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SCMR Edition 2020

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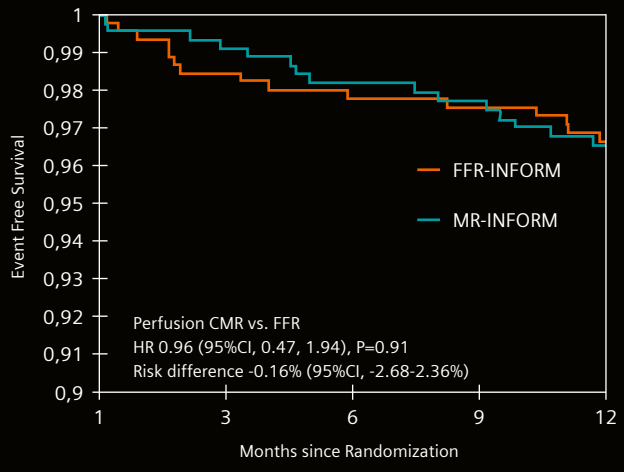

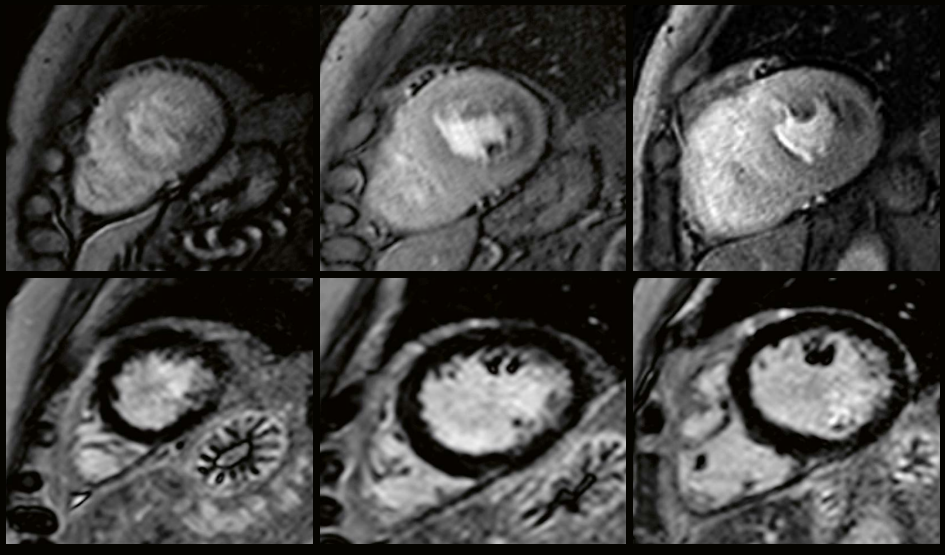

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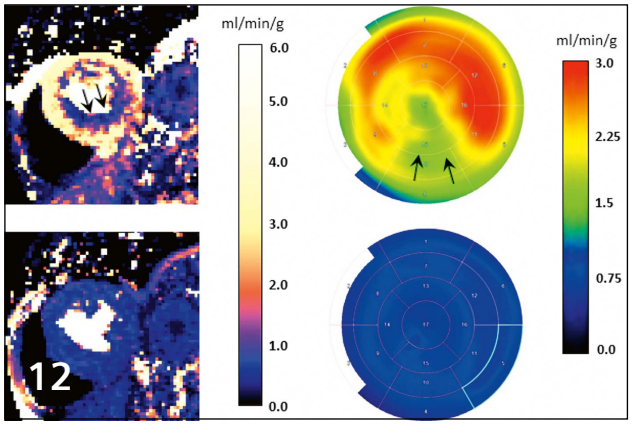
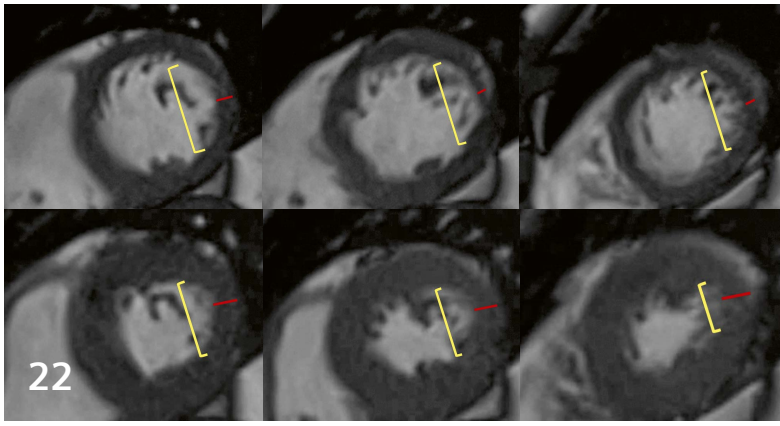


Quantitative CMR Perfusion Mapping[1]

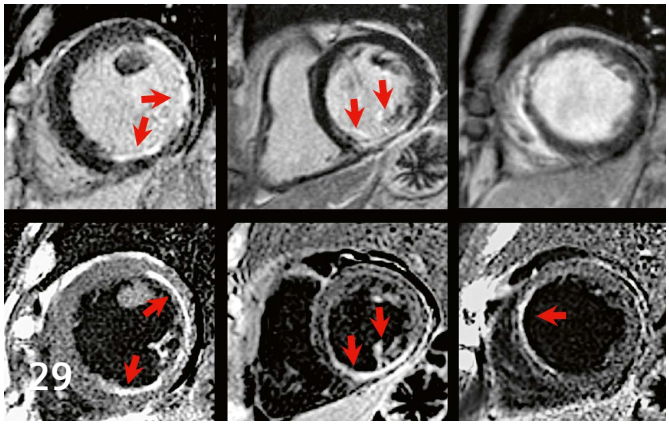


CMR for Ischaemia and Viability Detection in Coronary CTO

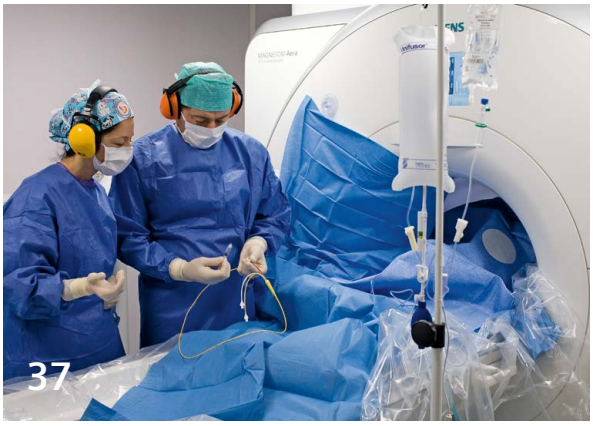
Editorial Comment

Cardiovascular Imaging

Interventional CMR



Flow-Independent Dark-Blood Delayed Enhancement (FIDDLE)[3]



Interventional CMR

Spotlight

Meet Siemens Healthineers

Cover courtesy of MR-INFORM Investigators.

[1]*Customer developed prototype. The product is under development and not commercially available yet. Its future availability cannot be ensured.*

[2]*The information shown herein refers to products of a 3rd party and thus are in their regulatory responsibility. Please contact the 3rd party for further information.*

[3]*The product is under development and not commercially available yet. Its future availability cannot be ensured.*

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Dear readers and colleagues,

It is a great honour to contribute as Editor of the MAGNETOM Flash SCMR 2020 Edition. Writing this as the decade is coming to a close, I chose to reflect about what are the things in store for cardiac MRI. As the merciless pace of the digital revolution in cardiology and healthcare at large heralds disruption and causes uncertainty, how will this affect the cardiac MRI field? Will this huge engineering achievement withstand the emerging digital apps at our fingertips [1]? Will the primary weakness of cardiac MRI, its enormous complexity and lack of scalability beyond the hands of experts, set its limitation? Or will the electricity-hungry magnets soon pose social and ecological problems? Can they be run by some source of renewable energy [2]? While these thoughts may sound perturbing, the field of cardiac MRI has also been an undeniable front-cover success story for over two decades, coping with a number of diverse challenges. As we celebrate the many achievements of cardiac MRI, we also will revisit some of the most pressing challenges to get a better sense of future direction.

CMR can provide a plethora of diagnostic information, but can it also guide clinical management?

Cardiac MRI is a masterpiece of healthcare engineering, and at the same time, the crown jewel of evidence-based imaging diagnosis. It never has been the usual R&D story, a spin-off with colossal growth, eventually taken over by big industry. Rather, CMR has remained in a distinguished niche, a niche which has given everyone space to thrive, to harness the demanding MRI physics and engineering, and the shelter to co-develop a more sustainable model for a complex technology. Once it achieved the impossible, i.e. seeing the beating heart, it did not cease to fascinate – seeing the heart in its entirety, in action, in-depth. Clinicians were quick to appreciate its particular clinically advantageous features; the accuracy, the absence of radiation, needles or rib-poking probes, but most of all, unlike any other imaging modality, the non-invasive histology, practically on the go. Clinicians also helped to enshrine these important and clinically relevant opportunities in the substantial body of clinical evidence – which is beyond due diligence – the validation work, clinical comparative and effectiveness studies, vouching for the precision, the quality and the depth of its clinical meaning [3].

Yet, the benefits of CMR remain a tricky sell when it comes to the mainstream clinical world. In reality, cardiac MRI is often the second to third line diagnostic technique, despite its obvious advantages, superior evidence and informative diagnostic readouts. Unlike any other diagnostic imaging, cardiac MRI remains too complex to be 'traditionally scalable' i.e. squeezed in between the largely self-driving 'knees and spines'. As such, it will be naturally turned to very late in the course of disease, after a long series of diagnostic procedures, and typically, much procrastination and deliberation about its potential benefits. The eventual 'go' frequently consists of an over-extensive wide-cast-net exam, trying to solve the riddle of a heart condition that remains not fully understood. The resulting lengthy nature of the eventual exam sets can

make cardiac MRI a "once in a lifetime" experience. In their own words, the weary patients having experienced little in a way of direct benefit from the first exam, will reproducibly express scepticism if asked to submit themselves to yet another lengthy exam. Clearly, cardiac MRI on such terms bears little appeal beyond the single use, a far cry from a routine diagnostic means, which could also serially monitor disease progress and the effects of treatment.

Clinical evidence must link CMR with improving patient outcome

A number of things can (and must!) help us to urgently evise this situation. We must celebrate the successes of the 2019 studies, including MR-Inform, Spins and the yet-to-be published Gadacad, as they recognisably add to and boost to our common cause. Other important unresolved aspects include uncertain long-term business prospects of the field, related to the largely non-existent reimbursement in most countries. The poorly vetted short-term commercial interests – huge expenses for scanners, still rather complex and time-consuming postprocessing softwares and the overwhelming maintenance charges, resonate with the convoluted arguments about the high costs of the technique. Perhaps the most important lesson here is the realization that it continues to be the massive enthusiasm together with the selfless face of medical vocation that presently sustains this field. These issues collectively hinder the realization of the accomplished hard work and ingenuity, making the path to roll-out the benefits of cardiac MRI rather stony.

On a positive note, the cardiology practice guidelines are evolving, and the role assigned to cardiac MRI is growing. Admittedly, the phrasing remains careful. CMR is at best described as 'a promising' diagnostic tool with a 'great potential' to illuminate the underlying aetiology of heart disease. This rather reserved stance about cardiac MRI continues to be defended by the many contraindications to MRI (although in reality only a few still persist) and the perceived lack of availability (a term used to summarily denote a lack of scanner access, skill and expertise). Interestingly, this argument is in stark contrast with the view that the overall MRI market is already saturated in terms of satisfying the imaging needs with an average 12–15 units per million inhabitants as is the situation the EU (with Germany leading at 35 units per million capita) [4]. Elsewhere, the highest per capita number of MRI units include Japan (n = 55), followed by the U.S. (n = 38). Approximately 5000 additional units are being produced each year, and many existing machines are being refitted and upgraded to keep them going. So, no lack of machines, or so it would seem. Furthermore, there is a well-rehearsed argument about overuse and so-called 'unnecessary' MRI imaging, since the incidence of the overall morbidity and mortality has not been reduced in keeping with constant increase in imaging over the years. Clearly, such arguments are based on the misconception that imaging the disease somehow equates with a cure. Unlike drugs or medical devices, diagnostic tests are not required to provide evidence that their use can positively enhance treatment strategy and patient outcome. The breakdown of organ-specific MRI scans is even more enlightening. Currently, the prevalent deployment of MRI units is for imaging of brain, spine and extremities (altogether 70% of scanner utilization worldwide), whereas cardiac MRI amounts to only 1% of all imaging [4]. In fact, this prioritization of non-cardiac indications may explain the lack of relationship between overall imaging and mortality, as current efforts cannot counter the magnitude of problems created by heart disease, the major contributor to morbidity and mortality worldwide.

A regulatory requirement for a more evidenced-based approach to imaging evaluated in terms of clinical effectiveness in delivery of medical care such as guiding treatment to change outcomes might in fact be of tremendous benefit to cardiac MRI. Something similar to the concept of companion diagnostics, where diagnostic testing which can be shown to guide effective treatment receives a licenced indication for its application. This concept could be beneficially expanded to all imaging modalities to distinguish between the methods available. This would ensure the best deployment of resources for a wider population. In other words, the current absence of regulatory pressure is eloquently exposed by an average level of evidence C supporting cardiac imaging in clinical guidelines, equating with expert consensus and not supported by evidence of improved outcome. In fact, there has never been a better opportunity for randomized clinical trials to demonstrate the benefit of cardiac CMR against a weak conventional standard of care, which is often either invasive, reliant on radiation or simply non-diagnostic [5].

CMR is particularly suited for assessing both ischaemic and non-ischaemic cardiomyopathies

The nature of heart disease has changed thanks to the considerable advances that have helped reduce the deadly share of ischaemic heart disease. With effective prevention and treatment of acute coronary syndromes, non-ischaemic cardiomyopathies now increasingly prevail as the cause of heart failure. Efforts to improve diagnostic approaches to the latter have been rather unsuccessful for several reasons. Firstly, these conditions are difficult to detect with the current first line diagnostic tools, such as echocardiography, which at best can recognize wall-motion abnormalities or severe systolic dysfunction, both of which

The unique capabilities of CMR are the essential must-haves of a modern diagnostic toolbox, primarily consisting of myocardial perfusion, late gadolinium enhancement (LGE) imaging and myocardial tissue mapping.

are hallmarks of ischaemic heart disease. On the contrary, non-ischaemic cardiac cardiomyopathies are characterized by a slow evolution of intrinsic global and diffuse myocardial changes over many months or even decades, with the pumping function being long preserved. Also, the onset of these conditions is not punctuated by the textbook 'heart-related' symptoms modelled on patients experiencing a heart attack. Rather, the symptoms ensue after decades of a subclinical course due to eventual development of heart failure, essentially synonymous with the advanced disease stages. The understanding of a modern cardiac patient is crucial to avoid the pitfalls of the classical approach to heart failure, which deliberates the recognition of the heart disease worthy of treatment to the late stages.

Clearly, this is also tantamount to the state of evidence for current treatment, as all trials have focused on these late disease stages, frequently beyond the remedial tipping point. Cardiac MRI has played an enormous role in bringing to light the above-mentioned pathophysiology, the in-depth understanding of non-ischaemic heart conditions, by recording the in-vivo patterns of tissue changes in symptomatic patients with overt heart failure [6], and increasingly, by collecting the phenotypical snapshots of disease evolution in subclinical stages [7]. This has led to important novel discoveries, including characterization of the relevant tissue substrates that drive disease and determine the prognosis. These unique diagnostic abilities are the essential must-haves of a modern diagnostic toolbox, primarily consisting of myocardial perfusion, late gadolinium enhancement (LGE) imaging and myocardial tissue mapping (as exemplified by the GoetheCVI® Examcard[1]).

Myocardial perfusion is essentially a concept transferred from another imaging modality, but much improved through high-spatial resolution and a better contrast afforded by gadolinium contrast agents [8]. Myocardial perfusion with CMR is the most accurate non-invasive functional test to determine the presence of relevant ischaemia, and of recently, to guide treatment with revascularization. The MR-INFORM clinical trial used a randomized clinical trial design to demonstrate that patients presenting with typical angina have a similar 1-year outcome, when receiving non-invasive treatment-guidance with cardiac MRI compared to invasive catheterization with FFR measurement [9]. LGE can visualize myocardial scar and its pattern, and by this recording the overall brunt, the cumulative toll of the disease, as well as the underlying aetiology [10–13]. The 2016 ESC guidelines for heart failure specifically highlight the role of CMR with LGE with regards to the type of scar (when present) in differentiation between the ischaemic vs. non-ischaemic pathophysiology [14]. A further advance comes by way of quantitative tissue characterization using T1 and T2 mapping. These magnificent imaging tools of non-invasive histology took their initial hints from the concept of myocardial T2* imaging in cardiac iron overload [15]. These quantifiable diagnostic tests are unique in providing the absolute values of myocardial tissue measurements, which reveal the presence of disease, reflect the disease character by indicating the underlying tissue substrate, as well as disease activity and stage of disease [5]. The mapping tools, more than anything else in cardiac MRI, build on its primary asset, to inform about the underlying pathophysiology – while the disease is still developing and as such potentially reversible – for delivering a timely cure, which may also improve mortality.

[1] *The information shown herein refers to products of a 3rd party and thus are in their regulatory responsibility. Please contact the 3rd party for further information.*

Quantitative tissue mapping tools are exciting, but meaningless without proper standardization

The widespread adoption of these novel tools suffers in an extension of the general issues surrounding cardiac MRI, because the 'must-have standard diagnostic toolbox' is neither standardized nor routinely available. What is more, it often needs to be purchased extra, making cardiac MRI an unattractive addition to the general imaging. The additional areas of uncertainty, distinctive to the mapping tools, pertain the overall lack of experience with quantitative imaging tools, a rather new concept to imagers. Mapping tools require a mental switch away from visualization [16] – into the area of analytical tests [17], i.e. recording a number and reading its meaning on a quantitative scale, with the reference ranges, abnormal, prognostically unfavourable range, etc. Perhaps more intuitive if thought along the lines of the blood markers. Any quantifiable tests, mapping tools included, require analytical validation, clinical qualification and standardization – prior to the application into clinical use. After deployment the tests must be subject to all the elements of quality control to ensure safe delivery of an intended, clinically meaningful result. For quantitative diagnostic tools, purchased for clinical use, the burden of standardization and validation remains firmly within the domain of the manufacturer or other providers of imaging biomarkers using the MRI technology. Equally important is that the MRI engineers, physicists and computational scientists, involved in developing either acquisition or postprocessing software realize that nudging of prepulses, pauses and beats in mapping acquisition or application of any correction factors in the postprocessing steps is a deviation from the original method, which must trigger a new cycle of analytical validation and qualification against a hard-core physiological meaning, even if this means years of intense work. Poorly calibrated and non-standardized quantitative methods simply cannot be used outside the research domain.

A further difficulty lies in qualification of imaging tests as conveyors of worthy clinical messages beyond the circle of trained imagers, i.e. capturing the attention of the intended recipients of our reports. An illustrative example is my long-held view that myocardial T2* measurement might be inherently more intuitive to the target physicians (i.e. haematologists) if it featured embedded in the blood results, as opposed to be sunk deep in an imaging report [15]. Such an approach might help to overcome the hesitation that ordering an imaging test – even for a crucial value – is rather excessive compared to 'a simple blood test'. T1 and T2 mapping suffer from a similar dissociation between image and its clinical application. Mapping results may appear more clinically worthwhile if they mentally trace the lines of cardiac biomarkers, such as troponin, or come framed similarly to histological results of endomyocardial biopsy. In fact, the first perceptible advantage of the mapping tools for the everyday clinician may be in receiving immediate clarity on the tissue processes, contrasting the weeks of delay until the results of the biopsy are available.

The most pressing need to achieve long-term viability of cardiac MRI is the evidence that a standardized cardiac MRI toolbox can improve treatment of heart diseases.

Urgent need for a standardized CMR toolbox to emancipate the discipline and increase access to serve patients

The most pressing need to ascertain the long-term viability of cardiac MRI is the evidence that the standard cardiac MRI toolbox can deliver a major change to improve the current approaches to treatment of heart diseases. Such evidence requires conducting well-controlled randomized clinical trials, assuring the value of cardiac MRI deployment for treatment purposes and improvement of prognosis, as exemplified by the aforementioned MR-INFORM clinical trial. Our own niche-like culture perhaps no longer helps the cause; we force the confusing technicalities (such as, about the image acquisition) on each other, as if to claim the supremacy of knowledge or skill, while effectively leaving most users clueless and unphased, as their primary interest is in the clinical benefits of the whole endeavour. With many sensational technical developments this remains rather elusive. The increasing technical maturity of cardiac MRI by faster scanning and a number of automated processes – clearly, an overdue homework, may allow more clinically oriented researchers and the large group of non-research dominated clinicians to finally move into the field without being overwhelmed by technical issues, a difficult and specific language and exams which require knowledge on artefacts and underlying physics.

In this context, we appreciate the many innovations of Siemens Healthineers MRI engineering which address the need for standardization and facilitate the ease of performing cardiac applications – especially the Cardiac Dot Engine, a tool which uses automation to support cardiac planning. Several articles in this edition address the capabilities of this powerful standardization tool. Another milestone which deserves our attention is the introduction of the MAGNETOM Sola Cardiovascular Edition system, a dedicated Cardiovascular MRI scanner, which heralds the emancipation of cardiac MRI as its own discipline. When speaking of emancipation, we should also recognize the important ground work being done around the world by giving voice to the quiet thoughts of the cardiac MRI clinical community, fighting the odds of the everyday reality. In this issue, we created a blog of shared experiences on starting out the local CMR services around the world, recalling the unique situations, as well as reiterating the common lines of the down-to-earth challenges. In the section titled "Cardiovascular MRI Around the World" we learn that in most cases the first stumbling block is the lack of a simple start-up toolbox for a cardiac MRI program. The emerging automated cardiac MRI approaches will certainly ease some of the current pressures experienced when starting a CMR program [18].

Finally, to really unfold the potential of cardiac MRI, the costs of running and maintaining the machines and effective postprocessing tools, as well as the need for lengthy training of specialized personnel must be overcome. If we achieve this, the pressing reimbursement issues – a crucial issue for viability of cardiac MRI – will be easier to solve. What is more, we cannot ignore the need to generate quality evidence based on standardized approaches and fully locked and approved diagnostic and therapy essays with strict quality control. We must demand that industry partners support us in performing large scale therapeutic trials using CMR as the central method for guiding therapy; by phenotyping and individualizing therapy, guiding patient management and – consequently – improving outcome. Only a sure place in clinical management based on its clinical effectiveness will render this method scalable and worthwhile. Even if the onus remains on those who sell technology to make it more affordable, and even if we cannot expect the everyday clinical CMR community to sustain this for much longer, it is up to us to shout out loud to change things, enabling us to better serve patients. In the end, it is we, who need life to have a meaning [19].

Valentina O. Puntmann

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Editorial Board

Review Board

The Status of CMR Stress Perfusion – Where Do We Stand After MR-INFORM?

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First pass contrast-enhanced stress perfusion with cardiac magnetic resonance imaging (CMR) has been performed clinically since the 1990's. However, clinical uptake has been sluggish due to

1. prior lack of clinical validation in multi-center studies;
2. insufficient training of qualified readers;
3. inadequate reimbursement for these procedures compared to other standard stress imaging procedures; and
4. inadequate support in international guidelines.

In fact, in the most recent (2012) U.S. guidelines in stable ischemic heart disease, CMR stress testing was given short shrift [1]. It received a Class IIa indication for patients with an intermediate to high pretest likelihood of disease with an uninterpretable ECG whereas stress nuclear myocardial perfusion imaging or stress echocardiography were given a Class I indication for similar patients. Thankfully these guidelines are in the midst of being updated. The most recent ACCF multimodality Appropriate Use Criteria in ischemic heart disease from 2014 [2] list CMR as only maybe appropriate for 1) symptomatic low risk patients with an uninterpretable ECG or unable to exercise or 2) symptomatic intermediate risk patients with uninterpretable ECG who are able to exercise, whereas stress SPECT and echo were rated as appropriate for both clinical scenarios. More recent ESC guidelines demonstrate high utility for CMR for excluding or including coronary artery disease when compared to invasive angiography, especially as compared to other imaging tests [3]. However, specific recommendations were not offered in regards to the use of particular stress imaging modalities.

When performing stress CMR, readers examine images for qualitative differences in contrast uptake in the first pass wash in of contrast in areas subtended by significant coronary stenosis (hypoperfusion) compared to those subtended by coronaries without significant stenosis during infusion of a vasodilator as a stress agent (typically adenosine or regadenoson). This approach to image analysis has performed well and shown to be superior to single positron emission tomography (SPECT) when accuracy was tested against invasive X-ray coronary angiography in both single center and multi-center studies [4, 5]. However, the gold standard for assessment of the severity of coronary artery disease has changed over time from quantitative coronary angiography to measurement of fractional flow reserve (FFR) using an invasive pressure wire in the cath lab. Smaller single center studies have demonstrated better accuracy of CMR perfusion against invasive FFR than against quantitative angiography since both of the former measures are physiologic rather than anatomic measures [6, 7].

The true measure of test performance is in its relationship to clinical outcomes. In that regards, the recently published MR-INFORM study adds a great deal to the literature supporting the use of stress CMR [8]. Nagel and colleagues studied 918 intermediate to high risk patients (either 2 or more CV risk factors or a positive exercise treadmill test) with typical angina to one of 2 strategies. The first strategy was a CMR-based strategy (MR-Informed) with revascularization only recommended for those with ischemia in at least 6% of the myocardium. The second was an invasive FFR-based strategy (FFR-Informed) in which revascularization was performed for FFR ≤ 0.80. The composite primary outcome included death, nonfatal MI, or target-vessel-revascularization within 1 year. Fewer patients underwent revascularization in the CMR group (36%) as compared to the FFR group (45%), $p = 0.005$. Despite this difference in revascularization rate, there was no difference in the primary endpoint between the 2 groups (3.6% vs. 3.7%, respectively) such that the threshold for noninferiority was met. The percentage of patients free from angina at 12 months was also similar between groups.

Thus, a noninvasive approach with CMR leads to similar outcomes to an invasive approach, despite a lower rate of revascularization. Although cost differences were not examined in the initial MR-INFORM publication, it is quite likely that costs would be less in the CMR group given the lower rate of revascularization. This finding has important implications for risk stratification in patients with suspected ischemic heart disease. Other imaging tests have been compared against each other, e.g. coronary computed tomographic angiography (CTA) against stress testing, primarily with SPECT and echo, in the PROMISE trial showing similar 3 year outcomes [9]. CTA with FFR analysis has been compared to invasive FFR in terms of accuracy [10] but studies in regards to hard outcomes are ongoing (the PRECISE Trial, NCT03702244). To date, other stress imaging tests have not been directly compared to invasive FFR-driven outcomes as was performed in MR-INFORM. Thus, the bar has been raised and CMR has leapt over the bar. Here is hoping that guideline recommendations and Appropriate Use Criteria ratings follow closely behind. Time will tell.

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Quantitative CMR Perfusion Mapping has the Potential to Change Clinical Routine for Assessment of Chronic Coronary Syndrome

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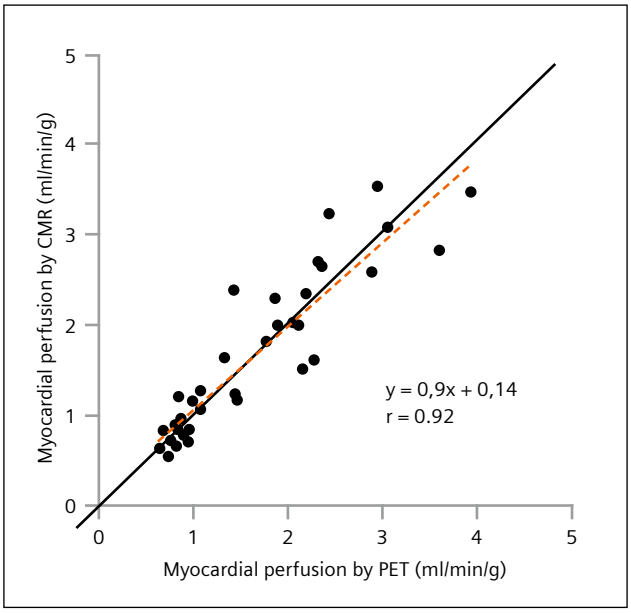
Background

Chronic coronary syndrome (CCS) is one of the most common causes of heart failure and death worldwide [1]. The diagnostic workup in patients with suspected CCS aims at establishing whether or not there is any significant coronary stenosis in need of treatment (percutaneous coronary intervention or coronary artery bypass grafting). Perfusion imaging during stress and at rest can identify clinically significant stress-induced myocardial ischemia in need of treatment. The vast majority of the research in this field during the last decades has been focused on diagnosing and treating atherosclerotic plaques causing stenosis in any of the three major coronary arteries. Very little focus has been on the myocardial vasculature beyond the coronary arteries, i.e. the coronary microcirculation. The primary reason for this has been the inability to quantify microvascular function in the clinical context. Up until recently, the only clinically feasible way to assess coronary microvascular function in patients had been cardiac positron emission tomography (PET). Cardiac PET is limited to few centers and is associated with cumbersome logistics and the need for radioactive isotopes. Hence, in order to make assessment of coronary microvascular function available to a larger group of patients, new diagnostic methods are needed.

Quantitative CMR perfusion mapping[1]

Myocardial perfusion imaging with cardiac magnetic resonance (CMR) has been available for more than 20 years. Traditionally, first-pass perfusion with visual assessment of relative myocardial perfusion distribution has been used. However, due to the complex relationship between signal intensity, blood flow and gadolinium concentration, qualitative visual assessment is not always reliable. Semi-quantitative methods have been proposed and validated [2]. Fully quantitative methods have, however, been lacking. The theoretical basis for fully quantitative perfusion with CMR has been known for several decades [3] originally based on the work by Leon Axel in 1983 [4]. In 2004, Christian et al. [5] showed experimental validation of a dual-contrast bolus technique for assessment of quantitative myocardial perfusion on a pixel-by-pixel level. The same year, Gatehouse et al. [6] showed the proof-of-concept of a dual-sequence, single bolus technique that could also be used for the same purpose. Later, both imaging techniques were shown to have clinical potential [7, 8]. In a collaboration between Peter Kellman and Hui Xue at the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, USA and the Lund cardiac MR group, Lund University and Lund University Hospital, Lund, Sweden, the dual-sequence, single bolus technique was recently clinically validated against cardiac PET [9] (Figs. 1, 2).



1 The relationship between CMR and PET for global myocardial perfusion (rest and stress included). The dashed line represents the line of regression. The solid line indicates the line of identity.
CMR = cardiac magnetic resonance
PET = positron emission tomography

[1] *Customer developed prototype. The product is still under development and not commercially available yet. Its future availability cannot be ensured.*

Potential clinical impact of quantitative CMR perfusion mapping

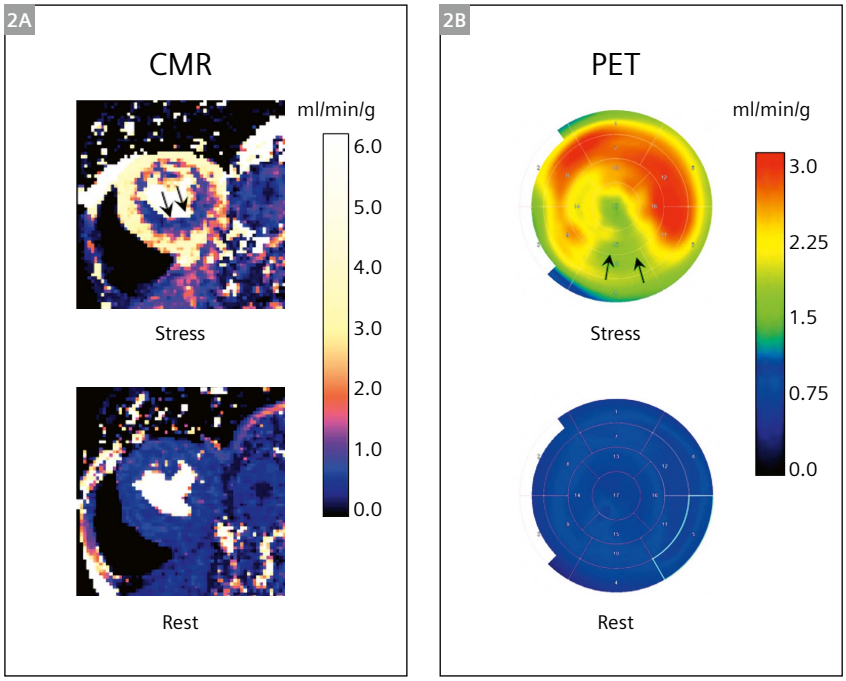
The potential of quantitative CMR perfusion led to a shift in clinical routine at Lund University Hospital in 2019. Instead of replacing a gamma camera used for clinical myocardial perfusion single photon emission tomography (SPECT), the regional healthcare politicians together with the head of the university hospital decided to replace this nuclear imaging method with quantitative CMR perfusion mapping. As a result, a dedicated cardiovascular MRI scanner (MAGNETOM Sola Cardiovascular Edition, Siemens Healthcare, Erlangen, Germany) was installed at Lund University Hospital in August 2019.

Quantitative CMR perfusion in clinical routine in patients with angina enables not only detection of significant coronary artery stenoses, but also assesses their severity. Consequently, this will enable more accurate diagnosis, presumably resulting in fewer unnecessary catheterizations and stents in patients with CCS.

Furthermore, a completely new group of patients with angina can be diagnosed, those with coronary microvascular dysfunction (CMD) [10] of which the majority are women [11]. In the WISE study (Women's Ischemia Syndrome Evaluation), 62% of women with signs and symptoms of ischemia did not have significant coronary artery disease (CAD) [12]. The pathophysiological mechanisms explaining CMD in the absence of obstructive CAD has been shown to partly be the same as for CAD, such as dyslipidemia, hypertension, diabetes and smoking. Coronary microvascular dysfunction has been shown to precede development of obstructive CAD [13]. Hence, the ability for early detection of changes in the coronary microcirculation may enable early detection of patients at risk of developing CAD.

The Cardiovascular Disease in Women Committee of the American College of Cardiology, in conjunction with interested parties (from the National Heart, Lung, and Blood Institute, American Heart Association, and European Society of Cardiology) recently published a consensus statement regarding patients with angina in the absence of CAD, referred to as INOCA (signs of Ischemia with Non-Obstructive Coronary Arteries) [14]. Many of these patients have CMD and an elevated risk for cardiovascular events (including acute coronary syndrome, heart failure hospitalization, stroke, and repeat cardiovascular procedures) compared with reference subjects. In this consensus report the authors state that: "Given the likelihood that multiple mechanisms may contribute to INOCA, improved understanding by specific phenotyping of these individuals beyond symptoms and ischemia is needed" [14].

Thus, due to this novel understanding of ischemia as a potential biomarker, the role of CMR for management of patients with angina will probably increase significantly in the coming years. Due to the quantitative nature of the recently introduced CMR perfusion imaging techniques, precise assessment of coronary microvascular function will become available to a larger group of patients.



2 A patient with stress-induced ischemia in the inferior LV wall with a significant stenosis in the right coronary artery. **(2A)** Rest and stress perfusion maps in a mid-ventricular short-axis view acquired using the dual sequence, single contrast bolus CMR perfusion mapping approach, showing stress-induced ischemia in the inferior LV wall (arrows). **(2B)** Rest and stress polar plot PET perfusion maps obtained by dynamic 13N-NH3 imaging showing stress-induced ischemia in the inferior LV wall (arrows) corresponding well with the CMR findings. The central part of the polar plot represents the LV apex and the periphery represents the basal parts of the LV.*

**The colors for PET and CMR perfusion maps are different and in concordance with colors typically used for each method. Furthermore, the color scales in this case are different for the two methods to optimize visualization of regional pathology.*
CMR = cardiac magnetic resonance
LV = left ventricle
MP = myocardial perfusion
PET = positron emission tomography
From Engblom et al. JCMR 2017;19:78. Reproduced with permission.

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Automated and Standardized CMR Exams Using Cardiac Dot Engine and Short CMR Protocols

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Which cardiac MRI protocol do I use for which purpose? This question remains an unresolved riddle for many users, whether they are new to CMR or are experienced imagers. For many the ease of image acquisition and the quality of the heart views – rarely experienced by any other cardiac imaging modalities – creates a strong temptation to dive deeper and image more. This position is often strengthened by the comparative harmlessness of MRI exams compared with imaging modalities which require ionizing radiation. However, there is seldom benefit and little clinical evidence that would justify doing more individual scans or introducing additional techniques. In fact, for many patients currently, the most lasting impression of a cardiac MRI scan is how very long it took. What comes to mind for many clinicians is the high cost, relative complexity, and lack of immediate therapeutic benefit.

1 Cardiac Dot Engine
Courtesy of Siemens Healthineers.

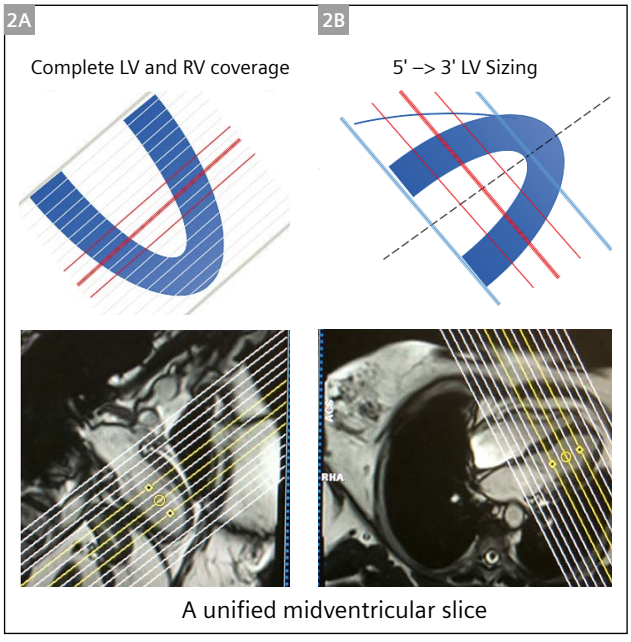
It is also important to realize that the complexity of cardiac MRI, with additional scouts as well as planning views and procedures, is unlike that for any other imaging modality. This calls for an efficient core strategy that is first targeted to the clinical question, and, second, supported by validation-qualification evidence. Any additional views need to be used sparingly, if at all, and best regarded as elective views, they need to be decided upon by the attending physician and performed under their direct supervision. In practice, this is often best performed by doctors themselves, which mandates a doctor's own personal scanning capability to competently decide between responsible and (excessive) defensive scanning.

Third, in imaging environments with shared arrangements over equipment and staff where cardiac MRI is squeezed between the 'knees and spines' with an expectation of 'scanning as usual', the opportunity to consider many cardiac-specific issues in patient preparation is often lost. Attending physicians must be integrated into patient preparation, principally to conduct efficient and competent patient communication, as they must make a judgment on the scan plan that fits best to address the clinical question based on a real person and not on paper-based information. Sufficient investment of time to explain the details of the scan procedures and the importance of breath-holding sets the expectations and motivates patients to cooperate positively. A healthy dose of simple humanity, such as in-room presence when administering adenosine or regadenosone is often what defines the outcome in terms of diagnostic image quality and overall patient experience.

At the Institute for Experimental and Translational Cardiovascular Imaging at the University Hospital Frankfurt we have developed Goethe CVI® Cardiovascular Imaging approaches[1] that addressed these considerations in creating standard operating procedures and imaging protocols for everyday use. Notably, our approach greatly benefits from Cardiac Dot Engine technology (Siemens Healthcare, Erlangen, Germany). This highly automated planning tool is, in our view, an essential 'must-have' for cardiac MRI. The Cardiac Dot Engine is based on a traditional feature, the placement of the '3 points' that define a 2-dimensional plane, and as such the imaging slice. There are several advantages to using the Cardiac Dot Engine. First, its built-in automation simplifies cardiac planning steps, thus importantly reducing the overall onboarding training period for new users. Second, although still far from a self-driving experience, planning with the Cardiac Dot Engine can reduce the concentration-burnout from a full day of cardiac scanning, which can require multiple exchanges of personnel. Third, it allows for greater standardization of all procedures, reducing the variation between patient studies as well as between centers. The Cardiac Dot Engine recognizably reduces the complexity of cardiac scanning, and helps to mitigate the current scarcity of doctors with advanced cardiac MRI training. In centers with more doctors at hand, shorter examination times and overall greater engagement of the doctors allows for their fully autonomous scanning and reporting – as in echo – reducing the reliance on even scarcer radiographer availability.

In the Goethe CVI® exam cards[1], we incorporated a 3-dimensional SSFP localizer allowing for isocenter definition and shim box positioning. This is followed by the Heart Scout, a rough oblique localizer of the heart's position in the chest, which is essentially a combination of the vertical and horizontal long-axis views. Then comes the crucial Cardiac Dot Engine step: Definition of the long-axis views, which involves the positioning of the dots on the relevant anatomical landmarks. This uses a combination of 3 dots per slice to achieve the three true long-axis views for 2, 3, and 4 chambers. These geometries are then acquired as cines. Next comes the short-axis geometry definition, whereby the whole heart stack is planned alongside the subset of 3 short-axis slices (basal, mid, and the apical). Crucially, both are planned perpendicular to the centerline of the long-axis views, with concordance of the middle slice between them. With just these 3 steps, the planning of basic cardiac geometries is complete.

The Goethe CVI® Examcards include acquisition of native maps, (stress-only) myocardial perfusion and late gadolinium enhancement in basic cardiac geometries. The three basic protocols then differ by reductionist approach



2 A unified midventricular slice with **(2A)** complete LV and RV coverage and **(2B)** 3' LV sizing.

[1]*The information shown herein refers to products of a 3rd party and thus are in their regulatory responsibility. Please contact the 3rd party for further information.*

to target the clinical question, for instance myocardial perfusion is performed when ischemia is suspected, or microvascular disease is deemed likely based on the pretest likelihood. In practice, most patients will undergo examination with myocardial perfusion imaging, as illustrated by examples of typical patients with either known coronary artery disease (previous stents, ongoing symptoms), those with multiple risk factors (e.g., metabolic syndrome), or systemic conditions where coronary vascular involvement is likely (e.g., systemic lupus erythematosus). Patients with atypical symptoms, commonly profound dyspnoea, will benefit from myocardial perfusion to clarify whether their symptoms correspond with 'angina equivalent'.

Patients with known pathological cardiac anatomy or cardiomyopathies and those who have had previous scans excluding significant myocardial ischemia, however, will undergo shorter protocols without myocardial perfusion. Patients who need repeat scans to follow up on myocardial inflammation/fibrosis and/or volumes/function will undergo native examinations only. Some patients will require a targeted expansion of the core protocols with MR angiography (aorta and renal arteries in hypertension scans), flows (Qp:Qs) or transaxial slices for congenital indications. The table time of a native scan is approximately 15 minutes, whereas other protocols (with myocardial perfusion and late gadolinium enhancement) are generally completed in under 30 minutes. This is an important contributor to an improved patient experience.

Goethe CVI® Approaches relate to a specific set of standard operating procedures and imaging protocols for cardiovascular magnetic resonance imaging and cardiac contrast tomography in everyday clinical use. Goethe CVI® exam cards are available for use, subject to a sharing agreement and a license fee. This arrangement with us involves two important considerations: First, the quality assurance when importing an exam card, as well as its maintenance to ensure that all functional parameters are preserved as originally envisaged. The second aspect encompasses the hands-on training of users for confident application. We offer several approaches to prospective users, either by Goethe CVI® fellowships or by way of a personalized, week-long observership training in collaboration with Siemens Healthineers. The details are provided on our website.

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16 Months of Exercise – A Case Study of Automated CMR with Cardiac Dot Engine

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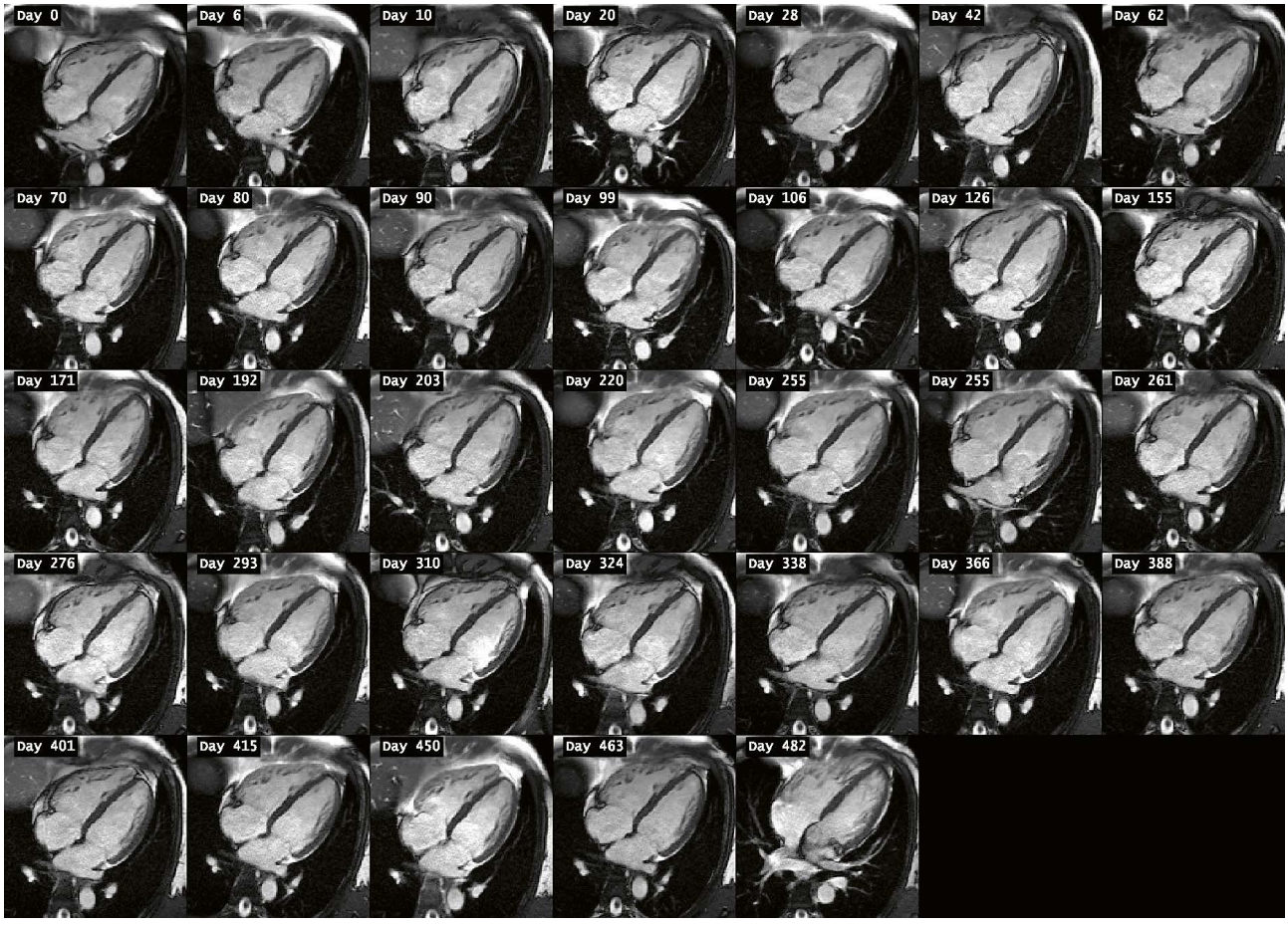
Introduction

Cardiovascular magnetic resonance imaging (CMR) provides valuable information for the clinical management of patients and is widely accepted as the gold standard for functional and viability imaging. However, CMR is a demanding imaging modality and it can be challenging to avoid inter-operator variability in both acquisition and interpretation. Positioning of standardized views such as the long axis views and short axis stack can be challenging for less experienced operators, and numerous sequence adjustments to optimize image quality require significant effort, all resulting in inconsistency between scans. Manual contouring of the myocardium for functional analysis is time consuming and can also be a significant source of variability for less experienced readers. Variability in both slice planning and manual contouring performed by different operators can negatively affect longitudinal studies where a high degree of reproducibility is required.

Aerobic exercise is well regarded as beneficial for cardiovascular health. The American Heart Association recommends at least 150 minutes of moderate-intensity



1 Automated slice prescription of a 4-chamber view using the AutoAlign component of the Cardiac Dot Engine over 16 months.

aerobic activity per week [1]. In this study, we sought to monitor and assess the effects of a high-intensity exercise training program on a healthy subject using CMR due to its potential for quantifying small changes in cardiac function. The exams were carried out using Cardiac Dot Engine technology (Siemens Healthcare, Erlangen, Germany) to minimize variability in this longitudinal study.

The Cardiac Dot Engine available on Siemens Healthineers MRI scanners provides a suite of guidance technologies designed to improve workflow by reducing operator burden during CMR acquisition and interpretation. The AutoAlign component of the Cardiac Dot Engine uses a machine learning based algorithm trained on 517 patient datasets to identify five anatomical landmarks – the base of the left atrium, aortic root, acute margin of the right ventricle, base of the left ventricle, and left ventricular apex [2–5]. From these landmarks, the standard 2-, 3-, and 4-chamber long axis views as well as the short axis stack are planned. The operator has the option to accept or adjust the position of the landmarks or view orientations if needed. The AutoTiming feature can be used to automatically adjust sequence parameters such as segments, phase resolution, and partial phase Fourier in a user configurable algorithmic manner to reduce scan duration for patients with diminished breath-hold capacity.

The InlineVF module automates the contouring of the endocardium and epicardium of the left ventricle and detection of the mitral valve basal plane. The left ventricular blood pool is segmented using an isoperimetric clustering algorithm [6]. Greyscale analysis with a shortest path algorithm is used to segment the endocardium and epicardium with inverse consistent deformable registration used to apply segmentation to all cardiac phases [7, 8]. A machine learning based cardiac anchoring technique is used to determine the basal and apical landmarks [5]. Together, the various automations in the Cardiac Dot Engine can reduce operator variability and is well suited for longitudinal studies where high reproducibility is required.

Methods

A single healthy 33-year-old male subject was enrolled in a high-intensity exercise program consisting of >150 minutes/week of high intensity aerobic exercise at >75% of age-predicted maximum heart rate (MHR). Exercise activity and heart rate were measured using an Apple Watch Series 3 (Apple Inc., Cupertino, CA, USA). CMR imaging was performed approximately every 2 weeks on a 1.5T MAGNETOM Aera (Siemens Healthcare, Erlangen, Germany). Cine imaging was performed with the following typical sequence parameters: 340 × 280 mm field of view, 1.5 × 1.5 mm^2 in-plane resolution, 6 mm slice thickness, 50° flip angle, 1.16/2.81 ms TE/TR, 13 views per segment, 36.5 ms temporal resolution. The AutoAlign feature of the Cardiac Dot Engine was used to automatically prescribe the 2-, 3-, and 4-chamber views as well as the short axis stack. The Cardiac Dot Engine was also used to automatically start and stop each scan by giving breath-hold instructions with an operator-defined rest interval between scans. InlineVF was used to calculate the ejection fraction, end-diastolic volume, end-systolic volume, stroke volume, cardiac output, and myocardial mass, with results reported inline during each CMR exam. Linear regression was used to evaluate potential trends.

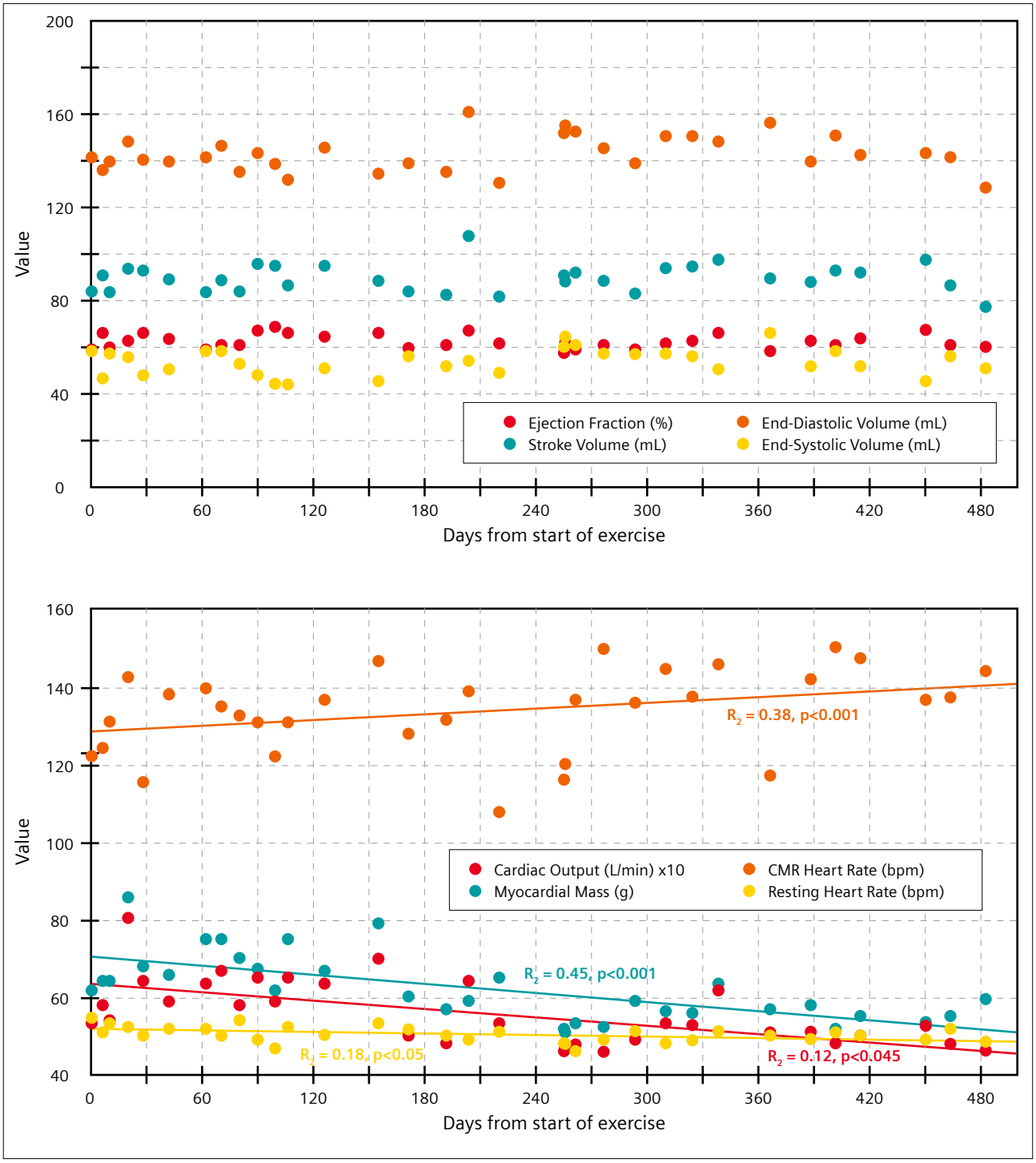
Results

The exercise program was well tolerated throughout the 16-month study duration, with an average of 154±5 minutes per week of high-intensity exercise. Daily "exercise minutes" categorized by the Apple Watch increased from 38±8 minutes in the 7 months prior to the start of the study to 58±6 minutes during the study. During exercise, the mean average heart rate was 159±6 bpm (85±3% of MHR) with a mean peak heart rate of 178±6 bpm (95±3% of MHR). Subject's weight remained unchanged over the course of the study. A total of 33 CMR exams were performed with a mean follow-up interval of 15±8 days.

	Overall	First 60 days	Last 60 days
Ejection Fraction (%)	62.6 ± 3.1		
End Diastolic Volume (mL)	143.7 ± 7.7		
End Systolic Volume (mL)	53.8 ± 5.6		
Stroke Volume (mL)	89.9 ± 6.0		
Cardiac Output (L/min)*	5.6 ± 0.8	6.1 ± 1.0	4.9 ± 0.4
Myocardial Mass (g)*	134.2 ± 10.9	129.3 ± 10.3	139.7 ± 4.2
CMR Heart Rate (bpm)*	62.2 ± 8.6	68.3 ± 8.9	56.0 ± 2.6
Resting Heart Rate (bpm)*	50.3 ± 1.9	52.0 ± 1.4	49.7 ± 2.1

* indicates a linear trend with $p < 0.05$. Resting heart rate was measured with an Apple Watch, and all other parameters are from Siemens Healthineers Inline VF.

Table 1: Cardiac structure and function over 16 months of exercise.



2 Trends of cardiac structure and function over 16 months of high-intensity exercise.

Automated slice planning with AutoAlign required no user intervention in 32/33 cases, where manual identification of a landmark was required in a single case. Slice orientation was highly consistent between studies (Fig. 1). Automated InlineVF analysis was successful in all cases (Table 1, Fig. 2). Ejection fraction and all volumetric measurements were unchanged over the course of the study. Myocardial mass increased 8% from the first 60 days to the last 60 days ($p<0.05$). Cardiac output dropped by 20%, coincident with an 18% decrease in heart rate during CMR and a 4% decrease in resting (sleeping) heart rate ($p<0.05$). Inter-study consistency was good for all parameters, with <10% coefficient of variation for all parameters in which there was no statistical change over the course of the study.

Conclusions

Automated CMR acquisition and analysis techniques were successfully applied to 33 CMR serial exams and used to quantify changes in cardiac function during a high-intensity exercise program. Increased myocardial mass was consistent with a previous study on exercise training [9], although previously reported changes in chamber volumes [10] were not found. Individual responses to exercise training may vary and subjects with >30 "active minutes" as measured by an Apple Watch may have less cardiovascular benefit from an additional high-intensity exercise program. The automated tools in the Cardiac Dot Engine reduce the burden of scanning and interpretation of CMR and reduce overall variability. High inter-study reproducibility of the imaging slice orientations is beneficial for direct comparison of images in serial follow-up studies and in more accurately quantifying small changes in cardiac structure and function.

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Cardiac Magnetic Resonance for Ischaemia and Viability Detection in Patients with Coronary Chronic Total Occlusions

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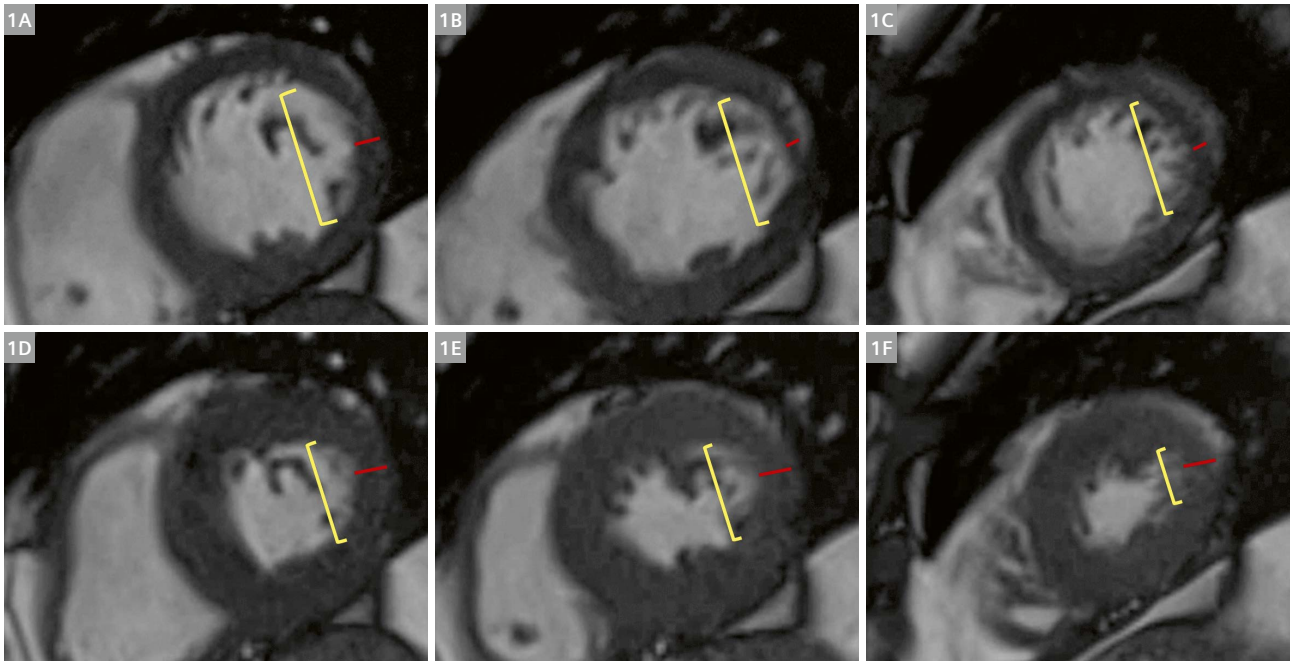
Introduction

The prevalence of coronary chronic total occlusion (CTO) is around 30% of patients undergoing coronary angiography. Percutaneous revascularization (PCI) of CTO lesions is attempted in only 10% of cases due to technical challenges and higher complication rates than in other settings. CTO-PCI leads to improved symptoms, functional class and quality of life, higher left ventricular ejection fraction and improved survival in observational studies [1–4]. However, there is no evidence of additional clinical benefit of revascularization over optimal medical therapy (OMT) in randomized clinical trials [5–9]. A possible reason for this is that the patients selected for revascularization have not been examined to confirm viability and ischemia in the CTO territory.



1 Baseline CMR in diastolic **(1A–C)** and systolic **(1D–F)** stop-frame in a patient with CTO of the Ramus, showing antero-lateral basal and mid segments thickening ~50%, suggesting ipokinesia.

Patients with CTO are heterogeneous, with different degrees of regional and global dysfunction, sub-endocardial or transmural scar and ischaemic burden. The study of these three components is crucial to identify patients who will have clinical benefit from revascularization, likely those with limited scar and wider ischemia. CMR is a robust technique that can accurately quantify left ventricular (LV) function, scar burden and myocardial ischaemia in a single examination, using a comprehensive, multi-parameter approach.

Study design

Our study (CARISMA_CTO) is the first study to systematically assess patients with CTO scheduled for PCI with a tailored stress CMR protocol (adenosine or dobutamine at high/low dose) according to LV function, correlating baseline parameters with those obtained after CTO-PCI (regardless of success) at 12 ± 3 months follow-up.

CARISMA_CTO could help in clarifying the best protocol for ischaemia and viability assessment by means of CMR to identify predictors of functional and/or clinical response to CTO-PCI. The final aim of the investigation is improving selection of candidates for revascularization by assessing their personal risk-to benefit ratio. Such individualized selection could help avoid potential PCI-related complications when the benefit of revascularization is unlikely.

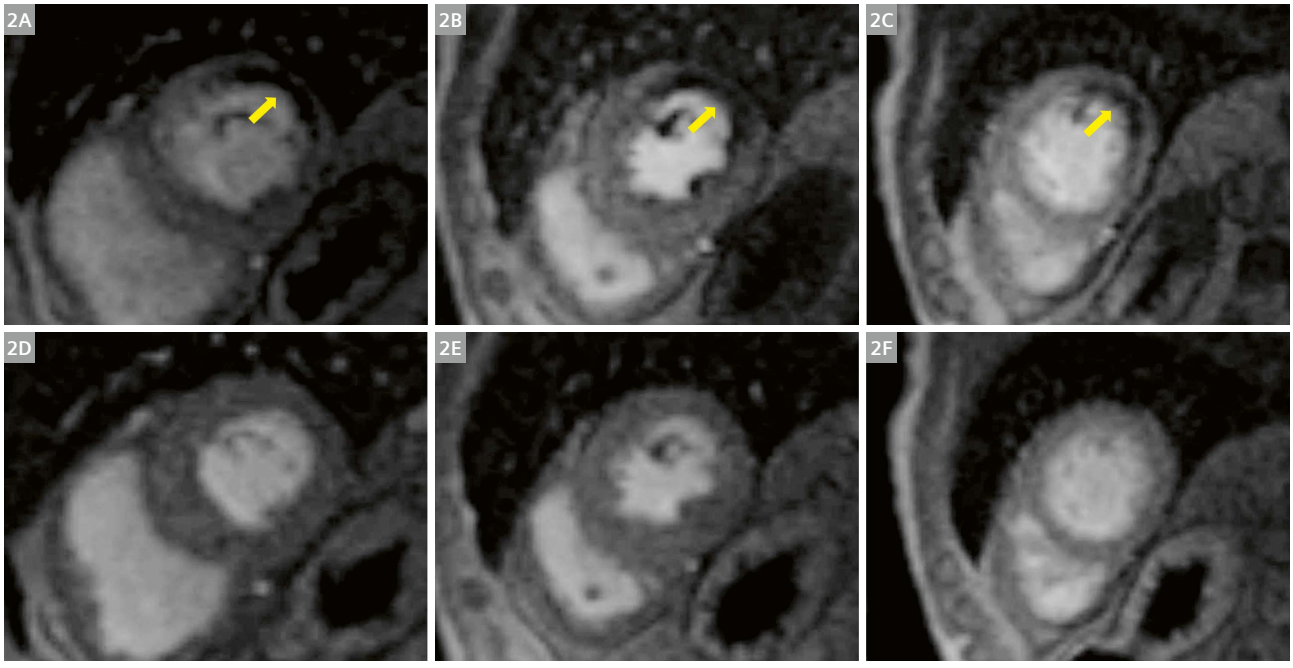
Methods

Patients will be identified at the time of coronary angiography. Coronary unstable/culprit lesions will be treated first and then patients will be followed-up for medical therapy optimization. Afterwards, within approximately 3 months-time, a baseline stress CMR examination will be performed before the CTO-PCI attempt.

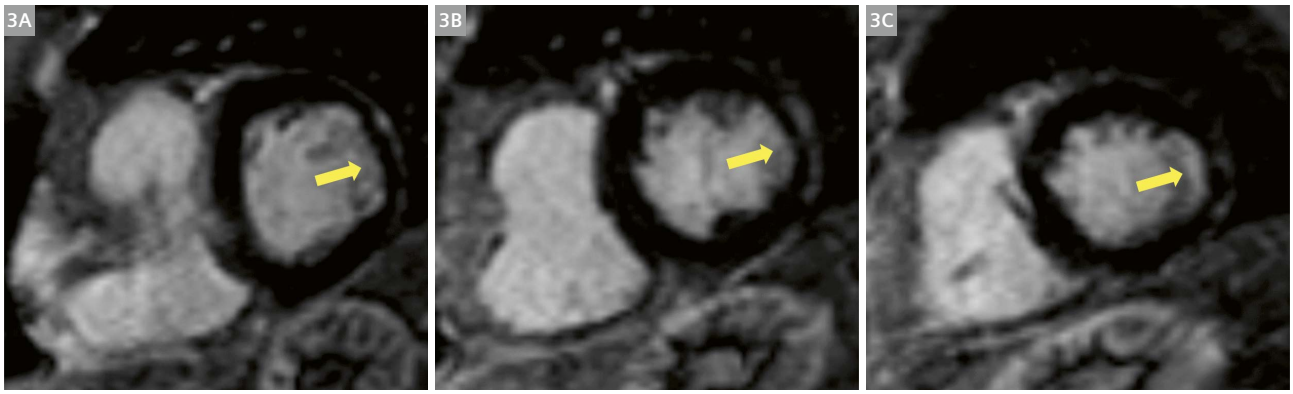
Eligible participants will undergo complete medical history, physical examination, Seattle Angina Questionnaire [10], 12-lead ECG, transthoracic echocardiogram and stress CMR. PCI operators will not be blinded to CMR results. Discussion between imaging expert and interventional cardiologist will be part of the decision making process. However, the PCI operator will be completely free to decide regarding the CTO-PCI opportunity. Both patients successfully treated with PCI and those with failed PCI and subsequently treated with OMT will undergo a stress CMR at 12 ± 3 months to longitudinally assess changes in LV remodelling and function, ischaemic burden and tissue characterization. At 12 ± 3 months a clinical evaluation, Seattle Angina Questionnaire, 12-lead ECG and transthoracic echocardiogram will be repeated. We will consider, as baseline therapy, that of baseline CMR examination and we will collect any changes in the following follow-up period.

Investigation CMR details

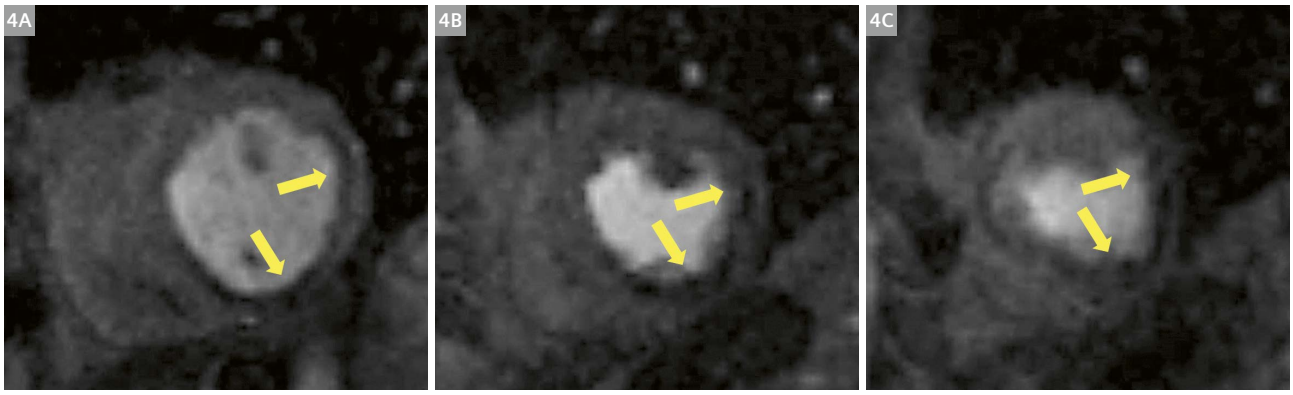
CMR studies will be carried out on a 1.5T scanner (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany; Discovery MR 450, GE Healthcare, Milwaukee,



2 Same patient as in Figure 1. **(2A–C)** first pass sequences during adenosine infusion show a perfusion defect in the lateral segments, from base to apex, suggesting a wide perfusion defect to the ramus territory. **(2D–F)** the same slices at rest condition: first pass sequences showing no perfusion defect in the same territory.



3 Same patient as in Figure 1. Late gadolinium enhancement (LGE) sequences showing < 50% LGE transmurality of the lateral segments. The presence of ipokinesia, perfusion defect and LGE extension < 50% suggest ischemia and viability in the ramus territory.



4 First pass perfusion during high-dose-dobutamine infusion in a patient with Ramus and Right Coronary Artery (RCA) chronic total occlusion, showing perfusion defect in the infero-septum, inferior, infero-lateral and antero-lateral segments, suggesting a wide perfusion defect to Ramus and RCA territory.

WI, USA; Philips Achieva, Philips Healthcare, Best, The Netherlands). Pilots, transverse white and black-blood images, long and short axis bSSFP cines to assess left and right ventricular volumes, function and mass will be acquired.

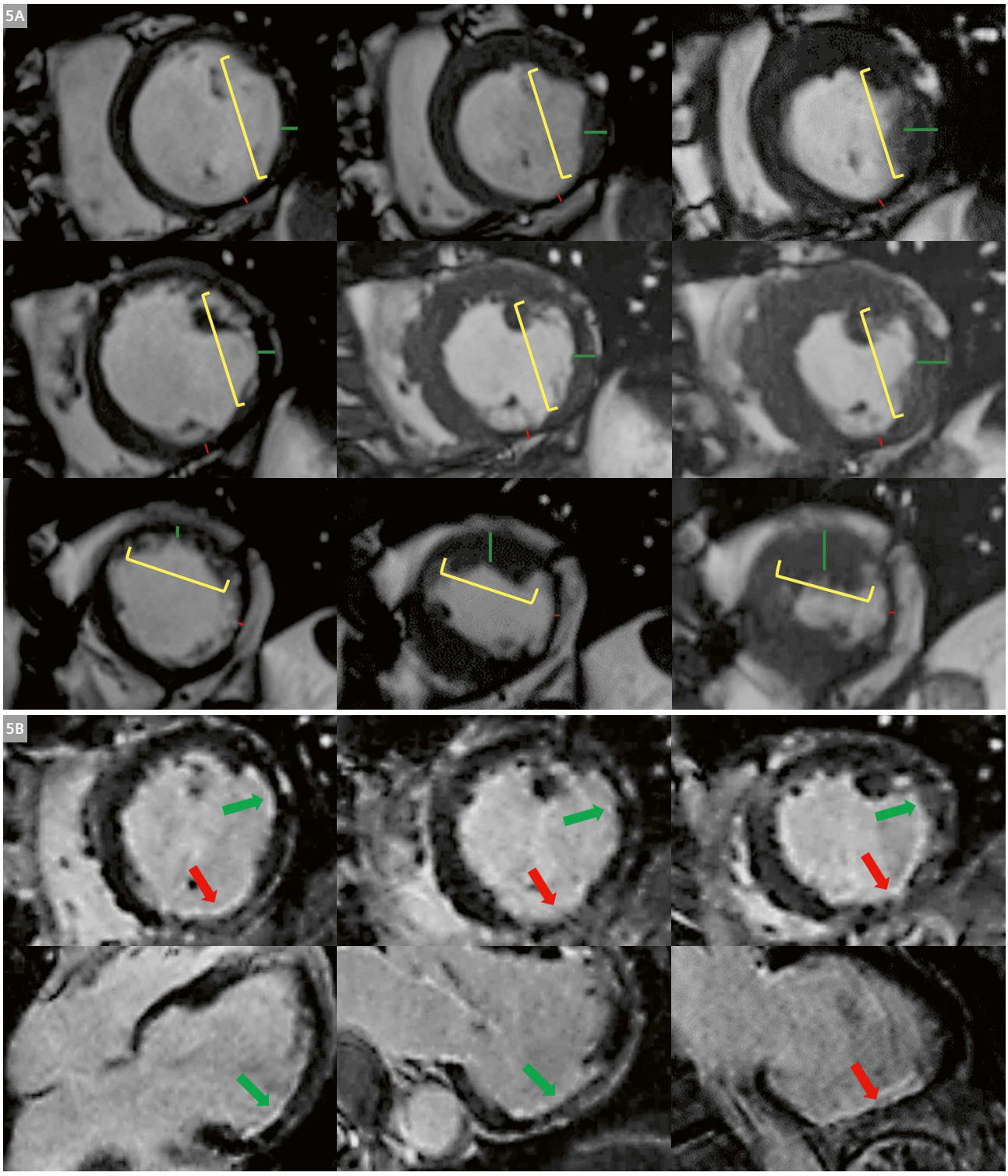
Stress CMR

Eligible patients will undergo stress CMR for viability and ischaemia assessment according to the following patient-tailored protocol:

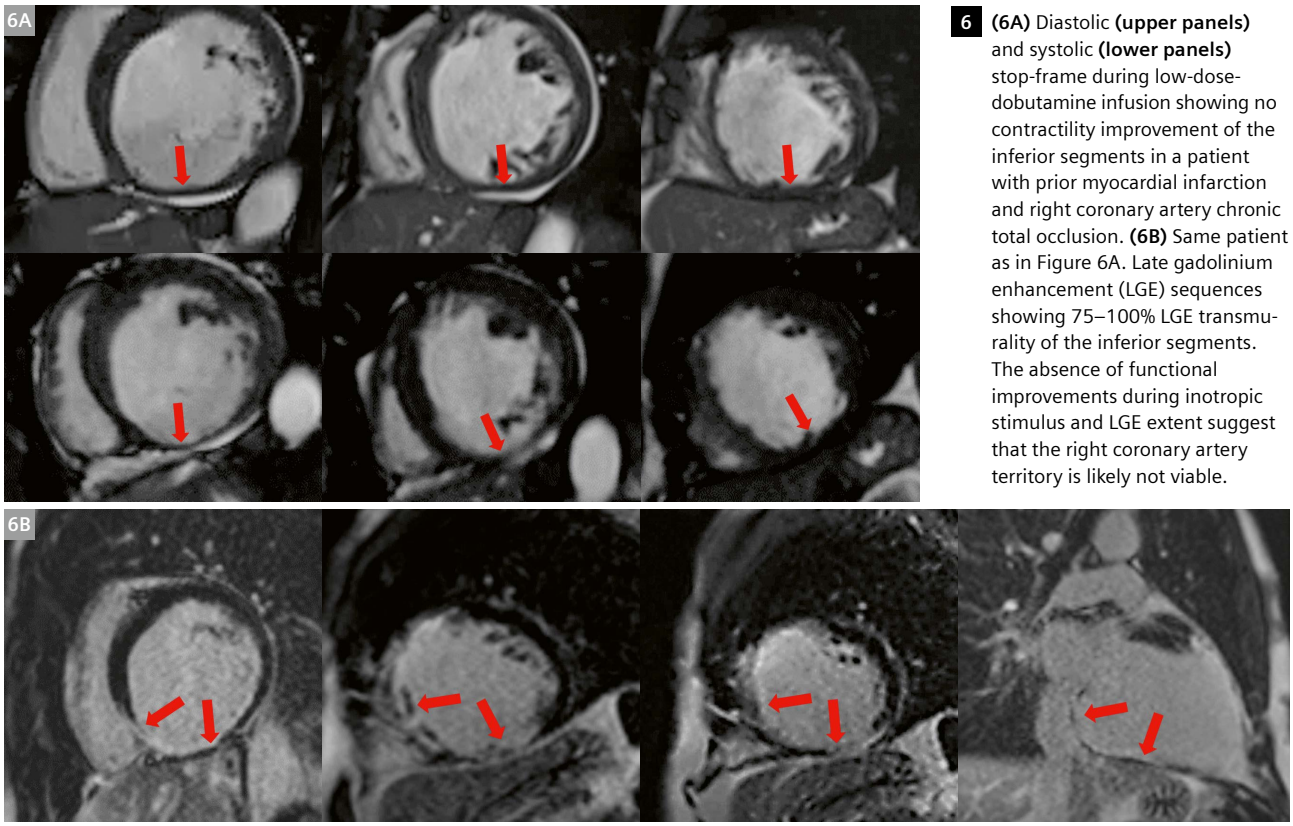
1. Patients with preserved LV systolic function (EF > 50%) and ≤ 2 hypokinetic segments (Figure 1)
   - Ischaemia assessment with adenosine stress perfusion test (Figure 2).
   - Viability assessment by means of LGE extent (Figure 3).
2. Patients with wall motion abnormalities (akinetic segments or > 2 hypokinetic segments) and preserved or moderately depressed LV function (EF ≥ 35%)
   - Ischaemia assessment by high-dose-dobutamine stress wall motion abnormalities and perfusion test (Figure 4).
   - Viability assessment by low-dose dobutamine kinetic response (Figure 5A) and LGE extent (Figure 5B).
3. Patients with severely depressed LV function (EF < 35%): Viability assessment by low-dose dobutamine and LGE extent (Figures 6A and 6B).

Adenosine stress perfusion

A T1-weighted saturation-recovery segmented *k*-space gradient echo pulse sequence with parallel imaging will be used to assess first pass myocardial perfusion in 3 short axis slices (basal, mid-ventricular and distal). For stress perfusion imaging, intravenous adenosine will be administered at 140 µg/kg/min. The perfusion study will start at the 4th minute of adenosine infusion, acquiring a series of 60 dynamic acquisitions. A bolus of 0.075 mmol/kg Gadobutrolo (Gadovist, Bayer S.P.A.) followed by a 20 ml saline flush will be delivered through an antecubital vein in approximately 3s. Patient's blood pressure and heart rhythm will be continuously monitored. A resting myocardial perfusion study will be undertaken 10 to 15 mins following the stress perfusion study, with a further injection of 0.075 mmol/kg Gadobutrolo.



5 **(5A)** Same patient as in Figure 4. Baseline diastolic **(left panels)** and systolic **(mid panels)** stop-frame showing antero-lateral and infero-lateral segments thickening < 50% and absent thickening of the inferior segments; **(right panels)**: systolic stop-frame during low-dose-dobutamine infusion showing contractility improvement of the antero-lateral and infero-lateral segments, thickening > 50% (likely viable), no improvement of the inferior segments (unlikely viable). **(5B)** Same patient as in Figure 4. Late gadolinium enhancement (LGE) sequences showing > 75% LGE transmurality of the inferior and 50–75% of infero-lateral and antero-lateral segments. Despite > 50% of LGE transmurality, dobutamine stress showed functional improvement of the infero-lateral and antero-lateral segments, which suggests the importance of a multiparametric assessment; in this case, it allows the detection of inducible ischemia and likely viability in the ramus territory, while the absence of inotropic response and LGE > 75% suggest a perfusion defect with likely no viability in the right coronary artery territory.



6 **(6A)** Diastolic **(upper panels)** and systolic **(lower panels)** stop-frame during low-dose-dobutamine infusion showing no contractility improvement of the inferior segments in a patient with prior myocardial infarction and right coronary artery chronic total occlusion. **(6B)** Same patient as in Figure 6A. Late gadolinium enhancement (LGE) sequences showing 75–100% LGE transmurality of the inferior segments. The absence of functional improvements during inotropic stimulus and LGE extent suggest that the right coronary artery territory is likely not viable.

Dobutamine stress test
Baseline 6 to 8 short-axis double-angulated cines covering the LV will be acquired adjusting the gap between sections, reducing the number of slices and the acquisition time (slice thickness 8 mm, gap ~4 mm). Dobutamine stress examination will be performed starting with 5 µg/kg/min up to 40 µg/kg/min plus atropine (up to 1 mg) if needed to reach target heart rate [(220 – age) × 0.85]. Dobutamine infusion will be carried out for 3mins for each step, acquiring short axis cines for global function, wall motion abnormality (WMA) assessment and comparison. At peak dobutamine infusion a stress perfusion imaging will be performed using 60 dynamic acquisitions during the administration of an intravenous bolus of 0.075 mmol/kg Gadobutrolo in approximately 3s. Rest perfusion imaging will be performed approximately 10 min following stress, using the same geometry and contrast medium as during stress. Termination criteria will be severe chest pain, development of new wall motion abnormalities, significant arrhythmia, hypertension (blood pressure > 240/120 mmHg), systolic blood pressure drop of > 40 mmHg and any intolerable side effect. A betablocker will be administered intravenously at the end of stress if clinically indicated.

Low-dose dobutamine study
Dobutamine infusion to assess viability only will be performed starting with 5 µg/kg/min up to 20 µg/kg/min for approximately 3 min (target 15% increase in heart rate × blood pressure) for each step. Six to eight short-axis stacks (slice thickness 8 mm, gap ~4 mm) will be performed to assess and compare global and segmental function.

Late gadolinium enhancement
When performed after perfusion, a final injection of 0.05 mmol/kg Gadobutrolo will be given following rest perfusion sequences, bringing the overall gadolinium dose to 0.2 mmol/kg. LGE images will be performed between 10 and 20 min after Gadobutrolo injection. The optimal inversion time to null signal from normal myocardium will be determined using a modified Look-Locker approach. Then a T1-weighted, segmented inversion recovery gradient echo contiguous short axis stack of the LV will be performed. Further slices will be acquired in the vertical, horizontal long axis or radial orientations as per clinical indication.

CMR analysis

The following details will be recorded:
- Evidence of ischaemia by visual comparison of rest/stress CMR perfusion (16 segments of the 17-segment

Study hypothesis	CMR capability of identifying at baseline predictive markers of response to CTO revascularization at 12 ± 3 months, in terms of myocardial viability and/or ischaemia.			
Viability definition	At least one of the following:	1. Late gadolinium enhancement transmurality ≤ 50%		
		2. Improvement in segmental function ≥ 1 grade during low-dose dobutamine		
Ischaemia definition	At least one of the following:	1. Perfusion defect (≥ 1.5 segments) assessed during peak infusion of adenosine or dobutamine		
		2. New wall motion abnormalities or worsening ≥ 1 grade during peak infusion of dobutamine		
Definition of outcomes	Time frame: 12 ± 3 months			
Primary outcome measures	Left ventricular mechanical improvement or ischaemic burden reduction in the CTO-territory after CTO-PCI, defined as the presence of at least one of the following:	1. Segmental function improvement ≥ 1 grade in the CTO-territory after CTO-PCI		
		2. Stress ischaemia improvement in the CTO-territory after CTO-PCI, defined as the presence of at least one of the following stress CMR (adenosine or dobutamine) findings: • Perfusion defect of < 1.5 segments or a reduction of ≥ 2 segments with perfusion defect • ≥ 1 grade improvement in segmental wall motion abnormalities		
Secondary outcome measures	Left ventricular mechanical global improvement, defined as the presence of at least one of the following:	Delta ejection fraction ≥ 5%	Delta end-diastolic volume ≥ 10%	Delta end-systolic volume ≥ 10%
		Quality of life improvement assessed by Seattle Angina Questionnaire (SAQ)		
		Major cardiac and cerebrovascular events (MACCE), defined as: All cause death, death for cardiovascular cause, life-threatening arrhythmia, hospitalization for heart failure, myocardial infarction, target vessel revascularization or stroke		

American Heart Association (AHA)/American College of Cardiology model, excluding the apical segment). A score of 0 (normal), 1 (subendocardial) or 2 (transmural perfusion defect) will be assigned to each segment.

- Evidence and extent of scar tissue (in 16 out of 17 myocardial segment model). A score of 1 (none), 2 (1–25%), 3 (26–50%), 4 (51–75%) or 5 (> 75%) will be assigned to each segment, based on the transmural extent of late gadolinium enhancement.

The total number of segments with perfusion defects and the quantification (grams/ LV mass) of the necrotic tissue will be scored for each patient.

A myocardial segment will be defined as viable if LGE transmurality will be ≤ 50%, not viable if ≥ 75%. LGE transmurality > 50% and < 75% will be considered as uncertain viability. Left ventricular cines will be analysed comparing segmental kinetic at baseline, 5 and 10 or 20 µg/kg/min (for viability assessment) and 30–40 µg/kg/min (for ischaemia assessment). Regional wall motion abnormalities (17 myocardial segment model) will be scored as 1 (normal), 2 (hypokinesia), 3 (akinesia) or 4 (dyskinesia).

A myocardial segment will be defined as viable if an akinetic/hypokinetic segment will improve to hypokinetic/normokinetic at low-dose dobutamine.

A myocardial segment will be defined as ischaemic if a normocinetic/hypokinetic segment will worsen to hypokinetic/akinetic at high-dose dobutamine. In addition, a bi-phasic response during the test will be considered a marker of myocardial ischaemia as well.

- Quantitative left and right ventricular analysis will include: end diastolic volume (ml), end systolic volume (ml), ejection fraction (%), left ventricular mass (grams), necrotic tissue mass (g) and all indexed parameters.

Discussion

Several observational studies and four randomized, controlled trials have examined the impact of CTO-PCI on clinical outcomes [1–14]. The current recommendation suggests that CTO-PCI should be performed when the anticipated benefits exceed the potential risks. At present, the main benefit and key indication remains symptom improvement (angina or dyspnea, which is often an angina equivalent in these patients).

Realizing the benefits requires successful CTO recanalization, the likelihood of which depends on the angiographic characteristics of the occlusion and the experience of the operator. Cautious selection of patients who can benefit from the procedure can lead to optimal

outcomes. Adding a selection of patients based on CMR confirmation of viability and ischemia could likely furtherly improve the clinical benefit of PCI in these patients.

To the best of our knowledge, this is the first CMR study systematically assessing in all-comers for CTO-PCI both viability and ischaemia with different and complementary approaches based on patient' characteristics and comparing the results with the same CMR protocol in the follow-up. CMR offers the possibility to assess viability by means of both LGE extent and low-dose-dobutamine inotropic response and to evaluate regional ischaemia by stress perfusion defect extent and wall motion analysis. This approach will allow individualizing the type and dose of stressor, obtaining the most informative data regarding viability and ischaemia for each patient.

Therefore, we'll analyze if these parameters at baseline could predict mechanical left ventricular segmental function improvement and ischemic burden reduction in the CTO territory (primary endpoint) and global LV mechanical improvement or clinical amelioration in terms of Seattle Angina Questionnaire and MACCE reduction (secondary endpoints) at 12 ± 3 months of follow-up.

Potential impact of CARISMA_CTO study

If this hypothesis is demonstrated, CMR assessment of viability and ischaemia should be recommended routinely before PCI in patients with CTO, to individually assess the risk-to-benefit ratio, avoiding potential PCI-related complications when the benefit is unlikely.

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Flow-Independent Dark-Blood Delayed Enhancement (FIDDLE)

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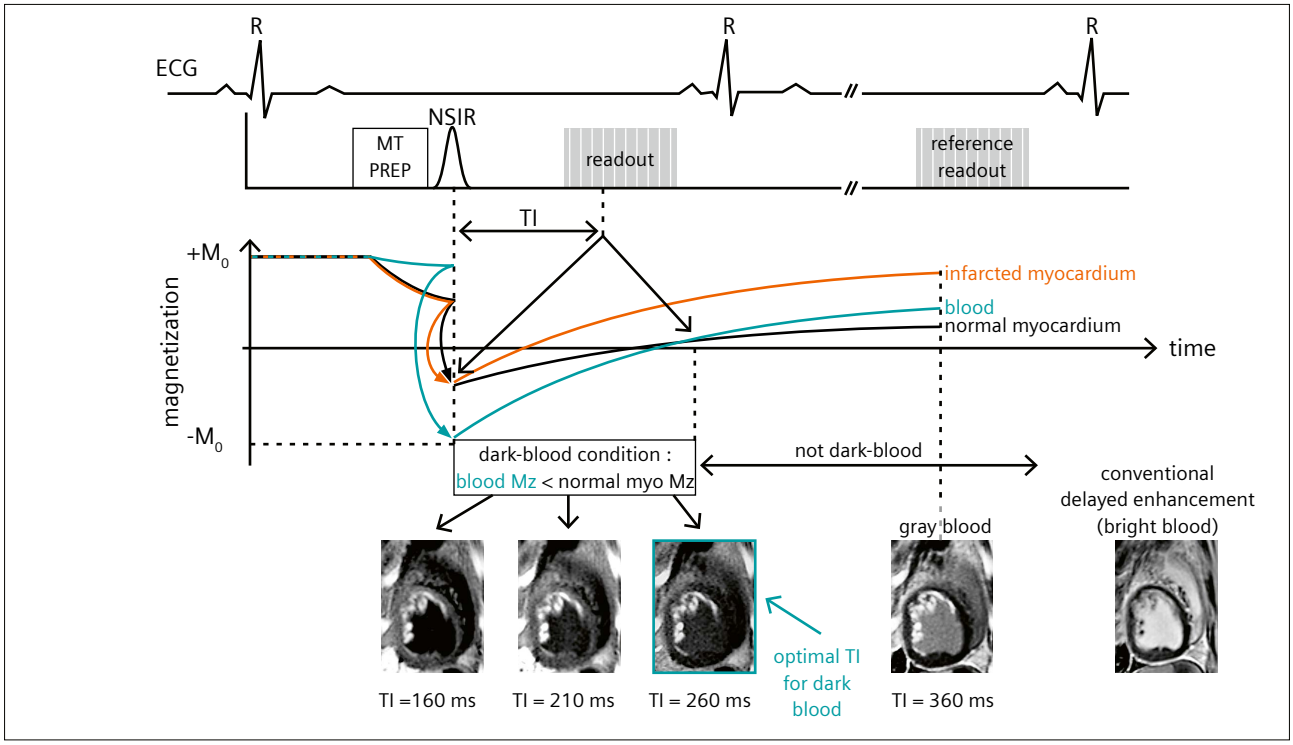
Abstract and key points

Delayed enhancement MRI is regarded as the imaging gold standard for the *in vivo* diagnosis of myocardial infarction. However, infarcted myocardium and ventricular blood pool possess similar signal intensities after contrast agent administration. Therefore infarcted myocardium immediately adjacent to the blood pool may not be detected in some cases. This problem is overcome in the flow independent dark-blood delayed enhancement (FIDDLE) technique[1] by improving the contrast between blood-pool and myocardium leading to an even higher accuracy in infarct detection than in conventional delayed enhancement. In this publication, we explain the mechanism behind creating contrast-enhanced dark-blood images with FIDDLE, and we give image examples in both ischemic and nonischemic heart disease patients.

[1]*The product is still under development and not commercially available yet. Its future availability cannot be ensured.*



1 Conceptual diagram of the FIDDLE sequence showing its core components: a tissue-signal-attenuating preparatory module, in this example using a series of magnetization transfer (MT) pulses (MT-prep); a non-selective inversion recovery (NSIR) pulse for imparting T1-weighting; a readout and reference readout for phase-sensitive IR (PSIR) reconstruction, and an inversion time (TI) which renders blood magnetization smaller than tissue magnetization (dark-blood condition). Even with TI outside the dark-blood condition (TI > 260 ms in this example), blood-pool signal is suppressed compared with conventional DE-MRI, improving the conspicuousness of infarcted myocardium. This is known as gray-blood imaging. ECG = electrocardiogram; M_0 = baseline longitudinal magnetization; M_z = blood or tissue magnetization.

The role of delayed-enhancement imaging in cardiac MRI

Cardiac MRI has emerged as a leading non-invasive imaging tool with a broad range of applications for cardiology. Much of the strength of cardiac MRI rests on its ability to differentiate healthy and diseased tissue using the delayed-enhancement MRI (DE-MRI) technique. The detection of myocardial damage is essential, as even small amounts of dead tissue are associated with a poor prognosis [1].

DE-MRI is regarded as the reference standard for the *in vivo* diagnosis of myocardial infarction (MI), owing in part to its high spatial resolution and excellent contrast between infarcted and normal myocardium. However, an important limitation is that the infarcted tissue and the ventricular blood pools possess similar signal intensities after contrast agent administration [2]. Hence, infarcted myocardium may be hidden if it is immediately adjacent to the blood pool, since there is poor delineation between bright tissue and bright blood. Thus, techniques that improve the contrast between blood-pool and adjacent myocardium were needed to improve the sensitivity of DE-MRI.

The evolution of dark-blood techniques

The development of dark-blood methods that provide blood-pool suppression after contrast agent administration required a break from conventional dark-blood techniques. Traditional dark-blood MRI [3, 4] depends upon the long T1 of blood (about 2 seconds at 3T) and sufficient blood flow between the dark-blood preparation and the data readout. The time between these two events allows inverted blood magnetization to recover to approximately zero and thus generate zero-blood signal, i.e. dark blood. However, after contrast media administration, the T1 of blood is greatly shortened, and thus the traditional method cannot be used to provide contrast-enhanced, dark-blood images.

Several approaches to improve discrimination of post-contrast blood-pool and infarcted myocardium have been proposed. Some are dependent on the motion of blood in the cavities, as either bulk flow [5, 6] or diffusion [7]. These techniques are limited in that 'slow blood flow' artifacts, which are bright and difficult to distinguish from subendocardial infarction, are likely to occur in patients with ventricular dysfunction, i.e. those most in need of cardiac imaging.

Other techniques have been proposed that are not dependent on blood flow. For example, Kellman et al. [8] describe a multi-contrast technique that acquires two separate images: one T2-weighted and one T1-weighted image. Liu et al. [9] describe a technique that is similar but combines T1- and T2-weighting in a single image. Foo et al. [10] describe a dual inversion time subtraction method which uses two acquisitions, at a long and short inversion time, respectively, to improve the delineation between infarcted myocardium and ventricular blood-pool. Peel et al. [11] describe a dual IR prep module to suppress blood-pool signal. However, none of these flow independent techniques have been adopted into clinical routine, perhaps in part due to the increased time and complexity of image acquisition. All of these methods result in images in which blood-pool signal is reduced compared to conventional delayed enhancement, but still higher than viable myocardium. Therefore, an endocardial layer that is partially infarcted may still be difficult to distinguish from the blood-pool.

A new class of dark-blood techniques such as Flow-Independent Dark-blood DeLayed Enhancement (FIDDLE) were developed in 2011 [12] to overcome these limitations and allow simultaneous visualization of contrast-enhanced tissue and a dark blood pool [13–15]. FIDDLE generates these contrast-enhanced dark-blood images through a combination of

- a non-selective tissue signal-reducing preparation module,
- a non-selective inversion recovery (IR) pulse,
- a phase-sensitive IR (PSIR) reconstruction [16], and
- the selection of an inversion time (TI) such that blood magnetization is lower than tissue magnetization and infarct magnetization is higher.

The resulting PSIR images simultaneously show contrast enhanced tissue and dark-blood (Fig. 1). It is worth mentioning that the blood is not dark because it is 'nulled' as in traditional dark-blood magnitude images. Instead, it appears dark in FIDDLE images, because they are PSIR images and as such depict the smallest magnetization as the darkest, irrespective of its absolute value.

Also owing to the PSIR reconstruction, a precise TI is not needed to yield dark blood, rather a range of TIs can be used, as long as the magnetization of blood is lower than myocardium; see the FIDDLE images with a range of inversion times fulfilling the dark-blood condition in Figure 1. However, among these TI values, choosing the longest one results in the best infarct-to-myocardium contrast. Interestingly, selecting longer TI values in FIDDLE can create gray-blood images with still better infarct-to-blood contrast than traditional (bright-blood) delayed enhancement.

FIDDLE variants

FIDDLE was designed to be flexible and modular in order to accommodate different preparation pulses, execution order, and readout type. Note that FIDDLE refers to the core concept of combining a tissue signal-reducing preparation and an IR pulse, both of which are spatially non-selective and therefore flow-independent. Based on

the FIDDLE concept, segmented and single-shot implementations exist, and the latter can also be combined with motion compensation (MOCO) [17].

Magnetization Preparation Configuration

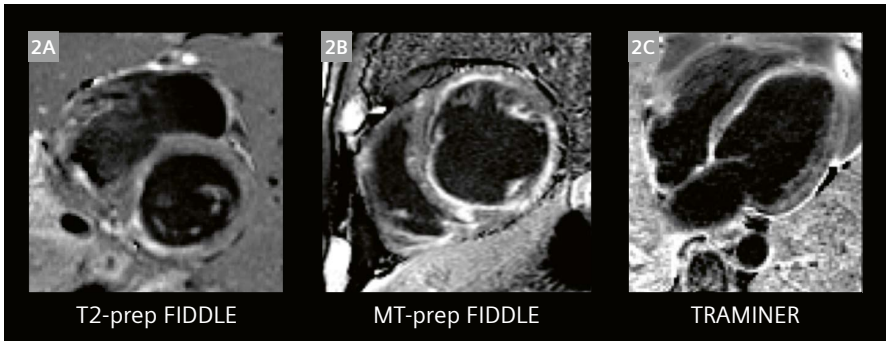
The position of the tissue signal-reducing preparation module relative to the IR pulse is flexible and can be placed before (prep-IR) or after the IR pulse (IR-prep). However, the IR-prep variant is more limited since the duration of the preparation module restricts the minimum inversion time that can be chosen. This constraint may not allow a short enough TI to result in a black-blood image, depending on the dose of contrast media given and the time elapsed after its administration.

The type of magnetization preparation is also flexible – the primary consideration is that the preparation module must attenuate tissue and blood to different degrees. Since its first description in 2011 [12] FIDDLE variants using a magnetization transfer (MT) preparation (MT-prep) [14], T2-preparation (T2-prep) [9], and an T2-rho preparation [15] have been employed. Examples of FIDDLE images with different preparation are shown in Figure 2.

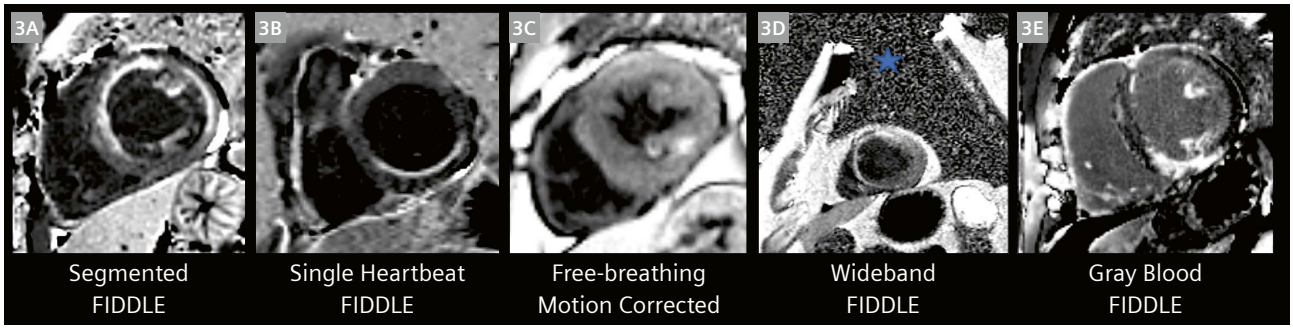
One common preparation for FIDDLE is MT-prep. An MT-prep employs a train of off-resonance MT pulses to saturate the macromolecular proton pool. This saturation is transferred to the main water pool resulting in a reduction in the detected magnetization that is proportional to the protein concentration of that tissue. The MT-prep variant of FIDDLE has been validated against histopathology in a canine model of MI and was shown to have higher diagnostic accuracy for the detection of MI in patients [14] than conventional DE-MRI.

T2-prep has also been shown to work well with FIDDLE. A T2-prep variant of FIDDLE combined with single-shot SSFP readout and motion correction to allow imaging during free breathing, demonstrated increased conspicuity of regions that were likely to represent subendocardial fibrosis [13] and demonstrated a higher rate of detecting hyperenhanced myocardium than conventional DE-MRI [18].

Yet another type of magnetization preparation for FIDDLE is the "T(Rho) And Magnetization Transfer And INvErsion Recovery" technique (TRAMINER) which creates separation between tissue and blood using a series of adiabatic BIR-4 pulses with a net flip angle of zero degrees. The BIR-4 pulses simultaneously impose T2-weighting due to the T2(Rho) relaxation in the spin-lock regime, and magnetization transfer contrast, both attenuating tissue magnetization while minimally affecting blood and effectively creating blood-tissue separation. TRAMINER has also been shown to result in a higher rate of detection of hyperenhanced myocardium compared with DE-MRI [15].



2 Clinical example images of different FIDDLE variants. **(2A)** T2-prep NSIR, **(2B)** MT-prep NSIR, and **(2C)** TRAMINER prep images all resulting in dark-blood images.



3 FIDDLE images (MT-prep NSIR) with different readout schemes: **(3A)** segmented acquisition, **(3B)** single-shot single heartbeat (reference and the MT-IR data readout occur in one heartbeat), **(3C)** free-breathing single-shot motion-corrected (MOCO), **(3D)** MT-prep wideband NSIR in a device patient, the blue star indicates the location of the device in the image, **(3E)** FIDDLE with a long TI to produce gray-blood images.

At the Duke Cardiovascular MR Center (DCMRC) we observed that MT-prep is superior to T2- preparation with regards to the homogeneity of the blood-pool. FIDDLE with T2-prep occasionally results in artifacts in the left atrial cavity, which appear to be secondary to non-uniform magnetization preparation, and this is particularly evident at 3T [18]. Additionally, unlike FIDDLE with MT-prep, FIDDLE variants with T2-prep can result in different blood suppression in the right versus the left ventricle. This is because deoxygenated blood in the right chamber has shorter T2 than the oxygenated blood in the left [18].

FIDDLE Imaging Variants

Its modular design allows FIDDLE to be adapted to a wide range of clinical settings. Figure 3 shows example images acquired with a selection of FIDDLE variants. All use off-resonance MT-prep.

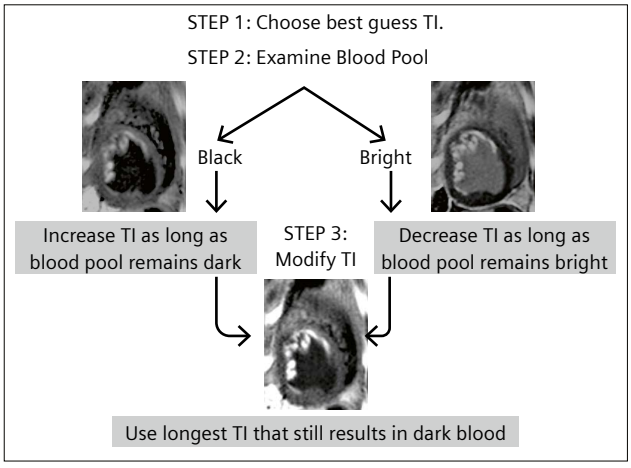
- **Segmented FIDDLE**: The most commonly used FIDDLE variant using a segmented, breath-held TrueFISP data readout combined with a MT-preparation (Fig. 3A). The segmented approach allows for high spatial and temporal resolution images to be acquired within a breath-hold. In patients who can hold their breath, this configuration provides the best diagnostic accuracy for assessment of myocardial damage.
- **Single-heartbeat FIDDLE**: For a fast overview of the entire heart or for patients who cannot hold their breath, FIDDLE has been implemented as single-shot TrueFISP technique (Fig. 3B). We use a single-heartbeat PSIR acquisition wherein reference- and IR-data are acquired in the same heartbeat [19]. This prevents spatial misregistration between the reference- and IR-data set, which can occur when running single-shot acquisitions with a trigger pulse of three during free breathing.
- **Motion-corrected, free-breathing, high spatial resolution FIDDLE**: A different free-breathing version of FIDDLE acquires multiple (usually eight) high spatial resolution single-shot images, which are motion-corrected and averaged together to improve signal-to-noise ratio (SNR) [17]. The motion correction algorithm corrects for in-plane motion between acquisitions and, similar to the single-heartbeat variant, reduces artifacts due to spatial misregistration (Fig. 3C).
- **Wideband FIDDLE for use with implanted cardiac devices**: This implementation uses a wideband (stretched adiabatic) IR pulse which provides a uniform inversion even in the presence of metal[2] (prosthetic valves, implanted cardiac devices, etc.) [20]. The MT-pulses are intrinsically robust towards poor B_0 homogeneity since they are applied off resonance. In addition, the wideband protocol is run with a GRE (FLASH) readout to reduce its sensitivity to metal (Fig. 3D).
- **Gray-blood FIDDLE**: If the inversion time is extended beyond that needed to fulfill the dark-blood condition (Fig. 1), a gray-blood image will result. While the blood-pool signal will be higher than that of normal myocardium, gray-blood imaging can still be helpful since blood-pool signal will be attenuated relative to conventional DE-MRI (Fig. 3E).

Clinical Implementation

From a breath-hold and clinical throughput standpoint, FIDDLE is essentially identical to conventional DE-MRI. No additional post processing or image registration is required, and all image reconstruction is completed at the time of image acquisition. The same dose of contrast media is used for FIDDLE compared to DE-MRI, and imaging can be performed at the same time-point after contrast agent administration. Moreover, spatial resolution, temporal resolution, and breath-hold duration (8–10 seconds) are also identical to DE-MRI. In other words, the implementation of FIDDLE can be regarded as a 'drag and drop' replacement for conventional DE-MRI.

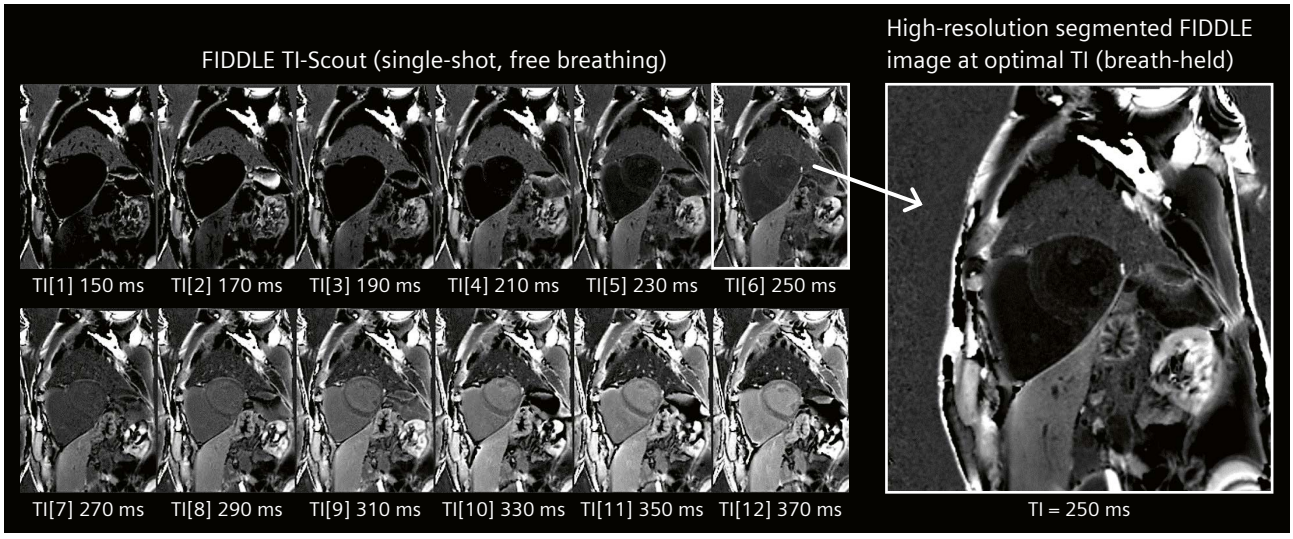
Setting the Inversion Time (TI)

Setting TI for FIDDLE is straightforward. One examines the image intensity of the blood-pool. If the blood-pool is not dark but gray or bright, TI needs to be reduced. If the blood-pool is dark, TI should be increased to the maximum value that still results in dark-blood. This algorithm is



4 Algorithm for manually setting TI of FIDDLE.

[2]*The MRI restrictions (if any) of the metal implant must be considered prior to patient undergoing MRI exam. MR imaging of patients with metallic implants brings specific risks. However, certain implants are approved by the governing regulatory bodies to be MR conditionally safe. For such implants, the previously mentioned warning may not be applicable. Please contact the implant manufacturer for the specific conditional information. The conditions for MR safety are the responsibility of the implant manufacturer, not of Siemens.*



5 A series of single shot FIDDLE images (PSIR by default) are acquired during a free breathing TI-scout scan. Each image has an increased TI compared with its predecessor (increments of 20 ms in this example). By exactly mimicking the magnetic evolution of the segmented sequence, the TI-scout creates single-shot images with the same image contrast as the segmented sequence for a given TI. The TI of the scout image showing optimal contrast (blood black and normal myocardium dark-gray) is plugged into the segmented sequence to obtain a segmented FIDDLE image with optimal contrast.

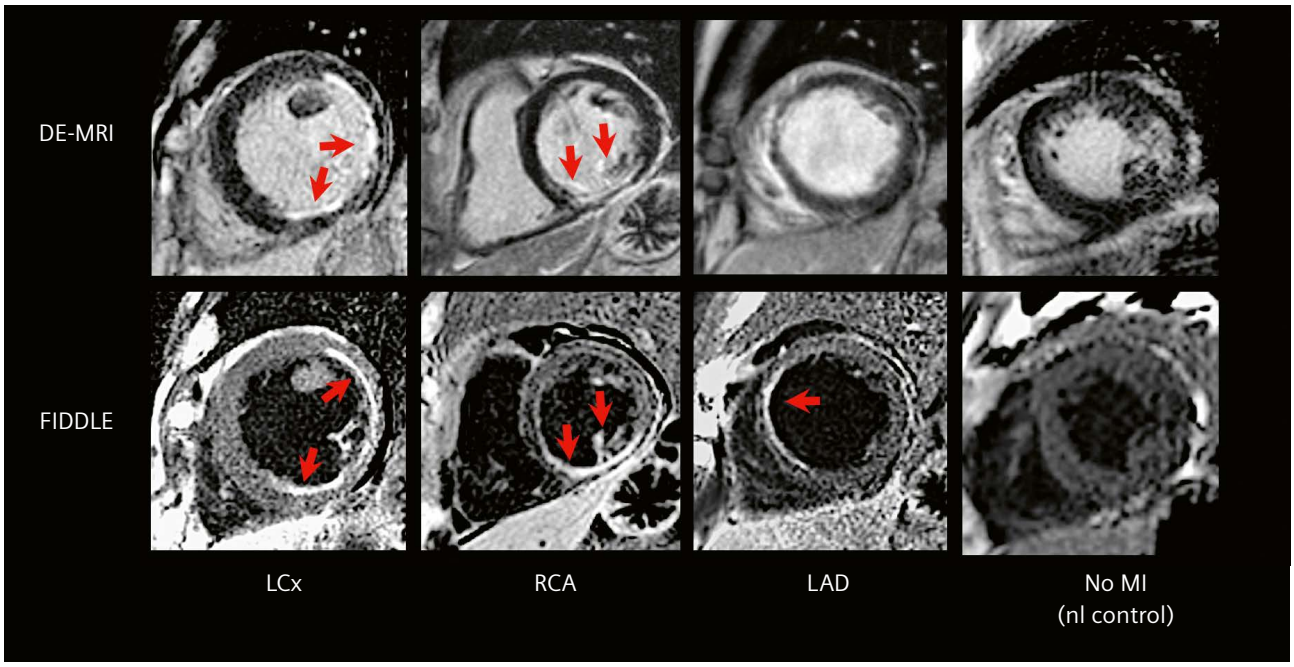
shown in Figure 4. For simplicity, our current practice is to use an initial TI that is purposely chosen to be too long (i.e. image is not dark-blood), and to incrementally reduce the TI until the dark-blood condition is fulfilled. Given its diagnostic performance and ease of use, FIDDLE has become a core component of the DCMRC clinical cardiac MR exam and is used daily at both 1.5 and 3T.
For new adopters of FIDDLE, a recently developed free-breathing FIDDLE TI-scout [21] allows one to find the optimal inversion time in a single-step and with high accuracy. Figure 5 shows a series of TI-scout images and the segmented FIDDLE image acquired with the TI found to be optimal by the scout. In contrast to the conventional TI-scout also known as Look-Locker sequence, the new TI-scout can also produce PSIR images, which are required for FIDDLE. Analogous to using the conventional TI-scout for DE-MRI the new TI-scout determines the TI at the time that it is run, but the optimal TI increases with time after contrast agent administration and TI should be continually adjusted.

Clinical scenarios and cases

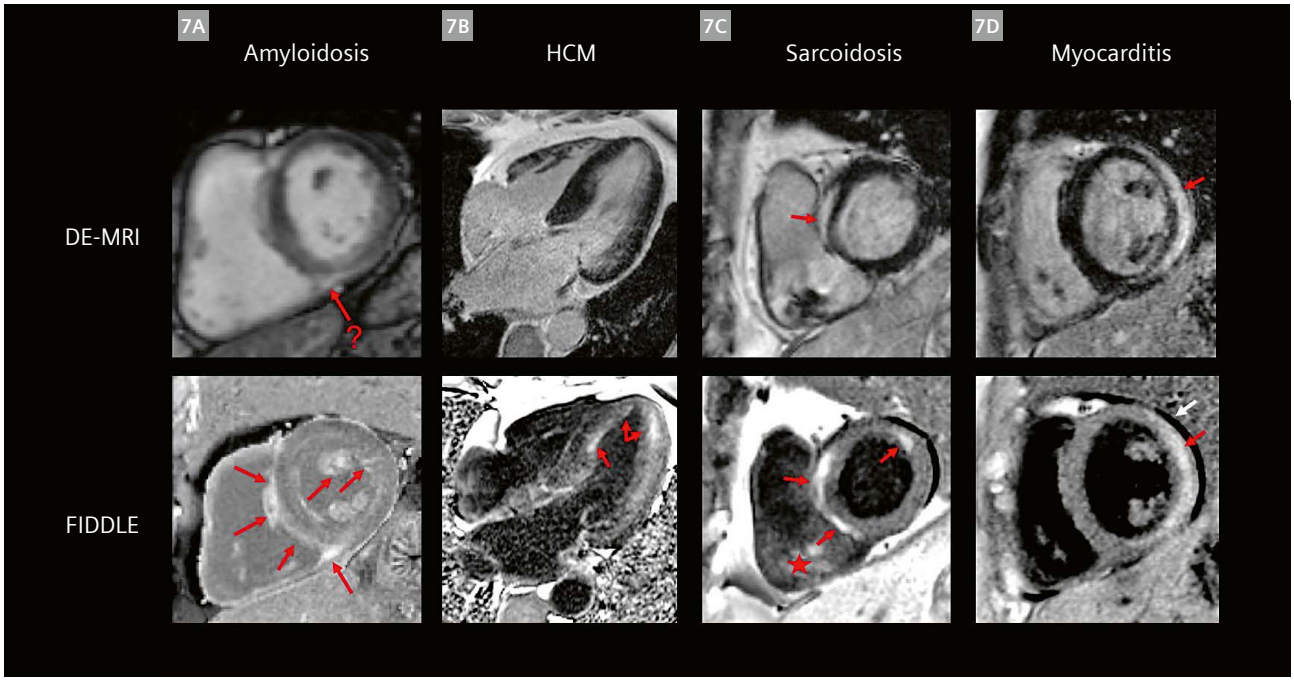
Myocardial Infarction
In a recent validation study, FIDDLE was shown to provide superior diagnostic performance for the detection of myocardial infarction (MI) compared with conventional DE-MRI [14]. Sensitivity and accuracy were significantly higher for FIDDLE compared to DE-MRI (96% vs. 85% and 95% vs. 87%, respectively). This improvement in diagnostic performance mainly came from improved detection of subendocardial infarctions, where the sensitivity of DE-MRI was only 80% compared to 98% for FIDDLE.

Although this result may suggest that the primary advantage of FIDDLE is in patients with small infarcts, this report also observed that some infarcts missed by DE-MRI were relatively large. Even when infarction was identified by DE-MRI, the data indicated that it was rare to visualize the entire length of the MI endocardial border, in contra-distinction to FIDDLE images for which the entire border was always visualized. Hence, infarct size measurements were more robust with FIDDLE than with DE-MRI; in comparison to pathology, there was reduced bias and smaller 95% limits-of-agreement with FIDDLE.

Figure 6 shows examples from four patients referred for myocardial viability assessment. In the first case, the patient had an occlusion of the left circumflex artery (LCx), and the hyperenhancement is well visualized on both the DE-MRI and FIDDLE images. In the next example, the infarct related artery was the right coronary artery (RCA), and while it is clear on DE-MRI that there is an infarct present in the inferior wall, the subendocardial border of the infarct is unclear. The third example is a patient with disease in the left anterior descending (LAD), which is difficult to identify on the conventional DE-MRI but is clearly visualized on the FIDDLE image. The final example is in a normal control patient with no CAD. In this case, a TrueFISP band in the anterior/anteroseptum gives a suggestion of hyperenhancement on the DE-MRI image, but the FIDDLE image clearly shows that there is no hyper-enhancement.



6 Comparison of conventional DE-MRI and FIDDLE images in patients with myocardial infarctions. The images are grouped by infarct-related artery (IRA): circumflex artery (LCx), right coronary artery (RCA), and left anterior descending (LAD). A control patient is shown on the right. See text body for details.



7 Example images in different nonischemic cardiomyopathies. In many of these cases, dark blood improves the appreciation of the location and extent of hyperenhancement. Red arrows indicate regions of hyperenhancement. In **7C**, the star indicates the RV lead from a cardiac device, which appears black on the conventional bright-blood DE-MRI, and bright on the FIDDLE image. In **7D**, the white arrow highlights that the PSIR reconstruction used with FIDDLE has the added benefit of rendering fluid (in this case a pericardial effusion) black, enabling better visualization of the epicardial surface.

Nonischemic Cardiomyopathy
There are no published comparisons of FIDDLE for the diagnosis of nonischemic cardiomyopathies (NICM). However, the DCMRC has used FIDDLE in nonischemic cardiomyopathy cases and found it to be equivalent, if not superior, to conventional DE-MRI. Figure 7 shows a series of example images in different nonischemic cardiomyopathies. In many of these cases, the suppression of the blood pool has allowed for improved appreciation of the location and extent of hyperenhancement.

Cardiac Amyloidosis
The first nonischemic cardiomyopathy (Fig. 7A) is cardiac amyloidosis. Cardiac amyloidosis (CA) can be challenging to image and as a result, studies on the prognostic value of DE-MRI in patients with CA have yielded inconsistent results [23]. A challenge in CA patients is that there is often global, diffuse hyperenhancement of the myocardium, which is why it can be difficult to appropriately set TI in DE-MRI to best visualize the abnormalities. FIDDLE mitigates this challenge as it uses a PSIR reconstruction and has a wide range of TIs over which the blood is suppressed, while providing differentiation of diseased and normal myocardium. In Figure 7A, the DE-MRI image does not clearly show any abnormal tissue, although there is a hint of possible hyperenhancement near the RV insertion site. However, the FIDDLE image depicts multiple areas of subendocardial hyperenhancement, as well as hyperenhancement of the RV side of the septum (see arrows).

Hypertrophic Cardiomyopathy
FIDDLE can also provide insight in cases of hypertrophic cardiomyopathy (HCM), where the hyperenhancement is diffuse and subendocardial, as is shown in Figure 7B. In this case, the DE-MRI image hints at possible diffuse disease along the lateral wall and apical septum, but the image characteristics are also similar to partial volume of trabeculations and blood pool. In the FIDDLE image, the blood pool is suppressed allowing the reader to clearly visualize the apical lateral hyperenhancement and the subendocardial mid-apical septal hyperenhancement (see arrows).

Cardiac Sarcoidosis
The suppression of the blood pool is particularly helpful in cases of cardiac sarcoidosis (CS), where the hyperenhancement is often on the RV side of the septum near the base of the heart. On conventional (bright-blood) DE-MRI images it can be challenging to differentiate LV outflow tract, RV blood pool and hyperenhancement in this setting, as is demonstrated in the CS case shown in Figure 7C. In the DE-MRI images, it is clear that there is hyperenhancement of the RV side of the anterior septum (see arrow), however it is ambiguous if the inferior septum is also hyperenhanced. On the FIDDLE image, it is clear that there is hyperenhancement of both the anterior and inferior septum, and there is also a small amount of hyperenhancement in the anterior lateral wall (see arrows). Also of interest, this is an example of wideband FIDDLE [20], the bright region in the RV blood pool (see star) is due to pacemaker leads.

Myocarditis
FIDDLE can also be used to identify regions of myocardial hyperenhancement in cases of myocarditis. In the example shown in Figure 7D, the hyperenhancement is well visualized on both the DE-MRI and FIDDLE images (see arrows). In the case of myocarditis, the suppression of the blood pool by FIDDLE does not provide a benefit over DE-MRI, however the PSIR reconstruction also renders the pericardial effusion black (see white arrow), allowing for a clearer visualization of the lateral epicardial border.

Conclusion

Despite the availability of an armamentarium of modern MRI techniques, the image-based diagnosis of myocardial disease can still be difficult. Finding new imaging methods that improve decision making, risk stratification, and management, is critical. The reduced variability associated with FIDDLE is expected to be important in clinical trials that employ infarct size as a surrogate endpoint. While studies have validated FIDDLE in patients with MI, FIDDLE provides a general approach to improve contrast-enhanced MRI of tissue pathology by separating parenchymal contrast-enhancement from blood-pool enhancement. Hence, the technique may have broad applicability in visualizing other pathologies throughout the heart and cardiovascular system, for example atrial fibrosis and aortopathies.

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Interventional Cardiovascular Magnetic Resonance: Initial Clinical Experience for Right Heart Catheterization

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Introduction

Right heart catheterization (RHC) is the gold standard technique to assess pulmonary blood pressures in the diagnosis of pulmonary hypertension. Blood pressures are measured invasively using a catheter navigated through the right chambers of the heart under X-ray fluoroscopic guidance in the cath lab.

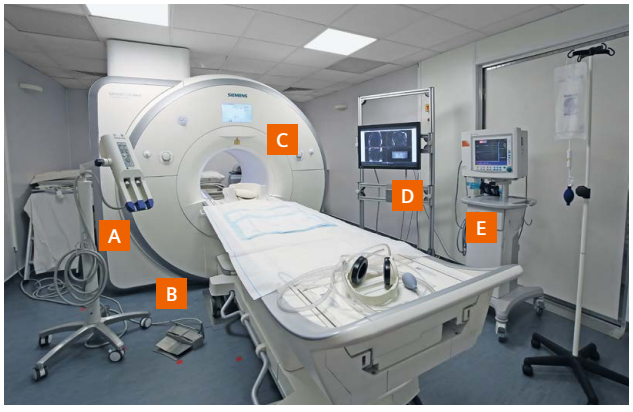
Over the past two decades, cardiovascular magnetic resonance (CMR) has emerged as a valuable technique for real-time guidance of cardiovascular procedures. Unlike traditional X-ray guidance, MR-guided catheterization is free of ionizing radiation and offers accurate measurements of cardiac function, volumes and blood flow, along with an excellent myocardial tissue characterization. The first MR-guided RHC procedures in humans were reported by Razavi et al. about 15 years ago [1]. In recent years, several centers have confirmed the feasibility, the safety, and the benefits of combining RHC with MRI [2–4]. Nowadays, the adoption of MR-guided RHC is progressively expanding from clinical research sites, using hybrid X-ray/CMR suites, to routine clinical practice with conventional CMR facilities.

Our institution is equipped with a 1.5T CMR scanner with a high throughput of about 5,500 CMR exams per year. We started an interventional CMR program in December 2018.

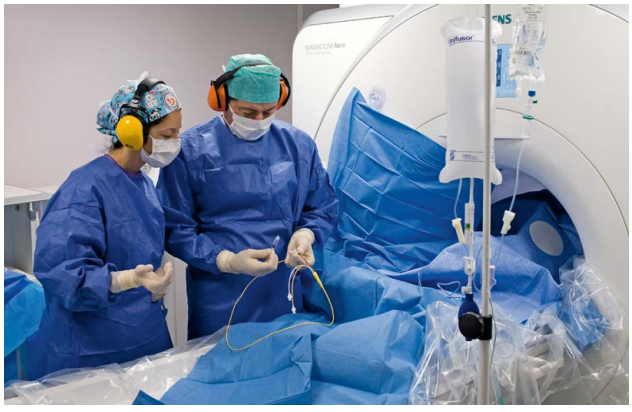
The aim of our study is to evaluate the feasibility and the safety of MR-guided RHC. 35 patients will be included by December 2019.

Methods

The research protocol was approved by the national Institutional Ethics Committee (2017-A03145-48). All patients provided informed written consent.



1 CMR suite and equipment: automated contrast injector (A), foot switch (B), 1.5T MAGNETOM Aera MR scanner (C), in-room monitor for Monte Carlo prototype display[1] (D), hemodynamic recording system (E).



2 The two interventional cardiologists filling the balloon of the catheter with a diluted solution of Gadolinium, so that the tip will be visible on CMR images. Their comfort is improved as they don't have to wear a heavy lead apron, that is mandatory in the cath lab for X-ray protection.

CMR suite and equipment

As shown in Figure 1, the procedures were performed in a conventional 1.5T CMR scanner (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany) with an 18-channel body cardiac coil. The MR room was equipped with an MR-compatible monitor[2] (prototype by EIZO GmbH, Rülzheim, Germany) to support real-time catheter guidance. Each procedure was performed with a 7 French three-lumen Swan-Ganz catheter (Edwards Lifesciences, Irvine, CA, USA) with femoral venous puncture. The balloon at the tip of the catheter was filled with a diluted gadolinium contrast solution (1/20, Dotarem, Guerbet, Aulnay, France), to allow its visualization on MR images as a bright spot (Fig. 2). Invasive blood pressures were recorded using an MR-compatible hemodynamic monitoring system[2] (non-commercially available). MR-conditional guidewires embedded with passive markers were available if needed (Nano4Imaging, Aachen, Germany).

Catheter guidance

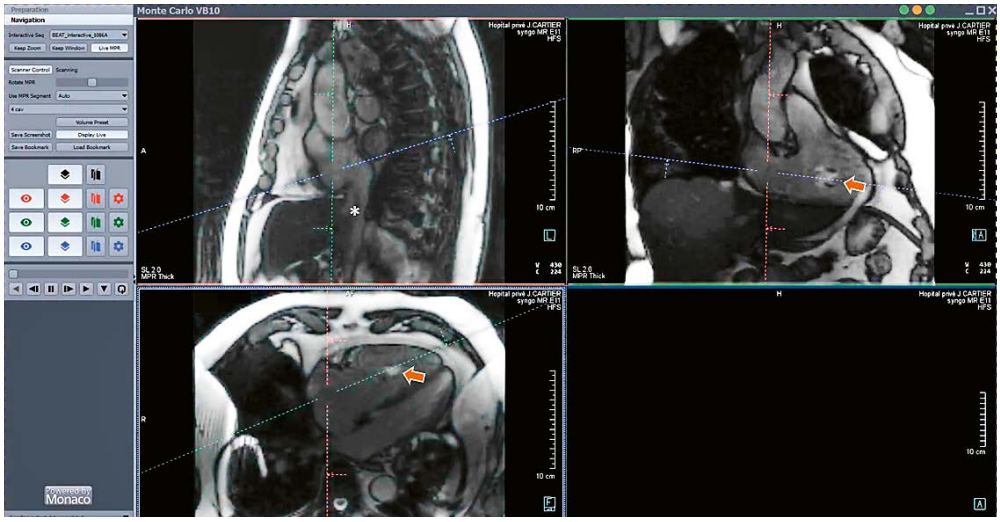
The MR-guided catheter navigation was done with an interactive real-time balanced steady-state free precession (b-SSFP) sequence (main parameters: TR/TE = 277/1.7 ms, FOV = 320 mm, matrix = 160, voxel size = 2 x 2 x 5 mm) allowing passive catheter tracking. Three planes were sequentially acquired with a frame rate of 1 per second. In addition, the workflow was supported by the Monte Carlo prototype[1] (Siemens Healthcare, Erlangen, Germany), consisting of an MR-compatible footswitch and a software application, installed on a remote computer connected to the MR host console. With Monte Carlo, the MR scans could be controlled and the MR images including the catheter tip were visualized (Fig. 3) on the mirrored in-room monitor and the screen in the control room. Reference views were planned by the technologist prior to catheter insertion: inferior vena cava long axis, 4-chamber view, right ventricular outflow track (RVOT) view, and bifurcation of the pulmonary artery (Fig. 4). Then, during catheter navigation, these views could be interactively selected and moved by the technologist to easily follow the catheter motion in real time.

MR-guided right heart catheterization procedure

The clinical staff consisted of two interventional cardiologists, two technologists, and a cardiologist specialized in CMR. Femoral venous access was obtained using ultrasound guidance. The catheter was inserted and navigated through the right heart. The interactive real-time sequence was used to visualize and follow the tip of the catheter, which appeared as a white spot in the images. Three different slices were updated every second and displayed on the in-room monitor for the cardiologists. All views could also be interactively modified, if needed. The sequence could be paused either by the interventional cardiologist using the foot switch or by the technologist via the Monte Carlo prototype. Communication between the cardiologist (in the MR room) and the technologist (in the control room) was ensured by the conventional MR communication system (Intercom). No additional MR-compatible communication system was available.

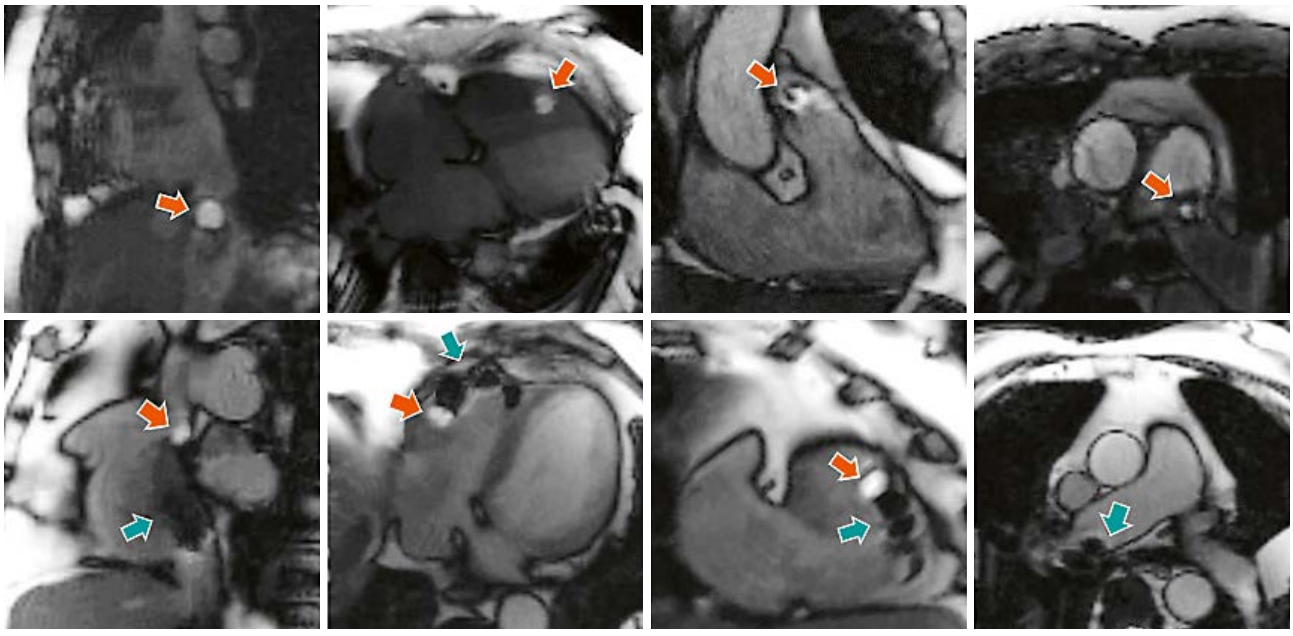
CMR diagnostic imaging

All patients underwent a diagnostic CMR exam directly after the catheterization procedure. Function evaluation was performed using a Compressed Sensing cine sequence with retrospective gating across two heartbeats. Two-chamber, four-chamber, two left-ventricle-outflow-track (LVOT), two right-ventricle-outflow-track (RVOT)



3 Monte Carlo interface showing three interactive views: vena cava long axis (top left, inferior vena cava depicted by an asterisk), 4-chambers (bottom left) and right ventricle outflow track view (top right). The tip of the catheter appears as a white spot in the images (orange arrow) and could be followed by the interventional cardiologist while it is navigated through the heart.

[1]Work in progress: the application is currently under development and is not for sale in the U.S. and in other countries. Its future availability cannot be ensured.
[2]The information shown herein refers to products of 3rd party manufacturers and thus are in their regulatory responsibility. Please contact the 3rd party manufacturer for further information.



4 Interactive real-time views used for catheter visualization without (top) and with a guidewire (bottom) in two patients. From left to right, as the catheter is navigated through the right side of the heart: vena cava long axis, 4-chambers, right ventricle outflow track and pulmonary artery bifurcation. The tip of the catheter can be seen as a white spot (orange arrow), corresponding to a diluted solution of gadolinium inside the catheter balloon. The guidewire is made visible by its markers creating signal void in the images (blue arrows, bottow row).

views were acquired, as well as a stack of 8-mm thick short-axis slices encompassing the whole ventricles. Aortic and pulmonary artery blood flow were measured by through-plane velocity-encoding phase-contrast sequences. Whereas cardiac output is usually measured by thermodilution in the cath lab, it was assessed non-invasively in our protocol, using the aortic blood flow sequence. The pulmonary to systemic blood flow ratio (Qp/Qs ratio) was calculated to exclude a potential left-right shunt. Then, a bolus of gadolinium was injected for first-pass perfusion imaging at rest. Late gadolinium enhancement imaging was acquired 10 minutes after injection. A real-time cine sequence could be added to assess the septal shift toward LV during inspiration in case of suspicion of constrictive pericarditis. All image viewing and interpretation were performed with *syngo*.via (Siemens Healthcare, Erlangen, Germany), using the 'MR Cardiac Analysis' workflow.

Results

Population

18 patients (67 ± 11 years, 11 men) were referred for MR-guided RHC from December 2018 to September 2019. Indications for RHC were pulmonary artery hypertension (15 patients), dilated cardiomyopathy (two patients), restrictive cardiomyopathy (one patient) and restrictive pericarditis (one patient).

Procedure

Hemodynamic measurement and diagnostic CMR were successfully completed in all patients without complications. The overall procedure was performed within approximately one hour, including less than 30 minutes dedicated to diagnostic CMR. A guidewire was used when manipulation of the catheter was more difficult, especially in very dilated right heart chambers. The other benefit of the guidewire was the passive markers that appear hypointense in images and help to visualize the catheter shaft.

Safety

MR-guided RHC showed excellent safety without any major adverse events. The interventional cardiologists reported a good noise tolerance using headset hearing protection. Dispensing with lead aprons, mandatory in the cath lab, improved the comfort of the operators.

Future perspectives

CMR has proven to be of great interest for the guidance of cardiovascular interventions such as hemodynamic characterization in pulmonary hypertension. The commercial availability of MR-conditional instrumentation will be the key to facilitating its adoption for more complex procedures, such as electrophysiology (EP) and radiofrequency (RF) ablation for cardiac arrhythmia (atrial flutter, atrial fibrillation and ventricular tachycardia). Pre-procedural

CMR is currently used for the assessment of scar distribution using high-resolution LGE imaging. Identification of arrhythmogenic substrate might enable an improved, targeted ablation strategy and have an impact on the procedural success [5]. However, it is even more attractive to replace X-ray fluoroscopic guidance with CMR, as direct visualization of lesion transmurality and gaps would potentially help to decide whether the ablation procedure is complete or not. It has been shown that RF lesions and surrounding edema could be well depicted with 3D non-contrast CMR sequences [6–8]. The feasibility of MR-guided EP and RF ablation in patients has been reported in a few early clinical studies [9–11]. Novel MR-conditional catheters are equipped with small coils that allow active tracking with automatic alignment of MR planes during catheter navigation. Further developments are under way to introduce these interventions into a routine CMR workflow (commercially available EP and ablation catheters, external defibrillators and other MR-conditional devices).

Conclusion

MR-guided RHC is safe and feasible in a fully clinical CMR facility. Patients benefit from a combined radiation-free RHC and a diagnostic CMR exam within one hour. Comfort of the interventional cardiologists is improved as they do not have to wear a heavy lead apron. This is a significant first step toward more sophisticated cardiovascular interventions under MR guidance, such as RF ablation for the treatment of arrhythmia. The direct visualization of RF lesions on MR images might be of particular value to assess the completeness of the procedure. This real-time feedback might help to avoid recurrence of the arrhythmia and thus the need to repeat procedures for improved and cost-effective patient care.

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Cardiovascular MRI Around the World

After decades of existence in an academic niche, Cardiovascular MRI is currently experiencing a phase of emancipation; moving beyond the research community and into clinical routine. With the support of international clinical societies and educational networks and the development of new technologies to standardize and automate CMR scans, cardiovascular MRI exams are now being performed across the globe. In the following article, we learn about the real-world challenges of setting up a CMR program in six different locations around the world. Although each location has its unique set of hurdles, a common theme is the need for standardization in order to permit scalability. Proving clinical benefit is not enough. CMR must be economically feasible and this can only be achieved by increasing scale, i.e. with shorter, standardized exams.

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Dr. Luca Arcari
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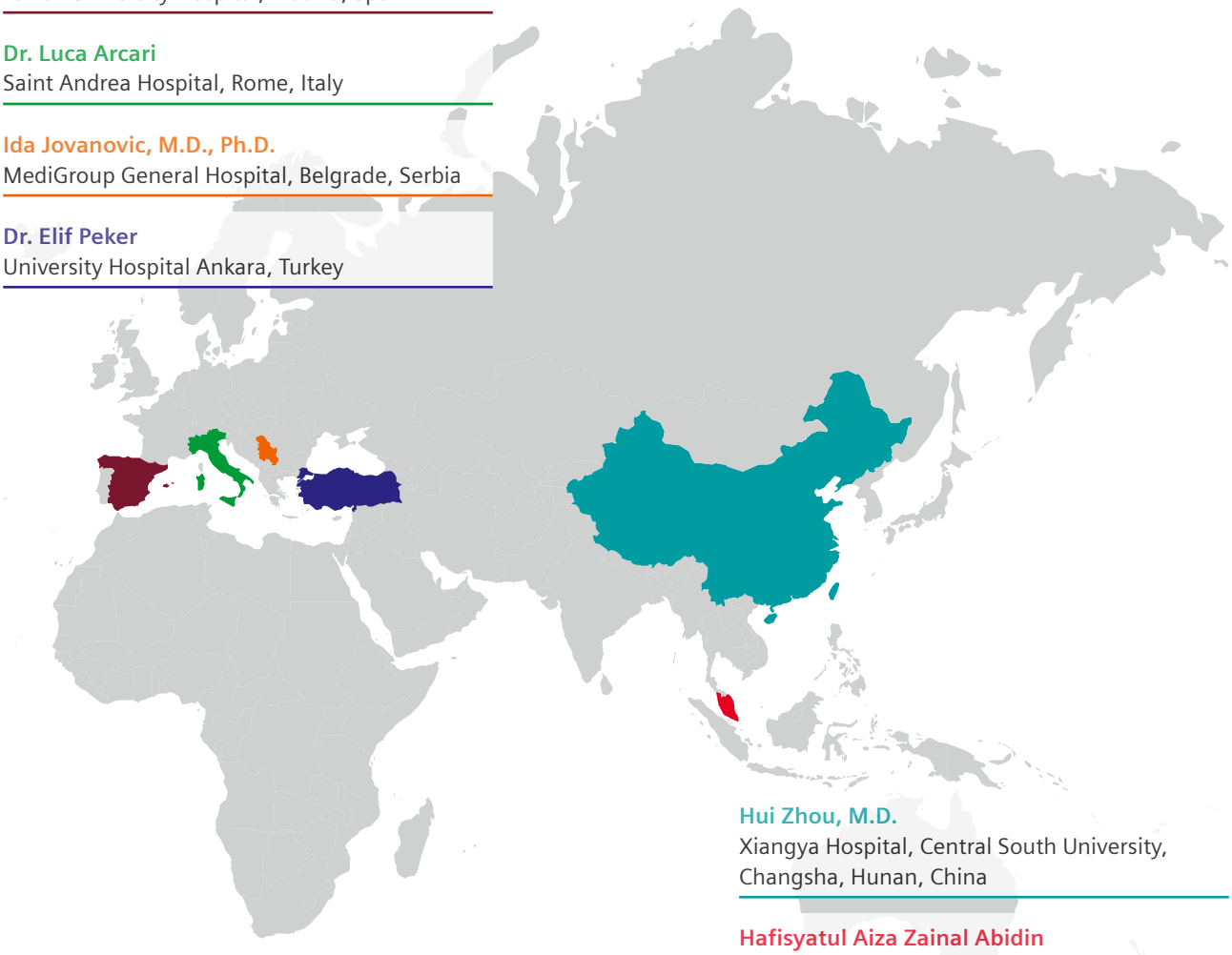

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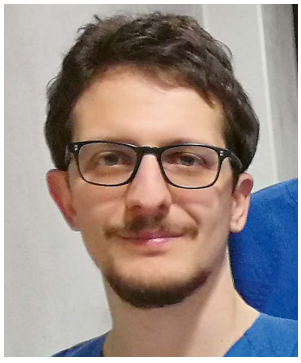
The First 3T Cardiac MR Scanner in Serbia

Ida Jovanovic, M.D., Ph.D.
Professor of Pediatrics and Cardiology,
Head of Pediatric Department and CMR team,
MediGroup General Hospital, Belgrade, Serbia

The first cardiac magnetic resonance (CMR) program dedicated to congenital heart diseases (CHD) in children and adults started in Serbia in 2010 at the University Children's Hospital in Belgrade. In a relatively short time, CMR was introduced into clinical routine in pediatric cardiology. The main goal was to describe cardiac anatomy, function, and flow quantification in complex CHD cases. In 2018, a 3T MAGNETOM Skyra scanner (Siemens Healthcare, Erlangen, Germany) was installed at MediGroup General Hospital in Belgrade and was the first top-level CMR equipment in the region. It took about two months to set up the new system. We faced many challenges, including coming to grips with the new software, sequence optimization for small children, 3D imaging of the whole heart, respiratory-navigated scanning, and similar. Artifacts were a significant problem at the beginning. However, this was mainly solved using good shimming. Special attention was paid to introducing emerging techniques for tissue quantification, such as T1 and T2 mapping, and ECV. The main reason for tissue quantification with CMR is the unique possibility to recognize early diffuse myocardial fibrosis, as the common pathological pathway toward loss of myocardial function. We are compiling our normal values for all parameters in both children and adults. In all patients, we obtain native T1 mapping whereas contrast media is only given if necessary for diagnostic reasons (such as MR angiographies, cardiomyopathies etc.). We try to avoid repeated contrast injections in young patients in whom further CMR follow-ups are planned. At our center, we celebrate the close teamwork between cardiologists and dedicated and experienced cardiac radiographers. We also foster cooperation with centers abroad, including University Hospital Frankfurt and Cardiothoracic Center Monaco.

Dr. Luca Arcari
Consultant Cardiologist, Subspeciality in Cardiovascular Imaging
Madre Giuseppina Vannini Hospital, Rome, Italy and
Saint Andrea Hospital, Sapienza University of Rome, Italy

"For the imaging cardiologist, cardiovascular magnetic resonance (CMR) represents a complementary tool that can provide answers to questions left unanswered by echocardiography. Is that "white spot" a scar? Is there regional viable myocardium? Is there diffuse fibrosis or edema to explain a global hypokinetic left ventricle? CMR can tell you this and more, often resolving the frustration of an unsolved problem. Yet, it takes a long time to master and implement the imaging technique. Training in centers with both expertise and volume is a must. I did my training at Goethe CVI, Frankfurt am Main, Germany. Personally, this gave me the opportunity to learn from mentors and fellows, cardiologists and radiologists from all over the world. What I learned from this experience is that, without specialist training, neither cardiologist nor radiologist can provide a high quality of service. Having said that, the hardest part comes later; namely, translating the experience gained abroad into a different local context. The return to reality may mean dealing with older machines, unexperienced personnel, a lack of interest from cardiologists, and the need to build bridges with those who are not willing to share technology that has limited availability. I finally found a role at Madre Giuseppina Vannini Hospital, Rome, Italy. The collaborative approach between radiologist Federica Ciolina and cardiologist Giovanni Camastra is an example of how a good clinical service can be delivered by combining experience and knowledge, working as peers. Fortunately, the newly installed 1.5T scanner (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany) is fully equipped the Cardiac Dot Engine as well as T1 and T2 mapping applications that enable us to shorten acquisition time and accurately quantify diffuse fibrosis and edema. Some gaps still remain, such as part-time availability of the machine and economic issues. However, the path to success looks much shorter now than it was at the beginning of the journey."



Matching Technological Advancement with Perseverance

Hafisyatul Aiza Zainal Abidin
Consultant Radiologist, CMR Department,
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Sungai Buloh, Shah Alam, Selango, Malaysia

Balancing an extremely high patient workload, achieving high quality diagnostic studies, and maintaining a great patient experience is a true challenge in CMR. Since it is increasingly used in clinical decision-making, it is important to ensure that the staff in the imaging unit are able to adapt to the dynamic changes required for attaining good image quality within minimal exam time. At the CMR department of the Universiti Teknologi MARA (UiTM), we recognize a number of technological and other advances that have helped us move forward.

Firstly, using the Cardiac Dot Engine on our MAGNETOM Aera 1.5T scanner (Siemens Healthcare, Erlangen, Germany) enables us to be time efficient. Setting up the routine and easy-to-follow protocol is key to maintaining quality in examinations performed. The Cardiac Dot Engine has made the transition possible while maintaining a similar standard among rotating nine radiographers. Nowadays, a standard rest protocol takes just about 30 minutes to complete from planning to late gadolinium enhancement sequence.

Secondly, it is also important to recognize that different gadolinium contrast agents have very different pharmacodynamics. The choice of agent as well as the appropriate dose of the contrast influences the timing of acquisition for late gadolinium enhancement imaging. We found that experienced use of a low-dose gadobutrol protocol results in increased scan efficiency and a small cost reduction. Using this technique, we achieve maximal contrast between myocardium and blood pool for precise scar detection.

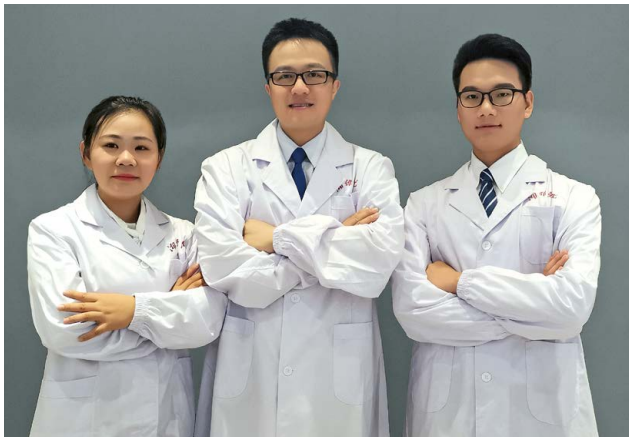
Thirdly, the era is now past where CMR examinations were known as tedious, complex, and time-consuming, so the patient experience has improved tremendously. Staff are now eager to engage in patient cooperation throughout the examination. Automated breathing commands allow operators to maintain a better focus on the quality of the images obtained rather than focusing on the technical aspects of the examination.

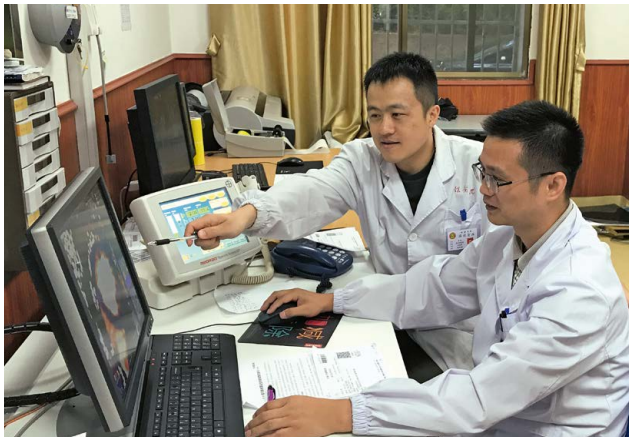
Finally, the courage to leave behind the 'traditional' long protocols and focus instead on the imaging that is proven to add benefit to the cardiology clinical care is key. It allows us to not only persevere with CMR, but also to ensure that we are able to move ahead together, taking advantage of the technological advancement in order to advance our skills and scientific knowledge.

Expanding the Role of CMR in China

Hui Zhou, M.D.
Associate Professor, Department of Radiology,
Xiangya Hospital, Central South University, Changsha, Hunan, China

The first magnetic resonance imaging (MRI) machine was introduced in China at the end of 1985. Later, the experimental and clinical application of cardiovascular magnetic resonance (CMR) was pioneered by Professor Huang Qichen at Nanfang Hospital. The first national scientific research project on CMR funded by the National Natural Science Fund was conducted by Professor Zhao Shihua of Fuwai Hospital in 1999. Although in many countries the application of CMR with the development of sequence technologies and clinical research seems to progress every day, the development of CMR in China remains limited. This is due to many factors such as equipment, investment, technical specifications, as well as clinical skill and expertise. Consequently, CMR is only performed at a few very specialized hospitals, unevenly distributed across various regions of China. The main challenges to the clinical application of CMR in China include long examination times, low reimbursement fees, large numbers of patients, and insufficiently skilled medical staff. The poor availability of adenosine or regadenoson mean that physicians focus on structural heart abnormalities and pay less attention to functional testing. Fortunately, more and more Chinese radiologists and cardiologists are attracted to this area and are investing in CMR training abroad. Many have returned with extensive experience and are positively promoting the standardization of CMR examinations in order to increase availability. For now, Chinese doctors have conducted a series of studies based on cardiac structure, function, and histological characteristics.





Chinese radiologists who have studied CMR abroad are positively promoting the standardization of CMR application in China.

Chinese CMR researchers are working to promote the application of CMR in China by standardizing the scanning procedures and diagnostic process, as well as by participating in international CMR research. So far, there have been few multicenter, large-scale clinical trials, and few Chinese hospitals have participated in international multicenter CMR research projects. Yet, as a national cardiovascular center, Fuwai Hospital has built the world's largest single-center database, with nearly 50,000 cases covering various cardiovascular diseases. The Chinese Expert Consensus on Clinical Application of Magnetic Resonance Imaging in Cardiomyopathy and the Chinese Expert Consensus on CMR Imaging Test Technology Standards were published in 2015 and 2019, respectively.

Dr. Elif Peker
Consultant Radiologist, University Hospital Ankara, Turkey

“I am a consultant radiologist and have been performing cardiac MRI at Ankara University Hospital for many years. I was very excited when I discovered that learning cardiac MRI would give me an edge in my career. However, I also understood I was taking on a big task as well as a risk due to my inexperience and the overall complexity of the modality. I started out by looking through the available sequences and protocols, without even knowing what sequence to use for what purpose! In those early days, our examinations took a painful 90 minutes. I found that one of the most challenging things was the pre-pulse delay in late gadolinium enhancement imaging. After a challenging beginning, I was determined to work hard and gain more experience. While I was not afraid to make mistakes, I also looked for people to learn from. I was grateful for the support of my colleagues Dr. İlhan Erden and Dr. Ayşe Erden. Dr. Hasan Yiğit first taught me some of the basics. I went to courses and congresses to learn about cardiac MRI from both a radiologist and a cardiologist perspective. I got to know the Frankfurt group through Dr. Puntmann’s webinars and the research on T1 mapping. I spent an incredible 6 months as a clinical research fellow driven by enthusiasm and hunger for learning, working hard and long hours on my research project. Nurses would find me asleep next to the workstation! And yet those were the days that I would happily relive again. The memory of this amazing experience lives on in my own great team that I work with today. Together, we enjoy passing on the knowledge to others by teaching cardiac MRI in Turkey.”

Silvia Valbuena López
Consultant Cardiologist, Specialist for Cardio-Oncology,
Department of Cardiology,
La Paz University Hospital, Madrid, Spain

“Being part of the CMR community is exciting. It means working with the top cardiac imaging techniques, which offer so many advantages. High quality images and accurate acquisitions of the heart structure obtained without ionizing radiation and increasingly without the use of contrast allow physicians to refine the diagnosis of and prognosis for so many patients. This information can mean notable improvement in their treatment and a reduction in uncertainty about their heart disease. The aspirations for CMR are enormous: It remains the technique of choice whenever there is doubt about diagnosing a particular cardiac condition or determining the extent of disease. But are current CMR methods truly capable of fulfilling these high expectations?

Many modern CMR imagers continue to perform lengthy studies, with a myriad of sequences to achieve a thorough cardiac and vascular examination. Unfortunately, this tendency which unfortunately continues to be the mainstay in many centers (even tertiary reference hospitals) reduces the availability of CMR time for a larger number of patients who could actually benefit from it. What is more, such lengthy studies are difficult to achieve in a patient population that is often very sick and struggles to lie flat or hold their breath for longer periods of time.

At our center, we focus our efforts on shorter exams targeted to address the key clinical questions. This allows us to increase the number of patients we can scan within the limited time the scanner is available. We found that our focused imaging strategies yield much better image quality in a much shorter time, reducing the usual struggles with tired patients, failing ECG gating or arrhythmias, and avoiding the vicious circle of repeating sequences with an exhausted patient.

Beyond technical issues, CMR expertise and staffing is a major issue. Access to training remains limited and you need to keep up with the constantly evolving developments in CMR to make the most of the latest advances. Cardiac MRI remains an elusive and difficult skill to learn, especially for radiographers. This means that qualified physicians often perform the examinations. For now, the true CMR believers remain committed to ongoing growth and self-improvement. A growing body of qualitative evidence that reiterates that CMR-guided patient care is not only more accurate but also more efficient continues to put pressure on the health authorities to distribute resources more fairly to also include our field. Together, we will try to reach the ultimate objective of medicine: to deliver the best care to our patients.”

Meet Siemens Healthineers

Siemens Healthineers: Our brand name embodies the pioneering spirit and engineering expertise that is unique in the healthcare industry. The people working for Siemens Healthineers are totally committed to the company they work for, and are passionate about their technology. In this section we introduce you to colleagues from all over the world – people who put their hearts into what they do.

Kelvin Chow

Kelvin Chow studied Engineering Physics during his undergraduate training at the University of Alberta (Edmonton, Canada) before completing a PhD in Biomedical Engineering at the same institution in his hometown of Edmonton, Alberta, Canada. He trained as a post-doctoral fellow at the University of Virginia (Charlottesville, VA, USA) and joined Siemens Healthineers as a Senior Scientist in 2016. Kelvin is part of the MR collaborations group, working together with researchers around the world to develop new MRI techniques. His primary research focus is on quantitative tissue characterization with cardiac MR. Together with colleagues and leading collaborators in the field, Kelvin's recent projects involve the ongoing development of MyoMaps, quantitative myocardial perfusion, and the Cardiac Dot Engine.

Chicago, USA

How did you first come into contact with MRI?
During the last year of my undergraduate studies, I explored various options for a master's research project. At that time, I met Dr. Richard Thompson, who showed me movies of the beating heart and visualizations of flow within the heart – I was hooked! It was (and still is) fascinating to me that we have the technology to acquire such detailed images that tell us about how our body works, all measured non-invasively using MRI. What started as a short master's research project turned into a doctoral thesis, a post-doctoral fellowship, and now a career with Siemens Healthineers.

What is the most fascinating aspect of MRI?
How there's always something new in MRI! The underlying basis for MR imaging is remarkably simple – apply a time-varying sequence of radiofrequency pulses and spatial magnetic gradients in the presence of a strong magnetic field. And yet, the pace of MRI advancements has not slowed in the last 40 years of development, with new techniques still being developed by simply changing the timing and pattern of pulse sequences. Advancements in hardware performance and computational power have also opened the doors to techniques once not thought to be possible.

MRI is also unique in the research world due to its incredible translational potential. A researcher can use their knowledge of MRI physics to design a pulse sequence, program it on their laptop, and use it to image a human subject ... all in a single day! The short development cycle from an idea to clinical application makes MRI one of the most exciting research fields to work in.

What do you think are the most important developments in MRI and in Healthcare?
Increased availability of medical imaging such as MRI is an important area of research in order to bring its benefits to a wider population. The value of information provided by MRI in the diagnosis and management of patients is well established in many diseases, but MRI is still a highly specialized technique that is not widely used. Developments such as highly accelerated imaging with Compressed Sensing and automated technologies such as the Dot Engines help to shorten scan times and reduce complexity in acquisition and interpretation, which are essential to expanding the availability of MRI to more patients.

The evolution of MRI and healthcare overall toward precision medicine also holds promise for improved patient care by personalizing treatments for each individual instead of applying the traditional "one-size-fits-all" approach. Precision medicine relies on accurate and comprehensive characterization of a patient's disease and overall health, an area where MRI excels.

For example, a single cardiac MRI exam can provide a wealth of information about the heart, including cardiac structure, function, viability of damaged tissue, and micro-structural changes that may precede disease progression. Development of accurate and precise quantification techniques such as these may provide valuable information for personalized treatments in the future.

Outside of work ...
In my free time, I am still a huge geek for anything technological. I enjoy being driven around by the artificial intelligence in my Tesla electric car, expanding my Lego collection, and dabbling in 3D printing. Last year, I started a high-intensity aerobic exercise program with the goal of running my first 5 km race, which I completed earlier this fall. Along the way, I had regular cardiac MRI exams in order to see for myself the benefits of exercise on my heart!

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