Artificial Intelligence: Learning About the Future of Cardiovascular MR

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Over the past 40 years, cardiovascular magnetic resonance (CMR) has evolved from an esoteric research tool to an indispensable clinical tool that routinely changes patient management across the breadth of modern cardiovascular practice. CMR is a versatile, non-invasive imaging modality that provides a comprehensive assessment of multiple parameters for cardiac function and morphology in a single protocol. It plays a major role in the diagnosis and management of cardiovascular disease (CVD). The prevalence of CVD is increasing annually and the conditions are among the leading causes of morbidity and mortality worldwide. This requires improvements in assessing, diagnosing, treating, and monitoring CVD patients. CMR will play a central role in achieving these goals. However, there remain major challenges for the widespread use of this technique:

(a) Complex technology with many pulse sequences and parameters to choose from
(b) Manual data analysis and interpretation
(c) Inherent cardiac and respiratory motion
(d) Duration of the examination

Methods using artificial intelligence (AI) have been proposed to address these challenges, but have also given rise to new questions about the methods' reliability, accuracy, generalizability, and robustness. In order to shape the future of CMR and establish where and how AI can play a role in it, we will showcase some CMR applications and scenarios that reflect the abovementioned challenges. We will highlight some AI methods for each step of the CMR processing chain and conclude with thoughts on remaining challenges and opportunities.

Learning about the heart in higher dimensions

CMR enables the acquisition of morphological, functional, and quantitative tissue parameters. Various sequences are devised that represent powerful tools for the non-invasive characterization of congenital or acquired CVDs, including ischemia, valvular diseases, and ischemic and non-ischemic cardiomyopathies. Cardiac function is commonly assessed with continuous acquisitions (cine, real-time) over multiple cardiac cycles. Perfusion imaging permits the assessment of physiologic and pathophysiologic functional parameters. First-pass perfusion is the clinical standard for measuring myocardial blood flow and detecting myocardial ischemia. Cardiac viability is traditionally studied with a gadolinium-based contrast agent in late gadolinium enhancement. Cardiovascular flow by phase-contrast imaging measures the velocity of blood in the cardiac chambers and great vessels. Coronary magnetic resonance angiography (CMRA) has the potential to diagnose coronary artery diseases. Quantitative CMR techniques like T1, T2, or T1rho mapping provide characterization of tissue properties that distinguish healthy from diseased tissue. More recently, MR fingerprinting[1] and MR multitasking have been proposed to provide multi-parametric data in a continuously measured acquisition under a free-movement scenario (with respiration and a beating heart). Multi-parametric CMR offers the promise of a more accurate diagnosis, early disease detection, and monitoring over time or of response to therapy [1].

These applications require either high spatial and/or temporal resolution, should ideally be acquired in 3D with whole-heart coverage to avoid slice misalignments or to allow reformatting into arbitrary image orientations, or are susceptible to cardiac and respiratory motion. The achievable image quality must be sufficient to detect and characterize CVDs, and is thus an inherent trade-off between imaging resolution, scan time, and signal-to-noise ratio (SNR), which are overall challenging requirements to meet. Moreover, to fully utilize the available information and/or to resolve the individual factors (motion, relaxivity, perfusion, etc.), joint data processing of all acquired data should be performed. This in turn yields high-dimensional data processing for CMR. To give an example, 5D cine imaging provides 3D spatial information of respiratory (1D) and cardiac (1D) motion-resolved data. If we jointly reconstruct motion-resolved data, we can share spatiotemporal information, i.e., sharing samples at a spatial location

[1]MR Fingerprinting is not commercially available in some countries. Due to regulatory reasons its future availability cannot be ensured.

between different respiratory/cardiac motion states by accounting for the underlying motion between motion states. The benefit is increased sampling efficiency and higher sampling density, which in turn can result in improved image quality. Furthermore, high-dimensional data processing naturally lends itself to the combination of several data processing steps, as shown in Figure 1. In our 5D cine example, the image reconstruction is combined with a motion correction/estimation procedure. The combination could also expand across several processing steps and we could develop a single AI network that performs this task for us. Let us say we are actually interested in assessing the left ventricular function using the 5D cine imaging. We could thus combine reconstruction, motion estimation, and image segmentation (to obtain left ventricular functional parameters) using as input the acquired MR raw data and outputting the left ventricular functional parameters (ejection fraction, end-systolic volume, and so on). While joint processing has its benefits, one could also be interested in obtaining the intermediate results of this joint processing chain – to perform quality assurance, for instance, or to further visually assess morphology and function. However, depending on the selected setup, architecture, and scenario, this may no longer be easily possible. On the other hand, we could have developed individual and finely tuned AI networks for each of the tasks. For the 5D cine example, an image reconstruction network is followed by an image registration network that merges individually reconstructed motion states on which a subsequent image segmentation network is performed. Intermediate results (reconstructed image, motion fields, segmentation masks) would be available, but we would lose the possibility to share information between and within processing steps.

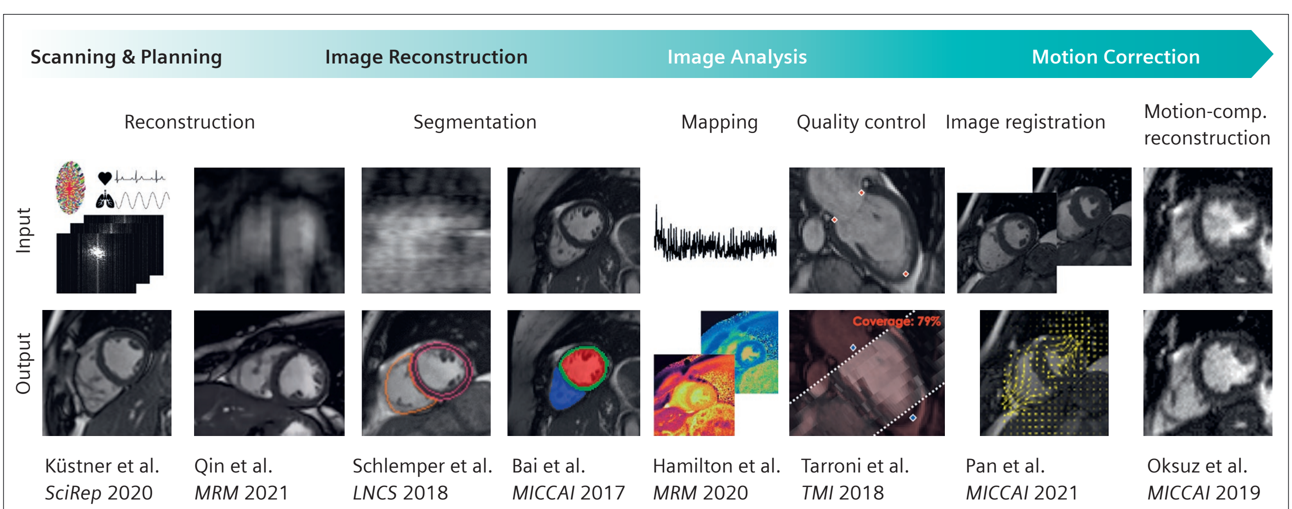
While the concepts of joint processing sound intriguing and have already been studied in several research settings, applying them to a clinical scenario in a reliable fashion is challenging. Furthermore, high-dimensional AI-based data processing is not trivial and currently still limited in most cases by the available graphics processing unit (GPU) memory and the availability of network building blocks to process data beyond 3D [2].

AI forming the CMR workflow

For a conventional CMR examination, several individual sequences are acquired, for which different processing steps are conducted. These include image acquisition, image formation, and diagnosis, as illustrated in Figure 1. These processing steps could be performed individually with highly optimized and tuned AI networks, or several steps could be combined end-to-end for outputting multiple results in so-called multi-tasking networks. While AI has the potential to improve each step of the imaging pipeline, it should be seen as a support for clinicians, not a replacement.

Scanning and planning

The most tedious and time-consuming part of CMR is planning the cardiac scan. The image quality depends on the experienced technician responsible for acquiring the data, and uncertainties might be introduced by incorrect planning. AI has the potential to speed up the whole planning workflow, resulting in increased patient comfort and reduced healthcare costs. Also, AI-supported planning allows for more standardized cardiac scans and reduces the complexity of cardiac view planning. Siemens Healthineers provides a solution for AI-based view planning with its myExam Cardiac Assist tool [3, 4].



1 Overview of clinical workflow supported by several artificial intelligence (AI) methods. Different AI solutions along the imaging and processing chain are illustrated for cardiac cine imaging. The inputs and outputs of the proposed AI techniques are also shown.

Image reconstruction

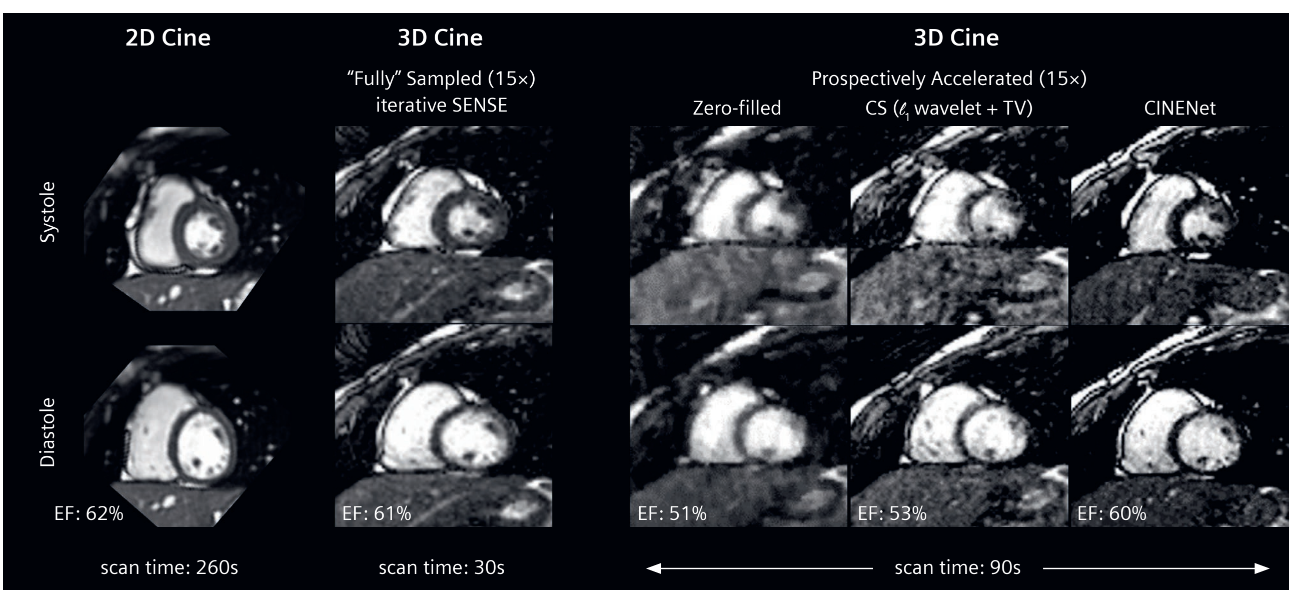
Traditional image reconstruction techniques suffer from long reconstruction times and limitations in acceleration under Cartesian sampling patterns. Furthermore, prior knowledge of the reconstructed images needs to be incorporated into the reconstruction procedure. However, this prior information is often too simple to characterize the complex medical images. AI provides the opportunity to gain this prior knowledge directly from the data. Dictionary learning is an early example of data-driven learning in Compressed Sensing (CS)-based MRI reconstruction, and involves learning directly from undersampled data how the individual dictionary entries should be combined. AI-based solutions now achieve image quality similar or superior to classic CS-based approaches, while reducing the reconstruction time tremendously from minutes and hours to seconds. Furthermore, the learned priors can deal with the characteristic, coherent backfolding artifacts that appear in Cartesian sampling schemes, which are standard in the clinical workflow.

However, learning only a data-driven image prior is not enough, and special care needs to be taken with the acquired *k*-space data. While purely image-driven networks are able to produce realistic-looking images, the images themselves are not consistent with the acquired *k*-space data. We refer the interested reader to a previous article in MAGNETOM Flash and to book chapters [5, 6] for more information on how to include the acquired *k*-space into a reconstruction network. In the current article, we focus on the application of AI-based solutions to (high-dimensional) CMR, including static and dynamic imaging.

Fuin et al. proposed a multi-scale variational network for CMRA [7]. For this static application, the reconstruction time could be reduced from ~5 minutes for a CS-based approach to ~14 seconds for the proposed learning-based approaches. Comparable image quality was achieved between the fully sampled reference scan and the 9× accelerated scan. The results show that the acquisition time can be reduced from 18:55 minutes for the fully sampled reference scan to 2:34 minutes for the 9× accelerated acquisition, while the image quality stays comparable.

An alternative approach for shortening the scan time while simultaneously increasing spatial resolution is to use AI-based super resolution. Images are acquired at a low image resolution and retrospectively reconstructed to the high-resolution target. This approach has been successfully applied to cardiac cine [8, 9] and CMRA [10, 11].

In the context of cine image reconstruction, Schlemper et al. proposed a data-consistent convolutional neural network (CNN), performing alternating single-coil data-consistency steps and image denoising with a 5-layer CNN [12]. This approach was improved by a recurrent approach to propagate information through the time dimensions and between iterations [13]. Separated convolutions in the spatial domain and temporal domain further improve reconstruction quality, yielding more accurate functional



2 Physics-guided deep learning-based image reconstruction for cardiac cine imaging. High imaging acceleration (15×) enables the acquisition of a 3D cardiac cine with isotropic resolution and left ventricular coverage in a single breath-hold of < 10 seconds. A deep learning-based image reconstruction, CINENet, provides high image quality in contrast to the zero-filled reconstruction (input to network) or a Compressed Sensing (CS) reconstruction. CINENet reconstruction of accelerated scan (9 seconds) is in good accordance with a separate (slightly accelerated, 2.5×) 3D cine (30 seconds) and a conventional multi breath-hold 2D cine (260 seconds). The 3D cine with CINENet reconstruction shows high agreement with the conventional 2D cine in terms of left ventricular ejection fraction (EF).

parameters [14] and allowing for accelerated 3D cine reconstruction [15]. An example for accelerated single-breath-hold 3D cine reconstruction compared to conventional multi-slice multi-breath-hold 2D reconstruction is depicted in Figure 2. The aforementioned approaches operate directly on the full image, but low-rank and sparse priors are less frequently studied. Building on the success of unrolled networks, recent works focus on learning a structured low-rank prior [16] or low-rank plus sparse decomposition [17] in the context of dynamic MRI reconstruction.

While most approaches apply CNNs primarily in the image domain, hybrid networks exploit information in complementary domains. Due to the dynamic component in cine images, we can exploit the data in various domains. Exploiting all available data in various spaces pushes the reconstruction results further. El-Rewaidy et al. use both *k*-space and image domain information for radial imaging, implementing CNNs in both domains [18]. Complementary information in *k-t* and *x-f* space was studied in Qin et al. [19].

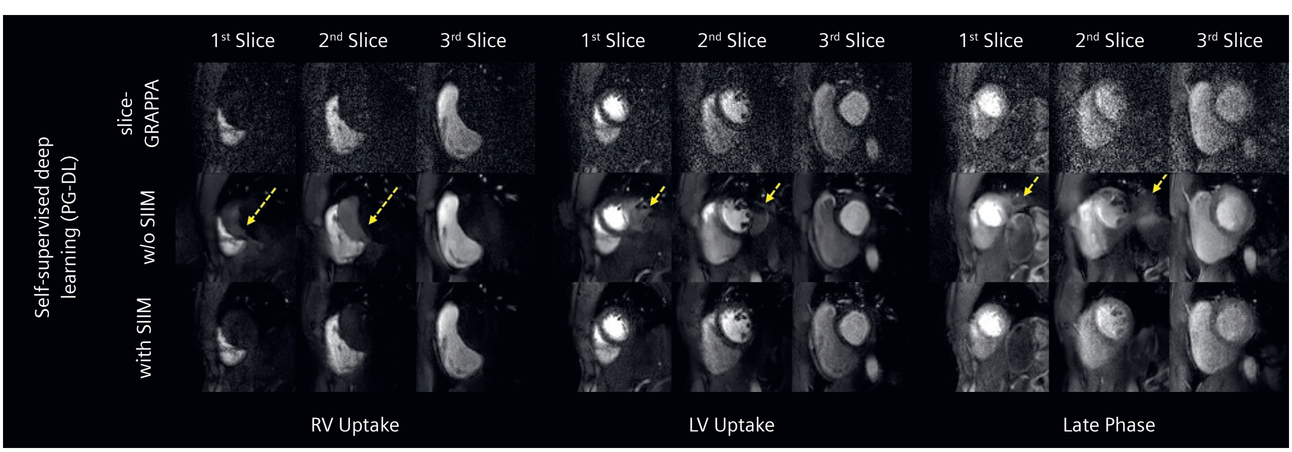
All aforementioned reconstruction approaches assume that fully sampled training data are available. The fully sampled data serve as a reference during training. However, training data is not always available, and is sometimes even impossible to acquire. Yaman et al. proposed a self-supervised learning approach that uses only the acquired training data points, with application to late gadolinium enhancement as depicted in Figure 3 [20]. The sampled data points are split into two disjoint sets, where the first set is used in the data consistency units of the unrolled reconstruction network, and the second set is used to evaluate the loss function during training directly in *k*-space.

Image analysis

CMR image segmentation and quantitative evaluation can be a challenging, time-consuming, and operator-intensive task. Segmentation of the chambers and myocardium is a mandatory postprocessing task. Automation of these tasks can therefore significantly reduce the time required for CMR image assessment.

AI-based solutions for image segmentation have been shown to be highly accurate and fast [21]. Considerable efforts have been directed toward cine imaging, as it is considered the gold standard for the assessment of cardiac chamber volumes and function [22]. The work of Morales et al. provided additional myocardial strain measures [23]. Segmentation methods have also been paired with predictions of important markers for cardiovascular disease, such as volume of pericardial adipose tissue [24] and scar-tissue areas [25]. Fahmy et al. automatically quantified left ventricular mass and scar volume in late gadolinium enhanced imaging [26], which showed strong agreement between the automated segmentations and the manual delineations. Farrag et al. [27] investigated the propagation of segmentation masks derived from cine imaging for the accurate segmentation of myocardial tissue in T1 mapping of a shMOLLI sequence. In contrast, the work of Hann et al. [28] segmented the myocardium directly in the shMOLLI data.

Segmentations have also been shown to provide valuable information for image reconstruction and motion correction tasks. Joint learning of motion estimation and segmentation for cine imaging was proposed by Qin et al. [29]. The results suggested that an efficient motion estimation network can bypass the need for high-quality reconstructions to achieve accurate image segmentation,



3 Physics-guided deep learning-based image reconstruction for dynamic contrast-enhanced MRI. A three-slice myocardial perfusion in the right ventricle (RV) uptake, left ventricle (LV) uptake and late phase is shown for different reconstruction techniques. A split slice-GRAPPA (top row) is compared to two self-supervised deep learning solutions (middle and bottom row) [63]. The difference between the deep learning methods is the use of signal intensity informed multi-coil (SIIM) encoding, which better models the underlying MR physics as indicated by the yellow arrows. *Image courtesy of Mehmet Akçakaya.*

indicating the superiority of high-dimensional data processing. Sun et al. [30] proposed a unified deep network architecture for joint image reconstruction and segmentation. The reconstruction and segmentation networks share network parts, acting as intrinsic regularizers for each other, while unshared network parts act specifically to the task (reconstruction or segmentation). Their results suggest that training a joint network is beneficial for high-quality segmentation of undersampled *k*-space data. While most multi-task networks aimed for an intermediate reconstructed image, Schlemper et al. [31] bypassed this step and directly predicted segmentation maps from highly undersampled dynamic CMR images of the UK Biobank data. Their results indicate that clinical parameters can be computed within an error of 10% if at least 10 lines are acquired for each cardiac phase using Cartesian sampling.

As sufficient image quality is a crucial factor in any further downstream task, Tarroni et al. devised an automated cardiac quality control [32]. The heart coverage, existence of inter-slice motion, and myocardial to blood pool contrast are automatically assessed. Their findings enable a reproducible and objective setting for large-scale and automated data processing.

Neural networks have also been proposed for quantitative CMR imaging to allow for accelerated myocardial tissue characterization. Jeelani et al. estimated quantitative T1 maps from a MOLLI sequence [33, 34]. The work of Fahmi et al. paired the quantification network with a segmentation to target the maps toward the myocardium [35].

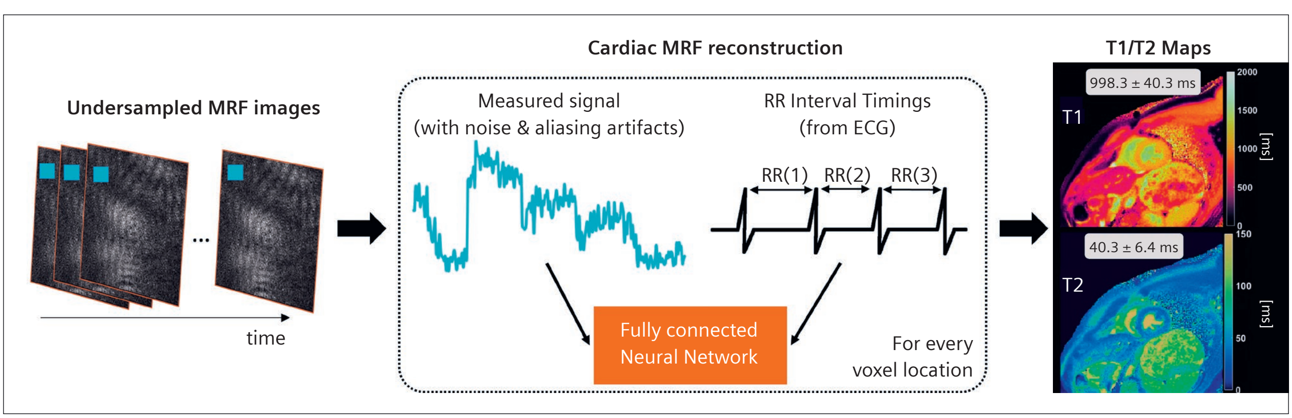
For multi-parametric acquisitions in MR fingerprinting, AI solutions have been initially proposed for non-cardiac applications [36] in order to bypass dictionary simulation and pattern matching and thereby reduce computation time and memory requirements. In CMR fingerprinting, sequence timings depend on the subject's cardiac rhythm. Hamilton et al. proposed an estimation of T1 and T2 maps directly from undersampled spiral images showcasing rapid and robust predictions [37], as depicted in Figure 4.

Myocardial tissue characterization has also been studied in the context of radiomics. In radiomics, the image data is converted into mineable high-dimensional data using a large number of handcrafted features targeted toward the image intensity, and structural and textural information. These features are then used to perform segmentation of myocardial tissue [38], differentiate between acute and chronic infarction [39], differentiate between causes of myocardial hypertrophy [40], discriminate between hypertensive heart disease and hypertrophic cardiomyopathy patients [41], and quantify myocardial inflammation [42].

Beyond purely imaging-focused approaches, AI methods have also been used to predict outcomes in patients with various cardiovascular diseases [43] and identify relationships between cardiac morphology and non-imaging information as provided by genetic variations [44].

Motion correction

Physiological motion is still one of the major extrinsic sources of image artifacts and requires appropriate handling during acquisition or reconstruction. In the case of CMR, we are primarily dealing with respiratory and cardiac motion, which result in non-rigid deformations of the heart and its surrounding environment. Respiratory motion and cardiac motion are in most solutions regarded as periodic, but they do not necessarily have a fixed frequency throughout the scan. In other words, a subject might hold their breath, or a heartbeat might be skipped and should therefore be treated as cyclic rather than periodic. Simplifications in modeling and correcting motion may be necessary to handle the motion problem and to build an appropriate AI solution.



4 Deep learning-based magnetic resonance fingerprinting (MRF) for myocardial tissue mapping [37]. A cardiac MRF sequence collects data within an ECG-triggered window under breath-hold from which the temporal fingerprint (measured signal) can be extracted for every voxel location. Together with the heart-rate interval timings, a fully connected neural network estimates the T1 and T2 values at each voxel location. *Image courtesy of Jesse Hamilton.*

AI-based image registration methods have been proposed to map motion states in motion-resolved images, outputting a motion field of the moving anatomies. Mappings can be expressed between a pair of images (e.g., end-systolic frame to end-diastolic frame), known as pairwise registration, or between a group of images (several diastolic frames) to a target image (end-systolic frame), known as groupwise registrations. Large non-rigid motion across multiple temporal frames can occur, and in the case of 2D imaging the existence of through-plane motion complicates the motion estimation process. Moreover, estimated motion fields should be diffeomorphic, i.e., a forward motion (end-systolic to end-diastolic) can be easily inverted to a backward motion (end-diastolic to end-systolic).

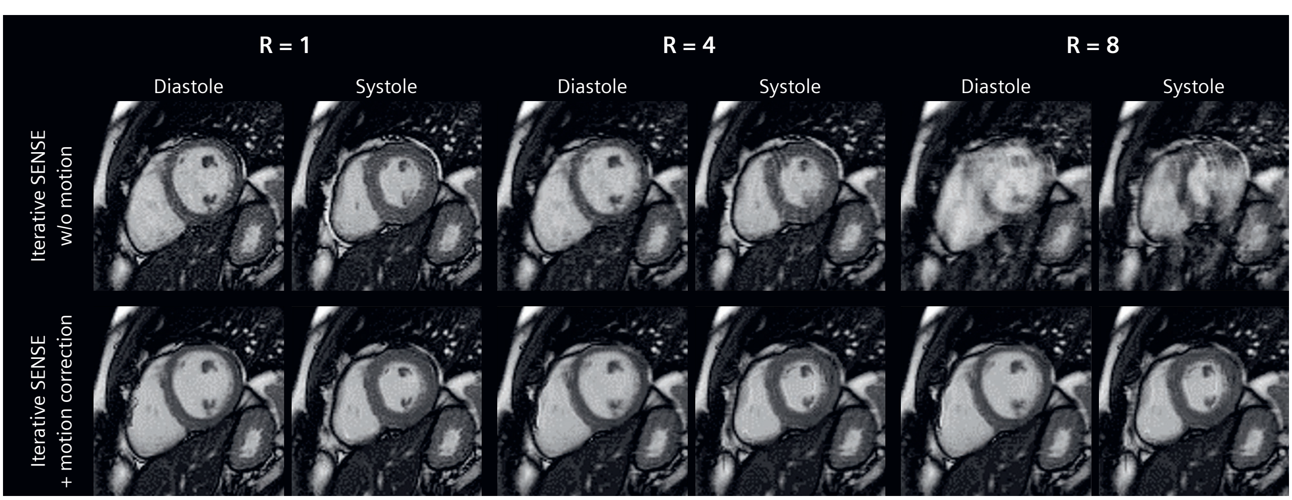
A fast and reliable motion estimation is therefore required that correlates these short- and long-term correspondences. AI methods have been proposed to operate on the reconstructed motion-resolved images (i.e., in the image domain) for pairwise registrations [45–47] or groupwise registrations [48]. Alternatively, registration could be carried out directly on the acquired raw *k*-space data [49]. Since it is often of interest to estimate motion from as little data as possible (providing high temporal motion resolution), motion estimation procedures have been challenged with data from accelerated acquisitions [49–51].

Instead of outputting a motion field, joint motion-compensated image reconstruction networks have been studied. Motion estimations are embedded with the reconstruction process in order to exploit the high-dimensional data [52–54], as highlighted in Figure 5. Further combinations with segmentation have been studied in [55], which introduced a joint framework for motion artifact detection, correction in *k*-space, and image segmentation. In this setting, the motion correction problem is reformulated as a reconstruction task. The motion artifact network detects motion-affected lines in *k*-space, which are then signaled to the reconstruction part for removal, yielding a motion-corrected image from which segmentations are derived. The results showed that joint processing was superior to sequential processing.

Adversarial training strategies as proposed in [56, 57] aim to correct for the motion in the image domain. These networks consist of two parts: a generator network which predicts motion-corrected images from simulated motion-corrupted ones, and a discriminator which tries to distinguish between the generated motion-corrected images (from generator) and real motion-corrected images. The goal is to fool the discriminator network to generate images that look like real motion-corrected images. Alternatively, motion embeddings can be learned with variational autoencoders that allow to distinguish between motion-affected and motion-corrected scans [58].

Current challenges, opportunities, and limitations

CMR imaging offers a great opportunity for deep learning due to the redundancy and the high dimensionality of the data. However, we also face challenges regarding acquisition time, SNR, the trade-off between spatial and temporal resolutions, and different types of motion, e.g., cardiac and respiratory motion, which makes the application of deep learning techniques more demanding. While deep learning approaches often outperform CS-based approaches in terms of pixel-wise quantitative scores, these approaches might tend to over-blur the temporal component. However, a



5 Motion-compensated image reconstruction for cardiac cine imaging. An image reconstruction is paired with a motion estimation network. The impact of sharing the available spatiotemporal information in a motion-corrected image reconstruction (bottom row) is shown in comparison to performing only a non-motion-informed image reconstruction (top row). For higher accelerations, sharing spatiotemporal data allows to increase sampling density and thereby improve image quality.

high resolution of the temporal dynamics is crucial for diagnosis and to detect subtle pathologies.

When using deep learning techniques, it is challenging to evaluate the quality and robustness of reconstruction approaches, especially in the case of subtle pathologies. However, we might get trapped in overly optimistic results if we use simulated data and neglect the unprocessed raw *k*-space data [59]. In a different line of work, the robustness of neural networks to small adversarial perturbations at the input was investigated [60]. Robustness of neural networks to changes in anatomy was studied in the context of static 2D imaging in [61], showing that domain shift has a marginal impact on image reconstruction when using unrolled networks and moderate acceleration. This observation regarding domain shift is different to image analysis tasks, where a subtle change might lead to mis-segmentation, for instance.

Deep learning approaches were intensively and individually studied in the context of scan planning, accelerated acquisition and reconstruction, and image analysis. While we often focus only on one part of this full imaging pipeline, deep learning provides many more opportunities to improve the whole workflow of CMR image acquisition for analysis and diagnosis. Future investigations of deep learning approaches will go deeper in supporting the choice of exam based on actual physiological scan parameters such as heart rate, or on the patient information obtained during the scan. Deep learning techniques will also support further acceleration in scan time to enable real-time interventional cardiac MRI [62]. We also observe a trend towards embedding different elements of the imaging pipeline into a deep learning approach and training this network end-to-end as shown in multi-task networks, or exploiting the available data, e.g., via motion fields, which will form the future of learning-based CMR imaging.

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