Myocardial First-Pass Perfusion Imaging with High Resolution and Extended Coverage Using Multi-Slice CAIPIRINHA

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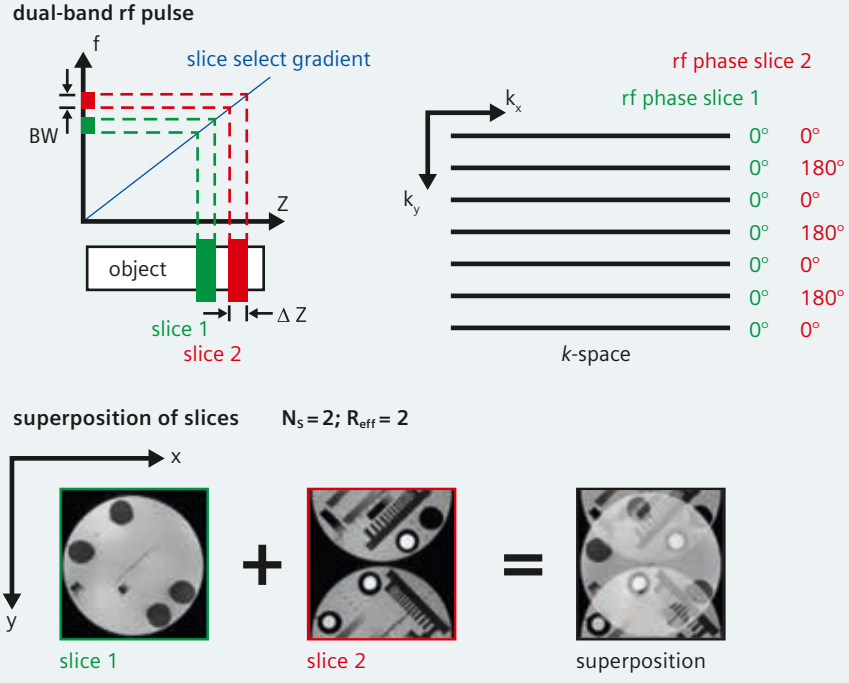
Background

Contrast-enhanced myocardial first-pass perfusion MR imaging (MRI) is a powerful clinical tool for the detection of coronary artery disease [1–4]. Fast gradient echo sequences are employed to visualize the contrast uptake in the myocardium with a series of saturation prepared images. However, the technique is strictly limited by physiological constraints. Within every RR-interval, only a few slices can be acquired with low spatial resolution, while both high resolution and high coverage are required for distinguishing subendocardial and transmural infarcted areas [5] and facilitating their localization, respectively.
Acceleration techniques like parallel imaging (pMRI) have recently shown their suitability for improving the spatial resolution in myocardial first-pass perfusion MRI [5–7]. Within clinical settings, 3 to 4 slices can be acquired every heartbeat with a spatial resolution of about $2.0 \times 2.0\,mm^2$ in plane [6]. However, for increasing anatomic coverage [8], standard parallel imaging is rather ineffective, as it entails significant reductions of the signal-to-noise ratio (SNR):

a) In order to sample more slices every RR-interval, each single-slice measurement has to be shortened by a certain acceleration factor R, which

1A **Conventional MS-CAIPIRINHA** for coverage extension
Multi-slice excitation and rf phase cycling



1A MS-CAIPIRINHA with two slices simultaneously excited ($N_S = 2$). A dual-band rf pulse is utilized to excite two slices at the same time (BW = excitation bandwidth). During data acquisition, each slice is provided with an individual rf phase cycle. A slice specific constant rf phase increment is employed (0° in slice 1, 180° in slice 2) between succeeding excitations. Consequently, the two slices appear shifted by ½ FOV with respect to each other. In this way, the overlapping pixels originate not only from different slices, but also from different locations along the phase encoding direction (y), facilitating a robust slice separation using pMRI reconstruction techniques. Using the two-slice excitation, effectively a two-fold acceleration is achieved ($R_{eff} = 2$).

inevitably comes along with an √R-fold SNR reduction.

b) During image reconstruction, the SNR is further reduced by the so-called geometry (g)-factor [9], an inhomogeneous noise-amplification depending on the encoding capabilities of the receiver array.

In addition, unless segmented acquisition techniques are utilized [10], the saturation recovery (SR) magnetization preparation has to be taken into account:

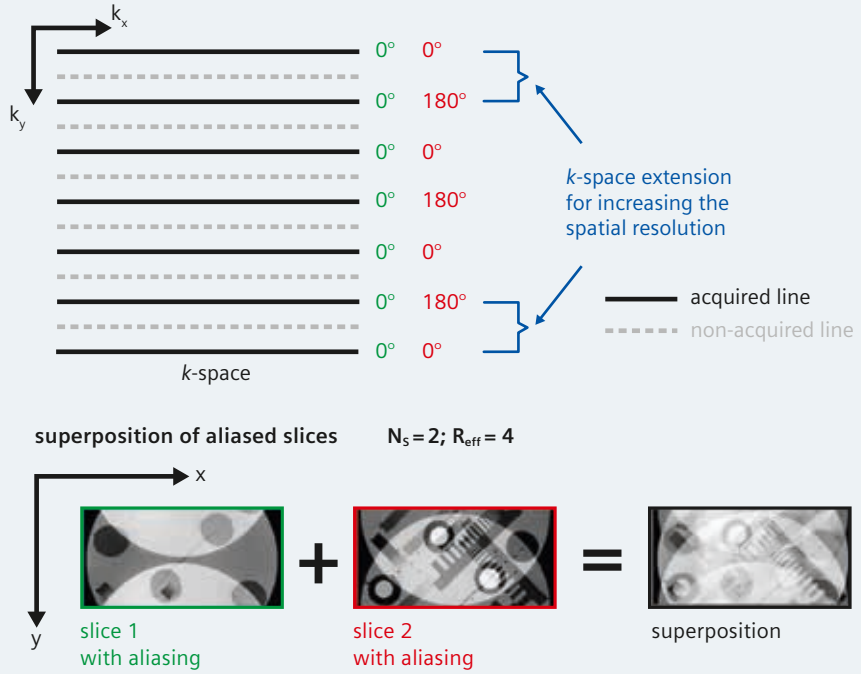
c) The preparation cannot be accelerated itself. Hence, the acceleration factor R has to be higher than the factor by which the coverage is extended. This leads to an increase of the SNR-reduction discussed in (a).

d) Subsequent to the preparation, the signal increases almost linearly with time. Thus, shortening the acquisition by a factor of R is linked to an additional R-fold SNR-loss.

As demonstrated recently [11], most of these limitations can be overcome by employing the **MS-CAIPIRINHA** (**M**ulti-**S**lice **C**ontrolled **A**liasing **I**n **P**arallel **I**maging **R**esults **IN** **H**igher **A**cceleration) concept [12, 13] for simultaneous 2D multi-slice imaging. By simultaneously scanning multiple slices in the time conventionally required for the acquisition of one single slice, this technique enables a significant increase in anatomic coverage. Since image acquisition time is preserved with respect to the single-slice measurement, the technique does not experience any SNR reductions despite the g-factor noise amplification of the required pMRI reconstruction [11, 12]. The MS-CAIPIRINHA concept can also be employed with acceleration factors that are higher than the number of slices excited at the same time. By utilizing this acceleration for increasing spatial resolution, the technique facilitates myocardial first-pass perfusion examinations with extended anatomic coverage and high spatial resolution.

A short overview of the concept is set out below, followed by a presentation of *in-vivo* studies that demonstrate the capabilities of MS-CAIPIRINHA in contrast-enhanced myocardial first-pass perfusion MRI.

1B **MS-CAIPIRINHA with $R_{eff} > N_s$** for improving coverage and resolution
Multi-slice excitation, *k*-space undersampling and rf phase cycling

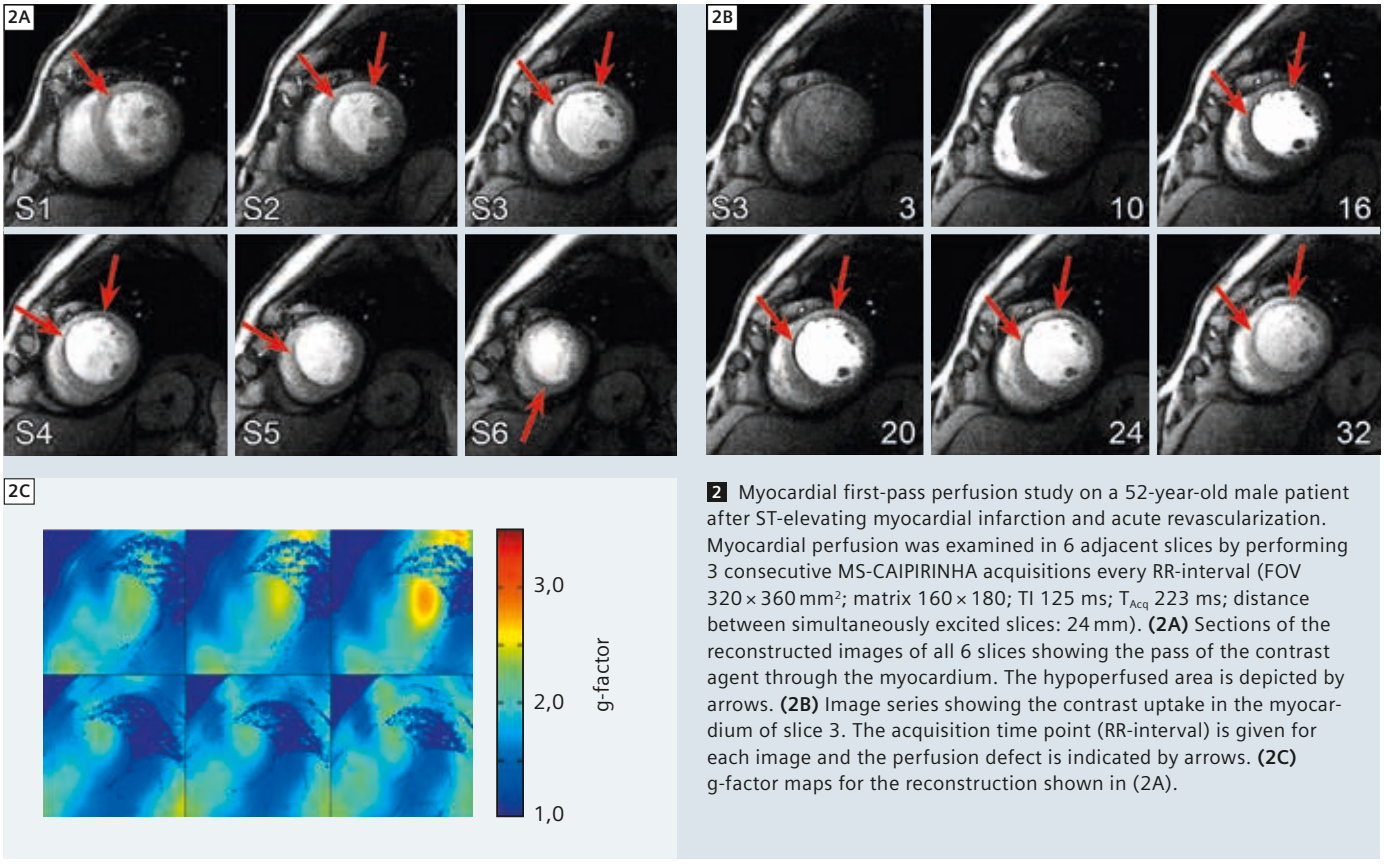


1B MS-CAIPIRINHA with an effective acceleration factor higher than the number of slices excited simultaneously. Again, two slices are excited at the same time employing the same rf phase cycles as in (1A), but *k*-space is undersampled by a factor of two. The slices and their undersampling-induced aliasing artifacts appear shifted with respect to each other by ½ FOV and can be separated using pMRI reconstruction techniques. Effectively, a four-fold acceleration is achieved ($R_{eff} = 4$). The additional acceleration can be employed to extend *k*-space and to improve the spatial resolution.

Improving anatomic coverage and spatial resolution with MS-CAIPIRINHA

MS-CAIPIRINHA

The MS-CAIPIRINHA concept [12, 13] is based on a coinstantaneous excitation of multiple slices, which is accomplished by means of multi-band radiofrequency (rf) pulses (Fig. 1A). Being subject to the identical gradient encoding procedure, the simultaneously excited slices appear superimposed on each other, unless the individual slices are provided with different rf phase cycles. In MS-CAIPIRINHA, the latter is done in a well-defined manner in order to control the aliasing of the simultaneously excited slices. Making use of the Fourier shift theorem, dedicated slice specific rf phase cycles are employed to shift the slices with respect to each other in the field-of-view (FOV) (Fig. 1A). The slice separation is performed using pMRI reconstruction techniques. However, the shift of the slices causes superimposed pixels to originate from not only different slices, but also different locations along the phase encoding direction. Thus, the MS-CAIPIRINHA concept allows the pMRI reconstruction to take advantage of coil sensitivity variations along two dimensions and to perform the slice separation with low g-factor noise amplification [12].



2 Myocardial first-pass perfusion study on a 52-year-old male patient after ST-elevating myocardial infarction and acute revascularization. Myocardial perfusion was examined in 6 adjacent slices by performing 3 consecutive MS-CAIPIRINHA acquisitions every RR-interval (FOV 320 × 360 mm²; matrix 160 × 180; TI 125 ms; T_{Acq} 223 ms; distance between simultaneously excited slices: 24 mm). **(2A)** Sections of the reconstructed images of all 6 slices showing the pass of the contrast agent through the myocardium. The hypoperfused area is depicted by arrows. **(2B)** Image series showing the contrast uptake in the myocardium of slice 3. The acquisition time point (RR-interval) is given for each image and the perfusion defect is indicated by arrows. **(2C)** g-factor maps for the reconstruction shown in (2A).

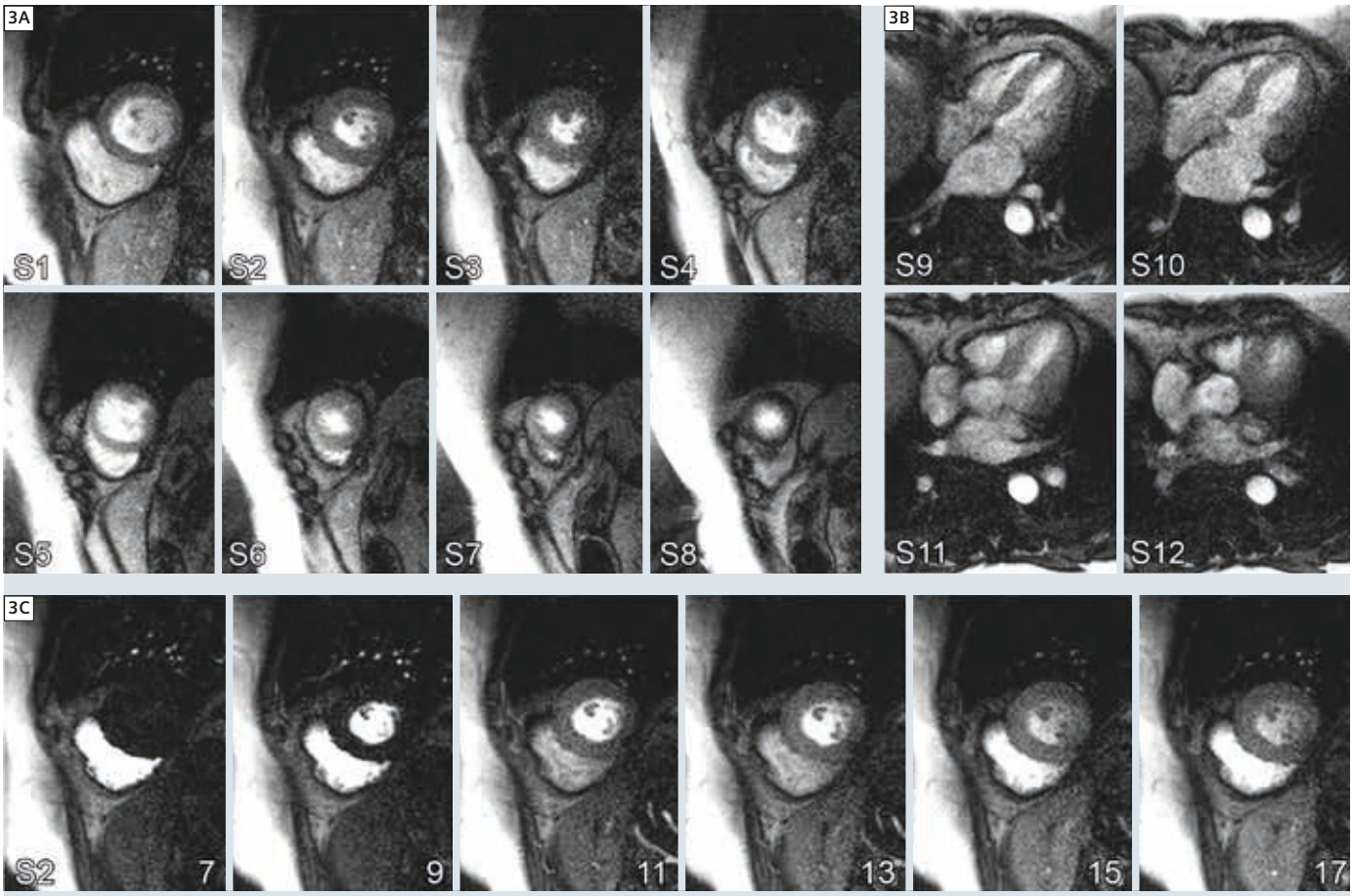
By conserving image acquisition time with respect to an equivalent single-slice measurement, the technique is not subject to any further SNR penalties. MS-CAIPIRINHA hence allows extending the coverage in 2D multi-slice imaging in a very efficient manner. Applied to myocardial first-pass perfusion imaging, the concept facilitates the acquisition of 6 slices every heartbeat with an image quality that is comparable to that of conventional 3-slice examinations [11].

Additional acceleration

While extending the coverage can be accomplished by simultaneous multi-slice excitation, improving the spatial resolution requires additional *k*-space data to be sampled during image acquisition. Of course, as the FOV and the image acquisition time are to be conserved, this can only be achieved by means of additional acceleration. However, the effective acceleration factor of MS-CAIPIRINHA is not restricted to the number of slices excited simultaneously. By applying simultaneous multi-slice excitation to an imaging protocol with reduced phase FOV, i.e. equidistant *k*-space undersampling, supplementary in-plane acceleration can be incorporated (Fig. 1B). The rf phase modulation forces the two simultaneously excited slices and their in-plane aliasing artifacts to be shifted with respect to each other in the FOV. As before, image reconstruction and slice separation is performed utilizing pMRI methods. Employed like this, the MS-CAIPIRINHA concept facilitates an increase of both, anatomic coverage and spatial resolution with high SNR efficiency. Since image acquisition time does not have to be shortened, SNR is only affected by the voxel size and the noise amplification of the pMRI reconstruction.

Imaging

Perfusion datasets were obtained from several volunteers and patients. The study was approved by the local Ethics Committee and written informed consent was obtained from all subjects. All examinations were performed on a clinical 3T MAGNETOM Trio, a Tim system (Siemens AG, Healthcare Sector, Erlangen, Germany), using a dedicated 32-channel cardiac array coil (Siemens AG, Healthcare Sector, Erlangen, Germany) for signal reception. Myocardial perfusion was assessed using a SR FLASH sequence (FOV 320 × 300-360 mm²; matrix 160 × 150-180; TI 110-125 ms; TR 2.8 ms; TE 1.44 ms; T_{Acq} 191-223 ms; slice thickness 8 mm; flip angle 12°). Two slices were excited at the same time (distance between simultaneously excited slices: 24-32 mm) and shifted by ½ FOV with respect to each other by respectively providing the first and second slice with a 0° and 180° rf phase cycle. In order to realize a spatial resolution of 2.0 × 2.0 mm² within the imaging plane, *k*-space was undersampled by a factor of 2.5, resulting in an overall effective acceleration factor of 5.



3 Myocardial first-pass perfusion study on a 51-year-old female volunteer with whole heart coverage. 6 consecutive MS-CAIPIRINHA acquisitions were performed every two RR-intervals (FOV 320 × 300 mm²; matrix 160 x 150; TI 110 ms; T_{Acq} 191 ms; distance between simultaneously excited short/long axis slices: 32/16 mm). **(3A)** Sections of the reconstructed short axis images. **(3B)** Sections of the reconstructed long axis images. **(3C)** Series of image sections showing the contrast uptake in the myocardium of slice 2. The acquisition time point (RR-interval) is given for each image. **(3D)** g-factor maps for the reconstructions shown in (3A). **(3E)** g-factor maps for the reconstructions shown in (3B). **(3F)** Measurement scheme. The acquisition was performed with a temporal resolution of 1 measurement every 2 RR-intervals.

All first-pass perfusion measurements were conducted in rest over a total of 40 heartbeats. All subjects were asked to hold their breaths during the acquisition as long as possible. Every RR-interval, 3 to 4 consecutive MS-CAIPIRINHA acquisitions were performed in order to sample the contrast uptake of the myocardium. For contrast enhancement, a contrast agent bolus (4 ml, Gadobutrol, Bayer HealthCare, Berlin, Germany) followed by a 20 ml saline flush was administered at the beginning of each perfusion scan. Image reconstruction was performed using an offline GRAPPA [14] reconstruction. The according weights were determined from a separate full FOV calibration scan. To evaluate the GRAPPA reconstruction, an additional noise scan was obtained and the g-factor noise enhancement was quantified [15]. All calculations were performed on a standalone PC using Matlab (The MathWorks, Natick, MA, USA).

Results

Figure 2 shows the results of a myocardial first-pass perfusion examination with 6-slices on a 52-year-old male patient (91 kg, 185 cm) on the fourth day after STEMI (ST-elevating myocardial infarction) and acute revascularization. Sections of the reconstructed images of all examined slices are depicted, showing the first pass of contrast agent through the myocardium (Fig. 2A). Also displayed is a series of image sections demonstrating contrast uptake in slice 3 (Fig. 2B). The GRAPPA reconstruction separated the simultaneously excited slices without visible artifacts. The g-factor maps (Fig. 2C) indicate generally low noise amplification. Thus, in comparison to the high effective acceleration factor of 5, the images provide excellent image quality. Both contrast and SNR allow for a clear delineation of the subendocardial hypoperfused area within the anterior and septal wall of the myocardium (arrows).

The results of a first-pass perfusion study with whole heart coverage are displayed in Fig. 3. In a 51-year-old female volunteer, first pass perfusion was examined in eight short (Fig. 3A) and four long axis slices (Fig. 3B). In order to accomplish the 12-slice examination and to achieve whole heart coverage, temporal resolution was reduced by a factor of two with respect to the examination displayed in Fig. 2. The contrast uptake of the myocardium was sampled with 1 measurement every two RR-intervals by performing 3 out of 6 consecutive double-slice MS-CAIPIRINHA acquisitions every heartbeat (Fig. 3F). Image reconstruction could be performed without visible artifacts and generally low noise amplification (Figs. 3D and E). Only in a few regions, the g-factor maps show moderate noise enhancement. In the images, the myocardium is homogeneously contrasted and the contrast agent uptake is clearly visible (Fig. 3C).

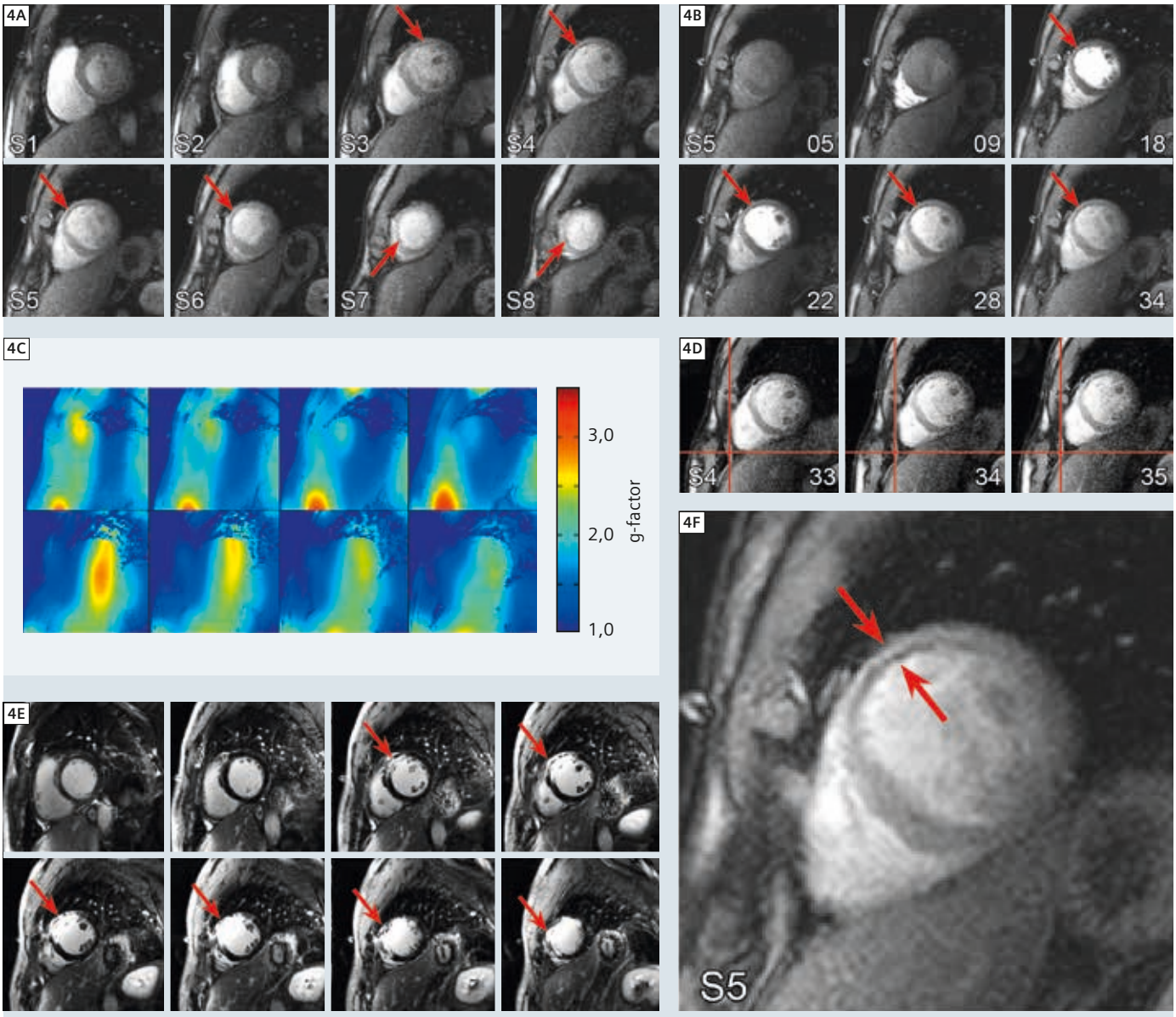
The findings of a first-pass perfusion study in a 48-year-old male patient (80 kg, 183 cm) on the eighth day after STEMI and acute revascularization are presented in Fig. 4. An overall of 8 slices were acquired with a temporal resolution of 1 measurement every RR-interval by performing 4 consecutive MS-CAIPIRINHA acquisitions after each ECG trigger pulse. Sections of the reconstructed images, showing the first pass of contrast agent through the myocardium in all 8 slices (Fig. 4A) are depicted together with sections demonstrating the process of contrast uptake in slice 5 (Fig. 4B). Despite the breathing motion (Fig. 4D), the GRAPPA reconstruction performed robustly and separated the slices without significant artifacts. The g-factor noise amplification is generally low and moderate within a few areas (Fig. 4C). In the images, the hypoperfused subendocardial region in the anterior wall can be clearly identified (arrows). As can be seen from the enlarged section of slice 5 (Fig. 4F), the technique provides sufficient spatial resolution to distinguish between subendocardial and transmural perfusion defects. These findings correspond well to the results of a subsequently performed Late Enhancement study (Fig. 4E) delineating a transmural infarction zone of the anterior wall (midventricular to apical).

Discussion

Contrast-enhanced myocardial first-pass perfusion MRI with significantly extended anatomic coverage and high spatial resolution can be successfully performed by employing the MS-CAIPIRINHA concept for simultaneous multi-slice imaging. Basically, two different acceleration approaches are combined: the simultaneous excitation of two slices on the one hand and *k*-space undersampling on the other. While the first directly doubles the number of slices acquired, the second provides sufficient acceleration for improving the spatial resolution. The proposed imaging protocols provide an effective acceleration factor of 5, which is sufficient for the acquisition of 6 to 8 slices every RR-interval with a high spatial resolution of $2.0 \times 2.0 \times 8\,mm^3$. Correspondingly, whole heart coverage can be achieved by sampling 12 slices with a temporal resolution of 1 measurement every 2 RR-intervals. Since the slices can be planned with individual thickness and pairwise specific orientation, the concept thereby provides high flexibility. With image acquisition times of 191 ms, it also supports stress examinations in 6 slices up to a peak heart rate of 104 bpm.

Employing a dedicated 32-channel cardiac array coil, the image reconstructions could be performed without significant reconstruction artifacts and only low to moderate g-factor noise amplification. Also in presence of breathing motion, the GRAPPA reconstruction performed robustly. The images provided sufficient SNR and contrast between blood, myocardium and lung tissue to delineate small perfusion defects and to differentiate between subendocardial and transmural hypoperfused areas.

Compared to conventional parallel MRI, the MS-CAIPIRINHA concept benefits from the high SNR efficiency discussed earlier. Simultaneous multi-slice excitation allows increasing the coverage without supplementary *k*-space under-



4 Myocardial first-pass perfusion study on a 48-year-old male patient after ST-elevating myocardial infarction and acute revascularization. 8 slices were acquired every RR-interval by performing 4 consecutive MS-CAIPIRINHA acquisitions (FOV 320 × 300 mm²; matrix 160 × 150; TI 110 ms; T_{Acq} 191 ms; flip angle 10°; distance between simultaneously excited slices: 32 mm). **(4A)** Sections of the reconstructed images of all 8 slices showing the first pass of the contrast agent through the myocardium. The hypoperfused area is depicted by arrows. **(4B)** Image series showing the contrast uptake in the myocardium of slice 5. The acquisition time point (RR-interval) is given for each image and the perfusion defect is indicated by arrows. **(4C)** g-factor maps for the reconstruction shown in (4A). **(4D)** Displacement of the heart due to breathing motion, example for slice 4. **(4E)** Late gadolinium enhancement. **(4F)** Enlarged section of slice 5. The technique allows distinguishing between subendocardial and transmural perfusion defects.

sampling. At the same time the g-factor noise amplification is minimized by exploiting coil sensitivity variations in both, slice and phase encoding direction. Thus, despite the doubled anatomic coverage, the image quality obtained is comparable to that of an accelerated measurement with standard coverage and high spatial resolution [5]. An important feature of the MS-CAIPIRINHA concept in myocardial first-pass perfusion MRI is the frame-by-frame reconstruction, which prevents the reconstructed images to be affected by temporal blurring. Moreover, arrhythmia and breathing motion only impact the underlying time frame and not the whole image series, as it is likely for reconstruction techniques incorporating the temporal domain [16–19].

Simultaneous multi-slice excitation is, of course, linked to an increase in the amount of energy that is deployed to the subject under investigation. Thus, limitations have to be expected at higher field strengths or when using sequences with larger flip angles, such as TrueFISP. At 1.5 Tesla, the application of the MS-CAIPIRINHA concept to TrueFISP has been successfully demonstrated utilizing advanced rf phase cycling [11].
In all *in-vivo* examinations, the distance between the two slices excited simultaneously was maximized in order to make use of the highest possible coil sensitivity variations in slice direction and to minimize the g-factor penalty. Thus, the spatial distance between consecutively acquired cardiac phases is large which might be a possible drawback for correlating hypoperfused regions of the myocardium. While the latter was feasible for all *in-vivo* studies, slice distance naturally can be reduced at the expense of slightly more noise enhancement.

Conclusion

Utilizing the MS-CAIPIRINHA concept for simultaneous multi-slice imaging, contrast-enhanced myocardial first-pass perfusion MRI can be performed with an anatomic coverage of 6 to 8 slices every heart beat and a high spatial resolution of $2.0 \times 2.0 \times 8\,mm^3$. Based on the simultaneous excitation of multiple slices, the concept provides significantly higher SNR than conventional in-plane acceleration techniques with identical acceleration factor and facilitates an accurate image reconstruction with only low to moderate g-factor noise amplification. Taking into account the high flexibility, simple applicability and short reconstruction times in addition to the high robustness in presence of breathing motion or arrhythmia, the concept can be considered a promising candidate for clinical perfusion studies.

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