



Real-time Magnetic Resonance Imaging

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Real-time Magnetic Resonance Imaging

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ABSTRACT

Real-time magnetic resonance imaging (**RT-MRI**) allows for imaging dynamic processes as they occur, without relying on any repetition or synchronization. This is made possible by modern MRI technology such as fast-switching gradients and parallel imaging. It is compatible with many (but not all) MRI sequences, including spoiled gradient echo, balanced steady-state free precession, and single-shot rapid acquisition with relaxation enhancement. RT-MRI has earned an important role in both diagnostic imaging and image guidance of invasive procedures. Its unique diagnostic value is prominent in areas of the body that undergo substantial and often irregular motion, such as the heart, gastrointestinal system, upper airway vocal tract, and joints. Its value in interventional procedure guidance is prominent for procedures that require multiple forms of soft tissue contrast, as well as flow information. In this review, we discuss the history of RT-MRI, fundamental tradeoffs, enabling technology, established applications, and current trends.

Key Words: Real-Time MRI, Fast Imaging, Interactive Imaging.

INTRODUCTION

Real-time magnetic resonance imaging (**RT-MRI**) enables rapid and continuous acquisition of images that allows visualization of dynamic processes as they occur. RT-MRI does not rely on any gating, synchronization, or repetition of the underlying movement or contrast dynamics. The quality of RT-MRI has experienced major leaps in the past 30+ years due to advances in MRI technology, including fast switching gradients, array receiver coils, and advanced reconstruction including parallel imaging, compressed sensing, and artificial intelligence. Over this same time window, RT-MRI has earned a substantial role in both diagnostic imaging and in the image guidance of invasive procedures. Diagnostic RT-MRI has proven most valuable in areas of the body that undergo substantial and irregular motion, such as the heart (e.g. arrhythmia), upper airway vocal tract (e.g. speech production), joints (e.g. instability), and gastrointestinal system (e.g. motility). RT-MRI for interventional guidance has proven most valuable for procedures that require multiple forms of soft tissue contrast, as well as flow information (e.g. right heart catheterization).

Historically, MRI has had a reputation of being a “slow” modality, especially compared to X-ray, CT, and Ultrasound. This perception is changing. On modern commercial MRI equipment, RT-MRI is now feasible, practical, and readily available. It is compatible with most MRI sequences, and notably includes proton density (**PD**) and T1-weighted (**T1w**) spoiled gradient echo (**GRE**), balanced steady-state free precession (**bSSFP**), and single-shot rapid acquisition with relaxation enhancement (**RARE**). RT-MRI can provide more than adequate spatio-temporal resolution, contrast-to-noise efficiency, and image quality for a wide array of applications.

The purpose of this review is to summarize current state-of-the-art RT-MRI technology and clinical applications, predominantly focussing on imaging of dynamic motion. We begin with a discussion of the history of RT-MRI and fundamental tradeoffs. We then review enabling technology, which includes hardware, acquisition, reconstruction, interaction, and post-processing. Next, we review the most common applications, including cardiac, interventional, upper airway, and musculoskeletal. Finally, we discuss current trends, including the use of machine learning and the use of high-performance low-field MRI systems.

There has been some recent debate regarding nomenclature for RT-MRI (1,2). In this manuscript, *RT-MRI* will refer to real-time acquisition that does not use any gating,

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4 synchronization, or repetition of the movement. We use the term *interactive RT-MRI*, when
5 latency between acquisition and image display is short enough to permit interaction (e.g.
6 guidance of interventions, or calculation of real-time cardiac output).
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10 11 12 **BRIEF HISTORY**

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14 Real-time techniques are commonly used in medical imaging; including live video for
15 gait analysis, fluoroscopy for diagnostic studies of the gastrointestinal tract, and ultrasound
16 to guide interventional procedures such as biopsies. Development toward fast MRI began
17 shortly after the first medical applications. This included the development of Echo Planar
18 Imaging (**EPI**) by Sir Peter Mansfield in 1977 (3), as well as introduction of fast low angle shot
19 magnetic resonance imaging (**FLASH**) by Haase *et al.* in 1986 (4), and fast spin-echo imaging
20 (**RARE**) by Hennig *et al.* in 1986 (5). Early clinical applications of real-time imaging include MR
21 fluoroscopic images of the head by Farzaneh *et al.* in 1989 (6), followed by techniques to
22 interactively control scan slice orientation and image contrast by Holzinger *et al.* in 1990 (7),
23 and real-time flow measurements by Riederer *et al.* in 1991 (8).
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33 More recent developments have enabled substantial progress in MRI acquisition
34 speed, which are discussed below. There has been tremendous growth in the number of
35 publications on RT-MRI, as shown in **Figure 1**. Many of the large vendors have adopted the
36 use of interactive RT-MRI for localization and scan plane/volume prescription. And several
37 diagnostic and interventional applications have developed and matured.
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43 44 **FUNDAMENTAL TRADEOFFS**

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46 MRI in general must balance a tradeoff between spatial resolution, temporal
47 resolution, signal-to-noise ratio, artifacts, reconstruction latency, and modeling assumptions.
48 This tradeoff is put to the test in RT-MRI, where temporal resolution is at a premium. **Figure**
49 **2** shows a scatter plot of spatial resolution (x-axis) versus temporal resolution (y-axis) from 22
50 recent publications that utilize state-of-the-art 2D RT-MRI techniques. These publications,
51 with acquisition details listed in **Supplemental Table 1**, were selected to include a diversity of
52 imaging methods and target applications, and to include work from different laboratories
53 both with and without specialized hardware and software capability. The general tradeoff is
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4 illustrated by a gray shaded bar, with fine spatial resolution and coarse temporal resolution
5 on the upper left (e.g. $1 \times 1 \text{mm}^2$ with 80 ms temporal resolution, 12.5 fps), and coarse spatial
6 resolution and fine temporal resolution on the right (e.g. $3.5 \times 3.5 \text{mm}^2$ with 20 ms temporal
7 resolution, 50 fps). Deviations from this line occur because the data span several different
8 applications, reconstruction methods, coil geometries, field strengths, and modelling
9 assumptions. The impact of these is discussed in detail in the Enabling Technology section
10 below. In general, moving towards the lower left requires using more advanced technology,
11 advanced modelling, and increased computational demand, or accepting worse SNR and/or
12 more severe image artifacts.
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23 ENABLING TECHNOLOGY

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25 RT-MRI is made possible by several system components that are included in most
26 modern high-end clinical MRI systems. These beneficial components are discussed in this
27 section. Items that are non-standard are clearly identified.
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32 Hardware

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34 The speed of MRI is fundamentally limited by NMR relaxation, and the time required
35 to cover k-space. RT-MRI therefore relies on time-efficient spatial encoding. One major
36 technological advance has been high-fidelity fast-switching shielded gradients, with eddy-
37 current precompensation. Modern systems offer this with gradients that can produce
38 $\geq 40 \text{mT/m}$ amplitude and $\geq 150 \text{mT/m/ms}$ slew rate on each physical axis with 50-100% duty
39 cycle. This enables GRE and bSSFP contrast with very short repetition times and enables
40 efficient k-space sampling (e.g. spiral or echo-planar). Spiral and EPI trajectories were among
41 the first technical advances to substantially broaden the set of applications that could be
42 addressed with RT-MRI (9).
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51 RT-MRI also benefits from the use of parallel imaging, which requires carefully
52 designed receiver coils arrays that provide diverse coil sensitivity along the likely directions of
53 spatial encoding and k-space undersampling. These coils should preferably preserve body-
54 noise dominance (10). Several MRI manufacturers and third-party vendors manufacture such
55 coils and optimized cardiac and torso coils are readily available. However, coils for nascent
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4 applications such as speech (11,12), and dynamic musculoskeletal imaging are not yet
5 standardized, and there is substantial room for development.
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8 Interactive RT-MRI requires the use of a flexible programmable console that can allow
9 “on-the-fly” changes to the scan plane, shim, and many other imaging parameters. Several
10 modern systems offer this capability, wherein many aspects of a pulse sequence can be
11 modified without substantial interruption (i.e. within a few milliseconds).
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19 High frame-rate RT-MRI has been fundamentally enabled by two gradient echo
20 sequences: GRE and bSSFP (**Figure 3A**). RF-spoiled and gradient-spoiled GRE sequences are
21 robust to artifacts and provide T1-weighted contrast with a short repetition time (**TR**). bSSFP
22 sequences (13) provide higher signal-to-noise ratio (**SNR**) efficiency than GRE, and provide
23 T2/T1 contrast, which is extremely advantageous in cardiac imaging because of the excellent
24 blood–myocardium contrast (**Figure 3A**, right). However, bSSFP has two important
25 limitations. One is sensitivity to off-resonance, which manifests as banding artifacts (14).
26 bSSFP RT-MRI is often used at $\leq 1.5T$ or at $3T$ with careful shimming over the region of interest
27 (**ROI**) and with the shortest possible TR. The second issue is a transient approach to steady
28 state, which can be problematic if the application requires frequent switching of the scan
29 plane or volumes, or if there is flow or motion through regions that experience the banding
30 artifact. Transient signal oscillations can be easily mitigated using catalyzation preparation
31 schemes, however it still takes time to reach steady state contrast.
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43 RT-MRI has been made possible by efficient k-space sampling trajectories (e.g. spiral
44 and EPI, described in the preceding section) and clever temporal undersampling schemes.
45 Although it is inefficient, 2DFT imaging may be used in both 2D and 3D imaging due to the
46 simplicity of reconstruction and robustness to artifacts. A wide range of \vec{k} - t under-sampling
47 schemes exists for accelerated 2DFT imaging (15–20). For example, one can use variable-
48 density pseudo-random \vec{k} - t sampling, which creates incoherent aliasing artifacts in a certain
49 transform domain that can be resolved by advanced reconstruction algorithms.
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56 **Figure 3B** illustrates more efficient sampling trajectories. EPI (3) is an alternative
57 where multiple Cartesian lines are acquired after each excitation, therefore k-space can be
58 filled only with one or fewer repetitions. However, its long readout time makes it vulnerable
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4 to ghosting and distortions from gradient waveform inaccuracy or off-resonance and near-RT
5 correction methods (21,22) have been proposed.
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8 Most preferred are radial and spiral samplings when higher spatial and/or temporal
9 resolution is desired. Both spiral and radial sampling naturally oversample the center of k-
10 space and this offers motion robustness and tolerance to undersampling. While radial
11 sampling is $\pi/2$ less efficient than Cartesian, its motion robustness and tolerance to
12 undersampling make it popular RT-MRI acquisition method (23). With moderate angular
13 undersampling along with the golden angle scheme (24), the streaking artifacts are usually
14 mild in appearance and incoherent over time. Alternatively, spirals can be very efficient
15 methods to cover k-space. Single-shot spirals can completely cover k-space, but the resultant
16 long readout time increases sensitivity to off-resonance, resulting in spatial blurring. Multi-
17 shot spiral acquisitions with a short readout time can be used to alleviate blurring. Both radial
18 and spiral imaging can be accelerated with the use of \vec{k} - t sampling strategies such as under-
19 sampling and random angle order schemes, e.g., bit-reversed (9) or golden angle (24,25)
20 (**Figure 3C**). For instance, radial or spiral imaging can be performed with an angle incremented
21 by the golden angle (222.5°) (24) or tiny golden angles (26). This, when undersampled,
22 produces relatively incoherent aliasing in the spatial and temporal domain (or in a transform
23 domain), which is well-suited for advanced reconstruction algorithms. The view order is an
24 added variable and the golden angle scheme is widely used as it additionally has the
25 retrospective field-of-view (**FOV**) tradeoff ability as opposed to the conventional scheme
26 (right, **Figure 3C**).
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43 RT-MRI has also benefited from 2D multi-slice imaging (11,27–31), which can be
44 performed by utilizing time-interleaved sampling of acquisition schemes described above
45 with a corresponding reduction in spatial or temporal resolution by the number of slices.
46 Alternatively, simultaneous multi-slice imaging (32) can be utilized to accelerate data
47 acquisition. Especially, controlled aliasing in parallel imaging results in higher acceleration,
48 also known as CAIPIRINHA (33,34), has shown substantially reduced aliasing artifacts. This
49 technique has recently been explored in some RT-MRI studies (35–37). 3D imaging has also
50 been explored by extending 2D acquisition schemes to 3D or by using novel 3D sampling
51 trajectories. Radial or spiral can readily be extended to 3D stack-of-stars (38) or 3D stack-of-
52 spirals (39,40) by adding phase encoding steps along k_z direction. Echo-volume imaging (41),
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4 a 3D extension of EPI, can achieve time-efficient 3D imaging and has primarily been
5 investigated for brain functional MRI (42). Combinations of two sampling schemes for 3D
6 imaging has also been explored, including EPI (43) and Cartesian sampling (44), each
7 combined with golden-angle radial sampling. There has also been interesting literature
8 where volumetric image can be efficiently obtained by RT-MRI acquisitions with automatic
9 advancement of the slice position (45). While 3D acquisitions allow for a more flexible \vec{k} - t
10 sampling strategy and therefore much redundant information to be exploited along the
11 additional dimension, the increased amount of data is challenging in terms of data processing
12 and reconstruction.
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22 Reconstruction

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24 RT-MRI data sampling and reconstruction varies with application. This is because there
25 is a trade-off between temporal resolution and reconstruction time (governed by the
26 complexity of the algorithm). The simplest reconstruction techniques use data sharing
27 strategies, for example keyhole or sliding window reconstruction (46). This simplicity enables
28 low latency reconstruction; however, the true temporal resolution is coarse.
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34 Higher levels of acceleration are achievable by undersampling, however zero-filled
35 reconstruction results in spatial aliasing that renders the images clinically unusable. One can
36 use parallel imaging to recover usable images, which can be performed in the image domain;
37 SENSitivity Encoding (**SENSE**) (47), or in k-space; GeneRalized Autocalibrating Partial Parallel
38 Acquisition (**GRAPPA**) (48). Parallel imaging of Cartesian data enables very low latency
39 reconstructions; hence its popularity in RT-MRI interventional applications.
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45 Reconstruction of undersampled non-Cartesian data is substantially more complex.
46 This is because the k-space points must be resampled onto a Cartesian grid in order to use
47 the Fast Fourier Transform (**FFT**), which increases computation demand (49). Additionally, in
48 non-Cartesian SENSE each voxel in the image domain can potentially alias with all of the other
49 voxels, resulting in the need for time-consuming iterative reconstructions (50). In non-
50 Cartesian GRAPPA the irregular gaps in k-space, result in the need for geometry-specific
51 GRAPPA weights (51,52) requiring large amounts of calibration data. These drawbacks often
52 restrict the use of non-Cartesian parallel imaging to applications where real-time visualization
53 is not necessary. One exception is through-time GRAPPA where multiple fully sampled non-
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4 Cartesian datasets are acquired and are used to learn the location-specific GRAPPA weights
5 (53–55).
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8 The level of acceleration achievable using parallel imaging, is in theory equal to the
9 number of independent coil elements along the direction of undersampling. In practice,
10 acceleration rates are often limited to 2-3 using Cartesian trajectories, and 3-4 using non-
11 Cartesian trajectories. Higher levels of acceleration can be achieved by combining temporal
12 and spatial encoding schemes. These techniques often leverage the fact that the MR data is
13 sparse in \bar{x} - f space, including; \bar{k} - t Broad-use Linear Acquisition Speed-up Technique (**BLAST**),
14 \bar{k} - t SENSE, \bar{k} - t GRAPPA (56). In these schemes, the reconstruction is constrained using some
15 prior information which can be used to determine the ground truth. These techniques often
16 preclude real-time reconstruction as this prior information is extracted from the data itself
17 (57), or as part of a pre-scan.
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26 Even higher acceleration factors are possible using constrained reconstructions (58),
27 compressed sensing (59) and regularized non-linear inversion (**NLINV**) (143). These methods
28 rely on object models, such as sparsity in a known transform domain, along with data
29 sampling that produces incoherent aliasing in the sparsity domain. Some of the most popular
30 sparsifying transforms for RT-MRI are finite differences, total variation, wavelet, and Fourier
31 transform, which can be applied to exploit spatial and/or temporal sparsity. This category of
32 methods enables acquisition of exceptionally high temporal and/or spatial resolution;
33 however, they rely on non-linear reconstruction that is computationally expensive, resulting
34 in high reconstruction latency that often limits clinical adoption.
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43 There has been substantial work towards reducing image reconstruction times. This
44 includes the use of coil selection (60) and coil compression (61) techniques. Modern Graphics
45 Processing Units (**GPU**) enable improvements in latency and throughput, through their
46 massively parallel architecture (62–64), and have enabled up to 27-fold reduction in latency
47 compared to conventional CPUs (65), making interactive RT-MRI feasible.
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52 In addition, the efficient k-space trajectories often used in RT-MRI are susceptible to
53 artifacts from linear time invariant gradient distortions, including eddy currents. Correction
54 of these has been shown to be feasible in real-time (22). However, artifacts from concomitant
55 fields (66,67) are more challenging. At present, these require the use of approximations (68),
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4 or the use of NMR field probes (69,70) in conjunction with a more sophisticated offline
5 reconstruction (71).
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8 Vendor-agnostic raw data formats have been developed to promote reconstruction
9 algorithm sharing and data sharing, for example ISMRM Raw Data (**ISMRMRD**) (72) and Raw
10 Array (**RA**) (73). The ISMRMRD format is designed to support simultaneous streaming of raw
11 data, pulse sequence waveforms, and physiology waveforms, to image reconstruction or
12 processing software (74). This streaming capability is important for fast reconstruction of real
13 time images.
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20 21 Post-Processing

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23 Offline processing, including segmentation, parameter quantification, and distortion
24 correction, of RT-MRI images is quite similar to traditional offline processing of CINE imaging
25 or even static imaging. However, there are many scenarios where in-line post-processing adds
26 value, particularly for interactive RT-MRI. The unique features of these methods in RT-MRI
27 are that they typically have to tolerate lower image SNR and have to satisfy maximum latency
28 requirements. Inline segmentation has been shown to aid monitoring of ventricular function
29 during cardiac interventions (75). Inline flow quantification has been shown to expedite
30 comprehensive cardiac examinations (76). And, inline off-resonance artifact correction
31 (deblurring) has been shown to substantially improves the sharpness of speech articulator
32 depiction (77).
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43 Interaction/Visualization

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45 RT-MRI applications often benefit from the synchronization with other
46 complementary real-time inputs. For cardiopulmonary testing, physiological monitoring of
47 ECG, respiration, expiratory gases may be synchronized with real-time cardiovascular imaging
48 (75). MRI-guided catheterization requires electrophysiological recording of high-fidelity ECG
49 waveforms, which can be challenging within the MRI environment, and hemodynamic
50 recording of invasive pressure waveforms (78,79). Real-time speech imaging requires
51 synchronization of audio signals with imaging data, which can be achieved with commercial
52 products (e.g. FORMI II+, Optoacoustics Ltd, Israel) (23,80).
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Additionally, for some applications, user interaction is required to modify parameters during imaging using real-time feedback to the scanner. Most notably, for real-time MRI guided intervention, the modification of slice position, slice thickness, slice orientation, image contrast, frame rate, and device imaging modules can each be toggled and modified interactively without a pause in the continuous stream of real-time imaging. Interactivity requires that images are displayed and manipulated in real-time, and that pulse sequence parameters are accessible to be modified on-the-fly.

Major MRI vendors have prototype or product graphical user interfaces for interactive imaging (e.g. Monte Carlo prototype, Siemens Healthcare, Erlangen Germany; iSuite, Philips, Best, The Netherlands; iDrive and MR Echo, GE Healthcare, Waukesha, Wisconsin, USA). Interactive imaging platforms are also available through independent MRI software vendors, most notably the RTHawk platform (Heart Vista Inc., Los Altos, CA, USA) (81). This platform is MRI vendor agnostic as long as a fully flexible stub sequence is available, but to-date, has been primarily developed on the GE platform. This system is compatible with interactive scan plane modification using a six degree of freedom 3D mouse (81).

Auxiliary equipment can also be used inside of the MRI suite for interactive modification of imaging. MRI-guided catheterization procedures use foot-pedals to leave interventionist hands available for device manipulation, which mimics traditional X-Ray catheterization suites. Other auxiliary equipment including computer mice, keyboards and tablets have been explored for interactive imaging (82), as well as gesture-based scan control (83). Furthermore, augmented reality and virtual reality equipment (84) may be attractive for interactive visualization of real-time imaging in the future.

APPLICATIONS

RT-MRI benefits a broad range of diagnostic and interventional applications. Here, we summarize the application-specific needs, imaging considerations, and the impact to date.

Cardiac

RT-MRI enables imaging of the cardiovascular system without the need for cardiac gating or respiratory compensation. This is particularly valuable in patients with cardiac

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4 arrhythmia (85,86) where cardiac gating fails (~10% of patients referred for diagnostic cardiac
5 imaging), and in patients who find breath-holding difficult (~10% of patients). It is also
6 extremely valuable in children with congenital heart disease (**CHD**), where it can be used to
7 lessen the need for sedation (87) and its associated risks.
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11 Real-time assessment of cardiovascular structures requires relatively high spatial and
12 temporal resolution to ensure accurate visualization and quantification. For example, Setser
13 et al. (88) recommend a minimum temporal resolution of 50 ms (20 fps), and spatial
14 resolution of 2 mm for functional RT-MRI of the left ventricle. Real-time ventricular function
15 imaging has been shown to achieve an excellent agreement with reference standard breath-
16 held, cardiac gated techniques, through combination of undersampled radial trajectories with
17 \vec{k} - t SENSE reconstructions in CHD (89), \vec{k} - t SPARSE-SENSE in patients with tachycardia (20)
18 and myocardial infarction (90), regularized non-linear inversion (91) and more recently, proof-
19 of-concept studies using machine learning reconstructions in CHD (92). **Figure 4a** and
20 **Supplemental Movie 1** contains a representative example of image quality. Spiral
21 trajectories, although less popular, have been combined with compressed sensing to achieve
22 high resolution imaging in children with CHD (93).
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33 Quantification of blood flow using phase contrast (**PC**) requires high spatial resolution
34 to mitigate partial volume effects; Greil et al. recommend that it is necessary to have 16 pixels
35 in the cross section of the vessel of interest to get accurate flow quantification (94). PC RT-
36 MRI has been used clinically to assess the respiratory and cardiac components of flow in
37 patients with Fontan circulation (95,96), to quantify flow in children with cardiac left-to-right
38 shunts (97), to investigate the effect of elevated intrathoracic pressure on blood flow (98),
39 and in CHD (99). **Figure 4b** and **Supplemental Movie 2** contains a representative example of
40 image quality.
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48 RT-MRI also enables imaging during exercise, which can be used to unmask subtle
49 changes in early cardiovascular disease (100). Studies have shown the ability to measure
50 ventricular volumes during exercise; to assess the effect of percutaneous pulmonary valve
51 implantation (101), to assess the mechanisms which augment cardiac output with exercise in
52 repaired tetralogy of Fallot (102), and to unmask right ventricular dysfunction in pulmonary
53 arterial hypertension (103). Real-time flow during exercise has also been used in patients with
54 Total Cavopulmonary Connection (104) and after surgical bypass of aortic arch obstruction
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4 (105). Continuous acquisition of real-time flow during ramped exercise over 10 minutes has
5 been shown (62), as well as combination with respiratory gas analysis to simultaneously
6 measure peak oxygen consumption (VO_2) enabling assessment of exercise capacity (106).
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10 Fetal cardiac RT-MRI is of interest as a potential secondary tool (after fetal
11 echocardiography) to characterize congenital cardiac malformations (107). It is one of the
12 most challenging applications of RT-MRI because of the very high heart rates, need for high
13 spatial resolution (tiny hearts), need for interaction (to follow movement of the fetus), and
14 desire to be conservative with SAR and acoustic noise (108). It has been attempted with some
15 success (109), however RT-MRI acquisition with retrospective metric-optimized-gating has
16 provided a promising approach for CINE MRI. **Figure 4c** and **Supplemental Movie 3** contains
17 a representative example of image quality of RT-MRI in the fetal heart.
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26 MRI-guided invasive procedures

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28 MRI-guidance of diagnostic and therapeutic invasive procedures employs
29 intraprocedural imaging to navigate devices and to assess procedural outcomes. Compared
30 to traditional image-guidance modalities such as X-ray and ultrasound, MRI offers flexible
31 image contrast and three-dimensional imaging capabilities that can improve tissue
32 visualization during a procedure. Real-time MRI is particularly valuable during complex device
33 manoeuvres and previous review articles have described the applications of real-time imaging
34 technologies to guide invasive procedures (110–112). **Figure 5** and **Supplemental Movies 4**
35 **and 5** contain illustrative examples.
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43 Many invasive procedures have been performed in patients in the MRI environment,
44 including MRI-guided biopsy (113,114); radiotherapy (115); thermal ablations such as
45 radiofrequency ablation (116,117), laser ablation, cryoablation (118), microwave ablation and
46 high intensity focused ultrasound (119); chemoablation; drug injection; electrophysiology
47 (120–122); and invasive pressure measurements (79,123,124).
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52 MRI-guided invasive procedures have unique requirements. Low-latency
53 reconstruction and in-room image display are essential, such that images can be used for real-
54 time device navigation and procedural decision making. Interactivity of imaging parameters
55 is critical to control image contrast and frame rate throughout the procedure. Image
56 processing, including image segmentation, registration and distortion correction, must also
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4 be performed on-the-fly (111). During many invasive procedures, devices (e.g. needles,
5 catheters, guidewires, sheaths) are imaged concurrently with target anatomy. Device imaging
6 is performed using either “passive” visualization, exploiting material properties, or “active”
7 visualization in which devices themselves are RF receivers, designed as loopless antennas for
8 imaging (125) or microcoils for 3D device tracking (126) (**Figure 5A, Supplemental Movie 4**).
9 Solenoid and loopless receiver coils positioned on invasive devices can also be applied for
10 small-FOV local imaging in MRI-endoscopy applications (127).
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Most in-bore biopsy procedures of prostate, liver, breast, and brain lesions use
standard T2-weighted, T1-weighted, diffusion-weighted, or dynamic contrast-enhanced
imaging for iterative confirmation of needle placement (113,114,128), with a few studies
employing high frame-rate dynamic needle guidance (129,130). MRI-guided cardiovascular
procedures are the most technically demanding, requiring rapid multi-planar imaging for
device navigation. Most commonly, a 2D Cartesian bSSFP acquisition is used, in combination
with parallel imaging, to achieve 5-10 frames/s, with magnetization preparation pulses for
contrast variation (**Figure 5B, Supplemental Movie 5**). 2D radial and spiral spoiled gradient
echo acquisitions have also been applied for cardiovascular procedures (131,132), and when
combined with regularized nonlinear inversion reconstruction, have achieved temporal
resolution of 42 ms (24 fps) with reconstruction delay of 27 ms (133).

RT-MRI thermometry, using proton resonance frequency shift imaging, is important
to monitor thermal ablations with high temporal resolution. Multi-slice single-shot EPI
acquisitions with real-time image registration methods have been developed for
thermometry and dosimetry during cardiac RF ablations (134,135) (**Figure 5C, Supplemental
Movie 6**). The geometry of transcranial high intensity focused ultrasound (HIFU) therapy
devices restricts the number of receive coils that can be positioned around the head, and
undersampled stack-of-spiral and stack-of-stars EPI thermometry acquisitions (40,43) have
been developed for volumetric brain coverage with 75 ms temporal resolution (13 fps). 3D
dynamic keyhole imaging has generated high spatiotemporal resolution (1.5x1.5x6 mm³ with
455 ms temporal resolution, 2 fps) imaging for dynamic guidance of radiotherapy (136). This
work utilizes a super-resolution generative model for high-spatial reconstruction from low-
spatial and high-temporal resolution images.

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4 The unique set of requirements of MRI-guided invasive procedures continues to
5 motivate the innovation of RT-MRI acquisitions, as well as rapid inline image reconstruction
6 and image processing.
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10 11 Upper Airway

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13 RT-MRI enables imaging soft-tissue structures and muscles of the upper airway that
14 are coordinated in space and time to perform essential human functions such as speech,
15 respiration, and digestion. RT-MRI is preferred over other imaging and movement tracking
16 modalities because it allows for observing deep soft-tissues such as the velum, pharyngeal
17 wall, and the larynx in the arbitrary imaging plane without radiation or endoscopy. The nature
18 of the movements of the upper airway is not necessarily periodic and is unrepeatably. RT-
19 MRI can now be combined with intermittent tagging pulses to visualize internal deformation
20 in the tongue muscles (137,138) and be exploited to reconstruct 3D tongue shape or model
21 (139,140). Real-time visualization and interaction are also advantageous for the operator to
22 modify imaging parameters on-the-fly and to ensure subject's compliance with stimuli.
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32 **Figure 6** and **Supplemental Movies 7-9** illustrate representative research areas in
33 speech production (23,141), sleep apnea (36,37,142) and swallowing (143). Imaging is often
34 performed along with synchronized recordings of physiological signals such as audio signals
35 in speech (144), polysomnography signals used in sleep studies (36), and intraoral pressure
36 sensor used in swallowing (145) to aid real-time or retrospective analysis. Several clinical
37 applications have also been explored such as velopharyngeal insufficiency (146), apraxia
38 (143,147), and post-surgical assessment of glossectomy (147,148) and cleft-palate repair
39 (149,150). Many other applications and technical aspects of the upper airway imaging have
40 been described in review articles with focuses on speech (23,141,151), speech and sleep
41 (152), sleep (142), and image analysis techniques on RT-MRI of vocal tract motion (153).
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51 The upper airway imaging generally requires high spatial and temporal resolution
52 although specific imaging parameters would be dictated by the applications as shown in
53 Figure 1 in Lingala et al.(23). For speech, high temporal resolution, below 70 ms (greater than
54 14 fps) and spatial resolution of no more than 3.5 mm² are typically required to study a broad
55 range of speech events. For sleep, pharyngeal airway motion is relatively slower than vocal
56 tract motion as it involves closure of the airway, requiring lower temporal resolution than
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4 imaging for speech and swallowing. For swallowing, it is valuable to track both the
5 pharyngolaryngeal area and the lower esophageal sphincter and its surrounding area (154).
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8 Current state-of-the-art technique uses non-Cartesian sampling (radial or spiral
9 acquisition) and parallel imaging, combined with constrained reconstruction. This has enabled
10 2D dynamic images with spatial resolutions of 1.3 to 2.4 mm² at high temporal resolutions of
11 10 to 60 ms (100 to 17 fps) from highly under-sampled MRI data (11,54,55,145,155–158).
12
13 Imaging 2D mid-sagittal plane is the most widely used as it is most informative thanks to its
14 entire vocal tract coverage from the lips to the glottis given a high temporal resolution.
15
16 Imaging a few 2D planes (11,29,30), simultaneous 2D planes (36,37), or 3D (38) at the cost of
17 temporal resolution have also been developed. Recently, 3D stack-of-spiral acquisition
18 demonstrated imaging of the full vocal tract (FOV: 200x200x70 mm³) with high spatio-
19 temporal resolution (2.4x2.4x5.8 mm³, with 72 ms temporal resolution, 14 fps) during natural
20 speech (39).
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28 Imaging the upper airway has a unique challenge – tissue surfaces along the upper
29 airway are the main region of interest but are vulnerable to off-resonance effects. Those
30 include the movements of the articulators during speech or swallowing, the closure of the
31 velopharyngeal port in velopharyngeal insufficiency, and the collapse of the pharyngeal
32 airway in sleep study. Off-resonance at the tissue surfaces manifests as blurring or signal loss
33 with non-Cartesian sampling such as spirals and/or appear as banding artifact when bSSFP
34 sequences are used. Careful shimming is usually carried out with a focus on the tissue
35 boundaries. Current RT-MRI studies for speech production are most often conducted using
36 short-duration spirals (2.5 ms) and/or at lower field strength (1.5T or lower) MRI scanners, or
37 in conjunction with field inhomogeneity reconstruction (159–161) or more recently AI-based
38 deblurring (77).
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50 Musculoskeletal

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52 Musculoskeletal RT-MRI is used to reveal abnormal joint biomechanics which are
53 linked to joint disorders, usually in the context of pain, instability or movement restriction.
54 For example, abnormal knee kinematics is known to contribute to the development and
55 progression of osteoarthritis. Common musculoskeletal applications include the knee, wrist,
56 spine, temporomandibular joint, foot, and hip (162), with a selected few illustrated in **Figure**
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4 **7** and **Supplemental Movies 10-12**. These have vastly different spatio-temporal resolution
5 and coverage needs.
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8 Early work used semi-static approaches (multiple static images in fixed postures).
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10 Systematic studies have since determined that biomechanical models derived from RT-MRI
11 are substantially different from those derived from semi-static approaches (163), making RT-
12 MRI the current method of choice. Musculoskeletal movements are voluntary, and can
13 sometimes be performed through controlled dynamics, for example where movements are
14 repeated and synchronized with a metronome or periodic visual stimulus. However, voluntary
15 synchronization is imprecise, subject-dependent, and impractical for patients with pain.
16
17 Retrospective gating can be applied using additional sensors (164) or self-gating approaches
18 (165), assuming that the timing variations have a negligible impact on kinematic estimates.
19
20 Movement can be more precisely controlled by a physical apparatus, but this does not lead
21 to realistic physical effort, which is often needed to reproduce the abnormal movement
22 and/or the symptom being studied (e.g. pain). Finally, it is possible to synchronize using
23 external muscle stimulation (166), which adds experimental complexity. For all of these
24 reasons, there is a need for RT-MRI, and often a need for an appropriate load (167).
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33 Musculoskeletal RT-MRI requires strong contrast between muscle, fat, and
34 surrounding fluids, and benefits from high SNR efficiency, making bSSFP the sequence of
35 choice (168). bSSFP can be augmented with phase-sensitive reconstruction for fat-water
36 separation (169). GRE may also be used with optional multi-echo fat-water separation (170).
37
38 Most studies in the literature were performed at conventional field strengths (1.5T and 3T) in
39 the supine position, which restricts movement and load bearing. For this reason, low-field
40 open-bore and upright MRI has been explored as an alternative to alleviate these restrictions
41 (171).
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48 In the knee, RT-MRI has provided valuable insight into patellofemoral pain, and used
49 to quantify kinematics (172), document the differences between the load-bearing and non-
50 load-bearing kinematics (173), and determine the effects of physical supports (172). RT-MRI
51 measurement of tibiofemoral kinematics can be further improved by using slice-to-volume
52 registration with 3D static scans (174,175). In the finger, 2D RT-MRI has provided insight into
53 joint cavitation, which is responsible for the cracking sound (176). In the wrist, 2D and 3D RT-
54 MRI have provided insight into ligament insufficiency, instability, and how aberrant
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4 kinematics may contribute to wrist pain (177,178). In the shoulder, low-resolution RT-MRI in
5 conjunction with high-resolution static MRI was used to better characterize rotator cuff
6 disease (179). In the temporomandibular joint, RT-MRI has been demonstrated with adequate
7 spatio-temporal resolution to track disc and condyle kinematics (180,181). In summary, RT-
8 MRI is a promising early-stage technique for studying musculoskeletal kinematic
9 insufficiency/abnormality and pain in several body regions.
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15 16 17 Other

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19 RT-MRI has also been used for other thorax and abdominal imaging applications. Real-
20 time cine imaging has been used to assess abnormal bowel motility following ingestion of an
21 oral contrast agent (e.g. mannitol). Bowel imaging is typically performed in a coronal
22 orientation and bSSFP imaging has been applied for imaging for 1-3 s temporal resolution per
23 3D volume (1 to 0.3 fps) (182,183). Dynamic esophageal imaging has been achieved using a
24 radial spoiled gradient echo acquisition with nonlinear inverse image reconstruction for 40
25 ms temporal resolution (25 fps) following the ingestion of pineapple juice (184). RT-MRI has
26 also been used in urethrography, to assess urinary function during bladder emptying (185),
27 in defecography, to assess the pelvic floor in mechanical and functional rectal disorders
28 (186) and to assess pelvic floor disorder and pelvic organ prolapse (187). These techniques
29 often use turbo spin-echo sequences to achieve T2 weighting, with 1.0-1.5mm spatial
30 resolution, and a temporal resolution of 1-5 seconds (1 to 0.2 fps).
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41 RT-MRI has also proven valuable for screening of fetal central nervous system
42 abnormalities, specifically the structural malformations (188–190). T2-weighted RARE
43 sequences (often with partial echo along the phase encode direction) are used for the
44 beneficial contrast between gray and white matter.
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48 This paper is focused on the use of RT-MRI in imaging physical motion; however it can
49 also be used to image contrast dynamics. Although this is beyond the scope of this article, this
50 includes dynamic contrast enhanced MRI (191), time-resolved angiography (192), as well as
51 functional MRI (42) including Arterial Spin Labelling (ASL) (193) and Encephalography (194).
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58 **CURRENT DIRECTIONS**

Increasing Role of ML/AI

In recent years, machine learning methods, especially deep learning, have enabled breakthroughs in computer vision and image analysis. The astonishing success of deep learning algorithms has penetrated areas of MR image reconstruction, artifact correction, automatic classification and segmentation, landmark detection, and so on.

Deep learning has huge potential in RT-MRI applications, for example in real-time visualization and/or immediate downstream analysis. There have been several early works on ML with success for RT-MRI applications, as illustrated in **Figure 8** and **Supplemental Movies 13-14**. This figure demonstrates the use of deep learning for various tasks; reconstruction of RT-MRI data (removing artefact from undersampled radial images, **Figure 8a**), improving image quality of RT-MRI (performing off-resonance deblurring, **Figure 8b**), and to enhance clinical impact (performing Needle detection and segmentation, **Figure 8c**). It has been shown to be popular for low-latency reconstructions of real-time MR data; in 2D cardiac imaging (92,195,196), MR-guided radiotherapy images (197), and 3D functional MRI (198). Additionally, it is popular for rapid post-processing of real-time data; including identification and segmentation of the vocal tract (199–202), as well as segmentation of the left and right ventricles from real-time cardiac MRI (203). Other applications include rapid needle detection and segmentation in MR-guided interventions (204,205), enabling real-time localization of the Fetal brain (206), spiral off-resonance deblurring in speech imaging (77), and combination of reconstruction and post-processing for real-time MR thermometry (207).

Some commercially available software has started using ML in real-time imaging, including HeartVista (208) which uses ML to automate the MRI exam, control the scanner and assist scan planning, and MeVisLab (209) for segmentation and annotation.

High Performance Low Field

Recent publications have suggested substantial opportunities for real-time imaging on high-performance low field (**HPLF**) MRI systems (210). These systems operate with a low static field strength (e.g. 0.35T and 0.55T) and incorporate contemporary high-performance hardware and modern imaging methods. Unlike historic low field MRI systems, these HPLF systems include fast shielded gradients and multi-channel receiver arrays. They are capable of non-Cartesian sampling, parallel imaging, and compressed sensing, and can exploit readily

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4 available computational resources. These systems have produced new capability and
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6 exceptional performance for cardiac, abdominal, and pulmonary RT-MRI, illustrated in **Figure**
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8 **9** and **Supplemental Movie 15**.

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10 The HPLF system configuration provides several advantages for real-time imaging. 1)
11 Many RT-MRI acquisitions are limited by off-resonance (e.g. bSSFP, spiral). Since absolute off-
12 resonance (in Hz) scales linearly with field strength, lower field strength systems relax this
13 constraint. For bSSFP acquisitions, longer TRs can be used without banding artifacts. For spiral
14 sampling, longer readouts can be used without blurring artifacts. 2) T2* is longer, making it
15 possible for efficient data sampling strategies, including spiral and EPI and to be implemented
16 with prolonged duration. This allows increased flexibility in trajectory design. Moreover,
17 artifacts related to susceptibility (e.g. blurring and ghosting) are reduced. 3) T1 is shorter at
18 lower field strength causing more rapid signal recovery between RF pulses. 4) Tissue heating
19 due to RF is reduced at low field, which permits high flip angle excitation and magnetization
20 preparation pulses, with diminishing concerns of patient safety during prolonged real-time
21 imaging. The net result is a favourable system configuration for real-time imaging.

22
23 HPLF is especially beneficial for MR-guided interventions, due to the favourable low
24 SAR properties. Reduced device heating will enable the application of commercial conductive
25 devices in the MRI-environment, and reduce the burden of design for new devices, which is
26 substantial at conventional field strengths ($\geq 1.5T$) (211). HPLF is also beneficial for real-time
27 speech imaging, where susceptibility gradients at air-tissue interfaces are the primary
28 constraint.

29
30 Finally, a HPLF system could be cost effective to manufacture, install and maintain,
31 which may increase accessibility for these real-time imaging applications outside of the
32 conventional Radiology environment (e.g. cardiology and point-of-care settings). Currently,
33 the B0 subsystem comprises roughly 30% of system cost (212). Therefore, a reduction in field
34 strength and potential complexity (i.e. simplified cooling and maintenance) could enable an
35 attractive value system.

36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 **CONCLUDING REMARKS**

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58 MRI has historically been applied to static imaging of the brain, spine, and joints, due
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60 to its relatively slow speed. Leaps in MRI technology and information extraction over the last

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4 two decades have made it possible to image more broadly, including areas of the body that
5 experience substantial motion and even irregular motion, and including the real-time
6 guidance of interventions. RT-MRI has a rich history and an even brighter future. It is a key
7 enabling technology for MRI to penetrate new diagnostic and interventional applications.
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10 11 12 13 **ACKNOWLEDGEMENTS**

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15
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19 Supplemental Movie 15.
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TABLES

Supplemental Table 1: Imaging parameters for 22 recent 2D RT-MRI publications that utilize state-of-the-art methodology, as selected by the authors of this review. Spatial and temporal resolutions are plotted in **Figure 2**.

App / Reference	Spatial Resolution (mm ²)	Temporal Resolution (ms/fps)	Notes
Cardiac			
Kowalik et al. 2012 (62)	3.5x3.5	20 ms (50 fps)	Flow to measure cardiac time intervals (1.5T) FOV: 500 x 500 mm Trajectory: Spiral PCMR Acceleration: x10 Reconstruction: Parallel imaging (UNFOLD-ed SENSE)
Bassett et al. 2013 (20)	2.0x2.0	47 ms (21 fps)	Ventricular volumes in Tachycardia (animal model. 3T) FOV: 260x260 mm Trajectory: Cartesian bSSFP Acceleration: x8 Reconstruction: Compressed sensing (<i>k-t</i> SPARSE-SENSE)
Kowallick et al. 2014 (98)	1.3x1.3	40 ms (25 fps)	Flow during Valsalva maneuver (3T) FOV: 192x192 mm Trajectory: Radial PCMR Acceleration: ~x20 Reconstruction: Non-linear inversion (NLINV)
Haji-Valizadeh et al. 2017 (90)	2.1x2.1	32 ms (31 fps)	Ventricular volumes in myocardial infarction (1.5T) and chronic kidney disease (3T) FOV: 300x300 mm Trajectory: Radial bSSFP Acceleration: x12 Reconstruction: Compressed sensing (GRASP)
Körperich et al. 2017 (96)	2.7x2.7	25 ms (40 fps)	Flow in Fontan Circulation (3T) FOV: 300x300 mm Trajectory: EPI PCMR Acceleration: x4 (plus Partial Fourier: 0.6)

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			Reconstruction: Parallel imaging (SENSE)
Allen et al. 2018 (86)	2.0x2.0	42 ms (24 fps)	Ventricular volumes in Atrial Fibrillation (1.5T) FOV: 380x380 mm Trajectory: Cartesian bSSFP Acceleration: ~x10 Reconstruction: Compressed sensing (SPARSE-SENSE)
Steeden et al. 2018 (93)	1.7x1.7	30 ms (33 fps)	Ventricular volumes in children (1.5T) FOV: 350x350 mm Trajectory: Spiral bSSFP Acceleration: x12 Reconstruction: Compressed sensing (similar to GRASP)
Kowalik et al. 2019 (99)	1.8x1.8	27 ms (37 fps)	Flow in great vessels in children (1.5T) FOV: 450x450 mm Trajectory: Perturbed spiral PCMR Acceleration: x18 Reconstruction: Compressed sensing (similar to GRASP)
Interventional			
Unterberg-Buchwald et al. 2017 (133)	1.6x1.6	42 ms (24 fps)	Endomyocardial biopsies (animal model. 3T) FOV: 256x256 mm Trajectory: Radial bSSFP Acceleration: ~x6 Reconstruction: Non-linear inversion (NLINV) with 27ms reconstruction latency)
Rogers et al. 2017 (79)	2.2x3.3	78 – 250 ms (adjusted dynamically) (13 – 4 fps)	Diagnostic catheterization (1.5T) FOV: 400x400 mm Trajectory: Cartesian bSSFP Acceleration: x1 to x4 Reconstruction: Parallel imaging (GRAPPA)
Chubb et al. 2017 (122)	0.8x0.8	100 ms (10 fps)	Active catheterization for ablation (3D point localization of point-source microcoils. 1.5T) Sequence: Dedicated tracking sequence (modified fast-field echo)
Heidt et al. 2019 (131)	1.7x1.7	294 ms(plus 18 ms fat)	Coronary catheterization with active guidewire (3T) FOV: 275x275 mm Trajectory: Radial bSSFP

		saturation per frame) (3 fps)	Acceleration: x1.5 Reconstruction: Gridding
Upper Airway			
Niebergall et al. 2013 (157)	1.5x1.5	33.3 ms (30 fps)	Speech task (3T) FOV: 192x192 mm Trajectory: Radial (FLASH) Acceleration: ~x13.3 Reconstruction: Non-linear inversion (NLINV)
Ilitis et al. 2015 (158)	1.5x1.5	10 ms (100 fps)	Upper airway (fast tongue movements in elite horn players. 3T) FOV: 192x192 mm Trajectory: Radial (FLASH) Acceleration: ~x40 Reconstruction: Non-linear inversion (NLINV)
Lingala et al. 2016 (11)	2.4x2.4	12 ms (84 fps)	Speech task (vocal tract shaping. 1.5T) FOV: 200x200 mm Trajectory: Spiral (GRE) Acceleration: x6.5 Reconstruction: Compressed sensing (SPARSE-SENSE)
Olthoff et al.2016 (145)	1.3x1.3	40 ms (25 fps)	Swallowing task (3T) FOV: 192x192 mm Trajectory: Radial (FLASH) Acceleration: ~x10 Reconstruction: Non-linear inversion (NLINV)
Lingala et al. 2017 (54)	2.4x2.4	18 ms (56 fps)	Speech task (1.5T) FOV: 200x200 mm Trajectory: Spiral (GRE) Acceleration: x4.3 Reconstruction: Parallel imaging (Through-time GRAPPA)
Freitas et al. 2018 (155)	1.5x1.5	38 ms (26 fps)	Speech task to visualize velopharyngeal motion (3T) FOV: 190x190 mm Trajectory: Radial (FLASH) Acceleration: x2.5 Reconstruction: Total Generalized Variation

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Ruthven et al. 2019 (55)	2.4x2.4	61 ms (16 fps)	Speech task (3T) FOV: 192x192 mm Trajectory: Radial (spoiled GRE) Acceleration: x5 Reconstruction: Parallel imaging (Through-time GRAPPA)
Musculoskeletal			
Fiorentino et al. 2013 (213)	1.6x1.6	331 ms (3 fps)	Rectus Femoris Knee Muscle movement (1.5T) FOV: 400x300 mm Trajectory: 2D Cartesian (spoiled GRE) Acceleration: x1 Reconstruction: Fourier transform
Krohn et al. 2016 (180)	0.75x0.75	67 ms (15 fps)	Temporomandibular joint movement (3T) FOV: 192x192 mm Trajectory: Radial (spoiled FLASH / refocused FLASH) Acceleration: ~x14 / ~x24 Reconstruction: Non-linear inversion (NLINV)
Henrichon et al. 2020 (178)	1.1x1.1	315 ms (3 fps)	Wrist movement (3T) FOV: 120x120 mm Trajectory: 2D Radial (FLASH) Acceleration: x1 Reconstruction: Gridding

FIGURE CAPTIONS

Figure 1: Publications involving RT-MRI. PubMed search: (("real-time MRI") OR ("real-time NMR") OR ("real-time magnetic resonance") OR ("real-time interactive MRI") OR ("RT-MRI")).

Figure 2: Scatterplot of 2D RT-MRI spatial and temporal resolution. Spatial resolution (x-axis) versus temporal resolution (y-axis) is plotted from 22 recent publications that utilize state-of-the-art methodology, as selected by the authors of this review, summarized in **Supplemental Table 1**. The gray shaded bar indicates the general spatio-temporal resolution tradeoff. All substantial deviations are due to variations in the field-of-view, use of parallel imaging, use of reconstruction constraints, and minimum acceptable signal-to-noise ratio.

Figure 3: Common sequences, sampling trajectories, and view orders used in 2D RT-MRI. **(A)** sequence diagrams of spoiled GRE and bSSFP, and the steady-state signal amplitude as a function of off-resonance Δf ; Simulation parameters: TR=5 ms; flip angle = 5° for spoiled GRE; flip angle = 60° for bSSFP; myocardium T1/T2=950/50 ms; blood T1/T2=1500/250 ms (representative of 1.5T). **(B)** Non-Cartesian sampling trajectories of undersampled radial, single-shot spiral, and single-shot EPI. **(C)** View orders of multi-shot spiral of conventional 13-interleaf bit-reversed and golden-ratio, and unaliased FOV as a function of the number of interleaves [Reproduced from Ref (25)].

Figure 4: Illustration of cardiovascular RT-MRI. **(A)** Real-time cine imaging using tiny-golden angle radial bSSFP sequence at 1.5T, with 12x undersampling and compressive sensing reconstruction (TE/TR = 1.3/2.7 ms, flip angle = 70° , in-plane resolution = 2.1 mm, 32 ms temporal resolution, 31 fps). A movie can be found in **Supplemental Movie 1** [Adapted from Ref (90)]. **(B)** Real-time PCMR using perturbed spirals at 1.5T, with 18x undersampling and compressive sensing reconstruction. Top: Magnitude images, Bottom: Phase images (TE/TR = 1.9/6.7 ms, VENC = 200 cm/s, flip angle = 20° , in-plane resolution = 1.8 mm, 27 ms temporal resolution, 37 fps). A movie can be found in **Supplemental Movie 2** [Adapted from Ref (99)]. **(C)** Real-time imaging of the fetal heart (shown by arrow in first column) demonstrating gross fetal movement. Golden-angle radial bSSFP sequence at 1.5T, with 27x undersampling

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4 and compressive sensing reconstruction (TR = 5.0 ms, flip angle = 70°, in-plane resolution =
5 1.0 mm, 74 ms temporal resolution, 14 fps). A movie can be found in **Supplemental Movie 3**
6 [Adapted from Ref (109)].
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11 **Figure 5:** Illustrations of RT-MRI for MRI-guided invasive procedures. Cardiovascular
12 procedures are the most technically demanding for RT-MRI, and therefore are provided. **(A)**
13 The position and orientation of catheter devices with two embedded microcoils are tracked
14 on a previously acquired 3D volume for an electrophysiology procedure. Real-time device
15 tracing is achieved using 3D gradient echo projection imaging (resolution 0.83mm, 10Hz
16 tracking rate) [Reproduced from Ref (122)]. **(B)** Interactive RT-MRI used to navigate
17 gadolinium filled balloon wedge end-hole catheter during diagnostic right heart
18 catheterization (bSSFP, TE/TR = 1.44/2.88 ms, flip angle = 40°, in-plane resolution = 1.8 mm x
19 2.4 mm, GRAPPA rate 2, 200 ms temporal resolution, 5 fps) [Adapted from Ref (123)]. **(C)** Real-
20 time MRI thermometry used to calculate thermal dose during therapeutic ablation procedure
21 (Gradient echo EPI, TE/TR = 18-20/110 ms, flip angle = 60°, in-plane resolution = 1.6 mm x 1.6
22 mm, GRAPPA rate 2, 200 ms temporal resolution, 5 slices/s) [Adapted from Ref (134)].
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35 **Figure 6:** Illustration of upper airway RT-MRI. **(A)** Speech production imaging using 13-
36 interleaved spiral GRE sequence at 1.5T (TE/TR = 0.8/6.0 ms, flip angle = 15°, in-plane
37 resolution = 2.4 mm, 12 ms temporal resolution, 83 fps) [Adapted from Ref (214)]. **(B)** Sleep
38 apnea study using simultaneous multi-slice radial GRE sequence at 3T (TE/TR = 3.7/6.5 ms,
39 flip angle = 5°, slice thickness/gap = 7/3 mm, 3 slices, in-plane resolution = 1 mm, 96 ms
40 temporal resolution, 10 fps) [Adapted from Ref (37)]. **(C)** Swallowing imaging of 10ml
41 pineapple juice using radial FLASH sequence (TE/TR = 1.33/2.10ms, flip angle = 8°, in-plane
42 resolution = 1.3 mm, 40 ms temporal resolution, 25 fps, 19 spokes) [Adapted from Ref (145)].
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51 **Figure 7:** Illustration of three Musculoskeletal RT-MRI applications. **(A)** Knee RT-MRI
52 highlighting flexion, extension, and the measurement of rectus femoris knee muscle moment
53 arms [Adapted from Ref (213)]. **(B)** Wrist RT-MRI illustrating a radial-ulnar deviation
54 maneuver, suitable for measuring dynamics of the scapholunate gap [Adapted from Ref
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4 (177)]. **(C)** Temporomandibular joint RT-MRI illustrating the ability to track condyle movement
5 during voluntary opening of the mouth [Adapted from Ref (180)].
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10 **Figure 8:** Illustration of three ML/AI-based low-latency applications. **(A)** Image reconstruction
11 of cardiovascular imaging; (left-to-right) the BH-bSSFP sequence and the RT radial sequence
12 reconstructed with gridding, GRASP, and the residual U-Net. [Adapted from Ref (92)] **(B)** Spiral
13 off-resonance deblurring of speech imaging; (left-to-right) GT, uncorrected, IR with GT field
14 map, and the CNN. [Adapted from Ref (77)] **(C)** Needle detection and segmentation for ex
15 vivo tissue RT-MRI; (left-to-right) Original image, needle detection and segmentation result
16 using Mask R-CNN, result comparison against a reference. [Adapted from Ref (205)]. Note
17 that “processing time” shown here is the time to run the neural networks and does not
18 include the time to do the pre-processing of the data. (BH: breath-hold, GRASP: Golden-angle
19 RAdial Sparse Parallel imaging, PT: processing time, GT: ground truth, IR: iterative
20 reconstruction)
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32 **Figure 9:** Demonstration of real-time bSSFP imaging using a high-performance low field
33 (HPLF) MRI system (prototype 0.55T Aera, Siemens Healthcare, Erlangen, Germany). **(A)** Real-
34 time bSSFP for MRI-guided invasive cardiovascular procedures (TE/TR = 2.0/4.0 ms, flip angle
35 = 45°, in-plane resolution = 2mm, slice thickness = 8mm, GRAPPA rate 2, 250 ms temporal
36 resolution, 4 fps). **(B)** Real-time bSSFP for dynamic intestinal imaging (TE/TR = 1.6/3.2ms, flip
37 angle = 90°, in-plane resolution = 1.2mm, slice thickness = 10mm, GRAPPA rate 3, 1.2s
38 temporal resolution for 6 slices, 0.8 fps). **(C)** Real-time bSSFP for dynamic respiratory imaging
39 (TE/TR = 1.21/2.4ms, flip angle = 70°, in-plane resolution = 1.8mm, slice-thickness = 15mm,
40 GRAPPA rate 2, 250 ms temporal resolution, 4 fps). Due to the reduced susceptibility, higher
41 quality imaging of lung parenchyma is feasible.
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SUPPLEMENTAL MOVIE CAPTIONS

Supplemental Movie 1: Real-time cine imaging using tiny-golden angle radial bSSFP sequence at 1.5T, with 12x undersampling and compressive sensing reconstruction (TE/TR = 1.3/2.7ms, flip angle = 70°, in-plane resolution = 2.1 mm, 32 ms temporal resolution, 31 fps) [Reproduced from Ref (90)].

Supplemental Movie 2: Real-time PCMR using perturbed spirals at 1.5T, with 18x undersampling and compressive sensing reconstruction. Top: Magnitude images, Bottom: Phase images (TE/TR = 1.9/6.7 ms, VENC = 200 cm/s, flip angle = 20°, in-plane resolution = 1.8 mm, 27 ms temporal resolution, 37 fps) [Reproduced from Ref (99)].

Supplemental Movie 3: Real-time imaging of the fetal heart (shown by arrow in first column) demonstrating gross fetal movement. Golden-angle radial bSSFP sequence at 1.5T, with 27x undersampling and compressive sensing reconstruction (TR = 5.0 ms, flip angle = 70°, in-plane resolution = 1.0 mm, 74 ms temporal resolution, 14 fps) [Reproduced from Ref (109)].

Supplemental Movie 4: Real-time device tracing achieved using 3D fast-field echo projection imaging (spatial resolution 0.83mm, 100 ms temporal resolution, 10 fps). The position and orientation of catheter devices with two embedded microcoils are tracked on a previously acquired 3D volume for an electrophysiology procedure. [Reproduced from Ref (122)]

Supplemental Movie 5: Interactive real-time Cartesian bSSFP imaging used to guide a gadolinium-filled balloon wedge catheter during diagnostic right heart catheterization procedure. Interactive modification of slice planes, number of multiplanar image slices, saturation pulse, and acceleration are demonstrated. bSSFP, TE/TR = 1.44/2.88 ms, flip angle = 40°, in-plane resolution = 1.8 mm x 2.4 mm, GRAPPA rate 2, 200 ms temporal resolution, 5 fps. RV: Right Ventricle, MPA: Main pulmonary artery, RPA: right pulmonary artery. [Reproduced from Ref (123)]

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4 **Supplemental Movie 6:** Real-time cardiac MR thermometry used for inline monitoring of
5 heat dose during therapeutic radiofrequency ablation (70W for 40s), demonstrated in an
6 animal model. Gradient echo EPI, TE/TR = 18-20/110 ms, flip angle = 60°, in-plane resolution
7 = 1.6 mm x 1.6 mm, GRAPPA rate 2, 200 ms temporal resolution, 5 slices/s. [Adapted from
8 Ref (134)]
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15 **Supplemental Movie 7:** RT-MRI of speech production (fluent speech – rainbow passage) using
16 13-interleave spiral GRE sequence at 1.5T (TE/TR = 0.8/6ms, flip angle = 15°, in-plane
17 resolution = 2.4 mm, 12 ms temporal resolution, 83 fps) [Reproduced from Ref (11)].
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22 **Supplemental Movie 8:** RT-MRI of sleep apnea events using simultaneous multi-slice radial
23 GRE sequence at 3T (TE/TR = 3.7/6.5 ms, flip angle = 5°, slice thickness/gap = 7/3 mm, 3 slices,
24 in-plane resolution = 1 mm, 96 ms temporal resolution, 10 fps) [Reproduced from Ref (37)].
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29 **Supplemental Movie 9:** RT-MRI of swallowing imaging of 10ml pineapple juice using radial
30 FLASH sequence (TE/TR = 1.33/2.10ms, flip angle = 8°, in-plane resolution = 1.3 mm, 40 ms
31 temporal resolution, 25 fps, 19 spokes) [Reproduced from Ref (145)].
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36 **Supplemental Movie 10:** Knee RT-MRI highlighting flexion, extension, and the measurement
37 of rectus femoris knee muscle moment arms [Reproduced from Ref (213)].
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42 **Supplemental Movie 11:** Wrist RT-MRI illustrating a radial-ulnar deviation maneuver,
43 suitable for measuring dynamics of the scapholunate gap [Reproduced from Ref (177)].
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48 **Supplemental Movie 12:** Temporomandibular joint RT-MRI illustrating the ability to track
49 condyle movement during voluntary opening of the mouth [Reproduced from Ref (180)].
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54 **Supplemental Movie 13:** Illustration of ML/AI based low-latency Image reconstruction of
55 cardiovascular imaging; Examples from two prospective patients; (left-to-right) the BH-bSSFP
56 sequence and the RT radial sequence reconstructed with GRASP, the residual U-Net, and
57 gridding. [Adapted from Ref (92)]
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Supplemental Movie 14: Illustration of ML/AI based low-latency Spiral off-resonance deblurring of speech imaging; (left-to-right) GT, uncorrected, IR with GT field map, and the CNN. [Adapted from Ref (77)]

Supplemental Movie 15: Real-time bSSFP imaging using a high-performance low field (HPLF) MRI system (prototype 0.55T Aera, Siemens Healthcare, Erlangen, Germany). **(A)** Real-time bSSFP for MRI-guided invasive cardiovascular procedures (TE/TR = 2.0/4.0 ms, flip angle = 45°, in-plane resolution = 2 mm, slice thickness = 8 mm, GRAPPA rate 2, 250 ms temporal resolution, 4 fps). **(B)** Real-time bSSFP for dynamic intestinal imaging (TE/TR = 1.6/3.2ms, flip angle = 90°, in-plane resolution = 1.2 mm, slice thickness = 10 mm, GRAPPA rate 3, temporal resolution 1.2 s for 6 slices). **(C)** Real-time bSSFP for dynamic respiratory imaging (TE/TR = 1.21/2.4 ms, flip angle = 70, in-plane resolution = 1.8 mm, slice-thickness = 15 mm, GRAPPA rate 2, 250 ms temporal resolution, 4 fps). [(A) Based on Ref (210), (B) and (C) Unpublished Data]

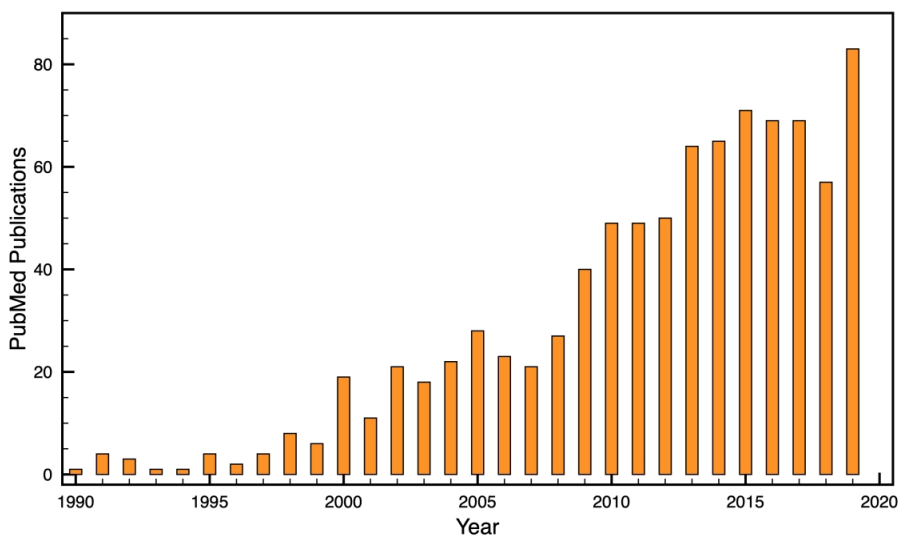


Figure 1: Publications involving RT-MRI. PubMed search: ("real-time MRI") OR ("real-time NMR") OR ("real-time magnetic resonance") OR ("real-time interactive MRI") OR ("RT-MRI").

1071x636mm (72 x 72 DPI)

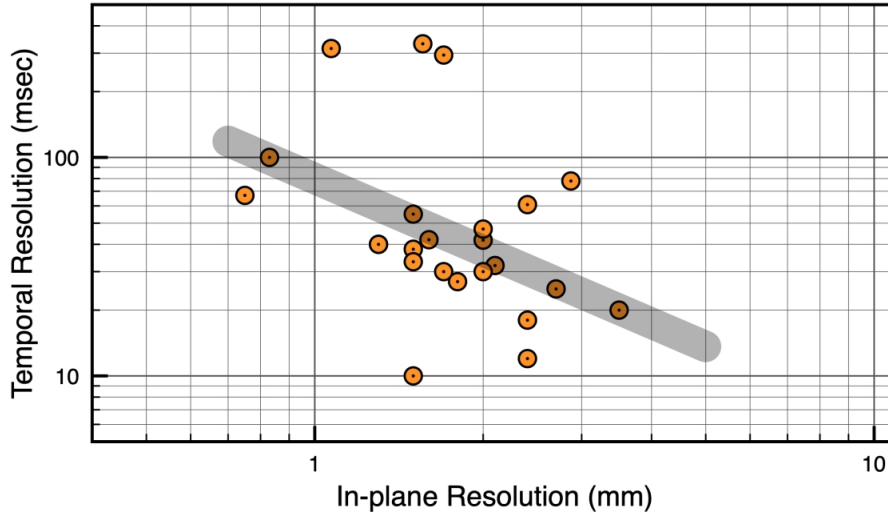


Figure 2: Scatterplot of 2D RT-MRI spatial and temporal resolution. Spatial resolution (x-axis) versus temporal resolution (y-axis) is plotted from 22 recent publications that utilize state-of-the-art methodology, as selected by the authors of this review, summarized in Supplemental Table 1. The gray shaded bar indicates the general spatio-temporal resolution tradeoff. All substantial deviations are due to variations in the field-of-view, use of parallel imaging, use of reconstruction constraints, and minimum acceptable signal-to-noise ratio.

822x478mm (72 x 72 DPI)

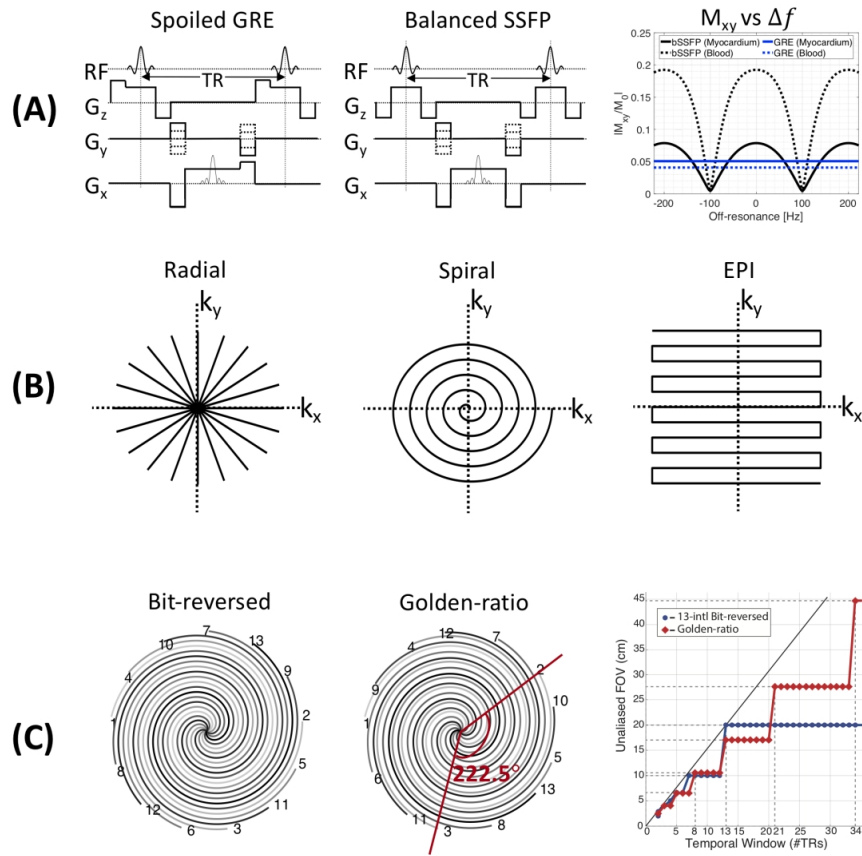


Figure 3: Common sequences, sampling trajectories, and view orders used in 2D RT-MRI. (A) sequence diagrams of spoiled GRE and bSSFP, and the steady-state signal amplitude as a function of off-resonance Δf ; Simulation parameters: TR=5ms; flip angle = 5° for spoiled GRE; flip angle = 60° for bSSFP; myocardium T1/T2=950/50ms; blood T1/T2=1500/250ms (representative of 1.5T). (B) Non-Cartesian sampling trajectories of undersampled radial, single-shot spiral, and single-shot EPI. (C) View orders of multi-shot spiral of conventional 13-interleaf bit-reversed and golden-ratio, and unaliased FOV as a function of the number of interleaves [Reproduced from Ref (25)].

179x177mm (300 x 300 DPI)

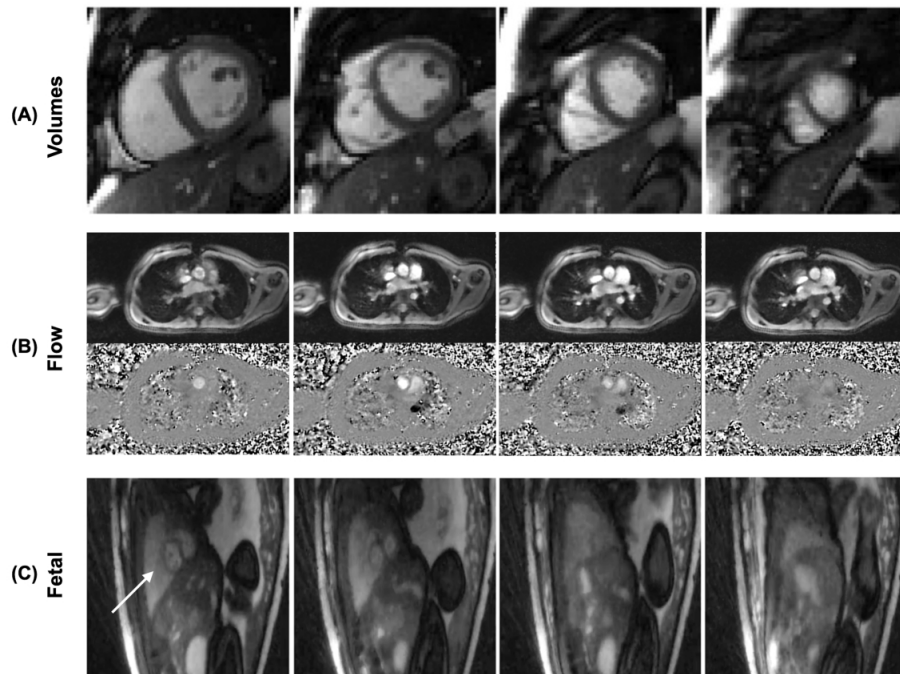


Figure 4: Illustration of cardiovascular RT-MRI. (A) Real-time cine imaging using tiny-golden angle radial bSSFP sequence at 1.5T, with 12x undersampling and compressive sensing reconstruction (TE/TR = 1.3/2.7 ms, flip angle = 70°, in-plane resolution = 2.1 mm, 32 ms temporal resolution, 31 fps). A movie can be found in Supplemental Movie 1 [Adapted from Ref (90)]. (B) Real-time PCMR using perturbed spirals at 1.5T, with 18x undersampling and compressive sensing reconstruction. Top: Magnitude images, Bottom: Phase images (TE/TR = 1.9/6.7 ms, VENC = 200 cm/s, flip angle = 20°, in-plane resolution = 1.8 mm, 27 ms temporal resolution, 37 fps). A movie can be found in Supplemental Movie 2 [Adapted from Ref (99)]. (C) Real-time imaging of the fetal heart (shown by arrow in first column) demonstrating gross fetal movement. Golden-angle radial bSSFP sequence at 1.5T, with 27x undersampling and compressive sensing reconstruction (TR = 5.0 ms, flip angle = 70°, in-plane resolution = 1.0 mm, 74 ms temporal resolution, 14 fps). A movie can be found in Supplemental Movie 3 [Adapted from Ref (109)].

149x111mm (600 x 600 DPI)

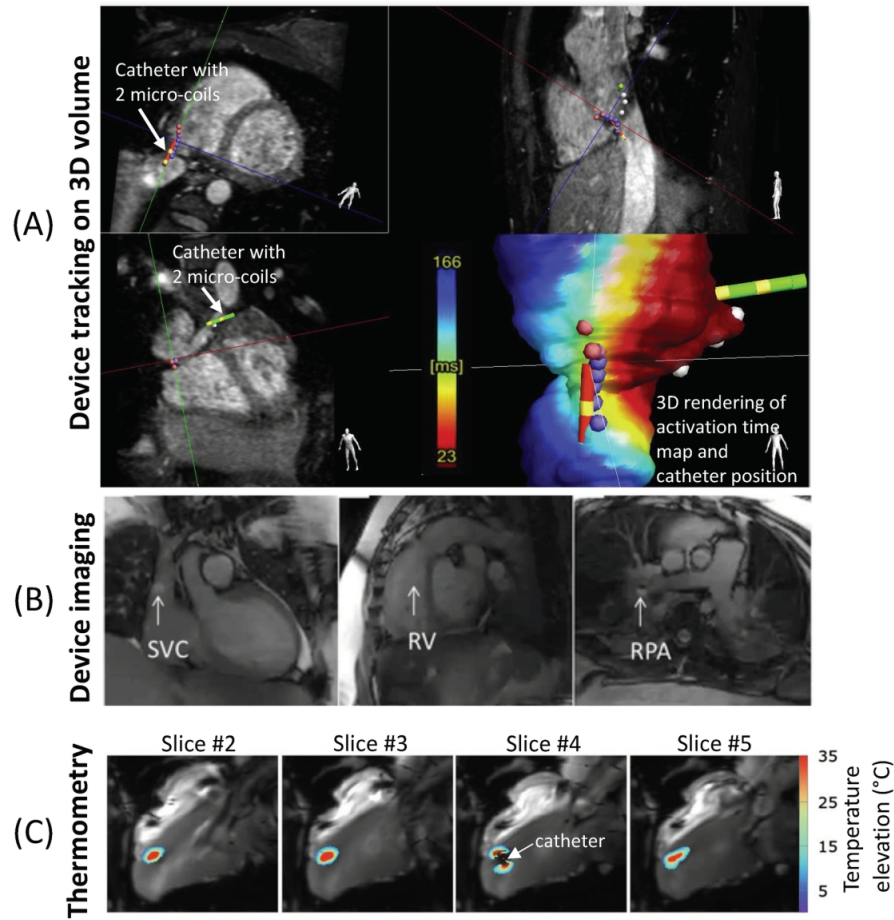


Figure 5: Illustrations of RT-MRI for MRI-guided invasive procedures. Cardiovascular procedures are the most technically demanding for RT-MRI, and therefore are provided. (A) The position and orientation of catheter devices with two embedded microcoils are tracked on a previously acquired 3D volume for an electrophysiology procedure. Real-time device tracing is achieved using 3D gradient echo projection imaging (resolution 0.83mm, 10Hz tracking rate) [Reproduced from Ref (122)]. (B) Interactive RT-MRI used to navigate gadolinium filled balloon wedge end-hole catheter during diagnostic right heart catheterization (bSSFP, TE/TR = 1.44/2.88 ms, flip angle = 40°, in-plane resolution = 1.8 mm x 2.4 mm, GRAPPA rate 2, 200 ms temporal resolution, 5 fps) [Adapted from Ref (123)]. (C) Real-time MRI thermometry used to calculate thermal dose during therapeutic ablation procedure (Gradient echo EPI, TE/TR = 18-20/110 ms, flip angle = 60°, in-plane resolution = 1.6 mm x 1.6 mm, GRAPPA rate 2, 200 ms temporal resolution, 5 slices/s) [Adapted from Ref (134)].

158x161mm (300 x 300 DPI)

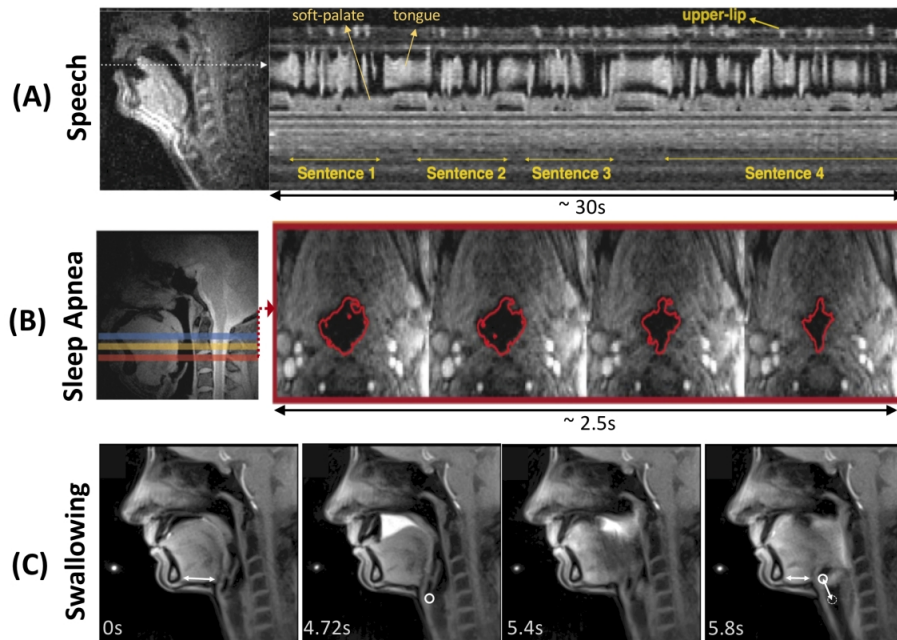


Figure 6: Illustration of upper airway RT-MRI. (A) Speech production imaging using 13-interleave spiral GRE sequence at 1.5T (TE/TR = 0.8/6.0 ms, flip angle = 15°, in-plane resolution = 2.4 mm, 12 ms temporal resolution, 83 fps) [Adapted from Ref (214)]. (B) Sleep apnea study using simultaneous multi-slice radial GRE sequence at 3T (TE/TR = 3.7/6.5 ms, flip angle = 5°, slice thickness/gap = 7/3 mm, 3 slices, in-plane resolution = 1 mm, 96 ms temporal resolution, 10 fps) [Adapted from Ref (37)]. (C) Swallowing imaging of 10ml pineapple juice using radial FLASH sequence (TE/TR = 1.33/2.10ms, flip angle = 8°, in-plane resolution = 1.3 mm, 40 ms temporal resolution, 25 fps, 19 spokes) [Adapted from Ref (145)].

208x156mm (300 x 300 DPI)

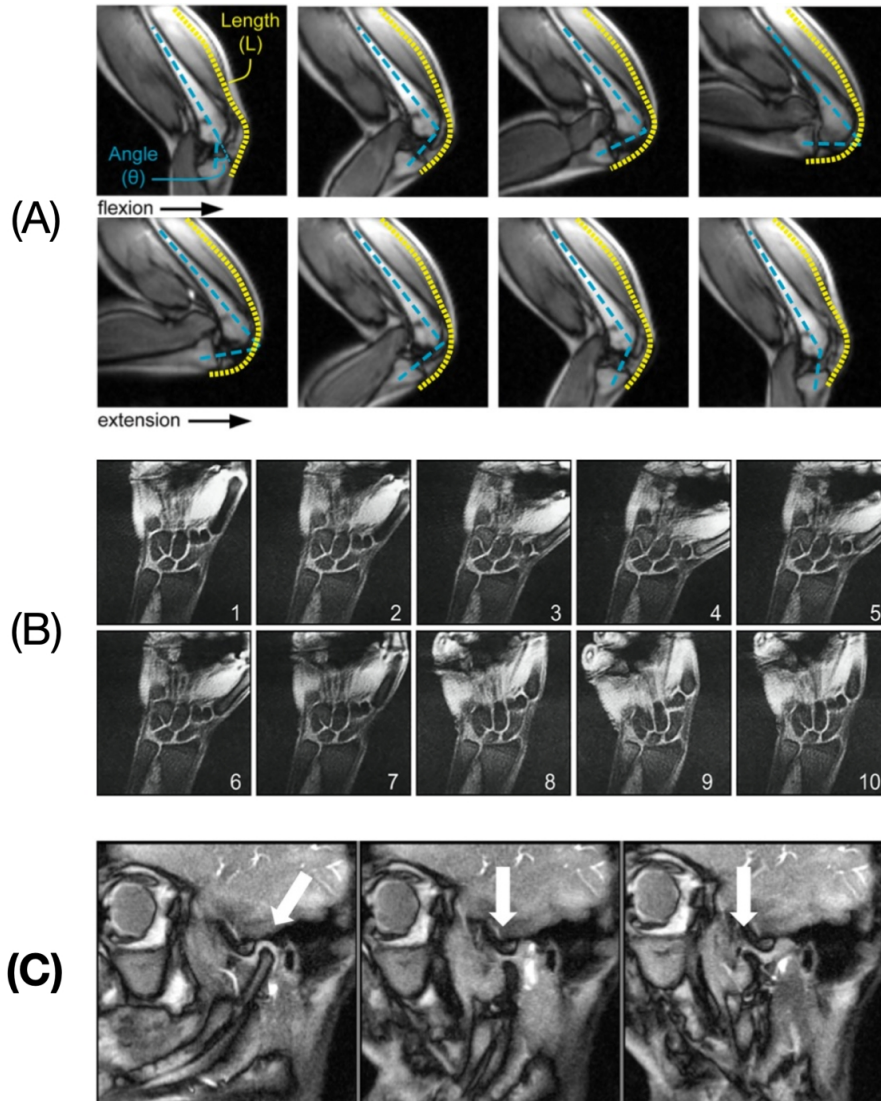


Figure 7: Illustration of three Musculoskeletal RT-MRI applications. (A) Knee RT-MRI highlighting flexion, extension, and the measurement of rectus femoris knee muscle moment arms [Adapted from Ref (213)]. (B) Wrist RT-MRI illustrating a radial-ulnar deviation maneuver, suitable for measuring dynamics of the scapholunate gap [Adapted from Ref (177)]. (C) Temporomandibular joint RT-MRI illustrating the ability to track condyle movement during voluntary opening of the mouth [Adapted from Ref (180)].

166x202mm (300 x 300 DPI)

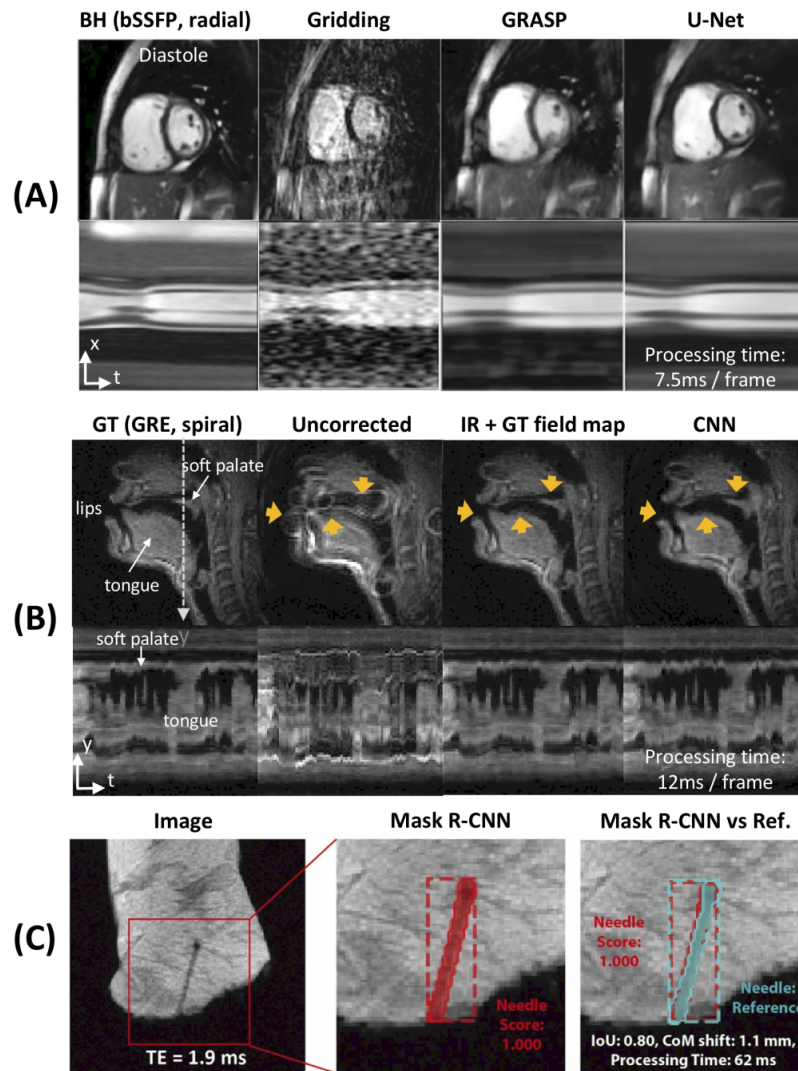


Figure 8: Illustration of three ML/AI-based low-latency applications. (A) Image reconstruction of cardiovascular imaging; (left-to-right) the BH-bSSFP sequence and the RT radial sequence reconstructed with gridding, GRASP, and the residual U-Net. [Adapted from Ref (92)] (B) Spiral off-resonance deblurring of speech imaging; (left-to-right) GT, uncorrected, IR with GT field map, and the CNN. [Adapted from Ref (77)] (C) Needle detection and segmentation for ex vivo tissue RT-MRI; (left-to-right) Original image, needle detection and segmentation result using Mask R-CNN, result comparison against a reference. [Adapted from Ref (205)]. Note that "processing time" shown here is the time to run the neural networks and does not include the time to do the pre-processing of the data. (BH: breath-hold, GRASP: Golden-angle Radial Sparse Parallel imaging, PT: processing time, GT: ground truth, IR: iterative reconstruction)

160x215mm (300 x 300 DPI)

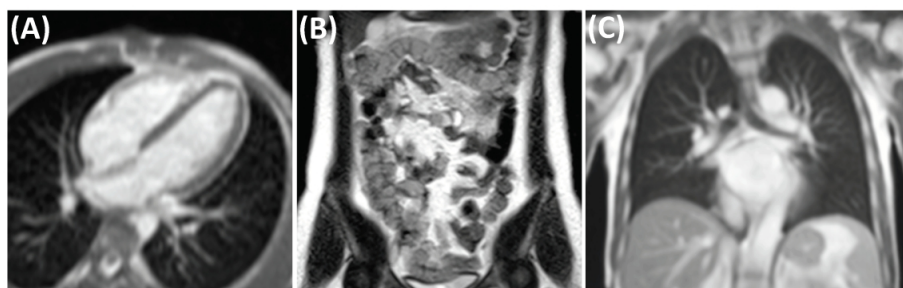


Figure 9: Demonstration of real-time bSSFP imaging using a high-performance low field (HPLF) MRI system (prototype 0.55T Aera, Siemens Healthcare, Erlangen, Germany). (A) Real-time bSSFP for MRI-guided invasive cardiovascular procedures (TE/TR = 2.0/4.0 ms, flip angle = 45°, in-plane resolution = 2mm, slice thickness = 8mm, GRAPPA rate 2, 250 ms temporal resolution, 4 fps). (B) Real-time bSSFP for dynamic intestinal imaging (TE/TR = 1.6/3.2ms, flip angle = 90°, in-plane resolution = 1.2mm, slice thickness = 10mm, GRAPPA rate 3, 1.2s temporal resolution for 6 slices, 0.8 fps). No bSSFP banding around the intestines is observed using the HPLF system configuration. (C) Real-time bSSFP for dynamic respiratory imaging (TE/TR = 1.21/2.4ms, flip angle = 70°, in-plane resolution = 1.8mm, slice-thickness = 15mm, GRAPPA rate 2, 250 ms temporal resolution, 4 fps). Due to the reduced susceptibility, higher quality imaging of lung parenchyma is feasible.

338x108mm (247 x 247 DPI)