from the preceding Look-Locker scan: one to null the normal myocardium and one to null the blood pool. The system then automatically calculated the two required delay times. Their results showed that
SIR-IR could simultaneously null both the blood pool and normal myocardium, rendering both tissues black with only the areas of MI appearing hyperintense. A 90% increase in scar-to-blood contrast was observed compared to conventional LGE. Furthermore, more foci of grade 1 hyperenhancement (1–25% transmural thickness) were found using SIR-IR compared to standard IR (17 vs 10 foci). Although scar-to-blood contrast improved, a 64% decrease in both scar-to-myocardium contrast and the signal-to-noise (SNR) ratio of the infarcted area was found. A similar trend was observed in the swine model. Furthermore, as this method relies on sufficient blood flow between the selective inversion RF pulse and image acquisition, it was found to work less reliably in patients with an LV ejection fraction < 40% where blood flow is reduced.

Later in 2012, Peel et al. proposed an LGE approach that also uses two inversion pulses [21], however, both inversion pulses were applied non-selectively (IR-IR) to render this method insensitive to blood flow (Fig. 9). Using simulations and phantom measurements the TDs were optimized to suppress multiple tissues within four different ranges of $T_1$ values (50, 100, 200, 300–1400 ms). Twelve patients with known MI were included and imaged with both conventional LGE and proposed IR-IR LGE. The results showed that IR-IR LGE, compared to conventional LGE, was able to achieve superior scar-to-blood contrast and increased confidence scores for presence of MI. Also, increased consistency between two experts for the assessment of scar transmurality and scar size was demonstrated. However, compared to conventional LGE, both scar-to-myocardium and myocardium-to-blood contrast were significantly reduced. Furthermore, when specific minimal $T_1$ values for tissue suppression (50 and 100 ms) were used, scar SNR was reduced compared to conventional LGE.

**No additional magnetization preparation**

Although all previous methods used additional magnetization preparation mechanisms to increase scar-to-blood contrast, similar effects can be achieved by shortening the TI to the point of blood pool nulling in a standard...
PSIR sequence (Fig. 10). Although the blood pool magnetization is nulled and appears black in the magnitude image, it appears dark-gray in the PSIR image as normal myocardium has even lower (negative) magnetization due to its longer $T_1$ relaxation time. The PSIR reconstruction mechanism is crucial as it reveals the negative magnetization of normal myocardium and makes it appear black in the resulting PSIR image (instead of bright in the modulus image).

In 2017, Holtackers et al. investigated the feasibility of this blood-nulled PSIR LGE approach without additional magnetization preparation in a small cohort of nine patients with MI and compared it to conventional PSIR LGE [22]. A dedicated noise scan without RF pulses was performed in each patient to enable accurate SNR and CNR measurements, showing a 99% increase in scar-to-blood contrast for blood-nulled LGE compared to conventional myocardium-nulled LGE, regardless of which method was used first. While scar-to-myocardium contrast was maintained, the myocardium-to-blood contrast decreased by 34% compared to conventional LGE. Numerical simulations illustrated the magnetization evolutions towards and during acquisition, which were significantly different for blood nulling than for conventional myocardium nulling, contributing to the observed contrast differences.

Later in 2019, the blood-nulled PSIR LGE approach was validated in an unselected cohort of 300 consecutive patients who were randomly allocated to either a 1.5 T or 3 T scanner of different vendors [23]. Of the 97 patients with ischemic scar tissue on blood-nulled PSIR LGE, eight patients (8.3%) were missed using conventional myocardium-nulled LGE and thus declared free of scar. This effect was observed regardless of which method was acquired first, and regardless of scanner field strength and vendor. Blood-nulled PSIR LGE showed significantly higher observer confidence and intra- and inter-observer agreement, and a significant 10% increase in total scar burden when compared to conventional LGE. As the blood pool appears dark-gray instead of black, blood-nulled PSIR LGE was able to detect all cases of intra-cardiac thrombus. It should be noted that no distinction can be made between the blood pool and scar tissue, in case both have an identical relaxation time.

Also in 2019, Foley et al. performed a study in which this blood-nulled PSIR LGE was compared against $T_1$-rho FIDDL and conventional LGE in a cohort of thirty patients with confirmed prior MI [24]. While both
blood-nulled LGE and $T_1$-rhe FIDDEE showed increased scar-to-blood contrast, only blood-nulled LGE was able to simultaneously maintain, and even exceed, scar-to-myocardium contrast compared to conventional LGE. Additionally, blood-nulled LGE demonstrated significantly higher reader confidence scores compared to both conventional bright-blood LGE and $T_1$-rhe FIDDEE.

Later, in 2020, the application of blood-nulled PSIR LGE was evaluated in a free-breathing 3D approach with high isotropic resolution ($1.6 \times 1.6 \times 1.6$ mm$^3$) \[25\]. As such acquisitions come with longer scan duration, the ideal TI to null the blood pool and obtain dark-blood contrast gradually increases due to continuous contrast washout. Therefore, a steadily increasing dynamic TI mechanism was developed to compensate for contrast washout and optimize contrast. This novel TI mechanism was evaluated in 50 patients and showed significantly better blood pool suppression compared to a conventional fixed TI. As a result, scar demarcation, observer confidence, and overall image quality significantly increased.

More recently in 2021, blood-nulled PSIR LGE was validated against histology in a porcine animal model with experimentally induced MI \[26\]. Although Bland-Altman analyses demonstrated high levels of agreement with histology for both LGE methods, conventional LGE showed a small but significant bias of -1.57%. In contrast, dark-blood LGE showed no significant bias when compared against histology (-0.03%). CNR analysis demonstrated a significant increase in scar-to-blood contrast for dark-blood LGE compared to conventional LGE, both at 1-week (167%) and 7-weeks (106%) post-MI.

**Discussion and future outlook**

Multiple dark-blood LGE methods have been described that suppress or null the blood pool signal while maintaining the bright signal from scar tissue (Table 1). Although mostly desired for improved detection of sub-endocardial scar areas, dark-blood LGE methods may also be beneficial for visualizing scar patterns in papillary muscles and thin-walled structures, such as the atria and RV.

---

**Fig. 10** Schematic overview of a standard phase sensitive inversion recovery (PSIR) LGE sequence where the inversion time is set for blood nulλng instead of normal myocardium nulλng. Note that only the PSIR grayscale is shown for this method, as only the PSIR images are used for clinical decision making. The faded parts of the diagram indicate the situation for conventional bright-blood LGE, where the Ti is set for normal myocardium nulλng.
| Magnetization preparation | Method name (acronym) | Year  | Number of subjects | Field strength | Blood \( M_z < \text{Myo} \_M_z \) | Blood appearance | Myocardium appearance | S-B CNR\(^a\) | S-M CNR\(^a\) | M-B CNR\(^a\) | Reference standard |
|----------------------------|----------------------|-------|--------------------|----------------|---------------------------------|------------------|-----------------------|----------------|----------------|----------------|-------------------|
| T\(_2\) preparation        | T\(_2\) prep-IR      | 2008  | 9 patients, 9 controls | 1.5 T          | No                              | Dark-gray        | Black                 | ↑              | ○              | ↓              | Standard LGE\(^b\) |
|                            | T\(_2\) prep-IR (FIDDE) | 2020  | 35 patients         | 1.5 T + 3 T     | Yes                             | Black            | Gray                  | ↑↑             | ↓              | ↓              | None              |
|                            | IR-T\(_2\) prep      | 2016  | 61 patients, no controls | 1.5 T          | Yes                             | Black            | Dark-gray             | ↑↑             | ↓              | ↓              | Standard LGE\(^b\) |
|                            |                      | 2017  | 172 patients, no controls | 1.5 T          | Yes                             | Black            | Dark-gray             | ↑↑             | ↓              | ↓              | Standard LGE\(^b\) |
|                            |                      | 2018  | 9 pigs, 42 patients, no controls | 1.5 T          | Equal                           | Black            | Black                 | ↑↑             | ↓              | ↓              | Absent            |
|                            |                      | 2018  | 5 swine, 45 patients, no controls | 1.5 T          | Equal                           | Yes              | Black                 | ↑↑             | ↓              | ↓              | Standard LGE\(^b\) |
| Magnetization transfer     | MT-IR (FIDDE)        | 2018  | 22 dogs, 20 patients, 11 controls | 1.5 T + 3 T     | Yes                             | Black            | Gray                  | ↑↑             | ↓              | ↓              | Histology + Standard LGE\(^b\) |
| Spin-locking (+MT)         | SL/MT-IR (TRAMNIR)   | 2017  | 40 patients, no controls | 1.5 T          | Yes                             | Black            | Dark-gray             | ↑↑             | ○              | ↓              | Standard LGE\(^b\) |
|                            |                      | 2019  | 73 patients, no controls | 1.5 T          | Yes                             | Black            | Dark-gray             | ↑↑             | ↓              | ↓              | Standard LGE\(^b\) |
| Multiple inversion pulses  | SIR-IR               | 2011  | 3 swine, 26 patients, no controls | 1.5 T          | Equal                           | Black            | Black                 | ↑↑             | ↓              | ↓              | Absent            |
|                            | IR-IR                | 2012  | 15 patients, no controls | 3 T            | Yes                             | Dark-gray        | Black                 | ↑              | ↓              | ↓              | Standard LGE\(^b\) |
| No additional magnetization preparation | Blood-nulled PSIR | 2017  | 9 patients, no controls | 1.5 T          | No                              | Dark-gray        | Black                 | ↑              | ○              | ↓              | Standard LGE\(^b\) |
|                            |                      | 2019  | 300 patients, no controls | 1.5 T + 3 T     | No                              | Dark-gray        | Black                 | ↑              | ○              | ↓              | Standard LGE\(^b\) |
|                            |                      | 2021  | 50 patients, no controls | 1.5 T          | No                              | Dark-gray        | Black                 | ↑              | ○              | ↓              | Standard LGE\(^b\) |
|                            |                      | 2021  | 13 pigs              | 1.5 T          | No                              | Dark-gray        | Black                 | ↑              | ○              | ↓              | Histology + Standard LGE\(^b\) |

\(^a\) Indicated values are relative to conventional (bright-blood) LGE with normal myocardium nulling: ↑ = increased, ↓ = decreased, ○ = maintained

\(^b\) Conventional (bright-blood) LGE with normal myocardium nulling

CNR = contrast-to-noise ratio, IR = inversion-recovery, M-B = myocardium-to-blood, MT = magnetization transfer, Mz = longitudinal magnetization, PSIR = phase-sensitive inversion-recovery, S-B = scar-to-blood, S-M = scar-to-myocardium, SIR = selective inversion-recovery, SL = spin-locking
Blood pool appearance

While these methods share a common goal, the methodologies to do so vary greatly. The appearance of the blood pool in the final image determines whether it is a black-blood or gray-blood method, in contrast to the conventional bright-blood LGE method (Fig. 11).

Black-blood methods are able to achieve excellent contrast between the black blood pool and bright scar tissue. The normal myocardium, however, often appears (dark-)gray instead of black (in conventional LGE). As a result, the scar-to-myocardium contrast is regularly compromised compared to conventional bright-blood LGE, potentially lowering the sensitivity for non-ischemic scar tissue. Other black-blood methods aim to simultaneously null both the blood pool and normal myocardium, thereby maintaining scar-to-myocardium contrast required for non-ischemic scar detection. With these particular methods, however, the myocardium-to-blood contrast required for anatomical reference is significantly reduced, potentially preventing one from assessing the exact location and transmurality of any bright area of scarring. Regardless of the appearance of the normal myocardium in black-blood LGE methods, the detection of intracardiac thrombi is compromised compared to conventional LGE as they appear equally black as the blood pool. However, by adjustment of specific sequence parameters, most black-blood methods can be adapted to gray-blood techniques [11].

On the other hand, gray-blood LGE methods are also able to achieve improved scar-to-blood contrast. As the blood pool is not completely black, the scar-to-blood contrast is usually not as high as in black-blood methods, however, still significantly increased compared to conventional bright-blood LGE. For most gray-blood methods, the normal myocardium appears equally black as in conventional LGE, thereby resulting in maintained or only slightly decreased scar-to-myocardium contrast. Since the blood pool appears darker than in conventional LGE, the myocardium-to-blood contrast is decreased, however, still adequate for anatomical reference. Additionally, as the blood pool is appearing gray instead of black, the detection of intracardiac thrombi is maintained using gray-blood LGE (Fig. 12) [23].

Besides the blood pool appearance, there is a fundamental difference between techniques that reduce the blood pool signal below that of normal myocardium versus those that result in blood pool signal that is still above normal myocardium. This distinction is important, for example in cases of patchy subendocardial scarring where the post-contrast T1 relaxation time is longer than that of blood. For methods where the blood pool signal is still above normal myocardium, the signal of this patchy subendocardial scarring will be in between that of normal myocardium and blood, and may resemble that of the blood-myocardium interface, which might render it invisible. For methods where the blood pool signal is below that of normal myocardium, the signal of patchy...
scarring will be in between that of normal myocardium and (dense) scarring. Although less clearly visible, patchy scarring will still be detectable. Table 2 provides an overview of the key differences between black-blood and gray-blood LGE, with conventional bright-blood LGE methods as a reference.

**Practical clinical utility**
The improved detection and visibility of subendocardial scar patterns make dark-blood LGE methods a useful tool in clinical routine settings. A 2021 study by Franks et al. showed that dark-blood LGE detects a higher ischemic scar burden than conventional bright-blood LGE and leads to a lower estimation of the myocardial ischemic burden when used in conjunction with perfusion imaging [27]. This can lead to disagreement around established thresholds of clinically significant ischemia used for revascularization decision making. However, since most studies focused on the detection of ischemic scar tissue, the diagnostic performance of these methods for detecting non-ischemic scar patterns remains largely unknown. Although multiple studies showed a decrease in scar-to-myocardium contrast, which in theory may hamper the detection of non-ischemic scar patterns compared to conventional bright-blood LGE, no general conclusions can be drawn yet. Even though dark-blood LGE methods may already replace conventional LGE in specific settings (e.g. ischemic heart disease and myocardial infarction with non-obstructive coronary arteries (MINOCA)), they remain as addition to conventional LGE in generalized cardiomyopathy scan protocols.

**Ease of use**
Compared to the single TI used for conventional LGE, most magnetization preparation schemes come with additional imaging parameters. These parameters include...
additional delays, durations, and specific RF pulse settings, such as the flip-angle, B1 strength, off-resonance frequency, and pulse train length and phase. Some have to be set only once when implementing and setting up the protocol, while others need to be adjusted individually for each patient. For some methods, this may require an additional T1 map [8, 9, 11] or contrast-scout scan [10] prior LGE imaging to calculate the optimal delay parameters. Other methods require repetitive pre-scans to empirically derive the optimal TI [18]. These requisites may require additional training and can prolong scan duration.

Apart from acquisition, the new types of image contrast may also introduce additional training for readers assessing these images. Techniques where both the blood pool and normal myocardium are nulled may require co-registration with cine images to determine and assess the myocardial borders. For methods that use additional magnetization preparation modules, readers need to be familiar with the T2, MT, and T1-rho effects on the cardiac structures and their appearance in various cardiomyopathies to assure accurate analysis of the underlying pathologies.

### Availability

Although the superiority of dark-blood LGE methods in detecting (sub)endocardial scar tissue compared to conventional LGE is already proven, clinical translation of dark-blood LGE is not straightforward. Most methods use additional magnetization preparation schemes that are not available in a commercial CMR system configuration. Software patches or work in progress (WIP) packages are required to perform those new preparation schemes on clinical CMR systems. Even though these may be made available by the vendors or have been implemented in individual centers for research purposes, legal regulations may prevent their use in routine patient care, hampering widespread clinical implementation. Methods without additional magnetization preparation mechanisms, however, are already readily and widely available on clinical CMR systems.

### Scar quantification methods

The improved scar-to-blood contrast achieved by dark-blood LGE methods may benefit the delineation and quantification of ischemic scar patterns. Kim et al. already showed that manual delineation of ischemic scar using dark-blood LGE led to significantly better sensitivity and accuracy (96 and 95%, respectively) than using conventional bright-blood LGE (85 and 87%, respectively) [14]. Differences in sensitivity and accuracy further increased when only slices with<25% transmural infarction were considered (98 and 95% vs 80 and 85%, respectively). Although Foley et al. found a 37.5% larger transmural extent of scar using dark-blood LGE compared to conventional LGE, no significant difference between both techniques was reported when using the full-width half-maximum (FWHM) quantification method [24]. This method, however, was found to under-estimate dark-blood LGE scar size by over 25% [28]. Instead, using manual contouring as reference, the signal threshold versus reference mean method with a 5-standard deviation (SD) threshold most accurately quantified infarct size on dark-blood LGE images, thereby outperforming the 6-SD, FWHM, and the Otsu auto-threshold methods. To the best of our knowledge, no semi-automatic quantification methods have been validated against histopathology for dark-blood LGE. As scar quantification is becoming increasingly important in recent years, future research should focus on validating quantification methods for dark-blood LGE to evaluate clinical benefit.

### Phase-sensitive inversion-recovery

The majority of dark-blood LGE methods use a PSIR sequence to reveal negative magnetization levels during signal readout. Without PSIR, these magnetization levels would be visualized similarly to positive magnetization levels of the same magnitude, potentially decreasing tissue contrast. PSIR therefore makes LGE image quality less sensitive to the chosen TI, leading to a reduction in image artefacts and potential misinterpretations. Additionally, in contrast to standard IR, PSIR is a two-beat sequence making it more robust to heart rate variations and cardiac arrhythmias as it relies

---

**Table 2** Black-blood versus gray-blood LGE with conventional bright-blood LGE as a reference

|                           | Black-blood LGE | Gray-blood LGE |
|---------------------------|-----------------|----------------|
| Scar-to-blood contrast     | ↑↑              | ↑              |
| Scar-to-myocardium contrast| O / ↓           | O              |
| Myocardium-to-blood contrast| ↓↓ / ↓          | ↓              |
| Assessment of scar transmurality | O / ↑          | ↑              |
| MI size quantification     | ↑↑ / ↑          | ↑              |
| MVO detection             | O              | O              |
| LV thrombus detection     | ↓↓              | O              |

Indicated values are relative to conventional (bright-blood) LGE with normal myocardium nulling: ↑ = increased, ↓ = decreased, O = maintained

*a* First value indicative for black-blood methods that simultaneously null both blood pool and normal myocardium (both appear black), second value indicative for black-blood methods with a dark-gray appearance of the normal myocardium

*b* Equal detection but might improve differentiation with thrombus

LGE = late gadolinium enhancement, LV = left-ventricular, MI = myocardial infarction, MVO = microvascular obstruction
to a lesser extent on a constant time delay between successive inversion RF pulses, averaging irregular heartbeats over two heartbeats. On the other hand, however, mismatches between the image (first heartbeat) and reference (second heartbeat) readout may lead to suboptimal image quality and scan duration inherently doubles when using PSIR instead of standard IR.

Field strength dependency
Although LGE CMR can be performed on both 1.5 and 3 T scanners, there are limited data for many of the dark-blood methods at 3 T (Table 1) as most were proposed and validated on 1.5 T. The increased field strength of 3 T may influence the performance of the additional preparation modules required for most dark-blood methods. As demonstrated in a recent study by Jenista et al., $T_2$ preparation at 3 T was prone to more in-flow artifacts in the left atrium and increased differences in RV-to-LV blood-pool suppression compared to 1.5 T [15]. Also, when using MT preparation, more in-flow artefacts were observed at 3 T compared to 1.5 T. However, no visible differences in blood suppression between the LV and RV were observed for MT preparation at both 1.5 T and 3 T. With only a few dark-blood methods (also) evaluated at 3 T [14, 15, 21, 23], other methods, in particular those using field strength dependent magnetization preparation modules, should also be evaluated at 3 T to assess their clinical utility.

Future research
While most novel dark-blood methods are compared to conventional LGE, only FIDDLE and blood-nulled PSIR LGE have been validated against histology [14, 26], and direct comparison studies evaluating different dark-blood LGE methods are limited [24]. Such comparison studies are mostly hindered by the limited availability of most techniques. Ideally, more direct comparison studies should be conducted to evaluate the individual performance of the various dark-blood LGE methods compared to conventional LGE with appropriate dose and timing [29]. Additionally, their effect on (semi-)automatic scar quantification methods should be investigated.

Exciting new avenues that hold promise for dark-blood LGE include the combination with image-navigated free-breathing 3D acquisitions with high isotropic resolution. 2D image-based navigators directly track the position of the heart itself and can correct for translational motion to enable 100% efficiency and thus more predictable scan durations [30]. Although the feasibility of 2D image-based navigators for conventional free-breathing 3D LGE has been investigated [31, 32], future work should focus on the implementation in dark-blood LGE approaches. The recent introduction of compressed sensing by the major vendors enabled widespread use of sparse imaging techniques, achieving acceleration factors that have not previously been possible to attain with parallel imaging alone. Additionally, artificial intelligence-based CMR reconstruction techniques may be used to further enhance the use of compressed sensing methods [33].

Conclusions
Dark-blood LGE methods are a promising new tool for non-invasive assessment of myocardial infarction. Although the discussed mechanisms improve detection of subendocardial scar, their weaknesses in terms of scar-to-myocardium contrast, blood appearance, availability, and ease of use, vary significantly. For a mainstream adoption of dark-blood LGE methods, however, clinical availability and ease of use are crucial.

Abbreviations
BIR-4: B1-insensitive rotation-4; CMR: Cardiovascular magnetic resonance; CNR: Contrast-to-noise ratio; DE: Delayed enhancement; FIDDELE: Flow independent dark-blood delayed enhancement; FWHM: Full-width half-maximum; IR: (Non-selective) inversion-recovery; LE: Late enhancement; LGE: Late gadolinium enhancement; LV: Left ventricle/left ventricular; MCODE: Multi contrast delayed enhancement; MI: Myocardial infarction; MT: Magnetization transfer; Mxy: Transversal magnetization; Mz: Longitudinal magnetization; MVO: Microvascular obstruction; PSIR: Phase-sensitive inversion-recovery; RF: Radiofrequency; RV: Right ventricle/right ventricular; SIR: Selective inversion-recovery; SD: Standard deviation; SL: Spin-locking; SNR: Signal-to-noise ratio; TEeff: Effective echo time; TI: Inversion time; TRAMINER: Transfer and inversion recovery prepared imaging; WIP: Work in progress.

Acknowledgements
Dr. Raymond Kim served as the JCMR Guest Editor for this manuscript.

Authors’ contributions
All authors collaborated in writing the manuscript, revising it critically for important intellectual content, and gave final approval of this version to be published. All authors have read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.
Author details

1 Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, PO Box 616, Maastricht 6200 MD, The Netherlands. 2 Department of Radiology & Nuclear Medicine, Maastricht University Medical Centre, Maastricht, The Netherlands. 3 School of Biomedical Engineering & Imaging Sciences, King’s College London, London, London, United Kingdom. 4 Department of Cardiology, Antwerp University Hospital, Edegem, Belgium. 5 Escuela de Ingeniería, Pontificia Universidad Católica de Chile, Santiago, Chile.

Received: 26 February 2021 Accepted: 17 May 2021 Published online: 22 July 2021

References

1. Kim RJ, Fieno DS, Parrish TB, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation. 1999;100(19):1992–2002.
2. Simoniott O, Kim RJ, Fieno DS, et al. An improved MR imaging technique for the visualization of myocardial infarction. Radiology. 2001;218(1):215–23.
3. Kwong RY, Chan AK, Brown KA, et al. Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. Circulation. 2006;113(23):2733–43.
4. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med. 2000;343(20):1445–53.
5. Kellman P, Chung YC, Simonetti OP, et al. Multi-contrast delayed enhancement provides improved contrast between myocardial infarction and blood pool. J Magn Reson Imaging. 2005;22(5):605–13.
6. Bandettini WP, Kellman P, Mancini C, et al. MultiContrast Delayed Enhancement (MCODE) improves detection of subendocardial myocardial infarction by late gadolinium enhancement cardiovascular magnetic resonance: a clinical validation study. J Cardiovasc Magn Reson. 2012;14:83.
7. Liu CY, Wieben O, Brittain JH, et al. Improved delayed enhanced myocardial imaging with T2-Prep inversion recovery magnetization preparation. J Magn Reson Imaging. 2008;28(5):1280–6.
8. Kellman P, Xue H, Olivieri LJ, et al. Dark blood late enhancement imaging. J Cardiovasc Magn Reson. 2016;18(177).
9. Francis R, Kellman P, Kotecha T, et al. Prospective comparison of novel dark blood late-gadolinium enhancement with conventional bright blood imaging for the detection of scar. J Cardiovasc Magn Reson. 2017;19(1):91.
10. Basha TA, Tang MC, Tsoo C, et al. Improved dark blood late gadolinium enhancement (DB-LGE) imaging using an optimized joint inversion preparation and T2 magnetization preparation. Magn Reson Med. 2018;79(1):351–60.
11. Fahmy AS, Neissiu US, Tsoo CW, et al. Gray blood late gadolinium enhancement cardiovascular magnetic resonance for improved detection of myocardial scar. J Cardiovasc Magn Reson. 2018;20(1):22.
12. De Boer RW. Magnetization transfer contrast. Part 1: MR Physics. Medica-mundi. 1995;40(2):64–73.
13. Kim RJ. Duke University, Durham, NC (US). Blood signal suppressed enhanced magnetic resonance imaging. U.S. patent 9,131,870 B2. September 15, 2015.
14. Kim HW, Rehwald WG, Jenista ER, et al. Dark-blow delayed enhancement cardiac magnetic resonance of myocardial infarction. JACC Cardiovascular Imaging. 2018;11(12):1758–69.
15. Jenista ER, Wendell DC, Kim HW, et al. Comparison of magnetization transfer-preparation and T2-preparation for dark-blow delayed-enhancement imaging. JMRI Biomed. 2020;33(13):e4396.
16. Moran PR, Hamilton CA. Near-resonance spin-lock contrast. Magn Reson Imaging. 1995;13(6):837–46.
17. van Oorschot JW, EI Aidi H, Jansen of Lorkeers SJ, et al. Endogenous assessment of chronic myocardial infarction with T1(tro)-mapping in patients. J Cardiovasc Magn Reson. 2014;16:104.
18. Muscogiuri G, Rehwald WG, Schoepf UJ, et al. T1(tro) and magnetization transfer and INvErsion recovery (TRAMINER)-prepared imaging: A novel contrast-enhanced flow-independent dark-blood technique for the evaluation of myocardial late gadolinium enhancement in patients with myocardial infarction. J Magn Reson Imaging. 2017;45(5):1429–37.
19. Muscogiuri G, Gatti M, Dell’Aversana S, et al. Image quality and reliability of a novel dark-blood late gadolinium enhancement sequence in ischemic cardiomyopathy. J Thorac Imaging. 2019;35(3):326–33.
20. Farrell C, Rehwald W, Salerno M, et al. Improved detection of subendocardial hyperenhancement in myocardial infarction using dark blood-pool delayed enhancement MRI. AJR Am J Roentgenol. 2011;196(2):339–48.
21. Peel SA, Morton G, Chiribiri A, et al. Dual inversion-recovery mr imaging sequence for reduced blood signal on late gadolinium-enhanced images of myocardial scar. Radiology. 2012;264(1):242–9.
22. Holtackers RJ, Chiribiri A, Schneider T, et al. Dark-blood late gadolinium enhancement without additional magnetization preparation. J Cardiovasc Magn Reson. 2017;19(11):64.
23. Holtackers RJ, Van De Heyning CM, Nazir MS, et al. Clinical value of dark-blood late gadolinium enhancement cardiovascular magnetic resonance without additional magnetization preparation. J Cardiovasc Magn Reson. 2019;21(1):44.
24. Foley JR, Broadbent DA, Fent GJ, et al. Clinical evaluation of two dark blood methods of late gadolinium quantification of ischemic scar. J Magn Reson Imaging. 2019;50(1):146–52.
25. Holtackers RJ, Gommers S, Van De Heyning CM, et al. Steadily increasing inversion time improves blood suppression for free-breathing 3D late gadolinium enhancement MRI with optimized dark-blood contrast. Invest Radiol. 2021;56(5):335–40.
26. Holtackers RJ, Gommers S, Heckman LIB, et al. Histopathological validation of dark-blood late gadolinium enhancement MRI without additional magnetization preparation. J Magn Reson Imaging 2021. https://pubmed.ncbi.nlm.nih.gov/34169603/.
27. Franks R, Holtackers RJ, Nazir MS, et al. Novel dark-blood versus conventional bright-blood late gadolinium enhancement CMR: A pilot study comparing impact on myocardial ischaemic burden. Eur Heart J Cardiovasc Imaging. 2021;22(Supplement_1):jeaa356.303.
28. Kotecha T, Martinez-Naharro A, Lamb T, et al. Quantification of myocardial infarct size and microvascular obstruction using dark-blood late-gadolinium enhancement. Eur Heart J Cardiovasc Imaging. 2019;20(Supplement_2):48.
29. Kim RJ, Albert TS, Wible JH, et al. Performance of delayed-enhancement magnetic resonance imaging with gadoversetamide contrast for the detection and assessment of myocardial infarction: an international, multicenter, double-blinded, randomized trial. Circulation. 2008;117(5):629–37.
30. Henningsson M, Smink J, Razavi R, et al. Prospective respiratory motion correction for coronary MR angiography using a 2D image navigator. Magn Reson Med. 2013;69(2):486–94.
31. Bratis K, Henningsson M, Grigoratos C, et al. Image-navigated 3-dimensional late gadolinium enhancement cardiovascular magnetic resonance imaging: feasibility and initial clinical results. J Cardiovasc Magn Reson. 2017;19(1):97.
32. Munoz C, Bustin A, Neji R, et al. Motion-corrected 3D whole-heart water-fat high-resolution late gadolinium enhancement cardiovascular magnetic resonance imaging. J Cardiovasc Magn Reson. 2020;22(1):53.
33. Bustin A, Fuin N, Botnar RM, et al. From compressed-sensing to artificial intelligence-based cardiac MRI reconstruction. Front Cardiovasc Med. 2020;7:17.

Publisher’s Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.