Ultrafast Magnetic Resonance Imaging Procedures for the Assessment of Cardiac Function

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Table of Contents

Summary....................................................................................................................... 5

Zusammenfassung ........................................................................................................ 7

Chapter 1: Introduction .............................................................................................. 9

Chapter 2: Real Time Cardiac MRI ......................................................................... 11

  2.1. Assessment of Cardiac Function Parameters by
      Real Time Magnetic Resonance Imaging ............................................................... 11
  2.2. Real Time Interactive Magnetic Resonance Imaging ............................................. 27

Chapter 3: Myocardial Motion Analysis................................................................. 43

  3.1. Ultrafast CSPAMM tagging.................................................................................. 43
  3.2. RingTag: Ring Shaped Tagging for Myocardial Centerline Assessment ............... 59
  3.3. Template Based Evaluation Procedure for CSPAMM Tagged Images .................. 77
  3.4. Magnetic Resonance Tagging under Ergometer Stress ......................................... 93

Chapter 4: Discussion & Conclusion ..................................................................... 111

Acknowledgments .................................................................................................... 113

Curriculum Vitae ...................................................................................................... 114
Summary

Fundamental understanding of the heart and its diseases is a challenging task due to the complexity of the heart structure and of the entire cardiovascular system. For the successful treatment and management of diseases, knowledge of the heart functionality is essential. Visualization by means of imaging modalities has thus drawn increasing interest over the last years. Magnetic Resonance Imaging (MRI) is a powerful tool which allows for the non-invasive assessment of the heart anatomy and function without exposure to ionizing radiation. The method enables the acquisition of arbitrarily oriented slice images or three dimensional image data sets with high temporal and spatial resolution to provide deepened insight into physiology and pathophysiology of the heart. In particular the accurate analysis of the heart wall dynamics has proven to be very useful. This is enabled by a unique MRI technique called Myocardial Tagging. Previous patient studies have proven the outstanding potential of this technique which offers new possibilities for understanding heart function.

The objective of the present thesis was the development and the application of high-speed imaging sequences for the assessment of the heart function. Such examinations are required for cardiac MRI in order to resolve the rapid cardiac dynamics as well as to reduce motion related artifacts.

A fast, hybrid acquisition technique was implemented and applied for anatomical imaging of the heart in real time. The function parameters as obtained after analysis of the real time images were compared with the results measured with a conventional, ECG gated gradient echo sequence. The effect of the time resolution on image quality was investigated and different prepulses for modifying image contrast were evaluated. The real time MRI protocol enabled the acquisition of image sequences with high temporal resolution and diagnostic quality. The imaging procedure does neither rely on cardiac synchronization, nor on breathing compensation techniques. Consequently, measurements are facilitated, especially in patients with irregular heart beats or inability of performing breath holds. It could be shown that important cardiac function parameters such as wall thickening and ejection fraction may reliably be determined using real time protocols. These high-speed acquisition techniques establish new application areas in MRI such as interactive imaging procedures or examinations under stress conditions.

For time constrained assessment of myocardial motion parameters, as existing under stress conditions, a tagging magnetization preparation was combined with an ultrafast image acquisition sequence. For prolonged tag line visibility and easier post processing, a constant tag line intensity was
achieved by optimization of the imaging flip angles. Acquisition times for such tagging experiments were reduced to few heart beats, which enabled the application for physically induced stress examinations. This setup was applied in a volunteer study for measurement of the heart kinematics under physical exercise. For time-efficient evaluation of tagging images a new evaluation software based on template matching of a physically modeled grid was developed. Conventional tagging measurements can thus be processed in a fraction of the previously required time.

For improved estimation of heart contractility and time efficient image evaluation, the tagging sequence RingTag was developed. Based on a user definable, convex ring saturation band, the deformation and displacement of a dedicated structure, such as the myocardial mid-line, may be tracked. The feasibility of this technique was demonstrated in phantom measurements as well as in volunteer examinations. The simple geometry of the ring saturation structure allows for time-efficient evaluation.

In conclusion, the application of ultrafast imaging techniques allows for magnetic resonance imaging in very short time and thus, enables to resolve highly dynamic processes and to reduce motion related artifacts. New application areas for MRI are established such as interactive imaging procedures or examinations under stress conditions. The comprehensive properties of MRI allow for the investigation of multiple aspects in a single examination what is often referred to as a diagnostic “one-stop-shop”. Consequently, ultrafast imaging techniques provide a powerful new tool for clinical diagnosis, as well as for basic physiological and pathophysiological research.

Die vorliegenden Arbeit befasst sich mit der Anwendung sehr schneller Abbildungsverfahren zur Erfassung der Herzfunktionalität. Messverfahren dieser Art werden für MRT am Herzen benötigt um einerseits die schnelle Herzbewegung zeitlich auflösen zu können und andererseits, um bewegungsinduzierte Artefakte zu unterdrücken.

Für die Untersuchung der Herzbewegung unter Belastung wurde eine Tagging-Präparationstechnik mit einer sehr schnellen Bildgebungssequenz kombiniert. Mit der Optimierung der Anregungswinkel für die Bildgebung erhält man einen konstanten Kontrast der Taglinien über alle gemessenen Herzphasen, was sich auch positiv auf die spätere Auswertung der Bilder auswirkt. Die Aufnahmezeit für Tagging-Untersuchungen dieser Art konnte so auf wenige Sekunden reduziert werden, was die Anwendung unter körperlicher Belastung erlaubt. In einer Probandenstudie konnten Variationen der Herzbewegung unter Belastung quantifiziert und somit die erfolgreiche Anwendung solcher Untersuchungen gezeigt werden.

Für die zeitlich effiziente Auswertung von Taggingbildern wurde eine neue Auswertungssoftware entwickelt, welche auf der dynamischen Anpassung eines physikalisch modellierten Gittermodells basiert. Die Auswertung konventioneller Taggingdatensätze kann so in einem Bruchteil der sonst benötigten Zeit erfolgen.


Zusammengefasst wird mit ultraschnellen MRI-Sequenzen das Erzeugen von Bildern in sehr kurzer Zeit und somit die Visualisierung von schnellen physiologischen Prozessen, sowie die Reduktion von bewegungsinduzierten Bildartefakten, ermöglicht. Neue Anwendungsgebiete, wie zum Beispiel interaktive Messverfahren oder Untersuchungen unter Stressbedingungen, werden erschlossen. Mit den umfassenden Eigenschaften des MRI wird das Untersuchen mehrerer Aspekte in einer einzigen Sitzung, was auch als “one-stop-shop” bezeichnet wird, praktikabel. Ultraschnelle Bildgebungssequenzen sind ein neues, leistungsfähiges Werkzeug für die klinische Diagnose, sowie für die physiologische und pathophysiologische Grundlagenforschung.
Chapter 1: Introduction

Knowledge of the heart functionality is essential for the medical diagnosis and treatment of cardiovascular diseases. For this reason, medical imaging techniques play an essential role in order to assess primary attributes representing the heart state. In the last years, Magnetic Resonance Imaging (MRI) has established its role in cardiovascular imaging, initially mainly for anatomical imaging. However during the last decade, emphasis has been put on the assessment of cardiac function such as flow [1], myocardial motion [2], perfusion [3], coronary flow reserve, and even metabolism [4]. The manifold properties of this technique, as well as the achievable accuracy and reproducibility, have made MRI a valuable tool for clinic and basic cardiac research. From images representing the heart anatomy, the endocardial and epicardial walls may be extracted and parameters such as local wall motion or ejection fraction be determined [5]. Another very powerful MRI technique for the estimation of the heart function is Myocardial Tagging [6,7]. This unique method allows for assessing quantitative, temporally resolved motion parameters of the heart wall dynamics. Previous studies have already proven the applicability and potency of tagging examinations [2].

Until recently, cardiac MRI examinations consisted of multiple measurements of several minutes duration. These lengthy procedures were unpleasant for patients and diminished image quality as motion related artifacts are intensified over prolonged measurements. The progress of the gradient system performance of actual MRI scanners and the development of new powerful acquisition sequences allow nowadays for the acquisition of images in the order of seconds or even in real time. The application of ultrafast imaging procedures allows to resolve fast dynamic processes and shortens significantly required acquisition time. Therefore, ultrafast MRI protocols establish new application areas such as interactive imaging procedures or examinations under stress conditions. This kind of examination is of great interest in clinical cardiology because it may allow for more precise and earlier diagnosis of potential heart diseases. For the assessment of the fast contraction motion of the heart and for the suppression of motion artifacts, the availability of fast imaging methods is hereby essential.

Goal of this work was the exploration of ultrafast imaging sequences for the assessment of cardiac function. Chapter 2 of the thesis introduces real time imaging for the estimation of global and local heart function parameters. A fast, hybrid acquisition technique was implemented (TFEPI = Turbo Field Echo Planar Imaging) and applied for interactive anatomical imaging of the heart in real time.
Chapter 3 describes the application of ultrafast imaging sequences for the assessment of myocardial motion. For time efficient assessment of myocardial motion parameters using the tagging technique, the preparation sequence CSPAMM (Complementary SPAtial Modulated Magnetization) was combined with TFEPI. A dedicated flip angle adaptation scheme is discussed, which provides constant tag line intensity over the entire cardiac. In order to overcome the restriction in required time effort for processing tagging examinations, a new evaluation tool is introduced. In order to improve the estimation of the heart contractility the novel tagging technique called RingTag is introduced and demonstrated. Finally, a volunteer study was performed in order to assess variations of the heart motion under cardiovascular load and to demonstrate the feasibility of myocardial tagging under physically induced stress conditions.

References

Chapter 2: Real Time Cardiac MRI

2.1. Assessment of Cardiac Function Parameters by Real Time Magnetic Resonance Imaging


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Abstract

A hybrid real time cardiac imaging sequence was implemented and its potential for functional assessment of the heart was investigated. For real time imaging, a segmented k-space acquisition scheme was combined with an echo-planar readout sequence. Neither ECG gating nor synchronization to breathing motion was necessary. Since the acquisition did not rely on the regularity of motion patterns (breathing, myocardial motion), the image quality obtained was highly consistent among the volunteers. Frame rates of 20 images/s without view-sharing and with a temporal resolution of 46 ms were obtained with an in-plane resolution of 2.4 x 3.0 mm² on a commercial MRI scanner.

Real time images were acquired in twelve healthy adults. Quantitative parameters such as ejection fraction, myocardial mass of individual short-axis segments and short-axis cavity are calculated; the results are compared to those determined by a conventional segmented gradient-echo-planar imaging sequence.
Assessment of Cardiac Function Parameters by Real Time Magnetic Resonance Imaging

Introduction

Recently, the interest in cardiac MRI for the determination of both morphology and function of the heart became increasingly important. Still, this imaging modality is hampered by extensive motion of the heart.

For conventional MR imaging, the data acquisition period for one image is long with respect to one cardiac cycle. Thus, the data have to be acquired segmented during the same phases of multiple consecutive cardiac cycles. As a consequence, an image of one heart phase represents an average of the same time point in a series of sequential heart beats. However, one important precondition has to be fulfilled: The heart has to be repositioned exactly at the same location during data acquisition in subsequent cardiac cycles. Therefore, data acquisition periods need to be synchronized with the motion of the heart. For this purpose, the electrocardiogram (ECG) is commonly used for the synchronization to the cardiac cycle. However, there are several limitations associated with that approach:

1. Motion of the heart induced by breathing needs to be suppressed by respiratory breath-holds, gating or navigator echoes [1]. Averaging or coached breathing patterns, even though these breathing motion compensation schemes generally work satisfactorily, they further complicate the setup and prolong scanning times.
2. The ECG is sometimes unreliable due to the switching of the gradients and/or due to the magneto hydrodynamic effect [2] in the presence of the static magnetic field B0.
3. Under enhanced physiologic or pharmacologic stress levels, extra systoles and ventricular ectopies are more frequently observed and the hydrodynamic effect may be amplified due to increased flow.

These potential limitations may result in artifacts which reduce the reliability and the accuracy of k-space segmented cardiac MRI techniques regarding the determination of functional cardiac parameters such as ejection fraction, myocardial mass or volume.

Therefore, the availability of real time imaging of the heart without ECG gating would be a distinct advantage.

In the literature, approaches for RT cardiac imaging have earlier been reported [3-12]. Promising results were already shown in 1986-1988 [3-5], using single shot EPI based techniques. However, the in-plane resolution of these procedures was still insufficient, or image data were acquired segmented during consecutive cardiac cycles [5]. Single shot EPI techniques have relatively long echo times and are thereby prone to increased flow artifacts in the images. This problem may be minimized by the use of earlier proposed k-space segmented gradient echo schemes [9-12]. These methods yield mini-
mized TE and TR. However, since one RF pulse is needed for each measured k-space profile, the acquisition window for one image is prolonged when compared to the single shot echo-planar imaging approach.

Ideas to split the lengthy EPI train appeared early in 1987. A two-acquisition EPI sequence was presented [3]. Other groups subsequently presented hybrids of segmented k-space acquisition and EPI readout [13-15]. By the application of a hybrid technique consisting of segmented k-space acquisition and an EPI signal read-out, overall sampling time could be reduced and the steady state magnetization was increased when compared to segmented k-space gradient echo methods. This resulted in an overall improved signal to noise ratio [13]. The echo time could also be shortened with respect to single shot EPI methods which helps to reduce flow- or motion-related artifacts in the images. Due to the multiple RF excitations per cine frame, an inflow weighting can additionally be achieved which yields high contrast between muscle and blood.

In this paper, the application of such a hybrid technique for RT imaging of the heart is investigated in a study including 12 healthy adults. Quantitative parameters such as ejection fraction, myocardial mass of individual short-axis segments and short-axis cavity area were measured and are compared with the results obtained with a more conventional EPI technique.

**Methods**

Images were acquired in 12 healthy adult subjects using the RT and the conventional EPI protocol. Numerical results of the below described parameters were subsequently compared using Bland-Altman plots [16] showing the mean difference and the limits of agreement (± 2 standard deviations, corresponding to 95% confidence intervals) between both methods.

Imaging was performed on a commercial Philips Gyroscan ACS/NT 1.5T equipped with a Powertrak 6000 (gradient performance: 21 mT/m, 100 mT/m/ms). For signal acquisition, a 5-element cardiac synergy coil was used.

**Protocol for RT cardiac imaging**

For RT imaging, TF-EPI (Turbo Field Echo Planar Imaging) [13] was applied. For TF-EPI, each slice selective RF excitation is immediately followed by an EPI readout train (Fig. 1). Slice selection including a subsequent EPI readout is repeatedly applied in order to cover the entire k-space for one cine frame. Data acquisition for one image is then repeated to subdivide the RR interval into a number of
frames or heart phase images. The current implementation also allows for the combination of TFEPI with flow compensating gradients, pre-pulses such as MTC pre-pulses, spectrally selective fat saturation, T2 pre-pulses, saturation bands, or tissue tagging. The sequence can be applied with or without ECG gating in a ‘free-run’ mode where images are acquired continuously over multiple cardiac cycles. In the latter case, the timing of the sequence does not depend on the ECG.

Each image was acquired with a 128 by 52 scan matrix and a field-of-view (FOV) of 310 mm. This resulted in an in-plane resolution of 2.4 x 3.5 mm². In order to further reduce the number of profiles to be acquired and to minimize the effective TE, a partial Fourier scheme was used in which 62.5% of ky-profiles were sampled. The thickness of the imaged slices was 8 mm.

The number of EPI-readouts after each RF excitation was 8 with an effective TE of 3.7 ms. 4 RF excitations per cine frame were applied with a TR of 11.4 ms, resulting in an acquisition window (Tacq) of 46 ms. A constant RF excitation angle of 30 degrees was experimentally found to yield the best contrast between myocardium and the ventricular blood pool while SNR is maximized. Generally, 58 heart phase images were acquired sequentially in ‘free-run’ mode without ECG gating. Therefore, 2-4 cardiac cycles were covered in real-time. Two different views were imaged: A mid-ventricular short-axis view and a long-axis view of the heart for the ejection fraction measurements using the area-length method (ALEF) [17-21].

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**Fig. 1** Multi heart phase real time (RT) imaging sequence TFEPI (=Turbo Field Echo Planar Imaging). It combines a segmented k-space gradient echo acquisition with an EPI readout. A slice selection is immediately followed by a EPI-readout train. Slice selection and EPI readout are repeated multiple times (repetition time TR) to split the k-space in multiple segments. Total shot duration for one heart phase image is denoted as TS and the heart phase interval is Δt.
Protocol for conventional imaging

For comparison with the functional parameters derived from RT imaging, a multi slice, segmented, flow compensated ECG-triggered echo planar imaging sequence was utilized. The entire myocardium was covered with a stack of 14 short-axis views from apex to base. Per slice, 16 heart phase images were acquired with a temporal resolution of 42.9 ms. The number of EPI-readouts was 9, resulting in a TE of 6.6 ms. Other scan parameters were: Constant excitation angle of 30 degrees, FOV=380 mm, 128 x 103 scan matrix, slice thickness 8 mm, slice gap 2 mm.

To avoid severe breathing artifacts and misregistration by through plane motion, the individuals were asked for shallow breathing. The acquisition time was 12 cardiac cycles per 2D acquisition. This resulted in approximately 2 minutes scanning duration for the entire heart.

Image Evaluation

Myocardial contours (epicardium, endocardium) were manually outlined for both the RT and conventional images for end-diastole (ED) and end-systole (ES) using a commercial cardiac software package (EasyVision v4.2, Philips Medical Systems, Best, The Netherlands).

Volume parameters

For quantification of ventricle volume data, different calculation methods were applied for the two acquisition schemes:

For calculating the volume based on the real time data, a single long-axis image was evaluated using the ALEF method which is also frequently applied in echocardiography for approximating the cavity volume [22,23]. The ventricle volume was then approximated by:

\[ \text{Vol}_{\text{ALEF}} = \frac{8A^2}{3\pi L} \]

EQ. [4]

Hereby, \( A \) denotes the LV area in the long axis slice and \( L \) is the distance from apex to the mitral valve plane. This formula simply represents the volume of the half rotation ellipsoid for approximating the cavity volume (Fig. 2).
Volume data from the conventionally acquired multi slice EPI measurements was calculated by the Simpson’s formula [17,24,25]:

$$\text{Vol}_{\text{Simpson}} = h \sum_{n=1}^{N} A_n$$

EQ. [5]

Hereby, $N$ refers to the number of slices, $h$ to the distance between two slices and $A_i$ to the area of a slice where index $N$ denotes the most apical slice (Fig. 3).

**Parametric short-axis area**

Volumetric parameters are used for the estimation of myocardial mass and volume, as identified by the segmented epi- and endocardial borders of the short-axis images. The myocardial mass per slice is proportional to the myocardium seen on the short-axis times slice thickness. In the following, ventricle area denotes the area confined by the epicardial border. ‘Cavity area’ refers to the area outlined by the endocardial contour and ‘Mass’ is defined as the difference of both.

For the analysis of the area parameters, derived from the conventional EPI short-axis reference images, the mid-ventricular slice from the image stack was selected for optimized correspondence with the RT short-axis scan plane.
Using RT imaging, 15 to 20 heart phase images were acquired per RR interval. Due to the high blood muscle contrast in the short-axis images (Fig. 4), the endo- and epicardial contours of the myocardium could clearly be identified in all volunteers. On the RT images, flow- or motion-related artifacts appeared visually reduced when compared with the single shot EPI methods.

Fig. 3  
Approximation of the ventricle volume using Simpson’s formula: A conventional multi heart phase gradient echo sequence is applied for acquiring a stack of short-axis images (slices 1..N), from apex to the base of the heart, encompassing the whole ventricle. The volume is calculated integrating the areas (A₁..Aₙ) bordered by the endocardium.
The RT images consistently showed a superior visual image quality when compared to the conventional EPI approach. The images in Fig. 5 display double oblique long-axis views at ED and ES, acquired under real-time conditions in free-run mode. In some images, even the mitral valve can be identified. In a cine mode display, their motion was clearly visualized on a beat-to-beat basis.

In the ‘free-run’ mode, in which multiple heart beats were acquired sequentially, the motion of the diaphragm during free breathing could be observed in addition to the myocardial motion in the images. The comparison of the areas confined by the segmented myocardial short-axis contours demonstrated good visual consistency between the RT acquisitions and the conventionally acquired EPI images as seen in Fig. 4. Considering the cavity area, a good correlation between both methods could be found, as most data points fell within the confidence intervals (see Bland-Altman plots in Fig. 6a).
The differences between RT and conventional EPI were similar for ED and ES (up to 2.5 cm²). However, relative deviations at ES were found to be larger. Generally, the difference between RT and conventional acquisition is negatively biased (-0.338 cm² for ED and -0.637 cm² for ES using RT), which indicates a slight underestimation of the RT technique. Similar results were found for the ventricle area (Fig. 6b, -0.731 cm² for ED and -0.546 cm² for ES). From these two parameters, the local myocardial mass may be derived which suggests a good correlation between both acquisition methods (Fig. 6c). Bland-Altman analysis of EF demonstrates relatively good agreement between both techniques, as all data points are randomly distributed within the confidence intervals (Fig. 7). The difference between RT and conventional acquisition is 3.078 cm³, showing an overestimation of the ALEF calculated EF when compared to the multi heart phase measurement.
Assessment of Cardiac Function Parameters by Real Time Magnetic Resonance Imaging

Fig. 6  Bland-Altman plots of area parameters evaluated from the real time TFEPI acquired short-axis images and the conventionally triggered multi heart phase, gradient echo measurements. Dotted lines indicate the mean difference bias and the point-dotted lines are ± 2 standard deviations (corresponding to 95% confidence intervals).

The considered area values are the cavity areas (6a, bordered by endocardium) and ventricle area (6b, bordered by epicardium), both evaluated at end diastole (ED, left) and end systole (ES, right). Both acquisition methods show good correlation with a slight negative bias which indicates an overestimation of the conventionally acquired EPI images compared to the real time measurements. Bland-Altman plot 6c compares the myocardial ‘mass’ which results from the subtraction of the areas confined by the epicardium and the endocardium.
In good agreement with earlier findings by Setser et al. using an ECG-triggered RT technique [26], we found a good correlation between quantitative functional parameters assessed by RT imaging and a more conventional technique. By the application of TFEPI for RT cardiac imaging, the total signal sampling time per heart phase image could be significantly reduced when compared to segmented k-space methods [9-12]. Splitting of the k-space in multiple readouts helps to reduce echo time significantly (when compared with single-shot EPI) resulting in a reduction of flow- or motion-related artifacts for cardiac applications. With respect to single-echo segmented k-space acquisition schemes [9-12], fewer RF excitations are used. This yields a relatively increased steady state magnetization resulting in a potentially improved signal to noise ratio [13]. By the use of EPI readout trains, the k-space can also be sampled in a shorter period of time when compared to segmented k-space techniques. Consequently, TFEPI combines the advantages of segmented k-space methods (robustness, short echo times) with those of single-shot

**Discussion**

![Bland-Altman plot showing the difference between the ejection fraction estimated from real time acquired long-axis images using the ALEF volume method, and the Simpson’s calculation based on a stack of the ECG gated EPI measurements. The fairly good correlation can be found which indicates that the real time method may be used as a first, quick estimation technique of the ejection fraction.](image-url)
EPI (high speed, good signal-to-noise). The high muscle-blood contrast obtained for the RT short-axis images support automatic or semiautomatic segmentation procedures for epi- and endocardial contour detection.

In the ‘free-run’ mode, ECG gating is not required. As a consequence, no problems associated with arrhythmias, thoracic muscle contraction, extra systoles, ectopic beats, blood-flow related or gradient-induced distortions of the ECG are to be expected. The technique potentially also allows for visualization of beat-to-beat variations since data are not acquired segmented over multiple cardiac cycles. No view sharing [27] algorithm has been employed and all data for one heart phase image were acquired within an acquisition window of only 46 ms. This is already relatively close to echocardiographic frame rates of 25 ms/image.

In this study, the image quality of both the conventional EPI acquisition and the RT TFEPI scans allowed for manual segmentation of epi- and endocardial contours. In the RT short-axis images a high contrast between the ventricular blood pool and myocardium was found which may be explained by the enhanced in-flow weighting of the TFEPI imaging sequence. This is supported with the finding in the 4-chamber views in which the blood-to-muscle contrast is reduced as displayed in Figure 5. The ejection fraction derived from the RT long-axis images using the ALEF calculation showed relatively high variability (deviations up to 18%) which may be explained with the reduced image quality of the long axis views and the coarse volume approximation by the rotation ellipsoid. Despite the potential limitations of the ALEF method [19,21], functional results may be used as a reliable estimate. Further improvements could be achieved by including multiple long-axis views (biplane volume model) for better approximation of the ventricle volume [20,21]. A better frame rate and/or an increased coverage may also be obtained by the combination of TFEPI and parallel imaging techniques such as SENSE [28,29] or SMASH [30].

With the availability of high performance hardware equipment, instant reconstruction and processing of real time acquired data is possible [31]. This establishes the basis for real time viewing and data analysis techniques, which may allow for rapid evaluation during the examination.

In conclusion, by the application of TFEPI sequences, real-time cardiac imaging is feasible on commercially available MR systems. Image quality is no longer sensitive to variation of the heart motion in consecutive cardiac cycles. No ECG or respiratory gating or retrospective ordering is required to synchronize on intrinsic (ECG) or extrinsic (breathing, patient motion induced by physical activity) motion of the heart. This may yield important implications for the use of MR cardiac imaging as a tool for measurements under enhanced stress levels, and for the investigation of arrhythmic heart wall motion.
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Abstract

Interactive real-time examination of left ventricular function in healthy volunteers both under rest and stress condition has been performed. For this purpose, a system combining an interactive user interface, an ultrafast segmented echo-planar imaging sequence, and real-time reconstruction and display of the acquired images was designed. Magnetic resonance images were acquired at rates of up to 20 images per second with multiple receiver coils. By using a sliding window reconstruction technique, reconstruction rates of up to 60 images per second were achieved with a latency of <100 msec. The quality of the real-time images was evaluated both qualitatively and quantitatively and was found to be appropriate for the determination of left ventricular function. It is concluded that the combination of dedicated components provides a convenient modality for the high-quality visualization of left ventricular function under rest and stress at video frame rates with magnetic resonance imaging.
Introduction

Investigation of left ventricular (LV) wall motion is a well-established diagnostic method for the determination of heart function in humans. For this purpose, interactive real-time acquisition and display of dynamic heart images at video frame rates are a convenient and fast examination procedure. Given an accurate representation of heart motion at a sufficiently high frame rate, the exact determination of regional motion parameters by time-consuming computerized image processing may be omitted in favor of a qualitative visual inspection of the resulting movies. Relevant global functional parameters, such as ejection fraction and stroke volume, as well as regional functional parameters, such as wall thickening and radial shortening, may be estimated or graded segment-by-segment by an experienced physician, providing the means for reliable diagnosis, definition of treatment, and prognosis for patients with cardiovascular disease.

Clinically, the most widely used imaging modality for the assessment of LV function is echocardiography, which provides an image that displays a two-dimensional heart motion in real time with usually sufficient spatial resolution (1,2). During an examination, views may be changed quickly, and the acquired images are displayed almost instantly. Further advantages include the mobility of the device and its widespread availability. However, the number of accessible plane orientations is restricted by the limited number of windows transparent to echocardiography, and image quality is inappropriate in up to 10% of all studies (3, 4).

In contrast, magnetic resonance imaging (MRI) offers free choice of slice orientation at an excellent image quality. For instance, it has been shown recently that Dobutamine stress tests with MRI provide a significantly higher diagnostic accuracy compared with echocardiography (4). This method is likely to become part of an integrated cardiovascular MR examination, provided it offers the same user friendliness as echocardiography.

Recently, ultrafast MRI methods, such as echo planar imaging (EPI) (5) and spiral imaging (6), have been established widely as reliable imaging sequences. Compared with conventional techniques, which assemble data for an individual image over several cardiac cycles (7, 8), these sequences enable the so-called real-time imaging, i.e., the acquisition of complete images in times in which no substantial motion occurs. Thus, motion-related inaccuracies are avoided to a large extent, and both cardiac and respiratory triggering or gating are dispensable. When the resulting image series, which has been collected during a continuous measurement in a free-run mode, is viewed in movie-mode, cardiac function may be assessed qualitatively. If quantitative evaluation is needed, then additional postprocessing may be performed. In a comparison of real-time imaging sequences to conventional imaging...
Abstract

sequences a good correlation in ejection fraction and wall thickening was found (9). Thus, the available temporal and spatial resolution of current real-time imaging sequences is adequate for the assessment of cardiac function. However, current commercially available MR systems are not able to perform image reconstruction at a corresponding rate during the measurement. Therefore, neither real-time display of the images nor interaction during the measurement, as they have been demonstrated before on dedicated systems (10, 11), are used routinely.

The combination of a fast imaging method, a real-time reconstruction and display facility, and an interactive user interface has recently been presented (12). Spiral image acquisition with a single receiver coil in combination with a sliding window reconstruction technique provided image reconstruction of up to 20 frames per second with a delay of 750 msec between acquisition and display (13). The system has been demonstrated to be capable of assessing both global and regional cardiac function (3).

The goal of the current work was to improve on a similar concept of a real-time system in several concerns. Our aims were to reduce motion artifacts by shortening the acquisition time, to improve visual perception of motion by increasing display frame rate, to enhance the signal-to-noise ratio (SNR) by the application of multiple receiver coils, and to simplify interactive scan planning by shortening the delay time.

The immediate reconstruction and display of images acquired with advanced, ultrafast imaging sequences and multiple receiver coils requires considerable processing performance that current single processor systems do not provide. The application of multiprocessing is therefore inevitable. However, this demands a careful load balancing of the individual processing steps of the reconstruction and of the data transfer between the processors to assure optimal performance of the system. In addition to high reconstruction rates, short delays between user interactions and the display of the corresponding images are beneficial (14), especially when an ergonomic, interactive planning tool is employed. Typically, delay times <100 msec are considered, to give the user the impression of an immediate response. Minimizing this latency can be achieved by requiring the reconstruction to comply with the real-time constraints of the measurements. A system that fulfills these demands was realized in a dedicated hardware extension. The combination with an interactive user interface and an ultrafast, segmented EPI protocol resulted in a system that allows acquisition of 20 complete images per second with multiple receiver coils, sliding window reconstruction of 60 images per second, and image display after a delay of <100 ms.

In the first step, the benefit of a short acquisition time and the use of multiple coils were investigated. Then, the interactive real-time system was applied to the examination of LV function in humans under both rest and stress conditions.
Materials and Methods

All measurements were performed on a Gyroscan ACS-NT 1.5 T whole-body system equipped with the PowerTrak 6000 gradient system (gradient strength, 23 mT/m; gradient slew rate, 105 mT/m/ms; Philips Medical Systems, Best, the Netherlands). The subjects were placed in the magnet in supine position. An electrocardiogram (ECG) was taken for monitoring purposes. The MR transmit coil was the built-in body coil and the receiver coil was a dedicated five-element cardiac synergy coil with two circular front and three rectangular back elements. The imaging sequence was a segmented, interleaved EPI sequence (5). A nominal scan matrix of $128^2$ was acquired in combination with a rectangular field of view of 60%. K-space was sampled with half coverage (62%) in fold-over direction. Spatial resolution was $2.3 \times 2.3 \times 8 \, \text{mm}^3$. The excitation flip angle was $20^\circ$.

Effects of Acquisition Time

To generate different acquisition times, the number of excitations per image (and, inversely proportionally, the numbers of EPI readouts per excitation) were varied. The following four schemes were used: 1) 3 excitations, followed by 13 EPI readouts each, TR=16.0 msec, TE=4.6 msec, resulting in an acquisition time of 48.0 msec per image; 2) 5 excitations followed by 8 EPI readouts each, TR=12 msec and TE=3.7 msec, resulting in an acquisition time of 60 msec; 3) 15 excitations followed by 3 EPI readouts each, TR=8 msec and TE=2.9 msec, resulting in an acquisition time of 120 msec; and 4) 25 excitations followed by 2 EPI readouts each, TR=7.2 msec and TE=3.0 msec, resulting in an acquisition time of 180 msec. Short-axis (SA) and long-axis (LA) images were acquired in a healthy volunteer. For each acquisition scheme, the SNR was calculated in three regions of five consecutive images of the time series. In addition, three blinded users independently rated image quality of 100 randomly chosen and displayed images (25 for each imaging scheme) on a scale ranging from 1 to 5 (1, unusable; 2, poor; 3, acceptable; 4, good; and 5, excellent). The evaluations were performed separately for SA and LA images.

Effects of Number of Coils Used

SA and LA time series were measured in a healthy volunteer using the fastest of the above-described imaging schemes (i.e., acquisition time per image = 48 msec). Five image sets were generated by delayed reconstruction of the signals collected by one to five coils. The SNR was calculated in three regions of five consecutive images from the time series. SA and LA images were evaluated separately.
**User Interface**

A dedicated user interface allowing for interactive modifications of geometric settings and imaging parameters was used for scan planning. With the mouse as input device, a new imaging slice was defined on and relatively to previously acquired images displayed on four image panels. Once the desired imaging slice was defined, the continuous mode was switched on, and the real-time imaging sequence was started.

**Real-time Image Acquisition**

For the real-time imaging, the following two segmented EPI schemes were used: 1) with 2 active coils, 3 excitations with 13 EPI readouts each were applied at TR=16.0 msec, resulting in 48.0 msec acquisition time per image corresponding to 20 frames per second; and 2) with 4 active coils, 5 excitations with 8 EPI readouts each were applied at TR=11.5 msec, resulting in a 57.5 msec acquisition time corresponding to 17 images per second. The inherent T2* contrast of the segmented EPI sequence was changed optionally by the insertion of appropriate prepulses. Bright blood contrast was generated by suppression of myocardial tissue, which was achieved by the application of a T2 preparation pulse (15) (TE=20 msec, pulse duration 27.2 msec). Alternatively, black blood contrast in SA views was obtained by the application of saturation pulses in two parallel slices adjacent to the imaging slice, which reduced the signal of blood flowing in (16) (pulse duration=7.0 msec). Fat saturating prepulses (SPIR; pulse duration=16.3 msec) also were introduced to reduce fat shift artifacts. To limit the loss of temporal resolution, and because the effects were conserved for a longer time than the acquisition of a single image took, prepulses were applied not before each single image but only before every \( n \)th image, \( n \) being in the range 1-5. Values of \( n=5 \) and \( n=2 \) were found to be optimal for bright and black blood contrast, respectively. This resulted in a reduction of the acquisition rate by two images per second and one image per second, respectively.

**Reconstruction**

Dedicated reconstruction hardware was designed (17) that provides both a high reconstruction rate and a short latency time. It consists of ten high-performance digital signal processors (DSPs), which are interconnected by dedicated communication links in an optimized topology. The required data processing is subdivided into four pipeline stages to speed up the reconstruction. Preprocessing and distribution of the data are handled by a single DSP on the first stage. The next four DSPs perform the gridding algorithm (18) in parallel to resample the data acquired on gradient slopes onto a uniform
grid. In addition, they carry out a one-dimensional Fourier transform. Four additional DSPs perform the Fourier transform in the orthogonal direction and combine the individual single-receiver coil images into one multiple-receiver coil image by calculating the sum of squares. In the final pipeline stage, a single DSP produces the modulus images to be displayed.

The reconstruction employs a sliding window technique (19) to provide a high rate in image generation independent of the speed of the image acquisition. The reconstruction rate is determined automatically, such that the available performance of the system is exploited. The transmission of the reconstructed images to the display is decoupled from the timing constraints of the measurement. Its rate adapts automatically to the connected display. Whenever the display is ready to receive the next image, it will be provided with the last reconstructed image. The image display settings, such as level and window, are modified during the acquisition for constant, optimal contrast and also may be changed interactively while scanning. In combination with the above-described segmented EPI sequences used for real-time imaging, reconstruction rates were increased by a factor of 3 compared with acquisition rates, thus in the range 48-62 images per second.

**Assessment of LV function**

Real-time imaging and displaying of SA views at different cardiac levels (from apical to basal) as well as of LA views at different angles around the cardiac axis were performed. In cases fold-over interfered with the region of interest, a saturation pulse (pulse duration=4.6 msec) was added before acquisition of every second image (n=2), suppressing the signal of interfering tissue.

Healthy volunteers were investigated under conditions of both rest and stress. The stress condition was achieved by physical exercise on an MR compatible ergometer (Lode BV, Groningen, the Netherlands). Real-time images were inspected visually and evaluated qualitatively, and SNR values as well as contrast-to-noise ratios (CNR) between myocardial wall and blood were determined.

**Results**

**Effects of Acquisition Time**

An increase of acquisition time from 48 msec per image to 60 msec reduced mean SNR by 10% and 14% for SA and LA images, respectively; an increase in acquisition time to 120 msec reduced the SNR by 39% (SA images) and 15% (LA images), and an increase in acquisition time to 180 msec re-
duced the SNR by 39% (SA images) and 32% (LA images). The changes were highly significant for acquisition times of 120 msec and 180 msec for SA images and for acquisition times of 180 msec for LA images.

Mean image quality was 3.6, 3.4, 2.7, and 2.5 for SA images, and 2.8, 2.2, 1.6, and 1.9 for LA images for acquisition times of 48 msec, 60 msec, 120 msec, and 180 msec, respectively. Eighty-seven percent, 89%, 56%, and 45% of SA images, and 63%, 32%, 19%, and 28% of LA image was rated acceptable or better. For acquisition times of 120 msec and 180 msec, no LA image was rated as good or excellent, whereas 31% and 9% of LA images acquired in 48 msec and 60 msec, respectively, were rated in these categories. One percent, 3%, 17%, and 24%, respectively, of the SA images, as well as 16%, 23%, 55%, and 36%, respectively, of the LA images were rated unusable. SA images acquired in 48 msec were significantly better rated than those acquired in 120 msec and 180 msec. LA images acquired in 48 msec were rated significantly better than those acquired with all other acquisition times.

Effects of Number of Coils Used

Relative to the SNR obtained for a single coil, SNR was increased by 7%, 2%, 5%, and 9% for SA images, and by 2%, 2%, 0%, and 4% for LA images, respectively for 2-5 coils. The changes were highly significant for SA images acquired with 2, 4, and 5 coils.

Real-Time Display of LV Function

Both EPI schemes produced images of virtually identical quality, with SNR values between 10 and 20. In both SA and LA T2*-weighted images (i.e., acquired without application of a prepulse), a CNR value of 10 was found. Endocardial and epicardial borders were well delineated (Fig. 1). In LA views, the valves could be recognized clearly in the “movies” even though the blood in the ventricle was not displayed homogeneously in all images.

In images that were acquired immediately after application of the T2 preparation pulse (Fig. 2), CNR values of 15 in SA, and 12 in LA views were found. In images that were acquired immediately before application of the next T2 preparation pulse, the CNR values decreased to 10 for SA and 5 for LA views (Fig. 3). In LA views, the signal level of the blood in the LV was more homogeneous than in the T2*-weighted images. In SA views, the lateral epicardial wall was in some cases was not discernible from the background.
Fig. 4 shows images acquired after application of two parallel saturation slabs to obtain black blood. A CNR value of 11 was found during systole, whereas during late diastole, CNR decreased to CNR values of ≈5.

The application of SPIR pulses before every image \( (n=1) \) reduced the available SNR by approximately 80%. The loss was negligible (0-10%) for less frequent application of the pulse \( (n=3-5) \). However, image quality did not improve to a noticeable extent, and artifacts were not reduced. Images that were acquired during physical stress showed a reduction in SNR and CNR by approximately a factor 2 (Fig. 5).

---

**Fig. 1**  
*T2*-weighted images acquired at 20 images per second. Top: Short-axis views. Bottom: Long-axis views. The far left image in each row shows an entire image, and the remaining images in the row are zoomed clippings of later frames. Only every second image from the time series is shown (time interval between the images show = 96 msec).
Results

Fig. 2  Images acquired with a T2 preparation pulse before every fifth image, acquired at 18 images per second. Top: Short-axis views. Bottom: Long-axis views. Immediately before acquisition of the fourth image in each row, a T2 preparation pulse was applied. The first image in each row shows an entire image, and the remaining images in the row are zoomed clippings of later frames. Only every second image from the time series is shown (time interval between most of the images shown = 96 msec; time interval before the fourth image in each row = 123 msec).

Fig. 3  Left: Images acquired 240 msec after application of a T2 preparation pulse immediately before the next prepulse was applied. Right: Images acquired immediately after application of a T2 preparation pulse. Note the better suppression of myocardial tissue after application of the T2 preparation pulse.
**Discussion**

*Effects of Acquisition Time*

Despite the shorter echo time, images acquired with longer acquisition times were inferior with regard to both SNR and image quality. Whereas a distinct drop off in image quality is found between the acquisitions times of 60 msec and 120 msec for SA views, LA views acquired in 60 msec already were
noticeably worse than those acquired in 48 msec. In particular, the number of unusable images increased significantly with longer acquisition times, which also reduced considerably the diagnostic value of the real-time movies. The SNR values reflected a similar, but somewhat less pronounced behavior. Thus, a very short acquisition time of 48 msec per image is thus preferable, especially for LA views, but SA images also profit from short acquisition times.

**Effects of Number of Coils**

The best results were obtained in cases in which either both front coils or, alternatively, all available coils were used. This may be explained by a better ratio of number of coils (influencing the signal) to the visible volume (influencing the noise). Therefore, depending on the region of interest, it is preferable to use either all coils on one side of the patient, or all available coils. However, the number of coils used must be traded off against acquisition time, because larger numbers of coils necessitate a longer minimal acquisition time.

**Real-Time Display of LV Function**

The high reconstruction rates of 48–62 images per second allowed the display of smoothly animated, real-time movies for all acquisition schemes. The generally good delineation of myocardial borders in both SA and LA views permitted fast estimation of wall motion and thickening.

In sequences in which a T2 preparation pulse was applied, SA views provided excellent contrast and LA views provided sufficient contrast between myocardium and blood. The endocardial border, thus, was well recognized. LA views provided an even better display of the valves than the T2* images. Occasional low contrast of the lateral wall to the background in SA views did not reduce the visual impression of cardiac function.

The application of saturation pulses in two parallel slices for SA views efficiently suppressed signal of blood flowing in, providing good black blood contrast. Contrast was optimal during systole due to the flow of saturated blood into the imaging slice. However, during late diastole, at times of virtually no through-plane motion of the blood, CNR decreased to acceptable values. Despite this loss in contrast, cardiac wall motion could still be followed in the movie. Furthermore, both wall motion and wall thickening were clearly recognizable. Because the application of SPIR pulses did not reduce artifacts but slightly reduced SNR and acquisition rates the application of SPIR pulses is not recommended in the cases examined here.
The reduction in SNR and CNR values obtained during the stress condition may have been caused by increased velocity of myocardial motion and blood flow, as well as by the motion of the subject during the physical effort. Further artifacts originated from radiofrequency leakage of the ergometer, producing white spots in the image. Nevertheless image quality was sufficient to demonstrate increased muscle contraction, leading to an increased ejection fraction and wall thickening. Due to better image quality compared with LA views, the effects were especially clearly visible in SA views. Despite the fact that images were not acquired with identical delays in cases prepulses were introduced (n>1), perception of the images displayed in real time was smooth. Visually, no jerks were noticed. This can be explained by the short duration of the prepulses in the range of 7.0–27.2 msec. The interleaved, segmented EPI sequences feature short acquisition times with relatively short echo trains. These characteristics seem advantageous for real-time imaging. The shortness of the acquisition time was beneficial for suppressing motion artifacts. Under the rest condition, images showed no significant image quality degradation. Under the stress condition, image quality still was sufficient for visual inspection but clearly lower than that seen under rest condition. Especially during rapid filling, in which velocities of up to 10 cm/seconds may occur (20), acquisition times should be shorter than the currently available 48-58 msec. Further k-space sampling reduction using sensitivity encoding (SENSE) (21) or simultaneous acquisition of spatial harmonics (SMASH) (22) may be advantageous, especially when measuring at higher cardiac frequencies. The SA views provided better image quality with higher SNR and CNR values than the LA views. This may be explained by the large in-plane motion in LA views during contraction and dilatation, producing severe misallocation artifacts, whereas the corresponding through-plane motion in SA views did not lead to a visible reduction in image quality. With the used reconstruction rates, the reconstruction hardware is not yet reaching its technical limits. With a single coil, 350 images of a size of 128^2 may be processed every second, whereas, at a matrix size of 256^2, approximately 100 images per second still are possible. The use of multiple coils reduces the available maximal reconstruction rate approximately linearly with the number of coils compared with single-coil acquisitions. With five coils, approximately 70 reconstruction per second are possible with the imaging parameters used.
Conclusions

A system set-up has been presented that allows MRI to be used as interactive real-time imaging modality. The interactive user interface allows for a fast definition and easy adjustment of the scan plane during the measurement. An ultrafast segmented EPI sequence acquires a full image within 48-58 msec, thus avoiding motion artifacts to a large extent. The reconstruction and display hardware is capable of handling the incoming data in real time with a time lag of <100 msec. The use of multiple coils provides optimal SNR over a large field of view.

The application of this system for the examination of LV function provides appropriate image quality for the estimation the relevant motion parameters and the assessment of cardiac function. Different contrast settings (T2*-weighted, bright blood, black blood) that provide complementary information are achievable by the application of prepulses.

Further studies will investigate the clinical use of the proposed imaging sequences. A protocol for a reproducible and reliable examination of LV function with real-time interactive MRI will be defined, and results will be compared to those obtained with other modalities.

Acknowledgements

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References


Real Time Interactive Magnetic Resonance Imaging
Chapter 3: Myocardial Motion Analysis

3.1. Ultrafast CSPAMM tagging

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Abstract

The combination of CSPAMM tagging with the imaging sequence TFEPI is presented which allows for the reduction of imaging time down to the lower limit of a 2 heart beat acquisition. For preserving constant tag line intensity over the entire cardiac cycle, a flip angle optimization scheme is applied which distributes the signal of the tagging magnetization equally over all heart phases. Due to the non-steady state acquisition procedure in the first two heart beats, an alternating tag line intensity artifact is established. In order to reduce this effect, a saturation prepulse is introduced at the beginning of the measurement.

Experiments were performed in phantoms as well in healthy volunteers in order to evaluate the result of the flip angle adaptation and the effect of prepulse for reducing the alternating tag line intensities.
Introduction

Tagging is a powerful magnetic resonance imaging (MRI) technique which allows for the temporally resolved assessment of tissue motion parameters. Based on the preparation of the tissue magnetization, spatial locations may be labeled in order to track them over time. Different tagging preparation sequences have been published which differ in the way saturation bands (tags) are generated, as well as in the geometrical representations [1-4]. Commonly applied techniques, such as SPAMM (SPatial Modulation of the Magnetization) [1] or CSPAMM (Complementary SPAMM) [3], produce a set of parallel tag lines or tag grid like patterns, respectively. After this tissue magnetization preparation, a conventional imaging sequence is used for acquiring the deformation of the tag lines which thus provide the basis for calculating various motion parameters [5].

Myocardial tagging is the application of tagging for the assessment of the heart muscle deformation and has shown to be very useful for the understanding and estimation of healthy and diseased heart states [6-9]. Imaging of the heart is in general associated with several difficulties such as motion artifacts originating from the inherent high motion components of the heart. Therefore, fast imaging sequences with high temporal resolution are requested, not only to reduce motion artifacts in the image acquisition, but also to increase patient comfort and throughput for economic reasons. Further, the availability of an ultrafast tagging measurement sequence would allow for the introduction of novel, powerful applications such as myocardial tagging under cardiovascular stress conditions.

<table>
<thead>
<tr>
<th>Imaging Technique</th>
<th>Breathing Scheme</th>
<th>Scan time (for 2 separate tag line directions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFE</td>
<td>1-4 breath hold</td>
<td>2 x 4 min</td>
</tr>
<tr>
<td>EPI</td>
<td>2 breath holds</td>
<td>2 x 12 sec</td>
</tr>
<tr>
<td>EPI</td>
<td>1 breath hold</td>
<td>1 x 12 sec</td>
</tr>
<tr>
<td>TFEPI</td>
<td>1 breath hold</td>
<td>4 heart beats</td>
</tr>
</tbody>
</table>

In recent years, new powerful gradient systems allowed for the implementation of always faster imaging sequences and consequently decreased imaging time significantly. With respect to this, it has been shown that tagging may even be performed in real time using SPAMM tagging [10]. However, this technique is hampered by tagline intensity fading which limits motion analysis to the systolic phase of the cardiac cycle. Further, due to the long-axis contraction of the heart [11], tagging using a static imaging plane implies tracking of different geometrical locations over time which may lead to falsified results. CSPAMM tagging on the other hand is able to overcome the previously mentioned drawbacks by using a subtraction technique, which prolongs tag line visibility and allows for the im-

Table 1  Table showing the development of the measurement times for CSPAMM tagging. The scan time increases the durations needed for the acquisition of two separate line tagged images in order to generate a grid image after multiplication.
Abstract

The implementation of a slice-following feature [3,14]. However, the two required measurements prevent from using CSPAMM for real time applications and consequently, strengthen the demand for a time efficient imaging procedure. The progress in the reduction of the acquisition time for CSPAMM measurements is illustrated in Table 1. In the following the combination of CSPAMM tagging with TFEPI (Turbo Field Echo Planar Imaging) is presented which allows for the reduction of the measurement time for a CSPAMM examination down to the lower limit of a 2 heart beat acquisition. TFEPI is a powerful imaging protocol which combines EPI (Echo Planar Imaging) with a variable number of RF excitations per read out train (Fig. 1) [12].

![Fig. 1](image.png)

Thus, the image acquisition can be very time efficient thanks to the multiple k-lines sampling provided by EPI while preserving a short echo time, which is important for reducing motion induced artifacts. However, the increased number of RF excitations in the TFEPI imaging procedure leads to an accelerated decrease of the tag line intensity since the information, which is stored in the longitudinal magnetization, is reduced with each imaging RF excitation applied. This decay may be prevented by a dedicated adaption of the applied imaging flip angles. Based on a previously published optimization scheme for single breath hold EPI CSPAMM tagging [14], an extension for the TFEPI sequence will be demonstrated.

CSPAMM tagging completed in the first heart cycles, implies transient imaging as steady state mag-
Ultrafast CSPAMM tagging

...ization is usually established during the first two heart beats. Thus, the different initial longitudinal magnetization levels of the first two images, which are acquired for the subtraction step in order to generate the final CSPAMM image, result in an alternating intensity of the tag lines, especially for short repetition times.

This undesired effect, which shortens tag lines persistency and complicates the later evaluation process, may be reduced by applying a steady state prepulse (SSPP) which intends to scale the initial $M_0$ magnetization before imaging to the expected steady state magnetization level. The development of the alternating tag line intensity will be explored and the effect of the SSPP will be demonstrated.

Methods

A useful mathematical formulation for calculating the tagging signal has been presented in [13]. The longitudinal magnetization of a tagging image may be described by

$$M_{z\text{tag}} = M_{ss} \cdot \text{TAG}(x)$$

where $M_{ss}$ stands for the steady state magnetization and TAG(x) for the tagging modulation function such as a cosine modulation. Over time this expression relaxes towards the equilibrium magnetization $M_0$ following

$$M_{z\text{tag}}(t) = (M_{ss} \cdot \text{TAG}(x) - M_0) \cdot e^{-\frac{t}{T_1}} + M_0$$

In this representation $M_{z\text{tag}}$ may be decomposed into two parts: the tagged magnetization part $M_T$ and a rest part $M_R$:

$$M_T = M_{ss} \cdot \text{TAG}(x) \cdot e^{-\frac{t}{T_1}}$$

$$M_R = M_0 \cdot \left(1 - e^{-\frac{t}{T_1}}\right)$$

Using equation [3], each heart phase specific excitation angle $\alpha_i$ for EPI can be calculated in order to get an equally distributed transversal magnetization. This condition can be expressed with the recursive relation

$$\alpha_{i-1} = \text{atan} \left(\sin(\alpha_i)e^{-\frac{\Delta t}{T_1}}\right)$$

where $\Delta t$ stands for the time delay between two excitations.
As demonstrated in [14], the last optimal imaging excitation angle $\alpha_{\text{last}}$ in the cardiac cycle can be obtained for single breath hold measurements by an iterative simulation process in order to achieve a maximal magnetization at beginning of each cardiac cycle. Further, if the last excitation angle $\alpha_{\text{last}}$ is known, all preceding flip angles for all individual heart phases can be calculated by using [5].

The flip angle optimization for TFEPI is an extension of the EPI calculation. Different as for EPI where each heart phase is imaged with an individual excitation $\alpha_i$, a variable number of $m$ excitations $\beta_j$, $j=1..m$ ($m =$ turbo factor) are applied in case of TFEPI (Fig. 2).

In order to preserve constant tag line intensity for all heart phases as obtained with the optimization for the EPI case, two requirements for the $\beta_j$ angles can be formulated:

1. each $\beta_j$ excitation must produce an equal amount of transversal magnetization in order to get constant tag line intensity, and

2. the total effect of all $\beta_j$ flip angles for each heart phase must comply with the $\alpha_i$ excitation for the optimized EPI case.

The first condition can be accomplished similar to the calculation of the $\alpha_i$ flip angles:

$$\beta_{j+1} = \text{asin} \left( \tan(\beta_j) e^{\frac{\Delta t}{T_1}} \right)$$  \[6\]
Ultrafast CSPAMM tagging

Given the first $\beta$ flip angle in a heart phase, all subsequent excitation angles may be calculated in order to achieve equal tag line signal.

The requirement that for each individual heart phase i the total effect of the $m\beta$ flip angles must agree with the optimized $\alpha_i$ RF excitation angle of the EPI protocol as obtained by [14], is approximated with:

$$\alpha_i = \cos \left( \prod_{j=1}^{m} \cos (\beta_j) \right)$$

[7]

Each heart phase is individually processed by iteratively increasing the first $\beta$ angle, calculating all subsequent excitation angles (equation [6]) and then estimating the total effect (equation [7]). The time remaining from the last applied $\beta$ flip angle until the beginning of the next heart phase is considered for calculating T1 relaxation (equation [4]). A valid set of heart specific $\beta$ flip angles is finally found, if the total effect of all applied $\beta$ angles agrees with the optimized $\alpha$ flip angle application from the EPI case, as calculated in [14].

In order to prevent the previously mentioned alternating tag line intensity effect, a prepulse (SSPP) was applied for the first heart beat, in order to reduce the initial $M_0$ magnetization to the expected steady state level $M_{ss}$ which was obtained by simulations and experiments. This SSPP sequence is implemented as a non-selective block pulse with a flip angle adapted accordingly to the heart rate of the subject [Fig. 3]. The total length of the prepulse is 2ms.

![Fig. 3](image)

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**Fig. 3** A prepulse is introduced at the beginning of the measurement in order to scale the initial magnetization to the expected steady state magnetization level (SSPP = Steady State PrePulse). This procedure allows for reducing transient imaging artifacts which are identified as an alternating tag lines intensity pattern.
All sequences were implemented on a Philips Gyroscan ACS/NT 1.5 T whole body scanner equipped with gradient system Powertrak 3000 (max. gradient strength 15 mT/m and max. gradient slope 40 mT/m/msec). For data collection a circular surface coil was used. In-vivo measurements were performed with young healthy volunteers and for phantom experiments a water bottle was used, of which T1 and T2 relaxation constants were matched to typical values of human myocardium. Simulations of the Bloch equations were done by means of a Matlab (MathWorks Inc., Natick, MA, USA) program, which allowed for visualizing the evolution of the magnetization for the imaging sequences EPI and TFEPI.

Results

The combination of CSPAMM tagging with TFEPI allowed for speeding up tagging experiments down to the lower limit of a 2 heart beat acquisition per tag line direction. The top row of Figure 4 demonstrates the comparison between a short-axis image measured with lower limit TFEPI CSPAMM in 4 heart beats, or about 4 seconds, for two separately acquired line directions, and a conventional EPI CSPAMM done in a single 12 second breath hold. Similarly, the bottom row shows long-axis images at end-systole imaged with TFEPI in 6 seconds and EPI in 15 seconds. It can be seen that acquisitions with lower limit TFEPI CSPAMM have a reduced signal-to-noise ratio compared to the EPI CSPAMM measurements, but are of sufficient good quality for accurate evaluation. However, the gain in acquisition time allowed for measurements within short restricted acquisition windows, as required for instance for stress examinations.
Ultrafast CSPAMM tagging

The rapid tag line signal decay for the application of the constant flip angles ($\alpha=8^\circ$ and $\alpha=25^\circ$) were verified in the computer simulations, as well as the effect of the constant tag line intensity over all heart phases as obtained for the case of the optimized flip angles (Fig. 5a). Additionally, the adaption of the tag signal towards the steady state magnetization within the first two heart cycles can be observed. Figure 5b depicts an enlargement of the 3rd heart phase, showing the identical tag line intensity curves as in Figure 5a. It can be seen that for the constant flip angle $\alpha=8^\circ$, the tag line intensity drops below the constant value of the TFEPI protocol (turbo factor=4) after the 10th of 16 heart phases. In case of a constant flip angle of $\alpha=25^\circ$ this already occurs after the 2nd heart phase.

Fig. 4  Comparison of images acquired with TFEPI CSPAMM (left column) and EPI CSPAMM (right column). The top row shows a short axis view of a human heart and on the bottom the long-axis is depicted. Despite the visibly smaller signal-to-noise of the TFEPI measurements, image quality is sufficient for reliable evaluation. The shortening of the required acquisition window by combining CSPAMM with TFEPI allows for faster measurements and the introduction of novel applications such as heart motion analysis under physically induced stress.
Corresponding results were found for the phantom experiments. For the three cases investigated, the maximal tag line intensity was extracted in each heart phase (Fig. 6, left) and pieced together to a new intensity bar, seen on the right side, which visualizes the temporal change of the maximal tag line signal. A higher starting magnetization level can be appreciated for the constant flip angles if compared

Fig. 5  
Graph a) shows the temporal change of the tagging signal during the measurement with EPI, flip angle optimized TFEPI and TFEPI with the constant flip angles $\alpha = 8^\circ$ and $\alpha = 25^\circ$. Graph b) depicts the magnification of the third heart phase. For constant flip angles the tagging signal level rapidly drops under the value of the optimized flip angles after the 10th heart phase for $\alpha = 8^\circ$ and even the 2nd heart phase in case of $\alpha = 25^\circ$. 

Corresponding results were found for the phantom experiments. For the three cases investigated, the maximal tag line intensity was extracted in each heart phase (Fig. 6, left) and pieced together to a new intensity bar, seen on the right side, which visualizes the temporal change of the maximal tag line signal. A higher starting magnetization level can be appreciated for the constant flip angles if compared
Ultrafast CSPAMM tagging

to the optimized flip angle approach. However, the temporal decay of the signal finally results in a lower level in later heart phases. Images of an in-vivo experiment are presented in Figure 7, comparing the optimized flip angles with the application of constant low excitation angles.

The effect of the non-steady state (transient) imaging in the ultrafast CSPAMM experiment can be appreciated in the simulation plots (Fig. 8) where the high magnetization components in the first two heart beats are visible. This can also be seen in the phantom acquisitions presented in the top row of Figure 9 where especially for high heart rates (right images; heart rate 120bmp) the alternating tag line intensity effect is obvious. The two images below demonstrate the SSPP application, which results in an equalization of the signal coming from the individual tag lines.

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**Fig. 6**  Tag signal decay demonstrated in phantom measurements. For better visualization, the maximum intensity value of each heart phase was extracted and pieced together to a new intensity bar as illustrated on the left. The right side shows the three cases: optimized flip angles and constant flip angles $\alpha=8^\circ$ and $\alpha=25^\circ$. 
Fig. 7 Demonstration of the flip angle adaptation in an in-vivo application of a volunteer. The top row shows images from four different time points over the whole cardiac cycle with applied flip angle optimization. The middle and bottom row demonstrate the application of constant flip angles with $\alpha=8^\circ$ and $\alpha=25^\circ$. 
Ultrafast CSPAMM tagging

Fig. 8  Visualization of the simulation results for the tag line shape change over 4 cardiac cycles with 16 heart phases each for EPI, flip angle optimized TFEPI with and without SSPP application and TFEPI with a constant flip angle of $\alpha=8^{\circ}$. It can be seen that the SSPP reduces the augmented magnetization level of the first heart phase, but cannot completely prevent this effect. For TFEPI with a constant flip angle the rapid tag signal decay can be observed.

Fig. 9  Phantom measurements visualizing the effect of the steady state prepulse (SSPP) for reducing the alternating tag line intensity effect. On the left, the acquisitions with a repetition time $T_R=1000$ ms (corresponds to a heart rate of 60 bpm) is shown and right the measurements with $T_R=500$ ms. The top row demonstrates the images without and the bottom row with SSPP.
The different magnetization levels and the varying tag line shape in the first two heart phases result, after subtraction, in an alternating tag line intensity in the final CSPAMM image (a). In heart phases 3 and 4, the steady state is already achieved, and tag line shapes are similar wherefore no dual intensity artifacts becomes visible.
Discussion

The TFEPI protocol is a powerful image acquisition sequence that allows for improving the time efficiency of CSPAMM tagging experiments. The possibility to adapt the number of EPI readout trains, or number of RF excitations per heart phase (equivalent to the turbo factor), respectively, allows for trade off between acquisition speed and short echo time for motion artifact suppression. The speed up in acquisition time for CSPAMM tagging experiments may allow for the introduction of novel applications, such as the measurement of myocardial motion during stress examinations.

The drawback of the rapid tag signal decrease by TFEPI, especially for high turbo factors, may be reduced by applying the flip angle optimization scheme. Tag line intensity can so be preserved, which prolongs tag line visibility and facilitates the later tagging evaluation.

In conventional, single breath hold CSPAMM experiments, the alternating tag line intensity effect is not visible as they are averaged out over the multi heart beat acquisition. However, the alternating tag line intensities cannot completely be diminished by the SSPP, which may be explained by the varying modulation shapes, particularly in the first two heart beats (Fig. 10). Whereas modulation for the first heart beat corresponds to a cosine shape, the following heart beats experience a modulation of already relaxed modulated magnetization from previous heart beats and thus have different tag line profiles. Subtraction of these two different modulation shapes accentuates the effect of the alternating tag lines intensities as seen in Figure 10a. After the 2nd heart cycle, modulation profiles are practically identical for both acquisitions, resulting in a diminution of the effect (Fig. 10b).

A possible solution consists in a continuous tagging preparation before the image data acquisition. By this procedure, steady state magnetization can be established before main data acquisition is initiated. In conclusion, a flip angle adaptation scheme for TFEPI CSPAMM tagging was proposed, which provides tag line visibility throughout all heart phases imaged. Further, the introduced SSPP sequence allows for reducing the alternating tag line intensity effect which otherwise may compromise tag line quality, especially for short repetition times.

The presented TFEPI CSPAMM sequence enables performing tagging experiments in few heart beats which establishes the basis for ultrafast tagging acquisitions as required for instance for physically induced stress examinations.
References

Ultrafast CSPAMM tagging


3.2. **RingTag: Ring Shaped Tagging for Myocardial Centerline Assessment**

M. Spiegel, R. Luechinger, J. Schwitter, P. Boesiger

*Magnetic Resonance in Medicine (submitted)*

**Abstract**

The analysis of the heart motion is essential for the understanding and estimation of the heart condition. Conventionally assessed endocardial ejection indices overestimate contractility, especially in hypertrophied hearts. However, this may be corrected if midwall circumferential fiber shortening is known which may be derived from the motion of the mid-line of the myocardium.

For this purpose the novel tagging procedure RingTag is introduced which allows for generating a freely definable, convex ring saturation band. Additionally, a prepulse called StarTag may be included which consists of tag lines arranged in a star-like manner, in order to improve analysis of circumferentially oriented motion components. For accurate reproduction of breath hold positions during acquisitions, a novel navigator guided breath holding technique is introduced. Multi heart phase imaging is done with a fast, single breath hold EPI measurement which includes optionally a labeling prepulse for implementing a slice-following property.

Results show that the RingTag sequence is able to create a well visible, variable convex saturation structure on the myocardium which can be tracked throughout the cardiac cycle and consequently allows for accurate analysis of the mid-line motion of the myocardium.

By increasing the flip angle of the RF pulse for the RingTag sequence, the procedure may also be utilized as a saturation pulse for suppressing signal coming from the area outside the user defined contour.
Introduction

The transmural gradient in myocardial thickening results in overestimation of contractile function by endocardial ejection indices, particularly in hypertrophied ventricles with increased relative wall thickness [1,2]. Shimizu [1] proposed a two-shell cylindrical model to calculate midwall circumferential fiber shortening (cFS). This approach confirmed reduced intrinsic contractile function in hypertrophied myocardium [1,2]. Further, the extent of fiber shortening is virtually limited by the afterload at end-ejection, i.e. the force acting in the direction of the circumferential fibers [3]. Therefore, the relationship between midwall cFS and circumferential wall stress at end-systole may serve as a load-independent measure of contractility [2]. Although conceptually attractive, the two-shell cylindrical model is limited by its geometrical assumptions. MR myocardial tissue tagging has shown to be a very powerful modality for the assessment of local myocardial deformation in healthy and diseased hearts [4-7]. It would be of great interest to apply MR myocardial tissue tagging for tracking of myocardial mid-line displacement during the cardiac cycle and thereby deriving information for calculating cFS [8,9]. Conventional tagging techniques such as SPAMM (SPAtrial Modulation of the Magnetization) [10] or CSPAMM (Complementary SPAMM) [11] use multiple RF excitation pulses combined with dephasing gradients to modulate the transversal magnetization in order to obtain a sinusoidal (or higher order) pattern of the longitudinal magnetization. This preparation is done immediately after the detection of the R-wave of the ECG, and is followed by a multi heart phase imaging sequence. Consequently, motion of the tagging pattern can be tracked and quantitatively described throughout the cardiac cycle [12]. However, the generation of line or grid shaped saturation regions may only allow for determination of the mid-line displacement to a limited extent because of the relatively low spatial resolution of the tag grid. Bolster et al. [13] developed STAG (striped tags) to perform tagging in polar coordinates which allowed for the production of saturation patterns which may be better adapted to the morphological structure of the heart. Nevertheless, this method does not allow for the exact labeling of a predefined structure as e.g. the mid-line of the myocardium. Therefore a new tagging technique called RingTag has been developed which allows for labeling of a ring shaped saturation band on the mid-myocardium. For improved tracking of circumferential motion components, the RingTag structure can be combined with the StarTag procedure which consists of additional saturation lines arranged in a user definable star-like manner [14].

We hypothesize that the RingTag technique enables fast and accurate tracking of the midwall line throughout the cardiac cycle. This information offers the possibility to directly measure cFS and to obtain afterload corrected estimates of myocardial contractility.
Methods

RingTag generation

The present implementation of RingTag includes a magnetization preparation prepulse which can be combined with various imaging sequences. Further, the implementation allows for the combination of the RingTag prepulse with additional prepulses such as StarTag or a fat suppression pulse.

The principle of the RingTag includes a block RF pulse together with a selection gradient for saturation of a line. If the RF pulse is applied with an off-center frequency (left side). If the selection gradient \( \vec{G} \) is temporally rotated around a chosen center point, as shown for the time points \( \vec{G}_0, \vec{G}_1 \) and \( \vec{G}_n \), the saturation band can follow a given convex contour (right side).

\[ \Delta \hat{x} = \frac{2\pi \cdot \vec{G} \cdot \Delta f}{\gamma \cdot G^2} \]

EQ. [3]

where \( \gamma \) is the gyromagnetic factor, \( \vec{G} \) is the gradient specifying the direction of the displacement and \( \Delta f \) the off-center frequency of the RF pulse (Fig. 1, left). By rotating the gradient \( \vec{G} \) with a constant angular speed around a user defined center point CP (in this implementation given by the center.
of gravity of the contour), the position of the selected saturation band can be changed in circumferential direction. By additionally varying the off-center frequency, a predefined shape can be prescribed where the saturation line follows the tangential line to the desired trajectory (Fig. 1, right).

This technique allows creating any prescribed convex contour. The inner area is hereby practically not affected by the saturation, whereas the outer part is continually suppressed. Off-center placement of the RingTag structure can be accomplished by adding an offset frequency component to the RF pulse, described by

\[ f_{\text{shift}}(m_{\text{off}}, p_{\text{off}}) = \gamma \cdot (G_m \cdot m_{\text{off}} + G_p \cdot p_{\text{off}}) \]  

EQ. [4]

where \( G_m \) and \( G_p \) stand for the selection gradient components in measurement and phase encoding direction, respectively.

The sequence of the RingTag pulse is shown in Figure 2. Sinusoidal selection gradients are applied at the same time with a RF pulse in which the off-center frequency is variable, depending on the desired shape (Eq. [3]). A spoiler gradient (\( G_s \)) is used to diminish remaining transversal magnetization. The duration of the RingTag prepulse depends on the number of sampling points for representing the gradient shape and is shown in Table 1, including the spoiler gradient with a length of 1.5 ms.
The effect of the RingTag sequence was simulated by a software package, written in PV-Wave (Visual Numerics Inc., Houston, TX, USA) and developed at our institute [15]. This program simulates the propagation of the magnetization by numerically solving the Bloch equations [16] in the presence of the RingTag excitation pulse (Eq. [3], Eq. [4]). The simulation package was connected to scanner system environment, enabling to exchange scanning parameters and thus, to directly simulate actually performed RingTag measurements.

<table>
<thead>
<tr>
<th>Nr Samples</th>
<th>Pulse Length [ms]</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>4.4</td>
</tr>
<tr>
<td>160</td>
<td>6.28</td>
</tr>
<tr>
<td>200</td>
<td>7.3</td>
</tr>
<tr>
<td>256</td>
<td>8.74</td>
</tr>
<tr>
<td>512</td>
<td>15.24</td>
</tr>
</tbody>
</table>

**StarTag pattern**

In order to be able to quantify circumferential shortening, selected points of the ring structure can additionally be labeled with freely definable saturation lines. Therefore additional saturation bands may be optionally added in a star like manner [14]. Each saturation band is generated by a single selective block shaped RF pulse. The total duration of the StarTag prepulse depends on the number of generated lines (Table 2; including a spoiler gradient of 1.5 ms duration).

<table>
<thead>
<tr>
<th>Nr Saturation Lines</th>
<th>Pulse Length [ms]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.31</td>
</tr>
<tr>
<td>4</td>
<td>4.62</td>
</tr>
<tr>
<td>8</td>
<td>7.69</td>
</tr>
</tbody>
</table>

**Imaging protocol**

Imaging is performed using a breath hold, flow compensated echo-planar imaging (EPI) sequence with a scan matrix of 128 x 80 data points, a FOV of 192 mm and scan percentage of 100%. This results in an in-plane resolution of 1.5 mm x 1.5 mm. Slice thickness is 8 mm, EPI factor 9 (6 read-outs per excitation). \( \alpha = 30^\circ \) and the echo time 4.1 ms. Imaging is done using partial Fourier sampling (62%
of k-space). In a breath hold of 15 heart beats, 16-20 heart phases are acquired with a heart phase interval of 30 ms.

The imaging sequence can be extended with a slice-following feature which guarantees imaging of the identical selected slice throughout the heart cycle [17], despite the long-axis contraction of the heart [18]. This is achieved by acquiring two images with a volume encompassing the desired slice, one with and the other one without labeling of the slice by the application of an inversion pulse. By subtraction of both images, signal from the labeled slice may be extracted. However, this feature is gained with a doubling of the measurement time.

The generation of RingTag and StarTag, as well the slice-following procedure are achieved by prepulses which can individually be enabled before the imaging procedure (Fig. 3).

![Diagram](image)

**Fig. 3** Application of the tagging prepulses: RingTag (black), StarTag (midgray) and slice-following labeling (light gray) are implemented as prepulses which can individually be enabled and are applied directly after detection of the R-wave. After magnetization preparation, imaging (white) is done with a conventional imaging sequence.

The definition of the RingTag structure is done on a scout scan by means of a planning software on the scanner console written in Java (Sun Microsystems Inc., Palo Alto, USA). The user specified saturation region is either defined by interactive mouse clicks identifying base points of the saturation band, or by outlining epicardial and endocardial contours with subsequent automatic calculation of the corresponding myocardial centerline. The defined geometrical structure is thereupon automatically forwarded to the acquisition software (Fig. 4).
Methods

Phantom experiments

In order to verify the accuracy and quality of the resulting RingTag structure, experiments were performed in a phantom with T1 and T2 matched to the relaxation values of human myocardium [23]. Series of experiments were performed, in which the length of the RingTag pulse and thus the number of sampling points for representing the pulse shape and the total flip angle of the block pulse were varied. By this procedure, an optimized parameter set could be determined for the in-vivo measurements. Beside ring shaped structures, as expected for midwall line definitions in human ventricles, also experiments with “extreme” trajectories like triangle-shaped or even concave contours were done.

Furthermore, to evaluate the potential of the RingTag sequence to suppress outer regions of a user defined, irregular, convex structure, phantom experiments were performed where high RingTag flip angles were used.

Fig. 4    The definition of the RingTag is done on a prescan (top right) by means of a user-friendly planning software (left). The desired structure can be specified by interactive mouse clicks or by segmentation of epi- and endocardial borders with subsequent automatic calculation of the middle line. After definition for the RingTag, the geometry is automatically forwarded to the scanner system and appears on following scan (bottom right).
**Navigator guided breath holding**

For in-vivo experiments consistent end-expiratory breath-held diaphragmatic position is essential for matching the prescribed tagging structure with the anatomy of the heart. This was ensured by using navigator guided breath holds. Hereby a 2D selective diaphragmatic navigator [19] was utilized to track the diaphragm position in real time (100 ms time resolution) [20,21]. During scout scanning, navigator measurements were performed repetitively before the actual image acquisition. After the onset of the end-expiratory breath hold, the diaphragm position was determined using the navigator data. In subsequent measurements the subject was then given instructions to inhale and slowly exhale until the target zone (previously stored diaphragm position) was reached (Fig. 5).

This automatically triggered the imaging sequence. At the end of the image acquisition, a navigator was performed again in order to reject image data for reconstruction in the case of insufficient patient cooperation or diaphragm drift during the sustained breath hold. This navigator based breath hold guiding technique allowed reproducing breath hold levels for serial measurements without shortening the time for the image data acquisition.

![Fig. 5 Navigator guided breath holding](image-url)
In-vivo measurements

Acquisitions were performed with healthy, young volunteers, as well as with patients with expected myocardial hypertrophy. After survey scans for localization of the heart, horizontal and vertical long-axis scans were performed to plan 5 short axis imaging planes, equally distributed from base to the apex of the heart. For each level, a first untagged scan was acquired on which the RingTag was planned. Then, a second image with applying the RingTag pulse was acquired. All scans were performed at identical breath hold levels, as determined using the navigator breath hold guiding technique. The breath hold position of the first measurement was used as the reference (definition of the target zone) for all subsequent acquisitions.

Data analysis

The acquired RingTag images were processed with a dedicated software package written in Matlab (MathWorks Inc., Natick, MA, USA). Taking the initial planned geometry of the RingTag as a starting point, the saturation structures were tracked automatically in the subsequent heart phases by incrementally adapting the position of the saturation ring to the inner intensity gradient of the RingTag. The temporary information over the heart cycle was included to determine the ring position in order to achieve a smooth deformation of the RingTag over time.

Experimental setup

The RingTag sequence was implemented on a Philips Gyroscan ACS/NT 1.5 T whole body scanner equipped with gradient system Powertrak 6000 (max. gradient strength 21 mT/m; max. gradient slope 100 mT/m/msec). For data collection we used in the phantom experiments a circular surface coil and in the in-vivo measurements a synergy cardiac coil with 5 elements (2 circular front and 3 rectangular back elements).
**Results**

**Phantom experiments & simulations**

By phantom measurements and simulations, a reasonable parameter set for the RingTag sequence could be determined. Gradient strength, length of the RingTag pulse (expressed by the number of sampling points representing the pulse shape), and the flip angle, show a critical influence on the saturation structure. In the presented experiments, the length of the RingTag pulse was set to 7 ms (172 sampling points) and the nominal flip angle for the block pulse was 800 degrees at maximal gradient performance. This resulted in a good saturation and exact agreement between the prescribed ring contour and prevented from unwanted effects such as enhanced sampling ring artifacts outside the contour.

Image series in Figure 6 demonstrate the simulation results for the evolution of longitudinal magnetization for a user defined shape. It visualizes how the desired structure is “peeled out of the magnetization surface”. Corresponding phantom images are shown in Figure 7. To illustrate the temporally resolved generation of the RingTag in phantom measurements, single time frames were created in individual acquisitions with piecemeal completed RingTag pulses.

The RingTag sequence is able to create even unconventional ring structures (Fig. 8 a-c). In these “extreme” examples, parts of the RingTag saturation band, where high angular velocities occur, have a reduced saturation effect if compared to parts with low angular velocities as e.g. in the edges of the contours (Fig. 8 a,b). This is a consequence of the constant angular speed of the RingTag selection gradient and the constant RF pulse amplitude applied.

As consequence of the RingTag generation principle, the procedure is limited to creation of convex structures. Concave trajectories can not be generated due the mutual canceling of ring parts during the creation process (Fig. 8 c).

Figure 9 demonstrates the effect of utilizing high flip angles for the RingTag RF pulse. This results in an enhanced suppression of tissue outside the ring structure, whereas the inner area is minimally affected.
Fig. 6  Simulation results of the temporal evolution of the longitudinal magnetization for a user defined ring structure by numerically solving the Bloch equations.
Fig. 7  Demonstration of the temporal resolved generation of a user-defined RingTag saturation band in a phantom. Each time frame was generated by an individual measurement with a partly applied RingTag pulse.
Results

Fig. 8  Demonstration of the generation of unconventional RingTag shapes. All kind of convex contour can be outlined, even long drawn out or contours with sharp corners. However, the RingTag production is limited to convex rings. Concave shapes show canceling of parts of the predefined saturation band as seen on the right example.

Fig. 9  Signal suppression outside the convex RingTag structure by applying a large flip angle. Image left shows the reference scan with indicated RingTag structure (dashed line). Middle image is the acquisition with the flip angle set to 800° and to the right with a 5 times larger flip angle. Below the intensity profiles of the three images is displayed. In light gray the left image, in midgray the middle image and in black the right image.
In-vivo measurements

RingTag measurements were successfully performed in volunteers and patients. The saturation band was clearly visible in all heart phases (Fig. 10). Measurements with slice-following showed lower SNR compared to non slice-following measurements, especially in the basal slices where the coil sensitivity was reduced. However, all measurements could automatically be postprocessed. Slice-following measurements enabled the motion analysis of the entire cardiac cycle. For the tagging approach without slice-following, tag fading was observed as known from conventional SPAMM imaging which limited its applicability mainly to the systolic phase of the cardiac cycle (Fig. 10, top).

The maximal tag saturation was achieved directly at the contour; regions towards the outside of the contour were less affected by the saturation pulse because of the relatively high angular speed of the saturation band following the prescribed trajectory. The intensity profile of the RingTag shows a characteristic steep inner gradient and a more flatten course towards the outside (Fig. 11). Thus, if the inner border is detected, the precision of the RingTag localization is not directly dependent on the saturation line width, but may be performed with very high, eventually even with sub-pixel accuracy [24].

The navigator guided breath holding procedure allowed to control the diaphragm position very accurately in volunteers as well in patients. By applying this technique, deviations for breath hold position could be minimized down to millimeter accuracy. In 171 measurements in 13 individuals (7 volunteers, 6 patients) the average deviation to the desired reference position was -0.33 mm for volunteers and 0.37 mm for patients. The drift during the measurement (difference between navigator measurement at beginning and end of the image acquisition) was 1.64 mm and 1.81 mm, respectively. The various measurements showed that consistent breath hold reproduction is crucial for precise placement of the RingTag saturation band on the myocardium. Otherwise, inaccurate placement of the RingTag on the myocardium was observed. Monitoring of diaphragmatic drift during breath hold allowed control of breath hold quality and rejection of data in case of insufficient patient cooperation.
Fig. 10  Images showing different time points of the heart cycle of a volunteer with applied RingTag and StarTag. Imaging was done with a flow-compensated EPI sequence (EPI factor = 9, in-plane resolution 1.5 by 1.5 mm², heart phase interval = 30ms). Top 8 images demonstrate the EPI acquisition without application of the slice-following prepulse; corresponding 8 images with the slice-following enabled sequence are shown beneath.
Discussion

A new tagging method has been presented which allows saturation of freely definable convex ring structures. The possibility to create a user definable saturation structure allows to track tissue motion and deformation within the myocardium along anatomically defined structures e.g. along the circumferentially oriented fibers of the mid-myocardium. Further, by enlarging significantly the flip angle of the RF pulse, an enhanced saturation of the outer region can be achieved. This effect may be applied for a time efficient saturation pulse to suppress tissue signal coming from outside the RingTag contour which might be useful in spectroscopic imaging (outer volume suppression of fat regions in the scull area), spiral imaging (reduction of off-resonance artifacts) applications or small FOV imaging.

At the current state, the RingTag generation lacks a mathematical description which would allow for weighting of the RF amplitude in the RingTag sequence in order to obtain a constant saturation level in all parts of the tag. This could be beneficial in applications with extremely shaped contours as demonstrated in Figure 8c. For the presented applications however these limitations did not have a negative effect.
The possibility to align the freely definable RingTag saturation structure with mid myocardial circumferentially oriented fibers may allow to estimate circumferential fiber shortening or ventricular strain properties [22]. In combination with assessment of end-systolic stress, this approach may provide an afterload-corrected measure of left ventricular contractility. The combination of RingTag with high speed imaging sequences may even allow the assessment under stress conditions.

References

Abstract

Magnetic resonance tissue tagging is a powerful method for the quantitative noninvasive analysis of heart wall dynamics. However, post-processing of tagging images and thus determination of motion parameters is a time consuming task, which restricts usability and therefore complicates the introduction of myocardial tagging for clinical applications.

One established and sophisticated technique for performing tissue tagging is CSPAMM (Complementary Spatial Modulation of Magnetization). For evaluation of these images a software was developed previously at our institute, which was based on tag line extraction using active contours (“snakes”). However, long evaluation times strongly limited the practical use to smaller, non-clinical studies.

Here, a novel model-based approach is pursued. The new tag detection tool allows for time efficient processing of CSPAMM data sets. Tagging information, which appears in the images as a dark saturation grid on the myocardium, is extracted using a predefined geometrical model consisting of vertices connected by elastic edges. Under the influence of virtual forces, induced by image features and relative position of the vertices, the model is deformed and thus is able to adapt itself to the tagging grid, while preserving its main structural characteristics.

In this paper, the new software is introduced and compared to its predecessor regarding required processing time, applicability and resulting motion parameters. The evaluation time using the new approach was found to be significantly reduced by a factor of approximately ten. Manipulations on the detected grid structure were extremely simplified due to the inherent dynamic behavior of the template and the improved graphical user interface. Resulting motion parameters derived with both software packages showed only minor differences and good reproducibility for the parameters extracted applying the template based software.

In summary, the new evaluation tool enables processing tagging data in reasonable time and thus, increases the potential of myocardial tagging as a tool for clinical investigations.
Introduction

Cardiovascular magnetic resonance imaging (MRI) provides a flexible tool, which has become increasingly important in the diagnosis and management of heart diseases. The manifold features of this technique, such as accuracy and reproducibility, have made MRI a valuable tool for basic cardiac and clinical research. In order to reliably estimate the heart state, detailed knowledge of the cardiac wall dynamics has shown to be useful and sensitive for in-vivo diagnostic scanning [1-4]. MRI myocardial tagging is a sophisticated technique for accurate quantitative analysis of heart motion. Previous studies have proven the outstanding potential of this technique, offering new possibilities for understanding heart function [4].

For myocardial tagging, the tissue magnetization is modulated prior to a conventional imaging procedure in order to generate saturation markers that appear as dark structures in the images (“tags”). The modulation patterns are fixed with respect to the myocardial tissue. During the deformation process of the underlying tissue, the localization of the tags may be tracked over time by cine imaging. After detection of the tagging structures in the images, displacements of characteristic tissue landmarks can be registered and represented as motion parameters [5]. Different types of tagging magnetization preparation sequences have been proposed in the last years [6-13]. For the discussed evaluation software the tagging sequence CSPAMM (Complementary Spatial Modulation of Magnetization) [8,9] was considered. This method allows for the assessment of the systolic and diastolic phase of the cardiac cycle. Through plane motion induced by the long axis contraction [11] during the cardiac cycle can be avoided by the application of a slice following imaging technique [8]. By optimization of the RF excitation angles for imaging, constant tagging contrast can be achieved for all measured heart phase images, which is an important precondition for automated tag detection. These features distinguish CSPAMM from other tagging principles and yield in increased accuracy and reliability.

The objective of a tagging evaluation software is the accurate and preferably automatic detection of the saturation structure in the tagging image - usually a line or grid like pattern, which is subsequently deformed under the motion of the tissue. However, analysis has shown to be a challenging task and several approaches have been undertaken in order to facilitate and speed up this process [5,12-21]. Existing solutions make use of techniques such as manual identification of intersection points [12], polynomial curve fitting [13], optical flow [14], active contour models [5,15], straight line Hough transform [16] or template matching [17]. A dedicated software has previously been developed at our institute in order to evaluate tagging examinations [5]. In this paper the term MACAVA will be used.
Introduction

to refer to this tool. MACAVA is based on active contours (snakes) [22-26] and allows for the semi-
automatic detection of the line tags with subsequent motion parameter calculation and visualization.

However, MACAVA is concerned with several difficulties such as

- **Sequential processing**

  Each tag line is detected and processed individually. Because information from neighboring tag
  lines is not considered, parallel lines may fall together or cross each other. Further, the sequential
  procedure is unfavorable regarding time efficiency.

- **Exclusion of anatomical structure information**

  Snakes try to extract tag line structures over the whole image, from one image border to the next.
  Because of the limited region-of-interest (the ventricle), potential problems occur at the transition
  from myocardium to the surrounding tissue structures such as e.g. fat. In these zones tag lines
  may be non-continuous or roughly altered by mutual displacement of different tissue layers. How-
  ever, such image information corresponds to high external energy components acting on the
  active contours. Consequently, the snake line may begin to oscillate or does not adapt itself cor-
  rectly to the presented tag information.

- **Manual corrections**

  After separate detection of the two orthogonal tag line directions, both data sets are combined in
  order to obtain a grid structure. The calculation of the motion parameters takes all grid elements
  into account that are either on the myocardium or touched by the myocardial border. The edging
  elements are at risk to be geometrically dispersed because of corner points being on different
  anatomies i.e. some on the myocardium and others on the surrounding tissue. Therefore, these
  grid elements have especially to be considered by drawing corner points related to the points on
  the myocardium. However, adaptations of already detected structures are only possible by shifting
  single crosspoints of the grid. In order to preserve a temporally continuous and natural motion of
  the grid structure further corrections at the neighboring nodes, as well as at the corresponding
  points of the previous and subsequent heart phases, are required.

- **User interface**

  MACAVA is implemented in PV-Wave (Visual Numerics Inc., Houston, TX, USA), a develop-
  ment environment that itself is required for running MACAVA on dedicated operating systems.
  The user interface is rudimental and not appropriate for intensive user manipulations. This slows
  down the evaluation process and makes work cumbersome.

In order to overcome the drawbacks mentioned, a new approach for tag line detection named TEVAL
was implemented. In this paper the new method is described. It allows for time efficient processing
of tagging images. The basic idea of TEVAL is the detection of the tagging structures by using a pre-
defined template model that is able to adapt itself to the tagging saturation grid. This is similar to ac-
tive contour based techniques, but in contrast, a global adaptation process of a predefined structure
definite model. For the calculation of motion parameters as derived from the displacement informa-
tion of the tagging grid, processing routines from MACAVA were used for both evaluation packages. A data interface was implemented for TEVAL that enables forwarding the detected tagging grids to the calculation module of MACAVA.

Three tagging data sets of patients were processed independently by two independent operators using both evaluation tools, TEVAL and MACAVA, in order to compare processing time, user friendliness, and results.

**Methods**

**Overview**

The template model is realized as an elastic, discrete structure [24] consisting of nodes (vertices) arranged in a grid topology. They are connected by edges acting as spring elements (Fig. 1).

![Diagram of nodes and edges](image)

*Fig. 1* Nodes arranged in a grid topology are connected with edge elements which act as springs. For reasons of clarity the diagonal connections between all vertices, which contribute to the stability of the template, are not shown. If a node is displaced as result of an external force or by manipulation of the user, neighbor elements are also affected and begin to adapt themselves.

Internal and external forces derived from image features or induced by rearranged node positions, as the result of user manipulations, lead to a deformation of the template and consequently perturb the equilibrium in the model. During the evaluation procedure an iterative simulation process calculates the relaxation of the imbalance of acting forces until a stable state is found or it is stopped by the user.
By an appropriate weighing of the deforming components, the template is able to adapt itself to the existing image structures (dark tag saturation lines) and to sustain the initially defined topology. The myocardial borders, which are outlined at beginning of the evaluation, allow to cut the template grid to the geometry of the ventricle (Fig. 2). By this, computation time may be saved and the mentioned difficulties at the transition areas of different tissue layers can be avoided as the detection process is limited to tag crosspoints in the region-of-interest.

Fig. 2 Visualization of the cutting process of the automatically generated initial template grid. Only nodes lying on the myocardium are considered for the adaption process. By this restriction of the optimization to the true region-of-interest (short axis view of the left ventricle), computing time is saved and continuity problems of tag lines at the border of myocardium and the surrounding tissue are avoided. The right image shows only the part of the template which is actually matched to the tagging structure.

Template model

The forces affecting a template node can be separated into internal and external components (Fig. 3). Internal forces are defined between vertices and behave like spring elements. The components taking effect in direction of the four neighbors are called neighbor forces ($f_N$), and the components in direction of the diagonal adjoining nodes diagonal forces ($f_D$). The size of neighbor and diagonal forces is proportional to the deviation from the initial distance between the two points. Thus, these components may be of contracting or expanding nature and are responsible for the structural stability of the tem-
plate. User interactions such as moving cross points to new locations result in distance variations between nodes, which induce changes in the neighbor and diagonal forces and consequently take effect on the neighbor nodes.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{force_diagram.png}
\caption{Visualization of the force components acting on a vertex of the template. They may be divided into internal forces ($f_N$, $f_D$) which are necessary for maintaining the structure stability and external forces ($f_V$, $f_E$) which provide the information for the adaption process.}
\end{figure}

Beside the internal forces, external forces are either vertex forces ($f_V$) or edge forces ($f_E$), which are both related to image features. The vertex force for a dedicated template node is determined by considering the surrounding area, which includes normally the bordering 24 pixels ($c=2$) as depicted in Figure 4.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{vertex_force_calculation.png}
\caption{For calculating the vertex forces only image points from a limited region are considered ($2c+1$ by $2c+1$ elements). For each pixel in this area the gray intensity difference $f_{(i,j)}$ to the middle pixel with index (0,0) is calculated (image gradient) and weighed with its distance. The total vertex force for pixel (0,0) is finally obtained by summing up all individual pixel force components $f_{(i,j)}$.}
\end{figure}
For each pixel of this region one force component vector is calculated which is proportional to the image gradient (gray value difference between the two picture elements). The forces are weighed with the pixel distance in quadratic manner in order to realize a regional dependency of the image features and therefore local features become more important. The total force affecting a single node is finally obtained by summarizing all partial force components as denoted in Equation [8] with the index range \( \Lambda = \{-c, -c+1, \ldots, -2, -1, 1, 2, \ldots, c-1, c\}:

\[
\begin{align*}
    f_x &= - \sum_{i, j \in \Lambda} i \cdot \frac{f[x + i, y + j]}{(i^2 + j^2)} \\
    f_y &= - \sum_{i, j \in \Lambda} j \cdot \frac{f[x + i, y + j]}{(i^2 + j^2)}
\end{align*}
\]

If nodes only tend towards intensity minima the detection process may run the risk of neglecting the course of the tag line curve. Therefore edge forces are introduced which allow two nodes to be shifted parallel to the edge (Fig. 5). For this purpose, the image gradient on the perpendicular bisector of the edge is determined. The calculation of multiple gradients along the edge results in only marginally better results, wherefore only one gradient is considered which is also favorable with regard to required computing time.

The course of the simulation process is visualized as a flow chart shown in Figure 6. A program loop iteratively calculates the sum of all forces for a specific node and derives the respective acceleration, including a user definable elasticity factor \( \varepsilon \). For the according time step the new velocity can be determined and subsequently the displacement of the node. The updated velocity value is fed back with
Template Based Evaluation Procedure for CSPAMM Tagged Images

a damping factor $\delta$ which has equal to the elasticity factor influence on the dynamic behavior of the template. An elasticity factor greater than one lets the forces react as rubber connections and the damping factor between zero and one prevents the model from falling into an oscillating state.

In order to reduce computing efforts, the mass $m$ of a template node as well the incremental calculation time step $dt$ are set to one. When the template has achieved a stable state, a fine tuning of the grid structure is performed. In this step, the edge connecting two nodes is sampled and each corresponding line point is shifted in limited orthogonal direction to the actual gray value minimum of the image. By this, the fitting of the connection line of two vertices to the saturation structure is visibly improved.

**Processing sequence**

After loading the tagging image, the endocardial and epicardial contours of the left ventricle are outlined manually. An initial grid template is automatically generated by enlarging the grid distance and incrementally adding new grid rows and columns by successively identifying the gray value minima of the underlying image. This process to build up the initial template starts outside the indicated ventricle border and ends when the whole ventricle is covered by the grid template (Fig. 7). Although this simple algorithm works in most cases, it may fail in images of poor quality. Therefore, the template grid may also be predefined in size and grid distance and manually be placed on the tagging image.

At this point the template is tailored to the ventricle shape. After definition of the start template, the
simulation process is started, which adapts the grid to the given tagging structures (tag lines/grid). In case of inaccuracies of the detection process, the user is able to interact by moving crosspoints to different locations, where they undergo the adaption process again. Alternatively, crosspoints may be locked at their new location. After completion of one heart phase the detected grid structure can be copied to the following heart phases. For each copy process the internal forces are newly initialized which allows the template to always start adapting from a relaxed state. Consequently, the copied template serves as the starting basis for the detection of the tagging structure in the new heart phase which normally represents only a slightly altered structure.

If all heart phases are evaluated, the detection grids can be saved and exported into a data format which can further be processed by the MACAVA package.

![Fig. 7](image)

*Fig. 7*  The generation of the initial orthogonal grid structure in the first heart phase may automatically be performed. Starting at a point outside the ventricle the grid distance is successively increased and new grid rows and columns are introduced and adapted to the saturation grid. This process is iterated until the region-of-interest (the left ventricle) is fully covered by the template structure.

**Implementation**

The evaluation software was written in Delphi (Insprise Corp., Scotts Valley, USA) and runs under Microsoft Windows95/NT (Microsoft Corp., Redmond, USA) on a conventional personal computer. The user friendly user interface including features such as variable zooming, colored visualization of individual force components and display of previous and subsequent node positions supports convenient and efficient tagging image processing (Fig. 8). The parameter constants that influence the dynamic behavior of the template, such as elasticity, damping or weighing constants, can easily be
Template Based Evaluation Procedure for CSPAMM Tagged Images

adapted. Suitable parameters were determined on different tagging data sets and were fixed for the evaluations performed in this paper. A 300MHz Pentium II personal computer was used to calculate the presented results. The calculation of motion parameters and the visualization of these results were done on the identical machine with MACAVA running under Linux and PV-Wave.

Results

The duration for processing a single patient using MACAVA amounts up to approximately 4 hours, hereby strongly depending on the quality of the image data set. Tagging images of reduced quality implicate increased evaluation efforts caused by time-intensive user interactions in order to correct individual mis-detected snake contours.
The processing time for a patient tagging data set applying the TEVAL software was approximately 30 minutes. The generation of the initial template could be accomplished automatically for all evaluations. As differences of the tagging structure are relatively small from one heart phase to the next, only minor alteration of the template grid are required which supports the reliable automatic identification of the tagging lines. After detection of the tagging saturation structures, the implemented data interface allowed for transferring the grid structure data to the MACAVA package, where motion parameters were automatically calculated in less than one minute.

Corrections of the detected tagging structures can be done much easier and quicker with TEVAL as neighbor nodes automatically align to the manipulated cross points whereas with MACAVA all adaptations have to be made individually for multiple vertices. Border nodes which have to be manually tracked with MACAVA, generally adjust automatically with TEVAL because of the structure maintaining character of the template.

The comparison of the results from TEVAL and MACAVA demonstrated good correlation (Fig. 9, Fig. 10). The curve shape of the considered parameters showed to be consistent referring to peak values. However, deviations are seen for velocity parameters in the first heart phases of the cardiac cycle (Fig. 10).
Fig. 9  Display of the circumferential shortening (left column) and radial shortening (right column) parameters of three different patients. Each tagging data set was processed with TEVAL and MACAVA by two independent evaluators. The results obtained with the TEVAL program shows a good correlation with the MACAVA evaluations.
Accurate and time efficient evaluation of tagging images is relevant for the successful introduction of myocardial tagging into clinical cardiology.

With the presented evaluation software TEVAL it is now possible to significantly speed up the processing time for tagging images. As the detection of the tagging structures is accomplished by matching of a complete, geometrically definite template, evaluations are less susceptible to local image artifacts. Consequently, the required processing time is much less dependent on the image quality of...
the data set than evaluations done with MACAVA. The motion of tagging crosspoints, which are expected to pursue a natural behavior which corresponds to continuous and smooth motion trajectories, are inherently supported by the template concept.

The user-friendly program interface of TEVAL supports efficient and convenient manipulation of the detected tagging structures. The software runs fast on a standard personal computer under Windows95/NT operating system, which is widely available and thus, simplifies the introduction of the evaluation software into other MR sites. However, the package lacks currently of a motion parameter calculation module. This functionality was replaced for this study by a dedicated data interface to MACAVA. In future, the complete motion parameter calculation may be integrated into the TEVAL software. By this, the software would not rely on the existence of MACAVA and consequently PV-Wave, which requires an expensive software runtime license. Other improvements could include the extension of the fine tuning step by a sub-pixel fitting strategy [27] or the temporal smoothing of the motion trajectories of intersection points.

Comparisons of the outcomes using both TEVAL and MACAVA demonstrated good consistency and reproducibility. The minor deviations between both evaluation methods may be attributed to the individual definition of the myocardial borders. As outlining of the endocardial and epicardial contours is manually aggravated in CSPAMM tagging images, the acquisition of additional anatomical images of the identical geometrical location might be helpful.

Although required processing time is enormously reduced employing TEVAL, user interaction is still required for the evaluation process. The recently published tagging processing method HARP (Harmonic Phase imaging) [28] seems to be a very powerful technique, which gives hope for a solution for fully automatic image processing. Further investigations have therefore to prove its applicability and comparisons with other evaluation concepts such as TEVAL have to be performed.

However, the availability of an evaluation software that enables processing tagging data in reasonable time increases the potential of myocardial tagging as a tool for clinical investigations.

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3.4. Magnetic Resonance Tagging under Ergometer Stress


Abstract

CSPAMM tissue tagging was combined with the ultrafast segmented k-space acquisition technique TFEPI, which allowed for shortening the total acquisition time down to few heart beats. The protocol was applied for performing tagging measurements under physically induced stress, enabling to analyze motion pattern alterations of the heart under influence of a cardiovascular load. CSPAMM tagging enabled imaging of the identical slice location throughout the entire cardiac cycle by its inherent slice-following principle. A manual correction procedure was performed for compensating bulk displacements of the body between measurements under rest and stress. A training procedure for improved reproduction of breath hold positions, based on the visual feedback of the real time acquired diaphragm position data, was introduced. Exercise was performed inside the scanner bore using an MR compatible ergometer. Measurements of thirteen healthy, young volunteers are presented. Results show significant changes in circumferential shortening (+23.77%), radial shortening (+35.96%) and rotation (+45.62%). Rise times were significantly decreased for circumferential shortening (-40.23%), rotation (-38.99%) and radial shortening (-40.61%).
Introduction

The investigation of the heart function under cardiovascular load is a widely accepted methodology in clinical cardiology for the early diagnosis and prediction of upcoming heart function deficits such as the disclosure of ischaemic myocardial sections [1-3]. The ability to reveal ischaemic symptoms earlier under cardiovascular stress than under rest conditions make examinations of this kind an important tool in daily clinical work. A commonly applied form of stress induction is the administration of pharmacological agents such as dipyridamole, dobutamine or adenosine. Various studies have proven the applicability and usefulness of this kind of examinations [4-7]. An alternative to pharmacological stress is physical exercise. For this purpose, clinically frequently used devices are the treadmill and the ergometer [8-10]. The advantages of physically induced stress experiments include the better resemblance of cardiovascular stress encountered in daily life, non-invasiveness and the absence of pharmaca. Further, it has been reported that physically induced stress performs equally well or even better than pharmacological stress with respect to sensitivity and specificity when investigating for coronary diseases [11,12]. Economic advantages may also be mentioned since physically induced stress examinations are much cheaper due to the renunciation of drugs. Limitations for physically induced stress examinations are the impracticability for subjects who are not able to perform physical exercise and the required patient cooperation.

During the stress examinations the heart function is routinely assessed by echocardiography (visualization of wall motion abnormalities), scintigraphic imaging (uncovering perfusion deficits) or observation of the ECG (detection of ST segment alterations). Generally, the earliest manifestation of myocardial ischaemia are abnormalities in the diastolic function. With more prolonged ischaemia, re-
Regional abnormalities in systolic function occur (Fig. 1) [13-15]. Consequently, the analysis of the heart kinematics over the entire cardiac cycle is essential for the early diagnosis and management of patients with suspected ischaemic heart disease [16,17].

Myocardial tagging is as a powerful MRI technique for assessing quantitative, temporarily resolved tissue motion parameters that may provide superior information content with respect to accuracy and significance when compared to other methods such as echocardiography [18]. However, tagging examinations under physically induced stress is concerned with multiple challenges:

- **Short Acquisition Window:**

  Physical exercise implicates augmented motion of the body, enhanced breathing and increased cardiac frequency. Studies observing the heart rate change after exercise stop indicate a rapid heart rate recovery after stress [19-21]. A study consisting of 55 measurements in 18 healthy subjects demonstrated a rapid decrease in the heart frequency (80% of max. heart frequency) after about the 10th heart beat (Fig. 2). This also agrees with findings in [22] where the drop-off occurs at about the 8th heart beat. If heart rate is assured to be valid measure for the stress state after exercise stop, the acquisition window for a breath held experiment is limited to the first few heart beats. Consequently, measurements preferably have to be done using fast acquisition sequences which allow for imaging in real time or by performing short breath holds directly after exercise.

Fig. 2 Heart rate recovery after exercise stop as assessed in 55 examinations with 18 subjects. After the 10th heart beat, the heart rate drops rapidly. Therefore, if the cardiac pulse is taken as a measure for the stress state, breath hold imaging has to be concluded within about the first 10 heart beats after exercise stop.
Magnetic Resonance Tagging under Ergometer Stress

• Acquisition at Identical Geometrical Levels of the Heart:
The heart motion patterns are complex and show specific characteristics for different geometrical levels of the heart such as for the apex, the mid-myocardium, or the base of the myocardium [23,24]. Thus, motion analysis has to be done related to dedicated geometrical locations. In case of a static imaging plane, the long axis contraction of the heart [25,26] has as consequence the acquisition of different positions over the cardiac cycle. Under stress conditions, enhanced cardiac motion must be expected which further strengthens the demand for a compensation mechanism for the long-axis contraction.

• Displacements of the Subject between Measurements under Stress and Rest
Due to the relatively long period between the time points for imaging under stress and rest, shifts of the subject may occur and have to be considered in order to prevent measurement and comparison of motion parameters originating from different locations of the myocardium. Further, for breath hold measurements the reproduction of similar diaphragmatic levels between rest and stress state have to be taken into account.

Progress in MR technology, such as the introduction of new fast imaging sequences and the availability of high performance gradient systems, enable the acquisition of cine frames in very short time, actually in real time [27,28]. Thus, the combination of ultrafast imaging sequences with myocardial tissue tagging could allow for the investigation of the heart condition under stress, even physically induced stress.
Introduction

Real time SPAMM (SPA\textit{tial} Modulation of the \textit{M}agnetization) tagging \cite{29} measurements during ergometer exercise have already been presented (Fig. 3) \cite{30}. However, the fading of the tag line intensity over time limits the motion analysis to the systolic phase of the cardiac cycle. Furthermore, no slice-following is provided which would allow for compensating the long-axis contraction motion of the heart. CSPAMM (Complementary \textit{SPAMM}) tagging \cite{31,32} is based on a subtractions technique and requires two measurements for a single image. This impedes the use of CSPAMM tagging for measurements in real time. However, the advantage of this technique is the incorporated slice-following feature. Hereby the imaging slice is labeled in order to measure the identical location over time, despite the long-axis contraction. Additionally, tag line intensity may be the preserved using CSPAMM which allows for heart motion analysis over the entire cardiac cycle and facilitates the image evaluation procedure due to improved tag line contrast.

We hypothesize that myocardial CSPAMM tissue tagging combined with an ultrafast imaging sequence may provide a powerful, accurate and quantitative assessment technique for cardiac stress examinations.

Fig. 3 \textit{Real time SPAMM tagging during ergometer exercise: 8 out of total 33 short axis images acquired in a ‘free-run’ mode (ECG triggering only used for initiating the scan) with a frame rate of 31 msec. Imaging was done with TFEPI (EPI factor = 13, turbo factor = 2, echo time = 4.5msec).}
Methods

CSPAMM tagging was combined with TFEPI (Turbo Field Echo Planar Imaging) [33], a fast and versatile imaging protocol which allows for performing acquisitions with high temporal resolution. The imaging procedure is an EPI based sequence where the read out trains are split up by a variable number of RF excitations, expressed by the turbo factor. This protocol combines the fast acquisition feature of EPI (multiple k-lines per excitation) while preserving a low echo time which is beneficial for reduction of flow and motion related artifacts. Finally, this implementation enables to shorten the measurement time down to 4 heart beats, which is the lower limit for CSPAMM tagging examinations if the two tag line directions are acquired separately. However, the increased number of RF excitations of the TFEPI sequence if compared with EPI, cause an accelerated decrease of the tag line intensity over time. In order to preserve and distribute the tag line signal equally over all heart phases, an RF excitation specific flip angle adaption was applied.

Imaging parameters for the CSPAMM measurements were a FOV 310 mm, a nominal scan matrix of 128² in combination with a rectangular FOV of 65%, scan percentage of 35%, 30 heart phases, EPI factor 11, turbo factor 3 (= three RF excitations each followed by an EPI readout), flip angle $\alpha=18^\circ$, and an echo time of 5 msec. For the high heart rates during stress two shots where required for each heart phase, doubling imaging time from 4 to 8 heart beats, but improving the temporal resolution from 42 msec to 14 msec (turbo factor = 1).

In order to address the raised questions concerning control over eventual body shifts and reproduction of similar breath holds, following strategies were pursued:

In order to correct displacements of the subject between stress and rest phases of the examination, long axis correction scans were completed in both stages of the experiment. This TFEPI long-axis measurement was performed within a single breath hold (FOV=300 mm, scan matrix of 128², EPI factor 9, turbo factor 2). For the scans under rest, which were acquired after a long recovery period, the
long axis control scan was compared to the corresponding image under stress. If a misregistration was notified, the apical short axis position was corrected in long axis direction by the distance measured on-line with the scanner viewing software (Fig. 4).

As CSPAMM tagging experiments have to be performed using breath holds, control of corresponding diaphragm levels in the measurements under stress and rest is important. In order to track the diaphragm position in real time, a M-mode pencil beam (navigator echo) [34,35] was placed on the right hemisphere dome and graphically visualized on an external PC. This allowed the volunteer to observe the own breathing excursion data over a mirror system on a back projection screen located in the examination room behind the scanner (Fig. 5) [36].

During the stress phase, exercise was shortly suspended in order to perform a breath hold, which allowed for defining a target zone at the end-expirational position. After stress, the feedback system was utilized to enable the individual to train the reproduction of the similar breath hold position as done before in the stress state by leading the position indicator of the diaphragm excursion into the target zone.

The examination protocol is summarized in Figure 6:
At the beginning survey scans were performed and the preparation for the following protocols was done in order to increase time efficiency for scanning. The second part was the stress phase where the individuals started cycling with an step-wise increasing load. After about 10 minutes of cycling the breath held tagging stress measurement were completed. For this, the individual interrupted cycling, performed a breath hold for the acquisition and restarted cycling immediately after the scan. After another 2 minutes of exercising the navigator scan was done in order to define the target zone for the breath hold training. The final part of the examination was the post stress phase which started after a recovery period of about 15 to 20 minutes. The long-axis control scan under rest was acquired and compared to the corresponding scan under stress in order to correct the scan plane in axial direction. Subsequently, the training procedure for breath hold position reproduction was done, followed by the final tagging acquisition under rest.

**Physical stress induction**

For inducing physical stress an MR compatible ergometer (Lode Technologies, Groningen, The Netherlands) was applied. This special bicycle device, mounted on a conventional patient table, enables cycling in supine position inside the scanner bore (Fig. 7). An external controller unit provides a freely adjustable, speed-independent (40-120 RPM) load within a wide range from 10 to 250 watts. In pre-
Methods

Presented investigations a step-wise increasing load up (20 W each 2 min) to average 80W for women and 120W for men, depending on their physical ability, is applied. Volunteers are cycling for an average of approximately 12 minutes.

**Tagging evaluation**

Tagging images were processed with the evaluation package Teval written in Delphi (Insprise Corp., Scotts Valley, CA, USA) and developed at our institute. This software, based on a template matching algorithm, allowed for the fast detection of the tagging grid. The calculation of the various motion parameters was done in the Macava package, also developed at our institute [37]. Motion parameters considered in this study were the circumferential shortening, radial shortening, rotation angle, area reduction and velocity components [37]. For better comparison all viewed parameter time series were matched on the time axis to 100% systole. In order to reduce evaluation time of the CSPAMM measurements acquired with two shots, only every second heart phase was analyzed which resulted in a final effective temporal (frame to frame) resolution of 28 msec.

The volunteer study included 13 healthy volunteers (9 men and 4 women) with an average age of 27 years.

**Equipment**

All measurements were performed on a Philips Gyroscan ACS/NT 1.5T whole body system (Philips Medical Systems, Best, The Netherlands). The CSPAMM tagging study was performed using the gradient system Powertrak 6000 (max. gradient strength 21 mT/m; max. gradient slope 100 mT/m/msec).
Magnetic Resonance Tagging under Ergometer Stress

MR data was collected with a synergy cardiac coil using the 2 circular front elements. For triggering the ECG was required and for monitoring the heart rate a pulsoxymeter (PPU), attached to the individual’s finger, was used since the ECG was disturbed during stress in most cases by the physical activity of the volunteer.

Results

Thirteen volunteers have been successfully examined and evaluated for heart motion alteration between rest and physically induced stress. During cycling the ECG was disturbed by the physical activity but instantaneously reinstated after exercise stop which allowed for performing immediately the breath hold measurements. Good placement of the especially for stress examinations developed electrodes (Skintact FS50C, Leonard Lang GmbH, Innsbruck, Austria) additionally supported the good ECG quality. The average heart rate during exercise was 125 bpm as determined by a pulsoxymeter device.

The very fast acquisition sequence and the high heart rates reduced image quality and SNR, but image were still well evaluable (Fig. 8). In the stress images, interferences from the ergometer, manifested as bright spots in the images, further reduced the SNR. Displacement corrections in heart axis direction after the stress measurement, based on the evaluation of the long-axis scans under stress and rest, resulted in shifts of maximal 8 mm (average 1.4 mm) toward base of the heart.

Fig. 8 CSPAMM tagging images over one cardiac cycle. Top row was acquired under rest conditions and bottom row under stress induced by an ergometer.
The average circumferential shortening increased from 11.99 mm to 14.84 mm (+23.77%) under stress (p=0.0071). The rise time from begin of motion until maximal shortening was decreased under stress by -40.23% (p<0.0001) from 262.28 msec to 156.76 msec (Fig. 9). For radial shortening the average value was augmented by 35.96% (p=0.0006). The rise time until peak rotational shortening was also decreased by -40.61% from mean 259.52 msec to 154.14 msec (p<0.0001) (Fig. 10). The rotation parameter under stress was in mean higher if compared to rest (increase from 3.77° to 5.49°, corresponding to +45.62%, p=0.01). The rise time was significantly decreased from 134.14 msec to 81.84 msec, i.e., -38.99% (p<0.0009) (Fig. 11).

Comparing the temporal progression of the velocity parameters demonstrated a more pronounced averaged value over all subjects with a highly increased mean peak velocity (rest: 31.23 mm/sec, stress: 62.73 mm/sec, +100.84%, p<0.001) (Fig. 12). Under rest, a flattening of the rotation velocity was seen before end-systole, whereas under stress a more linear transition from positive to negative velocity components was observed (Fig. 13). The averaged peak value under rest of 96.78 deg/sec was increased by +67.34% to 161.95 deg/sec under stress (p=0.01).

The average area reduction between rest and stress measurements showed a significant increase from 25.92 mm² to 32.07 mm², corresponding to +23.75% (p=0.009).
Fig. 10  Radial shortening under rest (dotted line) compared to under stress (solid line). The averaged radial shortening increased by 35.96%, from 2.92 mm to 3.97 mm. The averaged peak value over all volunteers increased from 5.10 mm by 22.63% to 6.25 mm (p=0.0062).

Fig. 11  Rotation under rest (dotted line) compared to under stress (solid line). The averaged rotation increased by 45.62%, from 3.77° to 5.49°. The averaged peak value over all volunteers increased from 7.39° to 10.00°, or 35.31% (p=0.0059).
CSPAMM tagging is able to overcome the disadvantage of a static imaging plane with the incorporated slice-following property and allows for motion analysis over the entire cardiac cycle. Consequently, this technique may provide more accurate parameters than conventional tagging techniques such as SPAMM. However, since CSPAMM measurements cannot be performed in real time, breath
hold acquisitions are required. The presented combination of CSPAMM tagging with TFEPI enables to shorten the acquisition time down to very short breath holds (lower limit) which is a prerequisite for measurements under physically induced stress.

The applied correction techniques tend to make measurements demanding and time consuming. Thus, for the investigation with patients the presented measurement setup is applicable only to a limited extent. It was also found that in most volunteers the target zone for the breath hold level under stress was similar to a fully exhaled breath hold under rest. This may be explained by the enlarged breathing range during exercise. In order to simplify the measurement protocol for future investigations, the maximal expiration could be chosen a priori for the rest exams.

The potential rigid body displacements of the volunteers, which are referred to the physical activity under stress, were in most cases fairly small. This may explained by the good position support given by the shoulder pads of the ergometer. Additional mechanical stabilization of the subject would allow for reducing body displacement to such small extent that it may even completely be neglected. However, the compensation technique for rigid body displacements could be facilitated by applying navigator echoes measurements in order to determine shifts and thus to automatically adapt the scan plane location. Further investigations have to be performed in order to clarify suitable correction procedures.

Unsolved problems for patient stress studies are still the insufficient supervision and limited accessibility of the individuals in case of an emergency. Because of the influence of the magnetic field on the ECG (magneto hydrodynamic effect), the ECG is not of diagnostic quality and does thus not allow for reliable assessment of the ST segment. A solution may be the application of the spatial vector analysis of the electrocardiogram which allows for the elimination of magnetic field induced ECG variations [38].

The estimated goal heart rate for conventional stress examinations which is reported in literature as 220-0.85*age, was not achieved for the young volunteer collective investigated. However, it has been shown that ischaemic reactions occur at much lower heart rates (~ 110-130 bmp) for supine bicycle exercise examinations [39-41]. This can be explained by the increased systolic blood pressure induced by the supine position which consequently results in higher rate-pressure products.

The comparison of motion parameters revealed significant variations between rest and stress states. Relatively large standard deviations were seen for the collective averaged parameter graphs because of individual variations, influenced by factors such as age, gender or training status. However, alterations of the averaged and peak values were found to be statistically significant.
In summary, the results indicate that accurate and quantitative analysis of myocardial motion using CSPAMM tagging may be performed even under physically induced stress conditions. Detailed insight into the heart kinematics under stress could allow for earlier and more accurate determination of cardiac problems. As myocardial tagging is a unique method for assessing detailed information on the myocardial motion, this could provide a powerful alternative assessment technique for stress tests compared to conventionally applied ECG analysis or echocardiography.

References


References


Magnetic resonance (MR) techniques are increasingly being used in clinical cardiology because they provide noninvasively unique information of heart anatomy and function. The versatile features, such as the ability to produce high-resolution, arbitrarily oriented anatomical images of heart and vessels, to analyze tissue motion, to quantify blood flow, to assess perfusion, and further function parameters, make MR an outstanding tool.

In this dissertation the application of ultrafast acquisition procedures for the estimation of the cardiac function has been discussed. Time-efficient acquisition techniques demonstrate to be useful for rapid visualization of cardiac dynamics, and are beneficial for the suppression of motion and flow related artifacts. Real-time protocols allow to assess cardiac function parameters without need for cardiac synchronization or breathing compensation. By dedicated computing devices, real time acquired data may be reconstructed on-line and thus, provide an instantaneous visual representation of the heart. With corresponding computing power, actual real time image processing becomes possible, which allows for immediate display of cardiac function parameters during the measurement. Such kind of quantitative feedback would be beneficial, for instance, during MR guided cardiac stress examinations. Other useful applications for real time measurement techniques include interactive planning procedures, which are useful for, e.g., quickly locating oblique coronary scan planes prior to high-resolution coronary MR angiography, or in MR-guided interventional procedures for the placement of catheters. For this, the integration of dedicated input and visualization devices would be appropriate, such as a “3D-mouse” for efficient spatial positioning of the scan plane or display of 3D rendered models (heart, catheter).

Myocardial tagging is an excellent tool for the analysis of the heart dynamics, which achieves to improve diagnostic accuracy and reproducibility. The presented reduction in scan time for CSPAMM measurements enables new applications such as examinations under physically induced stress condition. Myocardial tagging in conjunction with stress offers the potential to provide more accurate and reliable results for the detection of cardiac problems than conventional anatomical imaging. The developed RingTag tagging sequence enables tracking of the myocardial mid-line motion. This permits enhanced estimation of the heart contractility, which is only limited possible with currently available
tagging techniques. The post-processing HARP could possibly overcome this restriction, but future investigations have to validate usability of both methods. However, the RingTag sequence is the only technique, which allows for direct, on-line visualization of the myocardial mid-line motion.

In future, developments of 3D tagging techniques could provide motion analysis of the entire heart and improve the diagnostic value as the complicated fiber orientation of the heart muscle is taken into account.

In order for myocardial tagging to become a valuable and routinely applicable imaging modality, the time, as well as the amount of user interaction, required for quantifying motion parameters must be reduced considerably. Sophisticated image processing procedures, as presented in this work, enable to evaluate tagging examinations in reasonable time. This may increase the clinical relevance of myocardial tagging and open up possibilities for comprehensive studies. Novel evaluation strategies such as HARP could allow for fully automatic motion parameter determination. This could make possible on-line processing of tagging images and would allow immediate determination of quantitative motion parameters.

In summary, ultrafast acquisition procedures contribute to the uniqueness of cardiac MRI and increase its potential for clinical applications. The speed-up in imaging time provides improved insight into the fast cardiac dynamics. The shortening in examination duration might be an important step of cardiac MRI becoming a “one-stop-shop” modality, which would allow for the investigation of multiple aspects of cardiac function and anatomy in a single MR session, such as in-depth analysis of cardiac function, assessment of myocardial viability and visualization of the coronary arteries.
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Curriculum Vitae

I was born on Mai 23, 1970, in Melrose, Massachusetts, USA, as the first son of Marta and Armin Spiegel. In 1975, our family moved from USA to Heerbrugg, Switzerland, where I attended high school at the Kantonschule Heerbrugg. I graduated with Matura type C (natural sciences) degree in spring 1990.

From fall 1990 to 1995 I studied electrical engineering at the Swiss Federal Institute of Technology (ETH) in Zurich. I finished my studies with the final theoretical exams and the diploma work entitled “Auswerte- und Steuerelektronik für Magnetresonanz-Eingabeeinheit”, carried out at the Institute of Biomedical Engineering. In spring 1995 I received my diploma as a Dipl.-Ing. ETH.

In November 1995 I started working as a teaching and research assistant at the Institute of Biomedical Engineering of Biomedical Engineering of the University and ETH Zurich. As a member of the Biophysics group of Prof. P. Boesiger, I was involved in the development of methods for the fast acquisition and processing of data of the heart function by magnetic resonance imaging (MRI).