Quantification of the human heart wall motion by ultra-fast magnetic resonance myocardial tagging techniques

Author(s): Stuber, Matthias

Publication Date: 1997

Permanent Link: https://doi.org/10.3929/ethz-a-001843223

Rights / License: In Copyright - Non-Commercial Use Permitted
Diss. ETH No. 12208

Quantification of the Human Heart Wall Motion by Ultra-Fast Magnetic Resonance Myocardial Tagging Techniques

A dissertation submitted to the

SWISS FEDERAL INSTITUTE OF TECHNOLOGY ZURICH

for the degree of

Doctor of Technical Science

presented by

MATTHIAS STUBER

Dipl. El. Ing. ETH
born January 18, 1965
citizen of Tschappach SO

accepted on the recommendation of

Prof. Dr. P. Boesiger, examiner
Prof. Dr. O.M. Hess, co-examiner
Prof. Dr. E.M. Pedersen, co-examiner

Zurich 1997
PREFACE

The local function of the heart is still subject of basic research and is far from being fully understood. However, the lack of non-invasive methods for the assessment of the local heartwall mechanics is a severe limitation. This gap can be filled by the application of new magnetic resonance imaging (MRI) techniques. MRI combines the unique properties of non-invasiveness, absence of radio exposure, excellent soft-tissue contrast, and a high spatial and temporal resolution of the images. The further development and the adaptation of MRI methods towards cardiac basic research and clinical applications is a wide-ranging engineering task. Knowledge of electrical engineering, mathematics, physics, informatics and medicine have to be combined.

The results of the present work only became possible due to the interdisciplinary background of the Institute of Biomedical Engineering and Medical informatics of the University and ETH Zurich, Switzerland.

First of all, I am most grateful to Prof. Dr. Peter Boesiger, head of the magnetic resonance division at the institute, for giving me the opportunity to work as a member of the team. His open-minded, forward-looking guidance was always encouraging and had the major influence on this work. The excellent atmosphere in the group and the versatility of the projects were always very motivating for me. Further, I would like to thank to Prof. Dr. Otto Hess for collaboration, and his generous support in patient and volunteer studies and for the co-examination of my thesis. I am further indebted to Prof. Dr. Erik Morre Pedersen of Skejby University Hospital, Denmark, for helpful discussions and careful review.

I like to thank especially two colleagues who contributed to this work: I could profit from the great experience of Dr. Stefan E. Fischer. He introduced me into the well established tagging project and into the sophisticated methods he had already developed. Markus Scheidegger as the project leader of the cardiac imaging group, whose experience, readiness for discussions and indefatigable support with pulse programming accelerated the projects substantially. The project was also supported by Dr. Eike Nagel whose collaboration enriched this work considerably. I would also like to acknowledge
Preface

the work of Dr. Dieter Meier. His maintenance of the pulse programming environment contributed very much to the present results.

I am further indebted to Dr. Gérard Crelier and Dr. René Botnar for fruitful discussions and their friendship which could have been maintained over time and distance. I thank also to Xavier Golay, whose motivating and interdisciplinary work evoked a lot of synergy for common projects. I also owe my debt to Marcus Spiegel who continues the tagging project with enthusiasm.

Of course, I will not forget the help of my colleagues Corinne Duc, Patrik Kunz, Oliver Weber, Klaas Priessmann, Sebastián Kozerke, Henryk Faas, Markus Weiger and Andreas Trabesinger. Further, I would like to thank also for the collaboration with Peter Schmid, who supported the evaluation project. Local sources to which I owe a debt include all the students of the ETH who contributed to this work. I am grateful to Margrit Wyder, Felix Steinemann and Thomas Schertler for the careful analysis of the images and to Dr. Paul Dubach for the application of the tagging methods to clinical studies. Some friends and colleagues in London and Gottingen as hosts of a I should also not forget to thank to all the volunteers and patients who collaborated with patience: Most of all my brother Lukas who stayed in the scanner for several days without complaining, for careful proof-reading, for showing me a further perspective of the heart in his excellent novel and for being a friend.

My mother deserves also a lot of credit for the present work since she always encouraged me to go a step further with my education even if the circumstances have not always been so easy either.

Most of all, I would express my deepest thanks to my wife Franziska for her unselfish support, for her appreciation of my work, for taking care of our daughter Annina and her motivating collaboration on future projects.

My gratitude goes to all the contributors to the present edition.
SUMMARY

The quantification of the local heart wall motion is of increasing interest for physiological and pathophysiological research. Conventional techniques for the assessment of the local heart wall dynamics are either invasive, radio exposure has to be taken into account, or they do not provide sufficient information. This gap can be filled by the application of magnetic resonance imaging (MRI) techniques with preceding myocardial tissue tagging. Hereby, the magnetization of the muscle tissue is spatially modulated, or tagged prior to a multi-heart phase imaging procedure. The thus labelled tissue elements or artificial markers are fixed with respect to the muscle tissue and can be tracked on images which are acquired at different time points during the cardiac cycle. So far sophisticated magnetic resonance (MR) myocardial tagging techniques are time consuming and very prone to breathing induced motion artifacts. Even if new and exciting results have been acquired, the accuracy and the reliability of such methods are limited. Further limits are set by the lack of appropriate data analysis procedures allowing to derive quantitative motion data from MR tagged images. In the present work, new MR myocardial tagging procedures have been designed by combination of tagging procedures with ultra-fast imaging acquisition techniques. Furthermore an image analysis procedure for the quantification of the local heart wall motion has been developed. The new tools have been applied in vivo for heart motion analysis of healthy volunteers and patients with various heart diseases. Results are presented which give new and deep insights into local heart wall mechanics.

Methods

For the reduction of measurement time and for improvement of the accuracy of the results the myocardial tagging procedure is combined with a multi heart phase interleaved echo planar imaging technique. Therefore the image acquisition time is reduced from approximately 10 minutes to 10 seconds typically. By careful simulation
Summary of the procedure on basis of the Bloch equations, the radiofrequency excitation angles for imaging are adapted allowing the assessment of systolic and diastolic heart dynamics with optimized image contrast. Thus up to 25 heartphase images with a temporal resolution of 35 ms can be acquired. This allows to resolve even the fastest occurring motion components in the left ventricle, such as the systolic and the diastolic apical twisting and untwisting. By a slight modification of the scanning protocol, it also enables to perform real-time cardiac imaging under physiologically induced stress conditions. For the quantification of the local heart wall motion from the time series of tagged images, a semi-automatic computer procedure is implemented which is based on active contour models. Systolic and diastolic local motion parameters are calculated for different sites and layers of the myocardium.

Results

Heart motion of healthy controls and patients with various cardiac diseases such as aortic stenosis, infarction, left bundle branch block and heart transplants and of athletes with physiologically hypertrophied hearts has been investigated. The results of the studies show a complex motion pattern of the human heart: During the ejection phase of the ventricles, a torsional deformation with a counterclockwise rotation at the apex and a clockwise rotation at the base is observed. Simultaneously, a shearing between epi- and endocardial muscle fibre layers can be documented. In diastole, a fast apical untwisting precedes diastolic filling in the healthy heart. In most of the pathologies, modified local rotation patterns are found. Patients with a tendency for diastolic dysfunction show a prolonged duration of apical untwisting. A loss of epi- endocardial shearing in parallel with a reduced rotational amplitude occurs in infarcted regions of the heart.

Conclusions

By the application of ultra-fast imaging techniques, MR tagged images can be acquired in one short single breathhold period and thus, the sensitivity on breathing artifacts is suppressed. Therefore the reliability and accuracy of the method is improved. Together with the image analysis methodology, sophisticated MR myocardial tagging methods allow a detailed insight into the local heart dynamics. They provide a powerful new tool for basic physiological and pathophysiological research.
ZUSAMMENFASSUNG

**Einführung**


**Methoden**


Für die Quantifizierung der Herzwandbewegung ist eine halbautomatische Software, basierend auf aktiven Kontur-Algorithmen (=Snakes), implementiert worden. Diese Prozedur beinhaltet ausserdem die Definition von Parametern, die auf sensitive Art und Weise die Veränderungen im lokalen Bewegungsmuster wiedergeben können. Systolische und diastolische Bewegungsgrössen werden damit in verschiedenen Regionen des Herzmuskels berechenbar.

**Resultate**

Zusammenfassung

Schlussfolgerungen

Mit Hilfe von ultra-schnellen bildgebenden Sequenzen können markierte oder "getaggte" Bilder des Herzens während einer kurzen Atempause erfasst werden. Das bedeutet eine erhebliche Reduktion der atmungsinduzierten Bildartefakte, was sich schließlich in einer signifikant verbesserten Zuverlässigkeit und Genauigkeit der Methode ausdrückt. Zusammen mit der Auswertungssoftware erlauben moderne tagging-Verfahren einen detaillierten Einblick in die dynamische Funktion der Herzwand im gesunden und im pathologischen Fall. Somit steht eine neue Methodik für nichtinvasive, physiologische und pathophysiologische Grundlagenforschung zur Verfügung.
Zusammenfassung
# TABLE OF CONTENTS

- Preface: 1
- Summary: 3
- Zusammenfassung: 5
- Table of Contents: 9
- Chapter 1: 11
  - 1.1 Introduction: 11
- Chapter 2: 17
  - 2.1 Slice Followed Single Breathhold Myocardial Tagging: 17
  - 2.2 Towards High Resolution Myocardial Tagging: 41
  - 2.3 MR Real-Time Experiments in Cardiac Applications: 57
  - 2.4 Evaluation Strategies for the Quantification of the Local Heart Wall Motion by Magnetic Resonance Myocardial Tagging: 69
- Chapter 3: 93
  - 3.1 Alterations in the Local Myocardial Motion Pattern in Physiologic and Pathologic Hypertrophied Hearts: 93
  - 3.2 Long Axis Contraction of the Human Heart: 115
- Chapter 4: 125
  - 4.1 Discussion: 125
- Appendix A: 129
  - A.1 Slice Following Cardiac Imaging: 131
- Curriculum Vitae: 157
CHAPTER 1

1.1 Introduction

Background

Detailed knowledge of global and local heart wall dynamics is of great interest for physiological and pathophysiological research towards a fundamental understanding of myocardial function. Blood supply by the coronary arteries, local tissue perfusion and metabolism, the arrangement and the orientation of the myocytes, their connectivity and elasticity, and the generation and propagation of electrical signals strongly influence the heart wall motion. Thus, alterations in the local motion pattern may be very sensitive determinants for early diagnosis of various heart diseases.

Methods for the assessment of heart wall dynamics

In the 15th century, Leonardo da Vinci (1452-1509) made first experiments for the documentation of the heart motion. He observed the slaughter of pigs by piercing their hearts with a skewer. The motion of these needles outside the chest were directly related to the motion of the heart. Based on these observations he claimed that there must be a contraction and a relaxation phase of the heart responsible for the "circulation of air in the vessels of the body" (1). During the past years more sophisticated techniques have been applied. By surgically implanting radio opaque markers into the mid-myocardium of intact men the local heart wall dynamics was recorded radiographically (2). However such methods are highly invasive and thus their application is restricted to animals or to small collectives of humans. Non-invasive
methods such as radiography, computer tomography, ultra sound echoradiography, and conventional magnetic resonance imaging (MRI) allow the quantification of certain cardiac functions. Parameters such as wall thickness or chamber volumes, but also systolic ejection ratio and wall thickening are accessible. However, due to the absence of well defined structural landmarks on the images, local heartwall motion can not be detected and quantified reliably.

In 1988, new magnetic resonance myocardial tagging techniques have been proposed which allow to assess myocardial motion with high spatial and temporal resolution (3,4). For these techniques, prior to an ECG triggered multi-heartphase magnetic resonance imaging procedure, the muscle tissue of the myocardium is labeled by a spatially periodic modulation of the magnetization which is attached by special sequences of radiofrequency excitation pulses and magnetic field gradients. By such procedure line or grid tags can be applied. Then time series of heart images are acquired with high temporal resolution. In these images, the periodic grid of modulated magnetization appears as a dark grid which is fixed with respect to the muscle tissue. From the displacement, the rotation, and the distortion of this pattern during the heart beat cycle, the heartwall motion can be derived.

**Limitations of current techniques**

Standard myocardial tagging techniques suffer from a rapid fading of the tags which restricts their application only to the systolic phase of the human cardiac cycle. Furthermore, images of spatially fixed slices with respect to the scanner coordinate system are acquired. However due to the long axis contraction and the thus resulting through plane motion of the heart, tracing of always the same tissue elements on the different heartphase images is not achieved. This leads to high inaccuracy or even falsification of the results. Sophisticated subtraction based myocardial tagging techniques were developed (5-7). They suppress the rapid fading of the grid and allow to assess local heartwall motion throughout the entire cardiac cycle; tracking of always the same tissue elements is ensured despite the complex 3D motion of the heart. But measurement time for these techniques is rather long (approximately 10 minutes), their application is restricted to rhythmic heart motion and a repetitive breathhold scheme has to be applied in order to suppress breathing motion induced image artifacts. Hereby for
high image quality exact spatial repositioning of the heart for the different breathheld periods has to be guaranteed. Irregularities in breathing or patient motion lead to image artifacts which are much more severe for the sophisticated subtraction techniques than for standard acquisition procedures. Therefore, the accuracy and the diagnostic potential of the method might still be reduced for such techniques. Instantaneous or real-time (RT) imaging would consequently be the appropriate method to overcome these limitations. For conventional cardiac MR, RT imaging provides a powerful tool for imaging under physiologically induced stress conditions or for the investigation of arrhythmias. However, real-time imaging of the heart can not be combined with sophisticated myocardial tagging methods since they inherently require two acquisitions per heartphase image.

**Objectives**

The goal of the present work was the implementation of improved methods for the assessment and the quantification of local heart wall dynamics in healthy volunteers and in patients with different heart diseases. The accuracy and the reliability of sophisticated MR myocardial tagging techniques can be significantly improved if the sampled image data refer to the same breathhold i.e. measurement time is reduced to a very short period. Thus, subtraction based myocardial tagging procedures need to be combined with ultra-fast imaging techniques. In addition to the technical and methodological improvements, an image analysis procedure for the extraction of the local heartwall motion has to be defined. This includes the evaluation of new parameters which are highly sensitive to any changes in the local myocardial motion pattern. The application of the resulting techniques to clinical research studies is required and the so obtained results have to be discussed.

**Outline of the work**

In chapter 2 further developments of myocardial tagging techniques towards single breathhold applications are followed by a method for an increased resolution of the tagging grid. It also includes the discussion of ultra-fast imaging sequences for real-time applications i.e. instantaneous assessment of the heart wall dynamics under
physiologically induced stress. Finally, an evaluation procedure for the quantification of local heartwall dynamics based on temporally resolved MR tagged images is introduced. New results which have been obtained by the application of the new procedures to medical research studies are discussed in chapter 3: Local heartwall motion in volunteers, pressure overload patients with pathologically hypertrophied hearts due to aortic stenosis and athletes with physiologically increased myocardial muscle masses are compared. In this chapter, the long axis contraction of the human heart is investigated too and resulting strategies with respect to slice following imaging techniques are documented in the appendix.
References


1.1 Introduction

-16-
CHAPTER 2

2.1 Slice Followed Single Breathhold Myocardial Tagging

Abstract

Standard myocardial tagging techniques suffer from a rapid fading of the tags. This restricts their application only to the systolic phase of the cardiac cycle. In addition, such techniques acquire slices which are spatially fixed with respect to the scanner coordinate system. Thus, systolic long axis contraction results in through plane motion effects on time resolved short axis images. This results in interpretation errors and the results of the analysis are falsified. Therefore, sophisticated tagging techniques have been developed. With these techniques, fading of the tags can be suppressed allowing to assess systolic and diastolic heart wall motion. Furthermore, due to the slice following properties of these techniques, tracking of always the same tissue elements is ensured despite systolic long axis contraction. However, these methods have two major disadvantages. First, they suffer from relatively long acquisition times (~10 minutes). Second they are very prone to breathing artifacts. In the present work, a further development of such sophisticated tagging techniques is presented. The advantages of these methods are preserved, overall measurement time is significantly reduced (~10 seconds), and breathing artifacts can be suppressed by the application of a single breathhold scheme. This has important implications for the accuracy of the method and for the use of MR tagging as a quantitative tool for the quantification of systolic and diastolic function in the human heart.
2.1 Single Breathhold Tagging

Introduction

Myocardial tagging has proven to be a powerful tool for the noninvasive assessment of heart wall dynamics (8-15) with high spatial and temporal resolution. Quantification of the mechanical tissue properties of the myocardium and motion analysis based on MR tagged images have been reported (16-19). Standard myocardial tagging techniques suffer from the rapid fading of the tags, which restricts their application mainly to the systolic phase of the human cardiac cycle (13-15). This may be sufficient for certain applications. However, in a number of pathologies (22-24), diastolic dysfunction has been reported. Hence, MR techniques allowing to assess the systolic as well as the diastolic phase of the cardiac cycle within one examination are needed.

Besides the problem of the fading of the tags, long axis contraction of the heart may lead to through plane motion effects on short axis images if spatially fixed slices with respect to the scanner coordinate system are acquired (15). This means, not always the same tissue elements are visualized in the images which are acquired at different timepoints in the cardiac cycle. This finally leads to interpretation errors and falsification of the results of the analysis.

By these two reasons, (fading of the tags and through plane motion), CSPAMM myocardial tagging has been developed (14, 15). Applying CSPAMM, the lines or grid intersection points remain visible up to the very last acquisition in the cardiac cycle, and through plane motion effects can be avoided by the application of a slice following imaging procedure (15).

This technique basically involves subtraction of two acquisitions. This approach requires that an identical geometrical configuration can be achieved for both experiments. Thus, variations in repositioning of the heart caused by breathing may lead to severe image artifacts. These artifacts are weighted overproportionally (in comparison to standard imaging techniques) due to the subtraction procedure. For an accurate analysis of the heart wall dynamics, freezing of the breathing motion is strictly needed for this subtraction based techniques. This goal can either be achieved by the application of a multiple breathhold scheme (25), navigator controlled acquisitions (26) or single breathhold methods (SBH) (13, 21).
If repetitive breathhold schemes are applied (signal sampling e.g. only in the exhaled state) and assuming a physiological breathing of 12 to 15 breathing cycles per minute measurement time is easily four or even fivefold. This technique requires reliable patient collaboration, and patient comfort is reduced due to the longer mean scanning times. For navigator controlled techniques, measurement time is basically not reduced and reliable patient collaboration is still needed. However, the breathing level can be detected accurately. Therefore, equivalent spatial configurations can be recognized by the algorithms, which helps to improve image quality with respect to the application of repetitive breathhold schemes. SBH techniques still need patient collaboration, and in clinical applications, the breathhold intervals have to be short enough for patients not capable of holding their breath for longer periods.

MR tagging methods basically store information in the longitudinal magnetization of the tissue. This stored information decays not only under the influence of the spin lattice relaxation constant $T_1$ but also due to repetitive radio frequency (RF) excitation for imaging (15, 21). Consequently, imaging techniques with a low number of RF excitations for imaging are required.

By these reasons, CSPAMM myocardial tagging has been combined with an echo planar imaging (EPI) sequence. By the combination of CSPAMM myocardial tagging with a standard multi shot echo planar imaging sequence, double oblique slice followed grid tagged images can be acquired within a time period of only 12 heartbeats.

In the present paper, the theoretical background of the sequence is discussed. It includes the optimization of the signal derived from the modulated magnetization of the tagged slice. Additionally, some side effects, as they might appear as a consequence of shortened measurement times, are discussed. Subsequently an appropriate imaging strategy for in vivo single breathhold experiments is proposed and results are presented.
2.1 Single Breathhold Tagging

Methods

Theory

CSPAMM myocardial tagging (14) involves the periodic modulation of the magnetization in a thin slice of the myocardium (Fig. 1) with tagging slice thickness $dz$.

![Fig. 1. Situation for the planning of a double oblique short axis tagging experiment. A single oblique long axis view is overlaid by the graphic elements which are interactively used for planning. The gray, solid rectangle refers to the tagged slice of the thickness $dz$. The hatched rectangle documents the imaged volume that has to encompass the extent of the motion of the initially labeled thin slice during the entire heartbeat cycle. The thickness of this imaged volume is $ds$, and the offcenter of the tagged thin slice with respect to the imaged volume is $z_0$.](image)

This modulation is typically performed immediately after the detection of the R-wave of the ECG. Subsequently, a thick slice $ds$ (Fig. 1), encompassing the potential extent of the initially labeled thin slice, is imaged using a multi heartphase imaging sequence. This experiment consisting of labeling of a thin slice with subsequent imaging of a thicker volume is performed twice with an inverted modulation of the magnetization for the second experiment (Experiment A and B, respectively). Subtraction of the two acquisitions leads to an image derived only from the signal which originates from the labeled part of the magnetization in the thin slice. The signal from the imaged volume outside of the thin slice is suppressed due to the subtraction procedure. The signal of the tagged thin slice can be decomposed into two components: One component holding the tagging information and a second component which is built up as a function of time and is responsible for the fading of the tags. This second component is suppressed by the subtraction procedure as well. Consequently, only the signal derived from the tagged component of the magnetization in the thin slice remains after subtraction. The resulting signal intensity $I_k$ (for the $k^{th}$ heartphase image) after complex subtraction of the two acquisitions can be written as
Hereby, $I_{ka}$ is the signal containing the tagging information of the first acquisition (A) and $I_{kb}$ is the corresponding signal component for the second acquisition (B). $M_n$ refers to the steady state magnetization. $TAG(x,y,z)$ describes the modulation function of the magnetization, where $x$, $y$, $z$ are the spatial coordinates. $T_1$ is the time constant of the longitudinal relaxation and $t_k$ indicates the time of the $k_{th}$ RF excitation with the excitation angle $\alpha_k$. On condition that $TAG_B(x,y,z)$ equals $-TAG_A(x,y,z)$, equation [1] can be rewritten as

$$I_k = 2M_n TAG(x,y,z) \exp(-t_k/T_1) \prod_{i=1}^{k-1} \cos(\alpha_i) \sin(\alpha_k).$$

[2]

**Imaging pulse sequence**

Considering equation [2], the signal amplitude is not only scaled by the longitudinal relaxation of the magnetization, but also by the RF excitation angles of the imaging experiment itself. Thus, RF excitation for imaging inherently reduces the amount of the information stored in the modulated magnetization of the tissue. This fact has serious consequences for the evaluation of fast imaging sequences, which potentially can be

**Fig. 2.** CSPAMM myocardial tagging procedure in combination with a multi heartphase echo planar imaging (EPI) sequence. After a slice selection (RF pulse (a) and gradient (b)), the transverse magnetization is dephased with the tagging gradient (c). The RF block pulse (d) rotates the modulated transverse magnetization into $z$-direction. The sign of the modulation function is influenced by the sign of this RF block pulse (d). Gradient (e) finally spoils the remaining transverse magnetization. For the imaging part of the sequence, the presented EPI readout is performed for each heartphase with a corresponding RF excitation angle ($\alpha$) for imaging. Typically, the sequence is performed for each heartbeat.
2.1 Single Breathhold Tagging

combined with a tagging procedure. Fast imaging techniques such as segmented k-space methods (13), where sampling of one k-space profile basically requires one RF excitation, are limited with respect to the amount of the signal derived from the tagged slice [2].

For those techniques, the reduction in measurement time is linearly related to the number of RF excitations for imaging. This increased number of RF excitation pulses accelerates the decay of the stored information in the z-magnetization of the labeled slice. Consequently, imaging techniques where signal from multiple k-space profiles can be acquired by the application of one single RF excitation are favoured. This means that the combination of the tagging procedure with a multi shot echo planar imaging sequence is the most promising approach for the reduction of measurement time for CSPAMM myocardial tagging. Similar conclusions have also been claimed for SPAMM techniques (21). In Fig. 2, a tagging procedure (14) preceding a multi heartphase echo planar imaging sequence is presented. The tagging part of the sequence is triggered by the R-wave of the ECG and is immediately followed by the imaging part of the sequence. After the slice selective excitation (Fig. 2, a and b) of the magnetization in the thin slice \(d_z\) (Fig. 1), the tags are applied to the transverse magnetization (c). This modulation precedes an RF block pulse (d), which is either +90° or -90° yielding the positive \(TAG_a(x,y,z)\) or the negative \(TAG_b(x,y,z)\) modulation of the z-magnetization. By the application of the two RF pulses (a) and (d) interspersed by the tagging gradient (c), a sinusoidal line pattern is attached to the magnetization of the selected slice. For spoiling of remaining transverse magnetization, the dephasing gradient (e) is added to the tagging part of the sequence. In the imaging part, the slice selective excitation of the magnetization of the thick volume \(d_s\) (Fig. 1), is followed by an EPI readout train, where multiple k-space profiles are sampled. Variable RF excitation angles are used for a constant tag contrast in each individual heartphase image.

**Signal optimization**

The tag contrast basically decays not only due to spin lattice relaxation but also by the application of RF flip angles for imaging as documented in [2]. For constant signal amplitude for each RF excitation i.e. for the condition \(I_k = I_{k+1}\) from [2] the following condition can be derived:
\[
\tan(\alpha_k) \exp(\Delta t/T_1) = \sin(\alpha_{k+1}), \text{ for } k = \{1..n-1\}.
\]

This is the Mansfield formula extended with a tissue dependent term (14) \(\exp(-\Delta t/T_1)\). \(\Delta t = t_{k+1} - t_k\) is the heart phase interval or the time delay between two RF excitations for imaging. The RF angles \(\alpha_i, \alpha_n\) can be calculated iteratively by the application of an initial value for \(\alpha_n\).

If the tagging procedure is combined with a repetitive breathhold scheme, data acquisition is only performed every fourth or fifth heartbeat (14, 15). This means that the repetition time \(T_r\) (Fig. 3) is relatively long. Consequently the relaxation period \(t_{\text{relax}}\) (Fig. 3) lies between 4 or 5 seconds. Thus, the steady state magnetization modulated by the tagging procedure is almost at the thermal equilibrium before the application of the tagging pre-pulses. Although the last RF excitation pulse for imaging \(\alpha_n\) is set to 90°. Towards single breathhold methods, where data are acquired after the detection of each R-wave \((T_r \sim 1000 \text{ ms})\), the relaxation period \(t_{\text{relax}}\) is very short, which results in a decreased steady state magnetization, mainly if a 90° pulse is applied for the last \((n^{th})\) heart phase image. Thus, this last RF pulse angle has to be modified in order to obtain an increased steady state magnetization. Additionally to the condition [2] which guarantees constant signal intensity derived from the tagged magnetization of the thin slice \(dz\),

![Diagram](image)

**Fig. 3.** Temporal relationship between the detection of the R-wave of the ECG, the tagging part of the sequence and the imaging part of the sequence. The tagging procedures are typically performed after the detection of the R-wave of the ECG. The time interval in-between the tagging procedures is \(T_r\). The time between the \(n\) heartphase images is \(\Delta t\), and the time gap between the last RF excitation for imaging and the subsequent tagging procedure is \(t_{\text{relax}}\). The variable RF excitation angles for imaging are denoted as \(\alpha_i, \alpha_n\).
Fig. 4. Signal optimization for n=16 heartphases (T<sub>r</sub>=850 ms). a) Relative signal amplitude derived from the tagged component of the magnetization. The signal amplitude is plotted in function of the last RF excitation angle for imaging (α<sub>n</sub>) and for a fixed heartphase interval of Δt=35 ms taking multiple repetition times T<sub>r</sub> into account. The black dot indicates maximum signal intensity for a repetition time of 900 ms. Maximum signal intensity is ensured in this example if α<sub>n</sub> is set to 25°. b) Maximum relative signal amplitude which can be obtained by the optimized setting of α<sub>n</sub>. It is plotted in function of multiple Δt and T<sub>r</sub>. c) Last RF excitation for imaging in function of Δt and T<sub>r</sub>. Optimized for maximum signal intensity coming from the tagged component of the magnetization.
maximization of the signal amplitude $I_k$ is therefore a further requirement. Maximized $I_k$ can be obtained by the appropriate setting of $\alpha_n$ which always serves as starting condition for the recursion [3]. The optimization of $\alpha_n$ for constant, maximized tagging signal is achieved by a numerical simulation of the signal amplitude according to [1] and [3]. The dependency of the resulting signal amplitude $I_k$ as a function of $\alpha_n$ is calculated for 16 and 20 heartphases and for different values of the heartphase interval $\Delta t$ and the repetition time $T_r$. The results are presented in Fig. 4 and will be discussed later. For the investigation of the tagging pattern, the simulation is extended assuming a sinusoidal modulation of the magnetization. In Fig. 5 b), the corresponding result is shown ($T_r=900$ ms, $\Delta t=35$ ms, $\alpha_n=21^\circ$, $n=16$).

**Phantom experiments**

For the evaluation of the tag contrast and the tagging profile in absence of flow or motion induced artifacts, a stationary phantom is used. It consists of a plastic cylinder (diameter 10 cm) filled with a 2% agarose gel ($T_1 \approx 850$ ms). The phantom experiments are performed using the above described CSPAMM myocardial tagging procedure combined with a multi shot multi phase EPI sequence. Two phantom experiments with different $T_r$ are performed. The repetition time is 4000 ms for the first, and 900 ms for the second experiment. For triggering purposes, an artificial ECG is fed to the scanner. For both experiments the same heartphase interval of 35 ms is used for the acquisition of 16 phases. Optimal pulse angles $\alpha_n$ of 90° ($T_r=4000$ ms) or 25° ($T_r=900$ ms), respectively are used.

**Tag contrast**

In agreement to (21), the tag intensity is determined by calculating the average signal intensity along the center line of the tag in a region of interest ($=I_T$). Average signal amplitude of the "non tagged" part ($=I_L$) is derived from the center line of the lobe between two tag lines in the region of interest. The tag contrast is defined as the difference between these two signal levels. In order to indicate a relative amount of tag contrast, the difference is related to the maximum dynamic range (12 Bits) of the images. Hence, the tag contrast $C_{TAG}$ is defined as

$$C_{TAG} = \frac{I_T - I_L}{2^{12}-1}.$$ [4]
By the application of CSPAMM tagging, the signal amplitude of the tag lines in the images is theoretically zero throughout the entire heartbeat cycle. However, the presence of noise of any origin increases the signal level in these regions. Thus, the tag contrast (which theoretically is 100%) is slightly decreased in the images.

For the quantification of the persistence of the tags in single breathhold tagging experiments, the tag contrast is calculated according to [4] for each time frame of the previously described phantom experiments ($T_r=4000$ ms and $T_r=900$ ms) and for an in vivo example. For the phantom, the region of interest is positioned in the center of the image (isocenter of the scanner) and for the in vivo experiment, the region of interest is positioned in the septum of the myocardium for each heartphase (vertically tagged acquisition). The results of this analysis are shown in Fig. 6.

**Implementation**

CSPAMM myocardial tagging including slice following is implemented on a Philips Gyroscan ACS-NT 1.5T system (Philips Medical Systems, Best, The Netherlands) including the CPR3 software package for cardiac applications. For the acquisition of the images, a multiple heartphase interleaved echo planar imaging sequence with variable RF excitation flip angles is applied. The gradient performance of the system (prototype Powertrak 3000 gradient amplifier) is 15 mT/m for the strength and 50 mT/m/ms for the slope of the gradients. For signal acquisition, a prototype cardiac surface coil (Philips Medical Systems, Best, NL) is used. In Fig. 1, the situation for the planning (as implemented on the scanner) of a tagged short axis acquisition near the base of the myocardium is documented. The solid rectangle indicates the orientation, the position and the thickness $dz$ of the slice which is tagged at end diastole. The dashed rectangle refers to the volume imaged for multiple heartphases after the tagging procedure. The thickness $ds$ of this imaged slice is adapted to the long axis contraction at the given location on the myocardium. It has to be ensured, that the moving tagged slice is always encompassed by the imaged volume (in each heartphase), in order to guarantee the slice following properties of the sequence. In addition to the thickness of the imaged volume, the offcenter $z_0$ of the tagged slice with respect to the imaged volume can be defined. This allows to reduce the thickness $ds$ according to the amount of through plane motion at the given location. This finally leads to an increase of the wanted signal components.
with respect to the unwanted signal coming from the imaged volume excluding the tagged slice.

Complex subtraction of the corresponding heartphase images \[1\] is performed during reconstruction of the images. Grid tagged images are obtained by the combination of two orthogonal sets of line tagged acquisitions. Alternation of the line direction is performed runtime during the scan and is achieved by simply swapping phase encoding and readout direction.

**Examination protocol for in vivo applications**

In order to determine the double angulated imaging plane for a short axis view of the myocardium, two scout scans are performed. The first transversal scout scan is followed by a single oblique plan scan in cine mode. Here, the total amount of through plane motion with respect to the short axis is estimated. The result of this estimation is then used for the correct setting of the parameter \(ds\) and \(z_0\) of the imaged volume (Fig. 1). The double oblique short axis section is defined on the end diastolic image of this second scout scan.

For the tagging experiments, the subjects are asked to hold their breath in an exhaled state for 12 heartbeats. The line tags are applied immediately after the detection of the R-wave of the ECG (Fig. 3). The RF excitation angles for imaging are subsequently increased from one heartphase to the next according to the recursion of \[3\] and are calculated on basis of the numerical simulation presented in Fig. 4. Usually the heartphase interval is chosen as 35 ms. The number of heartphase images always depends on the individual heartbeat rate of the patients or volunteers and is adapted to cover the entire heartbeat cycle (\(n=15..20\)). The field of view is 300 x 300 mm with a scan matrix of 128. The thickness \(dz\) of the tagged slice (Fig. 1) is 6 mm. By the application of a reduced k-space (13, 14) acquisition scheme (30 % of \(k_x\)-profiles) and a rectangular field of view of 85 %, an inplane resolution of 2.3 x 2.3 mm is achieved on the images, resulting from the multiplication of the horizontally and vertically line tagged images. The number of \(k_x\)-profiles which are sampled after one excitation is always set to 9 (EPI factor). With this protocol, an echo time \(T_e\) of 5.4 ms is obtained.

For the suppression of artifacts caused by epicardial fat, a spectral selective presaturation pulse for fat signal suppression precedes the tagging procedure. In order to
2.1 *Single Breathhold Tagging*

obtain grid tagged time series of the orthogonally line tagged images, the two stacks are multiplied offline.
Experimental Results

Pulse angle optimization

In Fig. 4, the results of the simulation for constant and maximized signal amplitude $I_k$ (derived from the tagged component of the magnetization) as a function of $\alpha_n$ are shown. The relative signal amplitude always refers to the equilibrium magnetization $M_{eq}$ ($100 \% \sim M_{eq}\sin(90)$). The simulation is performed for $n=16$ heartphase images. In Fig. 4 a), the relative signal amplitude is plotted versus the last pulse angle of the iteration [3]. The heartphase interval $\Delta t$ is 35 ms. The resulting signal amplitude is plotted for various values of the repetition time $T_r$. For longer repetition times ($T_r > 2000$ ms), the optimum value for $\alpha_n$ does not differ significantly from $90^\circ$. However, if shorter repetition times are taken into account, optimum signal amplitude can only be obtained by carefully adapting this last RF excitation angle. If the curve referring to a $T_r$ of 900 ms is considered (Fig. 4, black dot), optimum $\alpha_n$ is $25^\circ$ which yields a relative signal level of 21 % for each heartphase. If the same parameter value is calculated for $n=20$ heartphases, the optimum angle is slightly reduced ($\alpha_n=21^\circ$) and the resulting relative signal amplitude amounts to 18 % for each heartphase. Consequently, there seems to be only a minor difference in signal amplitude between 16 and 20 heartphases. In Fig. 4 b), the maximum possible signal amplitude (on condition that the last pulse angle is set correctly) which can be obtained for a specific $T_r$ and $\Delta t$ is plotted. Longer repetition times and shortened heartphase intervals yield increased signal amplitude derived from the tagged component of the magnetization. This result is obvious, since both strategies result in a prolonged recovery time $t_{relax}$, which finally leads to an increased steady state magnetization. However, for adequate SBH applications in the human heart, the heartphase interval should be in the order of 35 ms (19), and a single breathhold experiment as mentioned above requires relatively short repetition times. In Fig. 4 c) the $\alpha_n$ which yields maximum signal amplitude is plotted as a function of the heartphase interval $\Delta t$ and the repetition time $T_r$. From this graph, the optimal setting of $\alpha_n$ for constant and maximized signal intensity $I_k$ can be obtained for a wide range of $\Delta t$ and $T_r$. 
Fig. 5. a) Simulation of the Bloch equations for a SBH tagging experiment ($T_e=900$ ms, $\Delta t=35$ ms, $n=16$, $\alpha_e=25^\circ$) in the presence of a sinusoidal modulation of the magnetization. The dashed lines document the situation right after the modulation of already modulated magnetization. They refer to the positive (triangles) and negative (dots) modulation pattern which, subtracted, result in the signal represented by the solid black line. b) Comparison between theoretically predicted (solid line) and measured (hatched line) shape of the tags in the phantom. The difference is documented by the gray line.
Higher order modulation

The optimization of the RF excitation angles for a maximized signal amplitude may lead to some side effects:

The last angle which yields optimum signal amplitude may differ significantly from 90° as shown in Fig. 4. Consequently, the remaining magnetization after the application of the n-th RF excitation angle for imaging is still modulated. Hence, a residual modulated magnetization remains and is transferred to the subsequent experiment. In Fig. 5 a) the influence of the modulation of such residual magnetization is documented with the previously described numerical simulation involving a sinusoidal modulation of the longitudinal magnetization in the tagged slice dz. A situation as occurring for the first heartphase image is presented. The DC component is not yet built up in this situation. For the simulation a repetition time $T_r$ of 900 ms, a heartphase interval $\Delta t$ of 35 ms and an RF pulse angle $\alpha_n$ of 25° are used for n=16 heartphases. Steady state magnetization is taken into account, and a repetitive ($T_r$) sinusoidal modulation of the magnetization is assumed. The solid black line shows the theoretically resulting shapes of the tags if modulation of residual modulated magnetization is assumed. Both dashed lines (circles and triangles) indicate the individual signals of the two acquisitions which have to be subtracted. For both experiments, an asymmetry of the lobes with respect to the x-axis can be observed. By the direct generation of a modulus image, alternating intensities of adjacent lobes would theoretically occur. However, complex subtraction of the CSPAMM technique compensates for these effects as documented by the solid black line.

Phantom and in vivo results

For the verification of the simulation results, a series of phantom experiments are performed. In Fig. 5 b), the theoretically predicted shapes of the lobes are compared to those derived from the previously described phantom experiment (First heartphase image, $T_r$=900 ms, $\Delta t$=35 ms, $\alpha_n$=25°, n=16). An excellent agreement between theory and phantom results is found. No intensity alteration of adjacentily positioned lobes or distortion of the tags due to modulation of residual magnetization is seen.

In Fig. 6, $C_{tag}$ derived from the two multi heartphase phantom experiments with different $T_r$ (4000 ms, gray bars; 900 ms, white bars) is plotted for 16 heartphase images.
2.1 Single Breathhold Tagging

Fig. 6. Tag contrast evaluation for two multi heartphase phantom experiments and one in vivo example. For the phantom experiments, \(n=16\) heartphases are acquired with a \(\Delta t\) of 35 ms. The first experiment (gray bars) is performed with a long repetition time (repetitive breathhold scheme) of \(T_r=4000\) ms. The corresponding \(\alpha_n\) is set to \(90^\circ\). The second experiment is performed under SBH conditions \((T_r=900\) ms, \(\alpha_n=25^\circ\)). For the in vivo example \(n=16\) heartphase images are acquired with a temporal resolution \(\Delta t\) of 37 ms. \(T_r\) (defined by the RR interval of the volunteer) is 900 ms and \(\alpha_n=25^\circ\).

and are compared to the results obtained in a single breathhold in vivo measurement. In the phantom the tag contrast remains constant for each heartphase as predicted by [3]. For the experiment with the shortened repetition time \((T_r=900\) ms) the tag contrast is slightly reduced but remains constant for each heartphase image, too. This slight reduction is caused by the smaller signal amplitude (Fig. 4) derived from the tagged magnetization of the thin slice. Consequently, the signal-to-noise ratio is decreased yielding a reduced tag contrast. The tag contrast in the in vivo experiment is decreased when compared to the corresponding phantom results \((T_r=900\) ms). It also slightly varies in function of time. This is presumably caused by the physiologically occurring flow and motion induced artifacts. However, the tag contrast in the single breathhold in vivo experiment is still surprisingly high and does not fade over time. Furthermore, a tag contrast of 50 % is far more than sufficient for a reliable detection of the tags up to the last, end diastolic heartphase image.

In Fig. 7, 20 apical double oblique heartphase images with a temporal resolution of 37 ms are presented. They are acquired with single breathhold CSPAMM myocardial
Fig. 7. 20 apical phases of the cardiac cycle imaged in a double oblique short axis plane of the myocardium (healthy volunteer). The images are acquired by the application of CSPAMM myocardial tagging in combination with an EPI slice following imaging procedure. The acquisition period lasts 12 heartbeats. The heart phase interval (time resolution) $\Delta t$ is 37 ms. The images are produced by the multiplication of horizontally and vertically line tagged images.
2.1 Single Breathhold Tagging

tagging in a healthy subject. The acquisition time was 12 heartbeats during one short
exhaled period, where the orientation of the tag lines was swapped runtime after 6
heartbeats. Obviously, no fading of the tags occurs for diastolic heartphase images and
the tag contrast remains constant, too.
Discussion

The combination of CSPAMM myocardial tagging with multi shot multi heartphase echo planar imaging is a promising approach. With respect to segmented k-space methods (13), the decay of the tagged component of the magnetization is reduced since less RF excitation angles for imaging are applied. Additionally, this results in an increased steady state magnetization with a subsequently improved signal to noise ratio. By the optimization of the RF excitation angles for imaging, constant tag contrast is predicted for each heartphase. By the appropriate setting of the initial value $\alpha_n$ of the iteration [3], the tagging contrast can be optimized also for short repetition times. Thus, single breathhold tagging experiments with signal sampling periods after the detection of each R-wave are feasible. Moreover, the results of the simulations for $n=20$ heartphases encourage for measuring such a high number of heartphase images.

Potentially, unwanted higher order modulation of the magnetization occurs if $T_r$ is short and the last RF excitation angle for imaging is less than 90°. In consequence intensity variations of the lobes between adjacent positions are expected. These effects would be disadvantageous for automatic image evaluation or structure extraction. However, since CSPAMM myocardial tagging requires two acquisitions by definition, such effects are automatically suppressed by complex subtraction of the corresponding images. These findings are in good agreement with the results from the phantom experiment.

In the phantom experiments, the theoretically predicted feasibility of a single breathhold tagging experiment could be successfully verified. The tagging contrast of the single breathhold experiment with a $T_r$ of 900 ms is only slightly reduced in comparison to the measurements with the longer repetition time ($T_r=4000$ ms). This originates in the reduced signal to noise ratio as occurring with shortened $T_r$.

By the visualization of the tagged volume and the encompassing imaged volume, planning of the tagging experiment is facilitated. Due to the freely selectable slice thickness of the imaged volume and its offcenter with respect to the tagged slice the parameters can be adapted with respect to the maximum expected through plane motion at the given location. Since the line direction is swapped runtime, grid tagged images can be obtained in one single breathhold period which avoids repositioning errors of the
2.1 Single Breathhold Tagging

heart due to different breathing levels in subsequent breathholds. With the complex on-line subtraction of the corresponding heartphase images, the line tagged acquisitions can directly be visualized after the scan.

In good agreement with the theoretical and the in vitro findings, a high tagging contrast during the entire heartbeat cycle can be documented in the typical single breathhold in vivo example of Fig. 7. Even though a high number of heartphase images (n=20) is acquired in this example, there is no fading of the tags for later heartphases and consequently systolic and diastolic heart wall motion is reliably accessible in vivo within one short single breathhold imaging experiment.

With the here presented single breathhold CSPAMM myocardial tagging technique, the advantages of the original technique (14, 15) have been maintained and the disadvantages such as sensitivity on breathing or increased measurement time are no longer a problem. In contrast to standard myocardial tagging methods (9, 13, 19), always the same tissue elements are imaged and the fading of the tags is suppressed. These are major preconditions for the reliable assessment of local heart function.
Conclusions

The present implementation of CSPAMM myocardial tagging combined with multi shot multi heartphase echoplanar imaging on a commercially available 1.5 T MR system has for the first time made it possible to acquire slice followed grid tagged images throughout the cardiac cycle during a short 12 heart beat breathhold interval. This has important implications for the accuracy of the method and for the use of MR tagging as a tool for quantification of systolic and diastolic function in the human heart.
2.1 Single Breathhold Tagging

References


2.1 Single Breathhold Tagging
2.2 Towards High Resolution Myocardial Tagging

Abstract

Magnetic resonance imaging with preceding tissue tagging is a robust method for the assessment of the local heart wall motion. However, one limitation of this technique is the low resolution of the obtained displacement map of the labeled points within the myocardium. By a new tagging technique which is based on the combination of two or more measurements of the same slice but with different grid positions, a highly improved resolution of cardiac motion data can be achieved. In combination with a multi heartphase echo planar imaging sequence, such images with doubled grid frequency can be acquired in one breathhold period.
2.2 High Resolution MR Tagging

Introduction

The evaluation of the regional heart wall motion is an important step towards the fundamental understanding of mechanical properties as well as the physiology of the heart (27, 28, 29). Magnetic resonance imaging (MRI) in conjunction with myocardial tissue tagging (30, 31) is the commonly used, noninvasive method for heart motion analysis. During end-diastole a number of myocardial points can be labeled by means of slice selective spin saturation or spatial modulation of the magnetization (32). The displacement of these labels can be derived from images which are acquired at different phases of the cardiac cycle. The labels or tags are subject to longitudinal relaxation, however they can be tracked throughout the entire heart cycle (33). Thus, not only systolic motion patterns can be evaluated, but also the diastolic untwisting and rapid filling phase of the ventricles are accessible. Especially, early diastolic motion parameters are of increasing medical interest, because these parameters are very sensitive to alterations in the heart mechanics (34). Myocardial tagging is basically a technique for the assessment of in-plane motion. In order to obtain the three-dimensional motion, the tagging technique can easily be extended by the evaluation of two orthogonal stacks of tagged images (35, 36) or by the tracking of always the same slice with respect to the heart (37) combined with the phase encoding of the through-plane motion (38).

Compared to the velocity phase contrast approach (39, 40), the analysis of the tagged images is performed directly on modulus images. The evaluation of the displacement of the labeled points can even be performed almost automatically (41-46). The accuracy of the assessed position of the labeled points within the myocardium is dependent on the contrast-to-noise ratio, on the shape and the frequency of the tagging pattern, and on the image resolution (47). Generally, the accuracy of the estimated tag position is better than the image pixel dimensions if curve fitting algorithms for the local minima segmentation of the image pattern are used (48).
The main limitation of commonly applied tagging techniques is the low resolution of the resulting trajectory map, as only a limited number of labels are marked on the myocardium. This reduced number of tags mainly hampers motion tracking of the right ventricle, since its wall thickness is relatively small with respect to the tag line distance. A higher resolution of the tagging grid would additionally be important for the assessment of strain and shear tensors of the myocardium (50). However, increasing imaging resolution in cardiac applications suffers not only from reduced signal-to-noise ratio and foldover artifacts, but also from an enhanced sensitivity to motion artifacts. Most obviously, an increased resolution of the tagging grid can be achieved by the increase of the tagging gradient ($G_{\text{tag}}$, Fig. 1, a). However, the grid spacing has to be a multiple of the pixel width (49) for an accurate tag line detection. Furthermore, the dynamics of the myocardium have to be taken into account if the grid distance is reduced by the tagging procedure: During the cardiac cycle, the grid or the lines are translated, rotated and distorted. This situation is documented in the k-space in Fig. 2. The circle in the center of k-space represents the main part holding the anatomical information. The convolution products of this anatomy and a cosine modulation on the image in horizontal direction is indicated, too (Fig. 2, a). Due to the local tissue contraction, the tag line distance locally decreases during systole. This means that the convolution products of the anatomy and the modulation function move further out in

Fig. 1. a) Conventional 1-1 SPAMM sequence modified by the application of a phase shift $\Psi$ between the two 90° tagging RF. b) The diagram shows the coordinate system of the magnetization, which rotates with larmor frequency, and the rotation axis achieved by the two RF pulses.
Fig. 2. Situation in k-space if the image is modulated by a cosine in vertical direction. The gray portion indicates the sampled region by the application of reduced k-space acquisition. a) The information of the anatomy is located in the center of k-space. The convolution products of the cosine modulation and the anatomy are located further out. b) Tissue contraction leads to a decrease in tag line distance. In k-space, the corresponding convolution products move still further out. c) Situation if contraction and rotation are considered in parallel. Due to the rotation of the object in the image domain a rotation in the frequency-domain or k-space results. Hereby, the convolution products might only partly be sampled.
k-space. However, it has to be ensured, that the relevant information is still sampled in order to get no low pass filtering on the raw data. This finally would appear similar to a fading of the tags on the images (Nyquist theorem). By the application of reduced k-space acquisition schemes in combination with line tagging overall measurement time can be reduced whereby the resolution perpendicularly to the tag lines is not affected (33, 26). Due to the rotational component of the heartwall motion, these reduced k-space acquisition schemes potentially lead to a similar problem as discussed for tissue contraction. According to the Fourier-Slice theorem, the convolution products of the anatomy and the modulation function rotate around the origin of k-space if the line tagged object is rotated. The rotation angle is identically in the image and in the Fourier domain. Hence, the convolution products might again move out of the sampled region due to rotation (Fig. 2, c). These effects have to be taken into account if the tag line distance is decreased by the tagging procedure. Finally, a higher resolution for the tagging grid results in a decrease of the relevant anatomical information on the images since the myocardium is obscured by the increased number of tags or gridlines.

Here we present an extension of the CSPAMM (37) tagging technique, which allows to shift the tagging grid to any position of the imaged slice. The resolution of the tagging grid can simply be doubled by the combination of two measurements with a 180° phase shift of the spatial modulation of the magnetization. This strategy is not only limited to tagging techniques based on the 1-1 SPAMM sequence, but can be adapted to any tagging sequence, such as a higher order SPAMM (32), DANTE (51), or SPAMM/DANTE hybrid techniques (52).

The next paragraph gives a description of the high resolution tagging strategy. Results obtained with this extension of the CSPAMM method are documented with in vivo examinations. Finally, the relevance of the new technique is discussed and compared to procedures by which the cardiac motion is assessed by velocity phase contrast.
2.2 High Resolution MR Tagging

Methods

Grid displacement and increased grid resolution

The method of placing the tagging grid at any desired position within the imaged slice is introduced for simplicity by the modification of a 1-1 SPAMM sequence.

Assume the rotating coordinate system of the magnetization to be \((x, y, z)\) and the gradient coordinate system to be \((s, p, r)\), \((s=\text{slice selection}, p=\text{preparation}, r=\text{read-out})\).

Fig. 1a) shows a one dimensional 1-1 SPAMM sequence with two 90° RF pulses and an interspersed tagging gradient in read-out direction and a final spoiler gradient in slice selection direction on which the following analysis is based. The transverse magnetization at the position \(r\) immediately before the second RF pulse is

\[
\begin{bmatrix}
M_x \\
M_y
\end{bmatrix} = \begin{bmatrix}
M_{ss} \sin(\Phi_{tag} \ r) \\
-M_{ss} \cos(\Phi_{tag} \ r)
\end{bmatrix}
\]

where \(M_{ss}\) stands for the steady state magnetization in \(z\) direction and \(\Phi_{tag}\) is the spatial tagging grid frequency,

\[
\Phi_{tag} = \gamma \int G_{tag}(t) \ dt. \tag{2}
\]

As a modification of the original SPAMM sequence, the second 90° RF pulse is applied with a phase shift \(\Psi\) relative to the first 90° RF pulse (Fig. 1b). This 90° RF pulse rotates a certain amount of transverse magnetization back to \(z\) direction, given by

\[
M_z = \begin{bmatrix}
-sin(\Psi) & cos(\Psi)
\end{bmatrix} \begin{bmatrix}
M_x \\
M_y
\end{bmatrix} \tag{3}
\]

In the case of spatial modulation of the magnetization by a gradient in-between the two 90° RF pulses, the resulting longitudinal magnetization becomes

\[
M_z(r) = -M_{ss} \left[\sin(\Psi) \sin(\Phi_{tag} \ r) - \cos(\Psi) \cos(\Phi_{tag} \ r)\right] \\
= M_{ss} \cos(\Phi_{tag} \ r - \Psi). \tag{4}
\]

Thus, the tagging grid can be shifted to any desired location by application of the second RF pulse with a phase shift \(\Psi\) relative to the first one. This simple result does not only hold for a 1-1 SPAMM or CSPAMM sequence but can be easily adapted to a higher order SPAMM (32) or DANTE (51) tagging sequence by the application of a phase shift to the tagging RF pulses linear dependent on its k-space position. The shift of the
tagging grid is then defined by the phase shift of the RF pulse generating the fundamental frequency of the spatial modulation of magnetization. For a one-dimensional CSPAMM sequence and without phase shift between the two RF pulses, the resulting tagging grid on a modulus image $A$ is described by

$$ TAG_A(r) = |\cos(\Phi_{tag} r)|. \quad [5] $$

If the second RF pulse of the CSPAMM tagging sequence is applied with phase shift of $90^\circ$ relative to the first one, a different tagging function,

$$ TAG_B(r) = |\sin(\Phi_{tag} r)|, \quad [6] $$

of image $B$ is achieved. The multiplication of two images which are modulated by the functions $TAG_A$ and $TAG_B$ results in an image with the double grid frequency,

$$ TAG_A(r) \cdot TAG_B(r) = \frac{1}{2} |\sin(2 \Phi_{tag} r)|. \quad [7] $$

Such an image would also violate the Nyquist or sampling theorem in the same manner as an image which is acquired with direct double grid frequency. However, if the two images $A$ and $B$ are evaluated separately, yielding the displacement of the labeled points of both images, displacements and trajectory maps with double resolution are achieved.

**Examination protocol**

High resolution CSPAMM myocardial tagging including slice following was implemented on a Philips Gyroscan ACS-NT 1.5T system equipped with the CPR3 software package for cardiac applications (prototype Powertrak 3000 gradient system, Philips Medical Systems, Best, NL). For the acquisition part of the sequence, a multi heartphase echo planar imaging sequence was applied. In order to obtain constant tagging contrast in each heartphase image, variable RF excitation angles for imaging were used (33). Further, a prototype cardiac surface coil (Philips Medical Systems, Best, NL) was used for signal receiving.

For the *in vivo* measurements signal acquisition was performed during four single breathhold periods in an expired state with an individual duration of 9 sec. The tagging sequence was applied immediately after the detection of the R-wave of the ECG. The field of view (FOV) was 290 x 290 mm with a sampling matrix of 128 data points. For the reduction of measurement time, a reduced k-space acquisition scheme (37) was used (35 % $k_x$-profiles). With a heartphase interval of 35 ms (temporal resolution), 16 to 20
2.2 High Resolution MR Tagging

heartphase images were generated depending on the individual heartbeat rate of the volunteers or patients. Four sets of time resolved stripe tagged images were acquired, whereby the shifting of the grid for high resolution tagging and the change of orientation (swapping of read-out and preparation direction) for the orthogonal set of line tagged images was performed run-time. The implementation allows a splitting of the acquisitions into 1, 2 or 4 single breathholds.
Results

The results obtained with the high resolution CSPAMM tagging method are documented in Fig. 3. The images show a temporally resolved double oblique short axis section acquired at an equatorial level of the heart of a healthy subject. The four sets of images were combined or multiplied off-line with a separate procedure. The tagging grid was applied at end diastole to a slice of 6 mm thickness with a tag line distance of 8 mm for each acquisition resulting in 4 mm line distance in the final images.

Fig. 3. Double oblique equatorial acquisition of the heart of a healthy volunteer (heart beat rate = 80). 16 heart-phases are acquired with a temporal resolution of 35 ms. The images are a result of the combination of 4 acquisitions of line tagged images. The initially modulated tag line distance was 8 mm and the resulting distance on the images is 4 mm.
2.2 High Resolution MR Tagging

The FOV was 290 x 290 mm using reduced k-space acquisition (35 % of k_x-profiles). The size of the sampling matrix is 128 x 96 (rectangular FOV). The thickness of the imaged slice is 25 mm and was adapted to the amount of long axis contraction at the given location. The temporal resolution is 35 ms, whereby the first image is acquired 25 ms after the R-wave of the ECG. By the use of an EPI-factor of 9 (9 sampled k_y-profiles per RF excitation), the scan can be split into four breathholds of 9 sec duration, each. The resolution of the trajectory map, segmented on the raw images, is 4 x 4 mm. Due to the application of the slice following tagging technique, always the same tissue of the myocardium is examined. This fact is important for an accurate segmentation of the heart wall (53). Further, these images show a high contrast between the blood within the ventricles and the myocardium. This facilitates the segmentation of the heart wall. The tagging contrast on the images remains practically unchanged for systole and diastole. Hence, motion data of the entire cardiac cycle can be extracted based on these images. The right ventricle is clearly visible in each heartphase image. Since the tag line distance is relatively small with respect to the thickness of the lateral free wall, the right ventricular motion can be tracked reliably as well.
Discussion and Conclusions

By using two measurements with shifted spatial modulation of the magnetization, the tagging grid spacing can be reduced down to the range of 4 mm. It is possible to circumvent the limitations associated to the Nyquist theorem even in the presence of rotation and/or tissue contraction. By the combination of the shifted grids, higher order terms of the modulation function are generated which do not have to be sampled originally. Image evaluation can be performed on the individual images before they are combined to high resolution tagged time series. This results in a more robust detection of the tag lines.

The need for multiple acquisitions to increase the grid resolution is a serious drawback. However, the application of a new tagging and imaging strategy holds the overall examination time in a reasonable range. The application of one-dimensional tagging sequences allows to acquire a reduced number of k_x-profiles in the imaging part of the sequence without loosing image resolution perpendicularly to the tag line orientation. Thus, measurement time can be significantly reduced without any loss in image quality.

The time for the acquisition of two one-dimensional tagged images is about half compared to the acquisition of a two-dimensionally tagged image (37). By the application of an EPI imaging strategy, overall measurement time can be reduced to 2 single breathholds of 9 sec duration, each. Consequently, the method is applicable to the major part of the patients. For individuals who are capable to hold their breath for longer periods (~20 sec), the measurement can be performed in one breathhold. The splitting of a measurement into multiple breathholds is a potential source of errors, since the reproducibility of the position of the diaphragm is not ensured for the different breathholds. Thus, the images which have to be combined do not necessarily refer to the same level of expiration and subsequent evaluation is hampered. Therefore, a patient feedback for the visualization of the breathing position would be helpful for the future.

The diaphragm position can either be detected by the application of a breath belt or by the use of MR navigators.

Compared to the velocity phase contrast (VPC) method, the spatial resolution of the displacement map obtained by the high resolution tagging techniques is similar. By using VPC, the signal phase has commonly to be averaged over multiple surrounding
pixels. Most limitations and properties are similar for both methods, such as the resolution of the resulting trajectory map and the possibility to investigate the cardiac motion of the entire heart beat cycle with a high temporal resolution. Both methods are also extensible to three-dimensional motion assessment (35) and towards strain quantification (54, 55, 56). Further, total measurement time is comparable for both approaches, as for the VPC method also four acquisitions with different velocity encoding directions are required. Even the evaluation of the images of both methods can be performed almost automatically. The most important difference in both methods is the accuracy of the resulting trajectory map. The accuracy of the VPC approach is dependent on time, due to the velocity integration from heart phase image to heart phase image (57, 58), and is in the range of several pixel widths. The accuracy of the tagging method is time independent and potentially within a subpixel range. This is the main reason for the wide field of documented in vivo applications of tagging techniques.
References


2.2 High Resolution MR Tagging


2.2 High Resolution MR Tagging
2.3 MR Real-Time Experiments in Cardiac Applications

Abstract

Cardiac magnetic resonance imaging would provide a significantly increased potential if imaging under physiologically induced stress becomes feasible. However, for standard MR imaging techniques, the data acquisition periods are relatively long when compared to the duration of the fastest occurring motion components in the human heart. Therefore, the image data have to be sampled during the same phase of consecutive heart cycles. An image of one heart phase represents an average of the same timepoint in a series of heartbeats. Hereby, an important precondition has to be fulfilled: The heart has to be repositioned exactly at the same location during data acquisition of the corresponding heart phases. Consequently, data acquisition periods have to be synchronized to the ECG and breathing or patient motion has to be controlled. However, this limits the application of cardiac MR to purely rhythmic motion and imaging under physiologically induced stress is not feasible either. In the present work, modifications of an ultra fast imaging technique allowing real-time imaging of the heart are discussed. First experiments with infarction patients and healthy volunteers are presented. It also involves image acquisition during exercise on an MR compatible bicycle ergometer.


**Introduction**

Mainly for diagnostic reasons, there are strong requirements to perform magnetic resonance (MR) imaging under physiological stress conditions. However, the resulting patient motion, the enhanced breathing activity (breathholding under physiologically induced stress conditions is not realistic) and the EMG signals overlaid to the ECG will strongly influence the image quality due to non reliable synchronization. Hence, MR imaging under physiologically induced stress can only be performed if real-time (RT) imaging sequences are applicable.

In the literature, approaches for RT cardiac imaging under rest conditions can be found (59-68). Impressive results were already shown in 1986 and 1987 (59-61). Hereby, single shot EPI based techniques were used. However, the in-plane resolution of the applied procedures were insufficient or consecutive heartphases are acquired in a single breathhold during multiple heartbeats. Single shot EPI techniques suffer from relatively long echo times and consequently, images are very sensitive to flow and motion induced artifacts. Therefore segmented k-space acquisition schemes were proposed (67, 68). These RT methods show echo times which are very short. However, the sampling time per heartphase is still relatively long (130 - 300 ms) with respect to the physiologically occurring motion components (70). In (71) a hybrid technique of segmented k-space acquisition and EPI readout phase is mentioned. By the application of a hybrid technique consisting of segmented k-space acquisition and an EPI signal readout, overall sampling time can be reduced and the steady state magnetization is increased. This results in an improved signal to noise ratio. Echo time is shortened with respect to single shot EPI methods which helps to reduce motion or flow induced artifacts. Due to the multiple RF excitations per heartphase, an inflow weighting can be achieved which yields a good contrast between muscle and blood. In the present paper, the application of such a hybrid technique for RT imaging of the heart is discussed.

This method has been applied to 10 infarction patients and 12 healthy subjects. The sequence was optionally applied without ECG triggering in a 'free-run' mode (61). Additionally to the purely anatomical images, real-time tagging images were acquired with a very high temporal resolution. In the healthy volunteers, RT imaging was even performed during physical exercise on an MR compatible ergometer.
Methods

Pulse sequence for imaging

RT imaging of the heart is performed using a TFEPI (= Turbo Field Echo Planar Imaging) imaging sequence (Philips Gyroscan ACS/NT 1.5T equipped with a prototype Powertrak 3000 gradient system: 12mT/m, 32mT/m/ms; CPR3 Cardiac Patch). This imaging technique has already been proposed in a different context for perfusion imaging studies (69). Slightly modified, it allows temporally resolved, double angulated RT imaging of the heart.

![Diagram of TFEPI sequence for real-time cardiac imaging](image)

Fig. 1. Multi heart phase real time (RT) imaging sequence. It combines segmented k-space acquisition with EPI readout. A slice selection (a) is immediately followed by a EPI-readout train (b). This procedure (Slice selection & EPI readout) is repeated multiple times (repetition time $T_r$) to split the k-space in multiple readouts. Total shot duration for one heartphase image is denoted as $T_s$ and the heartphase interval as $\Delta t$.

TFEPI is a method where every slice selective RF excitation for imaging is immediately followed by an EPI readout train (Fig. 1). Slice selection with subsequent EPI readout is repeated several times in order to split the k-space in multiple readouts. The so obtained data refer to the same heartphase image. Splitting of the k-space in multiple readouts helps to reduce echo time significantly. This is a very important precondition for the reduction of motion and flow induced artifacts in cardiac images. With respect to the segmented k-space acquisition schemes (67, 68), less RF excitations for imaging are used. This yields an increased steady state magnetization resulting in an improved signal
to noise ratio. By the use of EPI readout trains, the k-space can be sampled in a shorter period when compared to segmented k-space techniques. Due to these reasons, TFEPI is well appropriate for ultrafast cardiac MR imaging.

The current implementation allows the combination of TFEPI with flow compensating gradients or prepulses such as MTC prepulses, spectral selective fat saturation, T<sub>2</sub> prepulses or tissue tagging. Optionally the sequence can be performed without ECG triggering in a 'free-run' mode. Therefore, the timing of the imaging sequence does not depend on the ECG which results in a facilitated setup and in a stable steady state magnetization.

**Imaging protocol for RT cardiac imaging**

For standard anatomical images, the field of view (FOV) is 300 mm and the size of the sampling matrix 128. By the use of a reduced k-space acquisition scheme (80 %), an in plane resolution of 2.3 x 2.9 mm results. All heartphase images are acquired in half-scan mode (62.5 % of k<sub>r</sub>-profiles) which does not affect image resolution. With an EPI factor of 13 (=13 sampled k<sub>r</sub>-profiles per RF excitation) and a rectangular FOV of 60 % totally 4 RF excitation angles per heartphase image are applied (T<sub>r</sub>=16.2 ms). Thus, signal sampling time (=T<sub>s</sub>) per heartphase image amounts to 65 ms. With these parameters, a temporal resolution Δt=75 ms and an echo time T<sub>e</sub>=4.5 ms is obtained. The thickness of the imaged slice is 8 mm and a constant RF excitation angle of α=30° results in a good contrast between muscle and blood. Generally 40 to 50 heartphase images are acquired in free-run mode (without using the ECG for triggering purposes). Therefore, up to 6 heartbeats can be visualized individually. For signal acquisition, a circular surface coil (diameter=20 cm) is used. The resulting images are reconstructed immediately after the scan.

For RT tagging experiments, basically the same parameters are used for the imaging procedure. However, by the application of line tagging in combination with a reduced k-space acquisition scheme (40 % scan percentage) which does not affect image resolution perpendicularly to the tagged lines, sampling time per heartphase (T<sub>s</sub>) is reduced to 30 ms (T<sub>e</sub>=3.8 ms). The repetition time T<sub>r</sub> is still 16.2 ms but only 2 RF excitations are used per heartphase image. Hereby, the temporal resolution can be significantly improved with respect to the purely anatomical images. For tissue tagging,
a 1-1 SPAMM sequence where two 90° pulses are interspersed by a tagging gradient is applied. Since the tagged information does not only decay under the influence of spin lattice relaxation but also due to repetitive RF excitation for imaging, the flip angles are set to 15° in order to achieve a prolonged tag persistence. In contrast to anatomical imaging, ECG triggering is still needed for the application of the line tags at end diastole.

Imaging under rest conditions

Under rest conditions, all the infarction patients and volunteers underwent the same procedure including the acquisition of anatomical and SPAMM tagged images under real-time conditions. Hereby, the above described protocols were applied. For both experiments, double angulated apical time series of short axis images were acquired during free breathing of the individuals.

Imaging under physiologically induced stress

In all the measured volunteers, RT images were acquired under physiologically induced stress conditions as well. Stress was induced with an MR compatible cycling ergometer (Philips Medical Systems, Best, NL) including a versatile load programmer. Hereby, the volunteer was laying in supine position in the magnet. The surface coil for signal acquisition was fixed to the chest with an elastic band. The volunteer was forced to increase the performance according to the time course of the programmed load. Hereby, the resistance for cycling increased linearly within 3 minutes to 120 Watts and then remained constant. For the determination of the heartbeat rate during exercise (where the ECG is additionally distorted due to thoracic muscle contractions), a peripheral pulse sensor which measures near infrared absorption in the finger tip was used. After cycling for 6 minutes (3 minutes of 120 W) real time anatomical and line tagged images were acquired during exercise. For real-time imaging under physiologically induced stress, the same imaging protocols as under rest including anatomical imaging and line tagging were applied.
With the present protocol for RT anatomical imaging, a temporal resolution of $\Delta t=75$ ms is achieved. Therefore, 8 to 12 heartphase images can be acquired per heartbeat cycle. For all patients and volunteers, the endo- and epicardial boundary of the myocardium can clearly be detected due to the enhanced blood-muscle contrast (Fig. 2, a & b). The steady state magnetization of the heart muscle is decreased due to the repetitive application of the RF excitation angles for imaging. In contrast, the magnetization of the blood which moves into the imaging plane has an increased steady state magnetization. Due to the relatively short echo times (with respect to single shot EPI methods), motion or flow related artifacts are not a limiting factor for the determination of the heartwalls (Fig. 2, a). For the free-run mode, where multiple heartbeats are acquired sequentially, the motion of the diaphragm during free breathing can be observed in addition to the heartwall motion on the images. The resulting bulk motion of the myocardium is visualized in the movie mode. During free breathing, in-plane bulk motion of the heart induced by the adjacent diaphragm amounts approximately to 1 cm.

In one infarction patient who had numerous arrhythmias, the fourth out of six heartbeats shows an extra systole on the images. This extra systole is followed by a delayed filling of the ventricles. Due to the frequently occurring arrhythmias in this patient, ejection fraction measurements were not reliable on standard multi shot EPI images. However, by the application of the RT technique, the determination of the ejection fraction becomes feasible. The image series in Fig. 2, b show a double oblique 4-chamber view acquired under real-time conditions. In these images even the opening and the closing of the mitral valve is seen. By the application of a reduced k-space acquisition scheme for line tagged acquisitions, sampling time per heartphase image is reduced resulting in a high temporal resolution of $\Delta t=35$ ms. Thus, up to 28 line tagged images acquired at different timepoints within the cardiac cycle can be visualized. However, due to the fading of the tags induced by spin lattice relaxation and RF excitation for imaging, the tags can not be tracked reliably for later heartphases under rest.

During physical activity, imaging is also performed in the free-run mode. The corresponding images are partly presented in Fig. 3, e & f. In the movie mode a
Fig. 2. RT imaging of the heart under rest conditions. 

a) 8 consecutive double angulated (short axis) heartphase images at a basal level of an infarction patient. The images represent the 3rd out of 6 acquired heart cycles. The spatial resolution is 2.3 x 2.9 x 8 mm and the temporal resolution is 70 ms. One shot (acquisition time per 128 x 128 image) lasts 75 ms and the repetition time T, is 16 ms (T,=4.5 ms). A constant RF excitation pulse angle of 30° was used. 

b) Four chamber view acquired with the identical parameters. The base is on the left hand side of the images and the apex on the right hand side. 

c) 8 out of 16 heartphases which are acquired under real-time conditions using SPAMM tagging. Every second acquisition is presented.
relatively complex motion pattern can be seen. A strong bulk motion of the chest wall induced by the physical activity itself is observed.

The thorax obviously seems to be not sufficiently fixed which means that the physical activity of the legs induces a thoracic motion. In parallel the motion of the chest is also influenced by the increased breathing activity due to physical exercise. On the images, strongly varying anatomical structures in the region of the right ventricle are seen in the movie. The in plane component of the bulk motion of the myocardium during activity amounts up to 50% of the left ventricular cross sectional diameter.

In some individuals, the ECG was strongly distorted due to the physical activity. Therefore ECG triggering for the application of the tags at end diastole is not sufficiently reliable in all cases. However, tag persistence is prolonged during physical activity when compared to the images acquired under rest.
Discussion

By the application of TFEPI for RT cardiac imaging, total signal sampling time per heartphase image was significantly reduced when compared to segmented k-space methods (67, 68). Due to the reduced echo time, TFEPI is less sensitive to motion or flow related artifacts than single shot EPI techniques (61). The relatively high muscle-blood contrast in the RT images supports the automatic detection of the heart walls for the determination of wall thickness, wall thickening or ejection ratio. In free-run mode, ECG triggering is not needed meaning that no problems are associated to arrhythmias, thoracic muscle contraction, blood flow related, or gradient induced distortions of the ECG. Generally, beat to beat variations can be visualized. In-plane and/or temporal resolution may still be too low for specific applications. However, by the further improvement of the gradient systems, these problems might be overcome in the near future.

For MR tagging experiments, ECG triggering is inevitable because the timepoint of the application of the tagging pattern has to be defined in order to interpret the deformation of the tags on the myocardium correctly. If reduced k-space acquisition schemes are applied for tagging experiments, the sampling period can be drastically shortened and the temporal resolution can be significantly improved. However, sophisticated tagging methods with slice following properties and a prolonged tag persistence (72, 74) cannot be applied in RT, since these methods are based on subtraction techniques.

The acquisition of anatomical and tagged images during exercise is demonstrated. Through plane motion effects are amplified due to bulk motion induced by cycling or the associated enhanced breathing activity. Consequently, not always the same layers of the myocardium are seen in the different heartphase images. This may lead to misregistrations and consequently to biased numerical results.

TFEPI is not yet embedded in an interactive environment (75, 77). However, this ultrafast sequence might be very helpful and time saving for planning (77). Hereby, a real-time reconstruction unit, and a user interface allowing for interactive planning (75) are strictly needed.
Conclusions

By the application of TFEPI sequences, real-time cardiac imaging is feasible on commercially available MR systems. Image quality is no longer sensitive on badly reproducible geometrical configurations in consecutive heartbeats. No triggering, 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 has important implications for the use of MR cardiac imaging as a tool for stress measurements and for the investigation of arrhythmic heartwall motion and means a significant improvement of conventional cardiac MR techniques. By a further improvement of the gradient system, even a higher spatial and/or temporal resolution can be achieved.
 References


2.4 Evaluation Strategies for the Quantification of the Local Heart Wall Motion by Magnetic Resonance Myocardial Tagging

Abstract

Sophisticated magnetic resonance tagging techniques provide powerful tools for the non-invasive assessment of the local heart wall motion towards a deeper fundamental understanding of local heart function. For the extraction of motion data from the time series of magnetic resonance tagged images and for the visualization of the local heartwall motion an image analysis procedure has been developed. New parameters have been derived which allow to quantify the motion patterns and are highly sensitive to any changes in these patterns. The new procedure has been applied for heart motion analysis in healthy volunteers and in patient collectives with different heart diseases. The corresponding results are summarized and discussed.
Introduction

Magnetic resonance imaging (MRI) provides a powerful tool for non-invasive diagnostics of the human heart. Morphological changes can easily be detected due to the extremely high soft tissue contrast of the images. Furthermore recently developed new MRI procedures also allow to derive various kinds of functional information. Often parameters such as wall thickening and ejection fraction are quantified, perfusion and metabolic processes are investigated. However, due to the absence of well defined structural landmarks the detailed motion analysis is restricted and locally dependent variations of the motion patterns can not be quantified reliably. For a deeper biomechanical understanding of the motion, more detailed information of the local motion pattern is needed. In some studies rotational components of the heartwall motion have proven to provide important diagnostic information too (80, 81). Such information can not be traced on images which are acquired with conventional imaging techniques. In 1988 new magnetic resonance myocardial tagging techniques have been proposed (82, 83) and further developments have been reported (82-88). For these techniques, prior to an ECG triggered multi-heartphase magnetic resonance imaging procedure, the muscle tissue of the myocardium is labeled by a spatially periodic modulation of the magnetization. Hereby a special sequence of gradients and radiofrequency excitation pulses is applied. By such procedure line tags or grid tags can be attached to the tissue. Then time series of heart images are acquired with high temporal resolution. In these images, the periodic grid of modulated magnetization appears as a grid pattern of dark stripes which are fixed with respect to the muscle tissue. From the displacement, the rotation, and the distortion of this pattern, the local heart wall motion can be derived. For diagnostic purposes and for biomechanical research, quantitative parameters have to be extracted from these image series. Since sophisticated tagging techniques are rather new (88) and MRI myocardial tagging is still mainly restricted to basic research, evaluation strategies have to be defined and adapted to the local requirements. In the literature some evaluation procedures have been published (90-97) by which temporally and locally resolved motion data and further parameters such as stress and strain are computed. However, since the images are acquired with different MRI tagging techniques, and since the extracted biomechanical or diagnostic information strongly
depends on the underlying questions, which are not necessarily identical for different studies, the procedures can not easily be adapted. Thus, new image analysis and evaluation procedures allowing the quantification of the required motion parameters are needed. Relevant parameters have to be defined which are sensitive to the problems to be investigated; they have carefully to be adapted interactively to the specific biomechanical or diagnostic questions. In many pathologies, specific alterations in the local motion pattern are expected and hence, strongly related parameters should be provided by the evaluation tool. More applications even exist for which these needs have not yet been defined and hence, the specific alterations of the motion pattern have to be extracted by the definition of new parameters.

If the setup including evaluation procedure and parameter definition once is arranged, by each evaluation a set of spatially and temporally resolved parameters results which has to be visualized in an appropriate way and which has to be interfaced to statistic programs for further processing. All these steps and iterations require a fundamental understanding of the MRI method and the underlying heartwall mechanics in healthy and pathologic cases. Therefore, the development of a powerful sophisticated evaluation procedure requires strong interaction between the participating specialists of cardiology, of biomechanics, of MRI, of image processing, and of statistics.

In the present paper, an evaluation tool for the visualization and the quantification of the local heartwall motion from tagged magnetic resonance images is presented. It includes an automated tag line detection on basis of active contour models (snakes) (90-94). Then the definition of sensitive motion parameters and their visualization in graphs or motion images are discussed and the relevance of the parameters describing the local heartwall motion are investigated. Finally results of some specific volunteer and patient studies are summarized for which the new tool has been applied.
Methods

Tagging method vs. structure extraction

For the assessment of locally and temporally resolved heartwall motion CSPAMM myocardial tagging is used (88). This method allows the assessment of the systolic and diastolic phase of the cardiac cycle since the often observed fading of the tags can be suppressed. Through plane motion effects as occurring due to long axis contraction of the myocardium perpendicularly to the spatially fixed acquisition plane can be avoided by the application of a slice following imaging technique (89). Hence, motion tracking of always the same tissue elements throughout the entire heart cycle is ensured. By the additional application of variable RF excitation angles for imaging, constant tagging contrast can be achieved for all measured heartphase images which is an important precondition for automated tag detection.

Evaluation strategy and MR imaging method are strongly related to each other in MR myocardial tagging. Basically, the motion data has to be extracted from the tagged time series of images. The modulated structures can be of different shapes or complexity (82-88). If a grid pattern is attached to the magnetization of the muscle tissue, 2D motion of any arbitrary point on the myocardium can be calculated using interpolation. However, a geometrically simple modulation pattern might be more advantageous for a computer assisted extraction of the motion. For detailed motion analysis, the accuracy and reliability of the data should not be restricted by such requirement. The local heartwall motion can also be obtained by acquiring two images with orthogonal one-dimensional stripe patterns, rather than the direct acquisition of an image with a two-dimensional grid pattern. By the multiplication of the orthogonally line tagged time sets of images, the same local trajectories can be extracted as it is the case for direct grid-tagging. Moreover, the application of line tags is advantageous due to the following reasons: First, a reduced k-space acquisition scheme (87, 89) can be used which results in a significantly reduced measurement time. Second, automated structure extraction is facilitated since only lines and not grid intersection points have to be identified. Finally, less anatomical information is obscured by line tags in comparison to grid tags.

Let us assume a vertically oriented set of line tags. Due to the modulation of the magnetization of the muscle tissue (in case of CSPAMM), the resulting locally
dependent signal intensity \( I \) for the \( k^{th} \) heartphase (\( k=1..n; n \) is the number of imaged heartphases) at the location \( y_0 \) can be written as

\[
I(x, y_0, t_k) = A \cdot \| \cos(\Phi(x, y_0, t_k) \cdot x, y_0) \|.
\]  \[1\]

\( A \) is the signal amplitude which is constant due to variable flip angles, \((x, y)\) are the spatial coordinates and \( \Phi(x, y_0, t_k) \) describes the frequency of the modulated cosine. Basically, this modulation frequency or the related tag line distance is defined by the tagging procedure. However, since the muscle tissue locally contracts and relaxates during the cardiac cycle the tag line distance or the modulated frequency which is seen on the images varies with time and with respect to the segment of the myocardium.

**Evaluation steps**

For visualization purposes, the orthogonally line tagged heartphase images are multiplied. However, the horizontally and vertically line tagged time sets of images are analyzed separately. To increase the robustness of the line tag detection, all the evaluation steps are performed on 6 times zoomed images (92). Automated line detection starts with the first heartphase image. On the first end-diastolic images distortions of the tags due to blood flow or muscle contraction has not yet started and the contrast to noise ratio is maximized. Thus, the tag lines are almost straight and structure extraction is most easy and reliable.

Line detection is achieved by using snakes (90-94) which are active contour models associated with an energy functional \( E(s) \):

\[
E(s) = \int \alpha(s) E(s)_{\text{Image}} + \beta(s) E(s)_{\text{Curve}} + \\
\gamma(s) E^{-1}(s)_{\text{Corr}} + \delta(s) E(s)_{\text{Cont}} \, ds
\]  \[2\]

where \( s \) denotes the arc length along the snake, \( E(s)_{\text{Image}} \) the local image or signal intensity, \( E(s)_{\text{Curve}} \) the curvature energy, \( E(s)_{\text{Cont}} \) the continuity energy and \( E(s)_{\text{Corr}} \) the correlation energy coming from the correlation of the local image part and the known modulation function or kernel. The coefficients \( \alpha, \beta, \gamma, \delta \) are used for the weighting of the different energy terms. They are adapted iteratively as proposed in (91). In the first iteration, the curvature energy is low weighted. This causes the snake to lie on the grid lines except at those areas, where anatomical borders or image artifacts occur. In a second iteration, \( \gamma(s) \) is increased which results in a more pronounced dynamic bending.
2.4 Image Evaluation

The last iteration step is then performed with a default value of $\gamma(s)$. Since a series of boundary conditions are given, a priori knowledge is used for the iterative detection algorithm:

- The spatial modulation function [1] of the tissue magnetization is defined by the tagging procedure or scan protocol. Therefore, a local cross correlation (95) of the image with a model modulation function is performed taking maximum tissue deformation $\Phi$ into account.

- In order to satisfy the Nyquist or sampling theorem, maximum detectable tag line displacement between consecutive heart phases is limited by the interstripe distance and the sampling time constant (heart phase interval).

- Maximum possible deformation of the myocardial tissue (<40%; experience from many patient- and volunteer studies) is used for determination of the minimum possible interstripe distance at end systole, when maximum tissue deformation occurs.

By iteratively minimizing the energy functional $E(s)$, the snakes finally follow the tagged lines on the MR images. Since line tagged images are used for detection, the snake elements ('snaxels') are only allowed to deviate orthogonally to the tag line direction. In this direction, full k-space information is sampled and hence, image resolution is not affected into the direction where the snaxels are allowed to deviate. With this restriction, the continuity term $E(s)_{\text{cont}}$ of [2] can be neglected, which considerably decreases computation time. After completely automatic line detection in the first heart phase image, user guided correction might be needed. Since blood pooling, motion artifacts and borders of adjacent tissues may lead to detection errors, a graphical user interface allowing user guided snake correction was developed (96). It allows the manual correction of snakes which are not detected correctly by the algorithm. Hereby, misaligned parts of the snakes can be shifted to the desired location. Subsequently, the snake algorithm searches again a minimum energy configuration based on [1, 2] with
the new boundary conditions defined by the user. Again, correction of misaligned points is only allowed perpendicularly to the orientation of the snakes. After completion of the line detection in the first heartphase image (whether there was user interaction needed or not), the line pattern is propagated into the subsequent heartphase image and serves as starting condition for the snake algorithm in that image.

If the tag line extraction is completed for all heartphase images and for both the horizontally and vertically line tagged time sets of images, the orthogonal stacks of the detected lines are combined. Hereby, the grid intersection points are computed automatically. This involves the embedding of each individual intersection point in the temporal and spatial neighborhood with respect to the other points. Thus, the trajectories of all the grid intersection points on the images are defined. After the definition of the grid, the epi- and endocardial heartwalls have to be traced manually in the first heartphase image.

**Coordinate system**

Due to the ring structure delineated by the endo- and epicardial heartwall, the center of gravity (COG) can easily be defined. For the initial definition of the location of any point on the myocardium, a polar coordinate system is introduced. Into radial direction, epicardial (Fig. 1, triangle), mid-myocardial (Fig. 1, circle) and endocardial (Fig. 1, square) points are defined in steps of $\Delta \varphi = 5^\circ$ into circumferential direction ($l = 0..71$). The circumferential component originates at the location where the right ventricular endocardium merges the antero-septal left ventricular epicardium ($l = 0$, Ref1). The septum is delineated by the connection of the center of gravity (COG) and the two reference points (Ref1 and Ref2). The left ventricle is further subdivided into the segments inferior, lateral and anterior.

![Fig. 1. Polar Coordinate system of the myocardium. Into radial direction, epicardial (square), mid-myocardial (circle) and endocardial points are defined in steps of $\Delta \varphi = 5^\circ$ into circumferential direction ($l = 0..71$). The circumferential component originates at the location where the right ventricular endocardium merges the antero-septal left ventricular epicardium ($l = 0$, Ref1). The septum is delineated by the connection of the center of gravity (COG) and the two reference points (Ref1 and Ref2). The left ventricle is further subdivided into the segments inferior, lateral and anterior.](image)
square) points are defined in steps of $\Delta \varphi (=5^\circ)$ into circumferential direction ($l=0..m-1$; $m=72$) on the first heartphase image (end-diastole). The circumferential component originates at the location where the right ventricular endocardium merges the antero-septal left ventricular epicardium ($l=0$).

The septum is delineated by the connection of the COG and two reference points (Ref1 and Ref2). The left ventricle is further subdivided into the segments *septum*, *inferior*, *lateral* and *anterior*. In consideration of the bulk motion of the myocardium during the cardiac cycle, the coordinate system is not spatially fixed but has to be recalculated for each heartphase. If this fact is not taken into consideration, translational motion of the heart might appear as a rotational component and the subdivisions or segments of the left ventricle (septal, inferior, lateral, anterior) would not always contain the same tissue elements either. All the points of the myocardium are geometrically embedded in the previously extracted grid. On basis of the trajectories of the grid intersection points, each arbitrary point of the myocardium can be traced by the application of shape functions (interpolation). Consequently, the trajectories of the epi- and endocardial points can be calculated for the entire cardiac cycle. Based on the epi- and endocardial trajectories, the contours in the remaining heartphase images and consequently the dynamic COG are computed automatically. The reference points which delineate the septum propagate in the same manner into the subsequent heartphases.

**Parameters**

The local heartwall motion is a result of the orientation of the muscle fibers, their contractility, capability for relaxation and the connecting collagen structure. If one of these parameters is changed due to pathology or any other adaptation, an alteration in the local heartwall motion and consequently in the trajectory map can be expected. In the following, several motion parameters are defined on basis of the local trajectories which may reflect such changes. Similar parameters can either be found in the literature or they have been introduced on basis of volunteer and patient studies. Furthermore, the trajectory maps are also used for stress and strain calculations in a related project which is not further discussed here (101).

All the individuals which are measured show different heartbeat rates. To avoid temporal jitter of the parameter values which thereby may be induced and to allow for
direct comparison of certain motion characteristics, the parameters are normalized to the end systolic timepoint which is well defined by the smallest contour of the inner cavity. By definition, 100% on the time axis refer to the end systolic timepoint. Diastole is then characterized by values above 100%. This normalization in time can be performed optionally; if not required the data may be given in function of time [ms]. On condition that the images are visualized as a view from the apex, the following parameters are defined on basis of Fig. 1 and Fig. 2:

**Radial shortening [mm]:** Describes the motion of a point on the myocardium towards the center of gravity. In heartphase $i$ ($i=0..n-1$; $n$=number of heartphases), the radial shortening $r_{sh,i}$ of a mid-myocardial point $Q_{li}$ and the dynamic center of gravity $M_i$ is defined as

$$ r_{sh,i} = |Q_{li,0} - M_0| - |Q_{li} - M_i|. \quad [3] $$

This parameter is identically calculated for the epi- and endocardial points $P_{li}$ and $R_{li}$, respectively.
Rotation, [Deg]; Torsion, [Deg]: Rotational component of the motion of $Q_{li}$ from its initial state around the dynamic center of gravity. For the $i$th heart phase, rotation of this mid-myocardial point $Q_{li}$ at the location $l$ with respect to the circumference is given as

$$\alpha_{li} = \arccos \left( \frac{(Q_{li} - M_l) \cdot (Q_{li} - M_l)}{|Q_{li} - M_l| \cdot |Q_{li} - M_l|} \right).$$

This parameter is identically defined for the epicardial and endocardial points $P_{li}$ and $R_{li}$. Torsion is defined as the difference of the rotation between apex and base in temporal coincidence.

Rotation velocity, [Deg/s]: Temporal derivative of the rotation defined above [4]. The rotation velocity of the mid-myocardial point $Q_{li}$ around the dynamic COG is defined as

$$\omega_{li} = \frac{\alpha_{(i+1)l} - \alpha_{il}}{\Delta t}$$

where $\Delta t$ is the time delay between two consecutive heart phases. This parameter is identically defined for the epicardial and endocardial points $P_{li}$ and $R_{li}$.

Circumferential shortening, [%]: Relative shortening of the distance between two adjacent points ($Q_{li}$ and $Q_{(i+1)l}$, $l=0..m$) with respect to the circumference on the endo- or myocardium. In the $i$th heart phase, circumferential shortening of these mid-myocardial points is defined as

$$c_{S_{li}} = \left(1 - \frac{|Q_{(i+1)l} - Q_{il}|}{|Q_{(i+1)l} - Q_{il}|}\right) \cdot 100\%.$$  

This parameter is identically defined for the epicardial and endocardial points $P_{li}$ and $R_{li}$.

Shear angle [Deg]: The shearing $\beta_{li}$ between the endocardial and the epicardial muscle fiber layers at the location $l$ in heart phase $i$ is defined as

$$\beta_{li} = \arccos \left( \frac{(Q_{li} - M_l) \cdot (R_{li} - P_{li})}{|Q_{li} - M_l| \cdot |R_{li} - P_{li}|} \right).$$

Wall thickness [mm] / Wall thickening [mm]: The thickness of the wall $WT_{li}$ at a given location $l$ in heart phase $i$ is

$$WT_{li} = |R_{li} - P_{li}|.$$
and the wall thickening $dWT_{i,j}$ at the same location amounts to

$$dWT_{i,j} = WT_{i,j} - WT_{i,0}.$$  \[9\]

**Area of inner cavity [mm$^2$]:** $A_{i,j}$ is the area delineated by the inner contour (cavity) in heartphase $i$.

**Muscle area [mm$^2$]:** The muscle area $A_{M,i}$ is defined for each heartphase by the difference of the area delineated by the epicardial ($A_{O,i}$) and the area of the inner cavity ($A_{I,i}$).

$$A_{M,i} = A_{O,i} - A_{I,i}.$$  \[10\]

Depending on the biomechanic or diagnostic question, the locally and temporally resolved data have to be reduced to the relevant information. Thus, the individual parameters of the equations [3-6] can be visualized or exported by the software as single values, averaged within the segments (septum, inferior, lateral and anterior), averaged in transmural direction (epi-, endo-, and mid-myocardium) or simply as means of the cross-sectional muscle area. Except for the transmural component, shear angle [7], wall thickness [8] and wall thickening [9] can be calculated identically. In studies where the

---

**FIG. 3.** End diastolic line tagged acquisition a) and the corresponding image b) overlaid with the automatically detected tag lines (=snakes). The combination of the horizontally and vertically line-tagged images overlaid with the detected grid is shown in c). Image d) represents the corresponding end systolic timepoint. Both images are additionally overlaid by the epi- and endocardial contours and the segments are indicated, too. In image e) the systolic trajectory map is displayed in combination with the tagged image. The trajectories are starting in red at end diastole and are ending in yellow at end systole.
parameters of a quantity of individuals are involved, the values may also be averaged over the corresponding collective.

Implementation

The evaluation procedure is implemented on an Alpha AXP Workstation (OpenVMS 6.2) and on a PC (LINUX 2.0). The programming language is PV-Wave 6.02. The images which are acquired on the scanner can directly be transferred to the workstations and be read by the program. The orthogonally tagged images can optionally be multiplied for visualization purposes or for the post correction of the calculated grid intersection points. The anatomical images can be overlaid with graphical objects such as grid, heartwalls or trajectories (Fig. 3). In Fig. 3a, a horizontally line tagged acquisition at end diastole is shown. In Fig. 3b, the tag lines which are automatically extracted by the snake algorithm are overlaid to the image. Fig. 3c (end diastole) and Fig. 3d (end systole) show multiplied line tagged images overlaid with the semi-automatically extracted grid, the contours of the left ventricle and the subdivision into segments. In Fig. 3e, the local systolic trajectories originating from end diastole are overlaid to the tagged acquisition. The selected configuration including the tagged anatomical images and the graphical overlays can be displayed in a movie mode. The software is also equipped with a visualization tool, where all the calculated parameters can be graphically visualized in 2D or 3D. Furthermore, the resulting data can be displayed in cine mode. For documentation, a PostScript or TIFF interface is added. It allows to transfer the graphics of the different parameters as well as of the anatomical images overlaid with graphical objects from the screen to a file of the desired format. The graphical overlays which should be displayed or put on the files can arbitrary be selected. For further data processing, all the data resulting from the evaluation software are transferred to ASCII-files (including normalization of time with respect to end systole and averaging within segments or over cross section if needed). All graphs presented in the "Results" are generated by these facilities.
\section*{Results}

\textit{Image analysis}

The evaluation procedure has been applied to several studies. Healthy volunteers (C=20), athletes with physiologically hypertrophied hearts (PH=12), aortic stenosis patients with pathologically hypertrophied hearts due to aortic stenosis (AS=12) as well as patients with infarctions (MI=30), hypertrophic obstructive cardiomyopathies (HCM=13), left bundle branch blocks (LBBB=12) and heart transplants (HT=4) have been examined.

In the grid identification procedure, for most of the cases user correction of the snakes was needed mainly to exclude artifacts caused by borders between adjacent tissue which often appears as a black line too. Manual intervention is also needed if patients post surgery are examined. The clips or wires in their sternum lead to local inhomogeneities of the static magnetic field and to distortions of the radio frequency fields. Thus, images are partly obscured and automatic line detection is hampered. With the present implementation of the software, overall evaluation time for one slice and 16 to 20 heartphases is in the order of 1 hour.

\textit{Examples and visualization of the results}

For each subject, the above described parameter values are automatically calculated for the entire heartbeat cycle. Since the evaluation procedure has been applied to more than 100 examinations, relevant parameters for specific diagnostic or biomechanic questions related to the heart could have been extracted.

In Fig. 4a, the apical left ventricular rotation angle of AS, PH and C is indicated. The values represent cross sectional mean values averaged over the individuals of the collectives. A positive slope indicates counterclockwise rotation and a negative slope refers to a clockwise twist. The data are visualized as functions of time normalized to the end-systolic timepoint (=100\%) of the cardiac cycle. in comparison to the healthy volunteers, the AS patients show an increased end systolic peak rotation with a subsequently prolonged and delayed untwisting during the filling phase of the left ventricle. In contrast, apical rotation of the physiologically hypertrophied hearts of the
athletes is neither changed qualitatively nor quantitatively with respect to the healthy controls.

In Fig. 4b, apical, cross sectional mean rotation velocity averaged over the individuals of the same collectives is plotted normalized to the end systolic timepoint. Values above 0 Deg/s refer to a counterclockwise and values below to a clockwise rotation. Maximum untwisting velocity during diastole occurs significantly delayed in the AS patients with a tendency for diastolic dysfunction. The rotation velocity of the athletes is unchanged with respect to the healthy controls.

By the combination of rotation and area reduction, the coincidence of contractile function and rotational behavior can be investigated simultaneously. Similar to pressure-volume loops, rotation-volume loops of AS, PH and C are plotted in Fig. 4c. The loops are oriented clockwise. Relative local ejection is plotted vs. end systolic rotation on the y-axis. The rotation data represent mean cross sectional values averaged over the individuals of the collectives. For C and PH, a fast early systolic twist precedes the filling phase of the ventricles where practically no rotation can be seen. In the AS
patients, this separation of systolic rotation and contraction does not occur while during diastole, untwisting occurs before filling in the healthy and in the athlete's heart. For the AS patients, a prolonged and delayed filling without decomposition of rotation and

\text{Healthy Volunteer} \quad \text{Infarction Patient}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig5}
\caption{a) Locally and temporally resolved rotation angle for all segments of a short axis section (septum, inferior, lateral, anterior). The rotation angle on the z-axis is plotted as a function of time and with respect to the myocardial segment. \textit{Left}: Typical myocardial rotation map of a healthy volunteer. \textit{Right}: The same map of a patient with an antero-lateral infarction. b) Same data but different form of presentation. The locally and temporally dependent rotation angle is coded into colors. \textit{Left}: Healthy volunteer. \textit{Right}: Infarction patient. A rotation defect can be seen in the antero-lateral segment of the infarction patient. Additionally, a prolongation of systolic twist and diastolic untwist can be detected in the healthy segment of the MI patient.}
\end{figure}
relaxation is observed. In Fig. 4d, such a rotation-volume loop of one healthy control and one MI patient is documented (mean cross sectional rotation). Obviously, not only contractile but also rotational components of the heartwall motion are absent in this patient. It clearly documents the reduced performance in this infarcted heart.

For average cross sectional values as presented in Fig. 4, alterations of the heartwall mechanics in adjacent segments or into transmural direction can not be visualized. If locally dependent variations with respect to the circumference of the myocardium should be detected, visualization of the data as presented in Fig. 5 and 6 is needed. In Fig. 5, a typical apical rotation pattern of a healthy volunteer is compared to that one of a patient with an anterolateral infarction. The segment of the short axis view (septum-inferior-lateral-anterior) on the y-axis is plotted against the time on the x-axis. In Fig. 5a, the local rotational amplitude is coded into the height of the graph. An altered rotation pattern can be documented in the patient. Rotation and untwisting are prolonged and adjacent segments are presumably not rotating synchronously. This form of presentation yields mostly a qualitative impression. Important information might be hidden due to the 3D projection. Therefore the same data can be visualized as shown in Fig. 5b, where the rotation angle is coded into a color in function of time and segment. For the healthy volunteer, a synchronous counterclockwise rotation of all segments during systole can be reported. However, the infarction patient shows distinct variations

Fig. 6. Locally and temporally resolved mid-myocardial circumferential shortening of a healthy volunteer (left) and a left bundle branch block patient (right). In the patient, a dispersion of maximum circumferential shortening with respect to the myocardial segment can be documented by the angle $\alpha$. 
of the rotation pattern for the different segments. A counterclockwise rotation in the non-infarcted region occurs simultaneously with a clockwise rotation in the region of the infarction. In this form of presentation, the position of the antero-lateral infarction can clearly be seen. For the infarction patient not only strongly varying regional differences but also a prolonged and delayed rotation in comparison to the volunteer are observed. The same presentation but for a different parameter is given in Fig. 6. On the left hand side the locally and temporally resolved circumferential shortening of a volunteer is shown. On the right hand side, the same parameter is plotted for a LBBB patient. The angulation (α) visualizes, that maximum circumferential shortening occurs not in temporal coincidence for all segments. Obviously, a temporal dispersion of contraction with respect to the circumference occurs in this patient. This is most probably the consequence of the blockade of the left bundle.

However, not only the circumferential components but also the transmural components of the heartwall motion contain important information. For the visualization of transmural motion of the myocardium, graphs as shown in Fig. 7, where apical rotation of a healthy control (left) and an infarction patient (right) are compared, are applied. The

![Fig. 7](image)

**FIG. 7.** Regional rotation angles of a volunteer (left) and an infarction patient (right) at end systole for epi- mid-myo- and endocardium. In both cases, an increased endocardial rotation with respect to the epicardium can be seen. This yields an epi-endocardial shear angle which is typical for patients and volunteers. In the region of the arrow, a significantly reduced rotational component without transmural shearing can be seen. The same data is shown underneath in a colored bulls-eye view.
ring structure represents the short axis section of the myocardium. In circumferential direction, the segments of the heart are located. The position of the septum and the major segments are indicated. Into transmural direction, the apical rotation is plotted for epi- mid-myo- and endocardium. The two graphs refer to the end systolic timepoint of the cardiac cycle. It can clearly be seen that the endocardium rotates more pronounced than the endocardiun. This tendency is typical and can be observed in the healthy volunteer as well as in the healthy segment of the infarction patient. Consequently there exists a shearing between epi- and endocardial layers of the muscle fibers. However, rotational amplitude and shearing are completely lost in the infarcted area (arrow). Underneath these two rings, exactly the same data is shown in a bulls-eye view where the colors indicate the rotational amplitude at end-systole. Again, the transmural shearing and the hypokinetic region in the infarction patient can clearly be seen. These types of graphs can be displayed in temporal animation in order to get an impression of the dynamic processes as well.
Discussion

Radial shortening most obviously proves to be an interesting parameter for the determination of local heartwall viability (103). However, interpretations based on this parameter have to be done carefully. Considering MI patients where part of the myocardium shows no more contractile function, it can often be observed, that the healthy segments of the heart compensate for that hypokinetic area. These healthy parts consequently show an increased contractility. On short axis sections, a motion of the healthy segment towards the infarcted region is the consequence. However, this results as well in a translation of the dynamic center of gravity towards the infarcted region (Fig. 1 and Fig. 2). This finally appears as a non-influenced radial shortening in the infarcted region. Hence, this parameter might not be well appropriate for pathologies with asymmetric contractile behavior.

For the AS patients (Fig. 4a), an increased end systolic rotation angle can be reported whereas the MI patients typically show a reduction in end systolic peak rotation (Fig. 4d). For all the pathologies which have been measured, the rotational amplitude or the duration of untwisting at the apex are significantly changed with respect to the healthy cases. Thus, apical rotation is most sensitive on pathologic alterations of the heart. In this context, the directly related parameter rotation velocity provides important information as well. For the quantification of the duration of contraction or relaxation periods, rotation velocity has been considered to be the parameter which expresses the related alterations most impressively. For the quantification of the duration of isovolumic relaxation e.g., the time delay between end systole and peak untwisting velocity has shown significant alterations for patients with non-adequate filling with respect to C. For AS patients who show a tendency for diastolic dysfunction, a significantly delayed timepoint of maximum untwisting velocity (with respect to C or PH) can be demonstrated (Fig. 4b).

Basically, a counterclockwise rotation at the apex and a clockwise rotation at the base is observed during the ejection phase of the healthy heart. This yields a baso-apical wringing motion or torsion which has shown to be significantly increased in aortic stenosis patients.
For a ring structure like a short axis section of the left ventricle, area reduction can most obviously be achieved by a shortening into circumferential direction. Therefore, *circumferential shortening* and its temporal behavior might be an important determinant for diagnosis (104). In LBBB patients, it can clearly be recognized that the shortening of the circumference is delayed depending on the segment of the short axis section (Fig. 6). For MI patients a typically reduced *shear angle* can be reported in the infarcted region of the myocardium (Fig. 7).
**Conclusions**

Advanced magnetic resonance myocardial tagging techniques in combination with sophisticated image analysis procedures provide powerful tools to achieve detailed quantitative results of local heartwall dynamics. They allow to get insight into the local and temporal motion behavior and the underlying mechanics of the heart. This essentially contributes to develop a deeper understanding of the heartwall motion. It also allows to obtain diagnostic information which can not be assessed by any other diagnostic modality. However, the diagnostic relevance has still to be proven in the future.

The scanning protocols and the evaluation procedure have shown to be strongly influenced by each other. The acquisition of line tagged images helps to reduce the measurement time and automatic structure extraction is facilitated since lines instead of grid intersection points can be tracked. Due to the implemented snake algorithm, overall evaluation time could be significantly reduced with respect to purely manual definition of the grid intersection points. The introduction of a convolution kernel with the known modulation function helped to improve the robustness of the tag-line detection. Since user interaction is allowed after detection of each timeframe, the propagation of errors can be suppressed. Fully automatic tag line detection is not possible with the present algorithm. Mostly the tissue borders which might appear similar to tagged lines, noise, or artifacts of any origin are the limiting factors. In these cases, the algorithm is not capable to trace the tagged lines correctly. Hereby, a priori knowledge of the operators and interaction are strictly needed.

The versatile visualization tools in combination with the presented parameters allow the detailed investigation of the locally and temporally resolved heartwall dynamics. Local variations with respect to the segments or the transmural position can be detected accurately. Due to the high temporal resolution of the MR images, the fastest occurring motion components on the heart muscle -isovolumic twist and untwisting at the apex- can be assessed and quantified. Since all the parameters can be exported to statistic programs, larger patient or volunteer studies can be performed and appropriate documentation of the results is ensured.
The package has been applied to numerous volunteer or patient studies. Therefore, a database of motion parameters of the healthy and the pathologic heart could be established. A control collective is strictly needed for the definition of the pathologic motion. Based on these studies, a series of relevant parameters could be extracted; so far, not all of them have been investigated for all the patient collectives. This will be a subject of further investigations.

The most limiting factor is the evaluation time which still is in the order of one or even more hours per time series of one slice (16-20 heartphases). On one hand, this is a result of the sophisticated MR imaging method which allows to assess such a high number of images during the cardiac cycle. On the other hand, user friendliness and the efficiency of the algorithms can be further improved towards applications in clinical routine diagnostics. The present implementation of the software restricts its application to the evaluation of 2D sets of slices. However, for highly accurate motion analysis, quantification of 3D motion will be needed, too (92, 96, 99, 100).
References


CHAPTER 3

3.1 Alterations in the Local Myocardial Motion Pattern in Physiologic and Pathologic Hypertrophied Hearts

Abstract

Alterations in cardiac rotation of aortic stenosis patients, healthy controls and rowers with physiologic hypertrophied hearts were investigated using magnetic resonance myocardial tagging. In controls and in rowers, the left ventricle performs a systolic wringing motion with a counterclockwise rotation at the apex and a clockwise rotation at the base. In the athlete's heart, apical rotation is unchanged in comparison to controls. In aortic stenosis patients systolic rotation at the apex is increased and diastolic untwisting is prolonged when compared to controls or athletes. The differences between physiologic and pathologic hypertrophy suggest the occurrence of structural alterations in the pressure overloaded heart.

Submitted to Circulation.
3.1 Hypertrophied Hearts

Introduction

Alterations in the local motion pattern of the myocardium have been previously described (105-108). In pressure overload hypertrophy, wall stress can be normal (adequate hypertrophy) or increased (inadequate hypertrophy, (109)). The left ventricle (LV) responds to the pressure overload by developing LV hypertrophy with addition of new sarcomeres in parallel to the existing ones. This results in an increase in wall thickness with little or no change in chamber radius (110). Consequently, an increase in left ventricular filling pressure with an upward shift of the diastolic pressure-volume relationship (=diastolic dysfunction) occurs.

The implications of left ventricular hypertrophy and altered loading conditions on the regional wall motion and relaxation rate were investigated in aortic stenosis patients. For comparison purposes, championship rowers with physiologic LV hypertrophy were examined as well. These two collectives were compared to controls with normal left ventricular function.

Multiple imaging techniques for the assessment of regional wall motion exist. These techniques are either based on anatomical landmarks (111) or radioopaque markers (112-115). However, such methods are either highly invasive, the implanted tantalum helices might falsify the local wall motion due to the trauma of implantation or only a few distinct natural landmarks can be traced. Furthermore due to the invasiveness of such techniques, only animals (114-115) and very few selected humans have been studied. By this procedure, it is not possible to acquire data of control collectives of healthy subjects, which is strictly needed for the determination pathologic features. Alternative non-invasive methods like echocardiography or conventional magnetic resonance imaging (MRI), do not allow to visualize the exact local motion pattern of the myocardium due to the absence of structural reliably traceable landmarks. In 1988, Zerhouni et. al. proposed an MRI method called magnetic resonance myocardial tagging which locally saturates or labels the magnetization (116). The labels, which might be attached as lines or grids, are fixed with respect to the myocardial tissue and can be visualized for different timepoints within the cardiac cycle. The method has successfully been applied and has been refined by several groups (117-130). By the appropriate combination of orthogonal sets of time resolved images, it is even possible to describe
the local 3D motion of the myocardium by interpolation (131,132). Since the tagging information decays under the influence of longitudinal relaxation, the fading of the tags restricts the application of these techniques to the systolic phase of the human cardiac cycle.

A further modification of the existing tagging techniques has been proposed by Fischer et. al. in 1993 (133). This technique (CSPAMM = Complementary SPAtial Modulation of the Magnetization) allows to assess systole as well as diastole, whereby the tagging contrast remains constant during the entire cardiac cycle.

If slices which are spatially fixed with respect to the scanner coordinate system are acquired, long axis contraction during systole results in through plane motion on short axis images. This means that not always the same tissue elements are imaged in the different heartphases and thus leads to interpretation errors and the falsified results of the analysis. However, by the combination of CSPAMM with a slice following imaging technique, the effects of through plane motion can be suppressed (134,135). Therefore, real 2D projections of the complex 3D motion pattern of any point on the myocardium can be traced reliably without interpolation for the entire heartbeat cycle.
3.1 Hypertrophied Hearts

Methods

Study population

A total of 34 subjects were included in the present analysis. 12 patients with pressure overload due to aortic stenosis (AS), 11 healthy volunteers (C) and 11 athletes of a world championship rowing team with physiologic hypertrophy (PH) were investigated using CSPAMM myocardial tagging. Patients with aortic stenosis underwent cardiac catheterization for diagnostic purposes. Therefore, LV peak systolic pressure (LVSP) was measured using fluid-filled catheters.

<table>
<thead>
<tr>
<th>Patients</th>
<th>n</th>
<th>Age [yrs]</th>
<th>HR [min⁻¹]</th>
<th>LVSP [mmHg]</th>
<th>Wall area apex [cm²]</th>
<th>Wall area base [cm²]</th>
<th>Cavity area apex [cm²]</th>
<th>Cavity area base [cm²]</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>12</td>
<td>58±13</td>
<td>74±10</td>
<td>211±29</td>
<td>33±8</td>
<td>33±5</td>
<td>7±3</td>
<td>14±3</td>
</tr>
<tr>
<td>PH</td>
<td>11</td>
<td>23±4</td>
<td>60±6</td>
<td>-</td>
<td>26±3</td>
<td>33±4</td>
<td>9±2</td>
<td>19±4</td>
</tr>
<tr>
<td>C</td>
<td>11</td>
<td>34±9</td>
<td>73±6</td>
<td>-</td>
<td>21±3</td>
<td>23±2</td>
<td>8±2</td>
<td>14±3</td>
</tr>
</tbody>
</table>

Table 1. Patient characteristics: Number of measured individuals, age and heart rate (HR). In AS patients, left ventricular peak systolic pressure (LVSP) is given. Wall area and volume of the lumen are indicated for end-diastole. These values are given for the base and the apex. All the values are means including one standard deviation.

In Table 1, the patient variables are summarized. Mean age, heart rate (HBR) as well as LVSP are listed. In order to document the severity of LV hypertrophy, wall area and cross-sectional volume of the inner cavity (lumen) were determined on an apical and a basal level of the LV. If the end-diastolic wall area at the apex is compared, the AS patients and the rowers show a significantly increased muscle area (33±8 cm² and 26±3 cm²) in comparison to the controls (21±3 cm², p<0.01; p<0.01). At the base, the AS patients and rowers show an increased muscle mass (33±5 cm² and 33±4 cm²) in comparison to the controls (23±2 cm²; p<0.01; p<0.01). The athletes show significantly enlarged lumen at the base (PH-C: p<0.05) and a moderately enlarged lumen at the apex. In comparison to the controls, the AS patients show a highly significant increased wall area at both levels of the heart. If the lumen of apex and base are compared for these two groups, the AS patients show no significant enlargement. If the rowers are
compared to the healthy subjects, an increased cross sectional muscle mass can be reported at apex and base of the athletes.

**Examination protocol**

In order to determine the double angulated imaging plane for the short axis views of the myocardium, two scout scans are performed. The first transversal scout is followed by a single oblique scout in cine mode. Then on the end-diastolic image of the second scout

![Diagram of pulse sequence for magnetic resonance myocardial tagging (CSPAMM).](image)

**Fig. 1.** Pulse sequence for magnetic resonance myocardial tagging (CSPAMM). Prior to the multi heartphase gradient echo imaging sequence (Imaging A), the tagging pattern is attached to the magnetisation of the selected slice (Tagging A). The entire sequence is applied twice, whereby the sign of the modulation function (Tagging B) of the magnetisation is inverted for every second acquisition (Imaging B).

two double oblique short axis slices for the tagging examination of apex and base are defined. The apical imaging plane positioned 1 cm above the apical endocardium, the basal plane 1 cm below the valvular plane.

For motion tracking at these levels, a slice following CSPAMM based tagging pulse sequence (133,135) implemented on a 1.5 T Gyroscan ACS II whole body system (Philips Medical Systems, Best, NL) is applied. By this technique a periodic sinusoidal modulation of the magnetization is attached to a thin slice of the myocardium (Fig. 1, 'Tagging A') immediately after the detection of the R-wave in the ECG. Subsequently, a thick slice encompassing the potential extent of motion of the selected thin slice is
3.1 Hypertrophied Hearts

imaged periodically during the cardiac cycle (Fig. 1, 'Imaging A'). A multi heartphase gradient echo imaging sequence in partial echo mode with a short echo time of $T_e=3.4$ ms is used which strongly suppresses motion or flow induced artifacts. The same experiment is then performed a second time, whereby the modulation is inverted compared to the first experiment (Fig. 1, 'Tagging B'). Subsequent subtraction of the two temporally resolved datasets ('Imaging A' and 'Imaging B') results in signal components which exclusively contain information of the initially labeled thin slice. Signals of the surrounding tissue of the thick slice are suppressed by the subtraction procedure (134).

Two sets of images with horizontally and vertically modulated stripe patterns respectively are acquired. By the multiplication of these two acquisitions, a grid pattern results with 8 mm interstripe distance typically as documented in Fig. 2. The time delay between the detection of the R-wave and the first image is 35 ms; the time interval between the subsequently acquired 16 to 20 heartphase images is 35 ms too. The field of view is 360 mm; it is sampled by an acquisition matrix of 256x256 points and an in-plane resolution of 1.4x1.4 mm. The thickness of the tagged slice is 6 mm; the thickness of the imaged volume is related to the long axis contraction and varies from 25 to 30 mm at the base and from 15 to 20 mm at the apex. Due to the location of the relevant tag information in a limited area of k-space, a reduced k-space acquisition is applied with a scan percentage of 35% (128,135). It considerably reduces overall measurement time, but does not affect spatial resolution for motion detection. In order to obtain constant tagging contrast for each heartphase, optimized RF-excitation angles are used (133). Breathing induced motion artifacts are reduced by asking the subjects to follow a repetitive breathhold scheme. They are given 4 to 5 heart beats to slightly inhale, then exhale and hold the breath for approximately one second during the signal acquisition period. The breathing is synchronized to the noise of the gradients. With this breathhold scheme, a physiologic breathing frequency of 12 to 15 cycles per minute can be achieved. All patients and controls are investigated in prone position using a cardiac surface coil for signal acquisition.

**Image analysis**

Representative apical time series of tagged images of AS and C are presented in Fig. 2. In the first step, an automatic line detection algorithm which is based on snake
algorithms (136,137) is applied to each line-tagged time frame. After the line detection in the first timeframe, the user is asked to correct manually mispositioned lines. All evaluation steps for which user interaction is needed are performed on images which are zoomed by factor 6. For the correction, parts of the lines, which also are called snakes, are only allowed to be corrected perpendicular to the orientation of the snake, i.e. the snake elements may only be corrected in the direction in which full k-space information

![Representative images](image)

*Fig. 2.* Representative images (n=8) in a healthy volunteer (above) and an aortic stenosis patient (below). For both examples, every second acquisition is shown out of a series of 16 images. The temporal resolution for the measured images is 35 ms and the spatial resolution 1.4 x 1.4 mm with a slice thickness of 6 mm.
has been sampled. The entire procedure is repeated for all heart phase images for both the horizontally and the vertically tagged sets of images. For each time frame the snakes of the previous image serve as starting condition for the line identification. The next step of the procedure contains the calculation of the grid intersection points on basis of the orthogonal, time resolved sets of lines. Furthermore the endo- and epicardial borders of the ventricle are determined by manual contouring on one selected heartphase image with a high contrast between muscle tissue and blood. Based on the knowledge of the local heartwall motion described by the previously defined grid intersection points, epi- and endocardial contours for subsequent and/or previous heartphase images are calculated automatically. The center of gravity of the left ventricular segment is used as reference point.

Fractional area change of the LV contour is calculated for basal and apical levels. End-systole is determined by searching the smallest left ventricular contour in the time
series of the images. In order to describe the local heartwall motion in a polar coordinate system, the two points where the right ventricular endocardium merges the left ventricular epicardium are additionally used as reference points. The interpolation of the original grid points using linear 'shape-functions' then allows to describe the local heartwall motion in equidistant steps with respect to the circumferential component of the polar coordinate system (Fig. 3).

Based on the motion of the grid intersection points, epi-endo- and mid-myocardial points are calculated every five degrees for each heart phase, resulting in 3x72 trajectories which are partly visualized in Fig. 3. The rotation of these points with respect to their initial position and to the center of gravity are then determined (Fig. 4).

Average rotation of the 72 myocardial points are discussed in the following for the apical and the basal level of the hearts of all the three collectives.

Isovolumic backrotation (=untwisting) has been shown to be a sensitive parameter for the description of diastolic relaxation and filling (125). Therefore, rotation velocity and its minimum during diastolic untwisting is calculated, too. For normalization purposes, all data are related to the end-systolic timepoint of the cardiac cycle. This means that 100% on the time axis refer to the end-systolic timepoint. However, if measurements of time intervals are discussed, absolute time values in ms are presented.

![Myocardial Point](Image)

**Fig. 4.** Quantification of the local rotation angles of epi-endo- and mid-myocardial regions. The angle is defined by the position of a specific tissue element at two different time points and the centre of gravity defined by the endo - respectively epicardial borders of the corresponding cardiac phase.
Statistics

All values are given as means ±1 standard deviation (SD). Comparison between the three groups of subjects are performed with a student's t-test for unpaired comparisons. A p-value of less than 0.05 is considered to be statistically significant.
Results

Quantitative evaluation with automated line detection throughout the entire heart cycle was possible in all patients and volunteers at the apical plane. However, at the base, some acquisitions had to be rejected, because the image quality was not considered to be sufficient for accurate data analysis. An insufficient quality was mainly observed in patients and in rowers. Due to the increased size of the hearts, basal slices are not that close to the surface coil as in the healthy subjects.

Rotation

In Table 2, the parameters which are discussed in the following are summarized for AS, C and PH.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Rotation</th>
<th>(\omega_{\text{max}}) [Deg]</th>
<th>(\omega_{\text{max}}) [Deg/s]</th>
<th>(\omega_{\text{min}}) [Deg/s]</th>
<th>(T_{\text{untwist}}) [ms]</th>
<th>Torsion [Deg]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Apex</td>
<td>Apex</td>
<td>Apex</td>
<td>Base</td>
<td>Apex</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>12±5</td>
<td>99±38</td>
<td>-80±29</td>
<td>-15±10</td>
<td>88±19</td>
<td>32±6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>7±2</td>
<td>89±33</td>
<td>-55±17</td>
<td>-21±9</td>
<td>47±23</td>
<td>16±8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH</td>
<td>6±2</td>
<td>91±33</td>
<td>-56±8</td>
<td>-36±9</td>
<td>51±23</td>
<td>17±8</td>
</tr>
</tbody>
</table>

Table 2. MR data: Maximal rotation (Rotation) at the apex [Deg], maximal rotation velocity (\(\omega_{\text{max}}\)) at the apex [Deg/s], maximal untwisting velocity at base and the apex (\(\omega_{\text{min}}\)), relaxation time (\(T_{\text{untwist}}\)) in [ms] and in percent of end-systole [x100% ES]. Torsional deformation [Deg] at end-systole is given in all 3 groups. All the values are means including one standard deviation.

Maximum rotation at the apex amounts to 6.8±2.0 Deg in C (Fig. 5a). Maximum rotation velocity (Fig. 5b) is achieved at the very beginning of the cardiac cycle (\(\omega_{\text{max}} = 89.2 \pm 33.1\) Deg/s). However, this value is assumed to be zero at the beginning of contraction. Hence, there is some fast apical rotation already before the acquisition of the first image (=35 ms after the R-wave of the ECG). Maximum untwisting velocity is observed during isovolumic relaxation (-54.8±16.5 Deg/s). Diastolic relaxation time \(T_{\text{untwist}}\) (=time delay between end-systole and maximum untwisting velocity) was 46.6±23.0 ms in controls or 16±7.6 % in relation to the end-systolic timepoint (106). In analogy to conventional pressure-volume loops, Fig. 6 shows an apical rotation-area loop of one cardiac cycle. The loop is oriented clockwise and starts with the isovolumic contraction of the LV. In controls, a fast rotation is observed at the beginning of systole,
Fig. 5. a) Mean cross-sectional apical rotation angle [Deg] including one standard deviation in aortic stenosis patients, controls and rowers during one cardiac cycle. The rotation angles are plotted as function of time normalized to the end-systolic timepoint [=100%]. b) Mean cross sectional apical rotation velocity [Deg/s] including one standard deviation in aortic stenosis patients, controls and rowers normalized to the end-systolic timepoint.
Fig. 6. Left ventricular rotation-area loop (apical plane) in controls, rowers and patients with aortic stenosis. The loop is separated in isovolumic contraction (1), ejection (2), isovolumic relaxation (3) and filling (4) of the left ventricle. Athletes show a normal contraction and relaxation pattern whereas in AS patients systolic rotation and diastolic untwisting is prolonged.

where the cavity lumen remain almost unchanged (Fig. 6, 1). This phase is followed by the ejection phase of the LV (Fig. 6, 2) where rotational motion is significantly reduced. After the ejection phase, a fast backrotation in opposite direction of the systolic rotation can be observed (Fig. 6, 3). During this period, almost no changes in cavity lumen are detected (isovolumic relaxation). In the subsequent filling phase (Fig. 6, 4), no major rotational component can be seen. This means, that there is a distinct separation of rotation and ejection or untwisting and filling, respectively in the healthy heart. At the base, a counterclockwise rotation in parallel to the apical rotation can be observed during isovolumic contraction (Fig. 7). However, the rotation velocity is reduced in comparison to the apex (Table 2, \( \omega_{\text{min}} \)). Immediately after isovolumic contraction, the clockwise untwisting of the base starts. Thus, the healthy human heart performs a wringing motion during systole, with a counterclockwise rotation at the apex and a clockwise rotation at the base (105-107,113,125). The opposite rotation of apex and base typically does not start before the ejection phase (Fig. 5a and 7). Maximum rotation at the apex was 5.7±1.8 Deg in rowers, whereas rotation velocity during isovolumic
3.1 Hypertrophied Hearts

contraction was measured $91.3 \pm 33.0$ Deg/s (Fig. 5b) and is within the same range as the controls ($p=0.9$). Maximum untwisting velocity was $-55.9 \pm 7.8$ Deg/s and is identically in controls ($p=0.9$). The time interval between the timepoint of the smallest lumen and maximum backrotation velocity ($T_{untwist}$) was $50.7 \pm 23.3$ ms ($=16.9 \pm 7.7 \%$ in percent of end-systole). This time interval is absolutely identical for rowers and controls. In the rotation-area loop of Fig. 6, a distinct separation of rotation and contraction or untwisting and filling can be observed in rowers. Again, apical untwisting in the rower's heart occurs during isovolumic relaxation (125).

However, at the base of the athlete's heart a high untwisting velocity (Fig. 7) can be observed when compared to controls ($\omega_{min} = -35.8 \pm 9.4$ Deg/s vs. $\omega_{min} = -21.8 \pm 12.4$ Deg/s; $p<0.05$). In the athlete's heart, a wringing motion with a counterclockwise rotation at the apex and a clockwise rotation at the base can be also found during systole. Similar to the motion in controls, the baso-apical wringing motion of the athlete's heart starts right after the isovolumic contraction phase. During early systole, base and apex rotate synchronously in counterclockwise direction. During the ejection phase, the base changes its rotation from counterclockwise to clockwise, yielding a
torsional deformation of the heart. At this timepoint, the rotation velocity at the apex is reduced. This is identically to the findings in controls.

Maximum apical twist amounts to 12.3±4.7 Deg in patients with aortic stenosis, which is significantly higher than in volunteers (6.8±1.0 Deg, p<0.01) or athletes (5.7±1.8 Deg, p<0.01). Rotation velocity in early systole is 98.7±37.8 Deg/s which is not different neither from controls (p<0.6) nor from rowers (p<0.7). However, maximum untwisting velocity is slightly higher with respect to controls (-80.0±28.8 Deg/s vs. -54.8±16.5 Deg/s, p<0.08) or athletes (-55.9±7.8 Deg/s, p<0.08). The untwisting time in AS patients is 88.43±19.3 ms (=33.4±6.3%). Compared to controls, untwisting time is prolonged not only for the absolute value (p<0.01) but also in relation to systolic ejection (p<0.001). AS patients show also a delayed untwisting with respect to the rowers p<0.05 (p<0.001 for percent changes). The rotation-area loop in Fig. 6 clearly shows the difference of AS patients in comparison to controls or rowers: Systolic contraction and rotation are in phase. During diastole, untwisting and filling of the left ventricle occur simultaneously. This means that there is no separation of rotation and contraction or untwisting and filling as seen in the normal heart. However, the wringing motion of the pressure overloaded heart due to aortic stenosis is maintained during systole.
MR myocardial tagging has the potential for studying non-invasively regional cardiac motion of the left ventricle with high spatial and temporal resolution. By the application of a sophisticated MR tagging procedure, the fading of the tags can be suppressed and, thus, systolic as well as diastolic motion becomes accessible within one single imaging procedure. Additionally, by the application of a slice following procedure, the effects of through-plane motion can be suppressed. As a consequence, motion of the same tissue elements can be traced reliably throughout the entire cardiac cycle. Due to the high temporal resolution (35 ms), rapid cardiac motions such as systolic twisting and diastolic untwisting can be recorded. By the use of line tags, as an alternative to rectangular grids, overall measurement time can be reduced and automated evaluation is facilitated.

**Rotation in the normal and in the athlete's heart**

During early systole, the normal heart rotates counterclockwise at the base and apex. The baso-apical torsional deformation is then built up during the ejection phase of the left ventricle (=systolic wringing motion). During the ejection phase, the apical rotation velocity is slowed down. This might be explained with the motion of the base, which starts to rotate in opposite direction (clockwise) at this timepoint and consequently hampers apical rotation mechanically. During isovolumic relaxation, a rapid apical clockwise untwisting which precedes diastolic filling of the LV can be reported (125). In the healthy heart, rotation and contraction or untwisting and filling, respectively are temporally separated motion components.

In the physiologic hypertrophied heart of the rowers, there is practically no qualitative and quantitative difference in the rotation pattern at the apex when compared to the healthy. Moreover, rotation and contraction or untwisting and filling are also separated similar to the controls. Thus, no evidence of altered myocardial systolic or diastolic properties are found in the athletes heart (138-140). In controls and rowers with physiologic hypertrophy basal clockwise and apical counterclockwise rotation can be observed during the ejection phase of the LV. Presumably, this is a consequence of the complex fiber orientation within the ventricular wall. This wringing motion helps the
left ventricle to achieve a high intraventricular pressure with minimal systolic shortening comparable to the wringing of a wet towel to squeeze the water out. By this mechanism the heart can minimize energy expenditure.

**Rotation in the pressure overloaded heart due to aortic stenosis**

Pressure overload hypertrophy is associated with an increased systolic rotation at the apex, where a decrease in rotation velocity after isovolumic contraction is hardly observed. Diastolic untwisting is prolonged and delayed into the filling phase of the left ventricle. At the base, practically no rotational motion is observed. This passive basal rotation behavior presumably is responsible for the unreduced apical rotation velocity during systole: Active basal untwisting which hampers mechanically apical rotation is absent. Due to the prolongation of systolic twisting and diastolic untwisting there is an overlap of cardiac rotation and contraction or untwisting and filling, respectively at the apex of the pressure overloaded hearts. In the pathologically hypertrophied heart due to aortic stenosis, systolic and diastolic function are altered. Pressure overload hypertrophy results in an addition of new sarcomeres in parallel with the existing ones (110). Furthermore, an increase in the amount of collagen with a consequently increased elastic stiffness has been reported (141-145). This rearranged fiber architecture might explain the stiffening of the valvular plane with a subsequently reduced basal rotation. However, the baso-apical torsional deformation of the heart is increased in AS patients. Consequently, an increase in torsional deformation seems to result from the loss of basal clockwise rotation. The increased torsional deformation is achieved by a more pronounced apical twist. Thus, these alterations in the 3D motion of the heart may explain the functional changes of the myocardium with the occurrence of diastolic dysfunction in aortic stenosis due to the prolonged and delayed untwisting which results in an overlap of relaxation and diastolic filling.

**Limitations**

The advantages of a longer tag persistence and the slice following procedure result in a doubling of measurement time. Furthermore, subtraction based MR imaging techniques
are prone to breathing artifacts. Therefore breathhold strategies or MR navigator controlled techniques are strictly needed.

Mean age was different in the 3 groups. Patients with aortic stenosis have a higher age when compared to controls or athletes (Table 1). Aging potentially might be a reason for altered systolic twist mechanics or relaxation of the heart. However, recent investigations concerning the age dependency of myocardial muscle mechanics are rather contradictory to such a hypothesis.
References


3.1 Hypertrophied Hearts


134. Stuber M, Fischer S.E, Scheidegger M.B, Boesiger P: Slice Following in Cardiac Imaging with Optimized RF Pulse Angles. in *Proc SMRM, twelfth scientific meeting*, 1993;1:418


3.1 Hypertrophied Hearts


144. Thiedemann KU, Holubarsch C, Medugorac I, Jacob R: Connective tissue content and stiffness in pressure overload hypertrophy: A combined study of morphologic, morphometric, biochemical, and mechanical parameters. Basic Res Cardiol 1983;78:140-155

3.2 Long Axis Contraction of the Human Heart

Abstract

During systole, the heart does not only perform a purely radial contraction with respect to the short axis. Simultaneously, a translational motion of the valvular plane towards the apex can be observed. If spatially fixed slices with respect to the scanner coordinate system are acquired, this long axis contraction results in through plane motion effects in perpendicularly oriented short axis images. Hence, not always the same tissue is visualized in these images which are acquired at different timepoints during the cardiac cycle. This leads to interpretation errors, the results of the analysis are falsified, and quantification of functional parameters associated to the heart becomes unreliable. In the present study, the severity of these effects is investigated. Long axis contraction is quantified on different levels of the myocardium for the left and the right ventricle in 8 healthy humans.
Introduction

The fiber architecture in the heart results in a highly complex locally and temporally dependent 3D heart wall motion. A wringing motion of the left ventricle (LV) with a counterclockwise rotation at the apex and a clockwise rotation at the base during the ejection phase has been reported. This potentially stores energy in the muscle tissue which is released during the isovolumic relaxation phase of the cardiac cycle. In the healthy heart, this results in a fast untwisting at the apex. Additionally to the baso-apical wringing motion, a shearing between epi- and endocardial muscle layers of the LV are observed. The thickening of the endocardial layers during systole is increased with respect to the epicardial layers. On short axis images, mostly a radial contraction of the left ventricle towards the cross sectional center of gravity is observed during systole. In contrast, the right ventricle (RV), which is of a completely different geometrical shape,

![End Diastole](image1)

![End Systole](image2)

**Fig. 1.** Basal images of the heart of a healthy human. **Upper row:** End diastolic acquisitions. **Lower row:** End systolic images. **Left column:** Images acquired with a tagging sequence including slice following characteristics. **Right column:** Images acquired with a standard tagging technique without slice following properties.
performs not a radial contraction towards its center of gravity. It rather moves towards the left ventricular center of gravity. However, the right ventricle is not passive and its ejection is not only induced by the thickening of the septum. It shows a distinct circumferential shortening. In parallel with these inplane motion components the heart shows also an interesting motion pattern with a translational component of the base towards the apex during systole.

If spatially fixed slices with respect to the scanner coordinate system are acquired, this long axis contraction leads to through plane motion effects in perpendicularly oriented (to the long axis) short axis images (146, 147). Thus, not always the same tissue elements are visualized in short axis images which are acquired at different timepoints during the cardiac cycle. If this long axis contraction is neglected, interpretational errors occur and the results of the analysis are biased. The consequences of such through plane motion effects are documented in Fig. 1: Basal short axis sections of the same human myocardium which were acquired with two different MR tagging-techniques are shown. In the upper row, end diastolic images are shown whereas end systolic acquisitions can be seen in the lower row. The two images in the right column were acquired with a technique without slice following capabilities (meaning that the signal was derived from spatially fixed planes with respect to the scanner coordinate system) “SPAMM” (148, 149). In contrast, the two images on the left were acquired with a slice-following technique “CSPAMM” (150, 151). It is obvious, that the anatomical structure of the end diastolic images in the upper row do not differ significantly for both techniques. However, on the end systolic images below, the image acquired with the standard imaging sequence shows a different anatomical structure when compared to the image besides. In the region of the arrow, anatomical details of the right ventricular outflow tract are visible. These structures are absent in the end diastolic image above, meaning that not always the same tissue is imaged for different heartphases using conventional imaging methods.

Through plane motion induced by long axis contraction is a serious drawback. Measurements of functional parameters associated to the heart such as wall thickening, ejection fraction, wall motion, stress/strain, flow in the coronary arteries, or perfusion e.g. might become unreliable and inaccurate.
In the present work, the amount of this through plane motion is investigated. Quantitative results of local long axis contraction in 8 healthy volunteers are presented for the LV as well as for the RV at different myocardial levels (base, equator, apex).
Methods

For image acquisition, a CSPAMM (151) based tagging sequence was used prior to an ECG triggered multi heart-phase gradient echo imaging sequence. Due to its slice-following properties, this tagging technique allows to assess directly plane projections of the three dimensional trajectories of any arbitrary cardiac point.

Double oblique images of the long axis (4-chamber view) were acquired in 8 healthy volunteers using a cardiac surface coil for signal acquisition. In Fig. 2 on the left hand side, an end systolic long axis acquisition overlaid with the local trajectories is shown. 16 heart-phases were acquired with a time interval of 35 ms. (FOV 360 x 360 mm; scan matrix 256 x 256; Tₑ 5.4 ms). In order to reduce motion artifacts caused by breathing, all volunteers were investigated in prone position using a repetitive breath-hold scheme (TR = four RR intervals) by which the breathing activity of the volunteer is synchronized to the data acquisition intervals. For the enhancement of the tagging contrast variable RF flip angles for imaging were applied. All measurements were performed on a 1.5 T whole body scanner (Philips Gyroscan ACS II).

In the stripe-tagged images, the intersection points between the anatomy of the myocardium and the dark tagged stripes were traced semi-automatically for each acquisition. Trajectories of 72 points on the myocardium (Fig. 2, left) were then calculated automatically for all heartphases. These trajectories represent the real 2D projection of a 3D motion. The projections of these trajectories onto the long axis (d, Fig. 2, right) were subsequently calculated at a basal, an equatorial and an apical level of the LV and the RV.
Results

The quantitative results are documented in Fig. 3. As expected, maximum systolic long axis contraction was observed for basal levels (points 1 & 2, Fig. 3, right). For the RV, this contraction amounts to $21.7 \pm 1.5$ mm (point 1, Fig. 3, right) whereas $11.9 \pm 3.7$ mm (point 2, Fig. 3) was measured for the LV. Thus, long axis shortening of the RV is significantly higher than of the LV ($p < 0.0001$). At the equator, the contraction towards the apex was still $10.5 \pm 2.3$ mm for the RV (point 3, Fig. 3) and $5.9 \pm 1.6$ mm for the LV (point 4, Fig. 3). On equatorial levels, the RV shows still a more pronounced long axis contraction than the LV ($p < 0.002$). At the apical tip (point 5, Fig. 3), a small backwards motion of the apex towards the base is observed ($-2.3 \pm 1.3$ mm) which is also documented in the example of Fig. 3 on the left hand side. On all sites and levels, the standard deviations of the mean are relatively small when compared to the mean long axis contractions (Fig. 3: For the right ventricular basal level e.g., the mean contraction is more than 14 times the standard deviation).

Fig. 2  **Left:** 4-chamber view of a healthy volunteer acquired at end systole. The tagged image is overlaid with the local systolic trajectories.  **Right:** Schematic 4-chamber view. The amount of systolic long axis contraction is quantified for the locations (1). (5).
Fig. 3. Mean long axis contraction ±SD [mm] of 8 healthy subjects. RV=right ventricle, LV=left ventricle. The quantified locations correspond to the points documented in Fig. 2 (right).

**Discussion**

Systolic long axis contraction in healthy volunteers amounts up to maximum values of 25 mm or even more for basal, right ventricular regions (lateral, free wall). In consequence, misregistration on the images may be severe in specific regions of the heart. Systolic long axis contraction of the right ventricle is significantly higher than for the left ventricle. This is observed for the basis as well as for equatorial levels.

At a basal level, the plane of the originally selected tissue of a myocardial short axis section is not only translated towards the apex but also tilted during systole. At the equator, the same behavior with a reduced amplitude can be reported. The contribution of the long axis shortening to the systolic volume change seems to be higher for the RV when compared to the LV since the right ventricular long axis contraction is significantly increased. Obviously, the right ventricular output performance is mainly achieved by a contraction in long axis direction. The apex of the human heart performs a relatively small translational motion towards the base. The standard deviations of the means are surprisingly small for the 8 volunteers. Therefore, the definition of a simple linear contraction model for the long axis is feasible.
Conclusions

On short axis acquisitions of the human heart, the amount of through plane motion exceeds by a factor of 2-4 the commonly used slice thicknesses in cardiac MR imaging. Hence, the accuracy of conventional cardiac MR is limited. Imaging techniques and strategies helping to overcome these through plane motion effects are strictly needed. A priori knowledge of the amount of the through-plane motion at a given location of the myocardium with respect to the long axis is helpful for the development of appropriate imaging strategies including any kind of slice tracking (146, 150, 152).
References


3.2 Long Axis Contraction
CHAPTER 4

4.1 Discussion

MR imaging methods

MR myocardial tagging allows the non-invasive assessment of cardiac motion at different sites and layers of the myocardium with a high spatial and temporal resolution. By the application of a sophisticated MR tagging procedure, the fading of the tags may be avoided and consequently systolic as well as diastolic heartwall motion becomes accessible within one single examination. By the application of a slice following imaging procedure, the effects of through-plane motion are suppressed and always the same tissue of the myocardium is measured in the different heartphase images. Optimized RF excitations for imaging enable to acquire up to 25 heartphase images with a constant tagging contrast and a temporal resolution of 35 ms. Thus, the fastest occurring motion components in the myocardium - apical twisting and untwisting - are recordable. By the combination of MR myocardial tagging with ultra fast imaging sequences, the measurement time can be reduced from approximately 10 minutes to a single breathhold period of 10 seconds typically. Therefore, the major limitations of the technique, the long measurement time and the sensitivity on breathing induced motion artifacts are no longer true.

By a slight modification of the scanning protocol, real-time imaging of the heart becomes technically feasible on commercially available MR systems. ECG triggering and breath controlling are not necessary under real-time conditions. Unreliable R-wave detection due to thoracic muscle contractions or charge separating flow in the presence of the static magnetic field does not hamper ECG triggering and consequently image quality anymore. Breathing or patient motion in general as occurring under physiologically induced stress are no longer limiting factors which influence the
geometrical reproducibility of each heartbeat in a sensitive way. Therefore, instantaneous imaging during physical exercise or the investigation of arrhythmic heart wall motion is feasible. Since tagging techniques with prolonged tag persistence and slice following characteristics inherently require two acquisitions per heart phase image, they are not applicable in real-time.

**Evaluation procedure**

The evaluation tool in combination with improved tagging methods provides a powerful tool for physiological and pathophysiological research in the human heart. It does not only generate quantitative data from tagged time series of images. Due to the various visualization utilities it allows also a deeper insight into the local heart wall motion and cardiac dynamics in general. With the various interfaces to standard image formats or ASCII, documentation of the results or further statistical processing of the data is ensured. Imaging strategies and evaluation procedure have shown to be strongly influenced by each other. Imaging of orthogonally line tagged time sets of images does not only result in a significantly reduced measurement time, but it also facilitates automatic evaluation procedures since lines are much easier to be detected than grids or grid intersection points. By the implementation of tag line detection based on active contour models, evaluation time per slice could be reduced significantly. However, it still is in the order of 1 hour.

**Heartwall motion**

During isovolumic contraction, the healthy heart rotates in the same direction at the base and at the apex. In the subsequent ejection phase, a counterclockwise rotation at the apex occurs simultaneously with a clockwise rotation at the base. This yields a baso-apical torsional deformation of the left ventricle. During the ejection phase, the apical rotation velocity decreases in the healthy heart. This can be explained with the motion of the base, which starts to rotate in opposite direction at this time point and consequently hampers apical rotation mechanically. Simultaneously with the torsional deformation of the left ventricle, a shearing between epi- and endocardial muscle layers
is observed. In diastole, a rapid apical untwisting is followed by the filling phase of the ventricles where practically no rotational component can be seen.

Pressure overload hypertrophy is associated with an increased rotational motion at the apex, where the decrease in rotation velocity during the ejection phase is hardly observed. During diastole, untwisting is prolonged and delayed into the filling phase of the ventricles. This might explain the occurrence of diastolic dysfunction with delayed and incomplete relaxation in these patients. At the base, practically no rotational component is observed in these hypertrophied hearts. Presumably, this results from the stiffening of the muscle tissue at the valvular level of the heart in these patients. In contrast to the healthy heart, an overlap of rotation and contraction or untwisting and filling, respectively is found in the pressure overloaded patients due to aortic stenosis.

In the physiologically hypertrophied heart of the rowers, there is practically no qualitative and quantitative difference in the rotation pattern at the apex when compared to the normal healthy subjects. Apical rotation is almost identical. Moreover, rotation and contraction or untwisting and filling phases are also separated similar to the controls. Thus, no evidence of altered myocardial systolic or diastolic rotational properties are found in the athletes heart. In infarction patients, a prolonged and delayed untwisting at the apex similar to the aortic stenosis patients occurs. Additionally, a reduced rotation component is observed in the infarcted region which is accompanied by the loss of epi-endocardial shearing of the muscle layers. In left bundle branch block patients with a defect in the conduction system, a temporal dispersion of maximum circumferential shortening is observed in the different segments of the left ventricle.

First results obtained in heart transplant patients show a reduced amplitude in apical rotation in the presence of rejection of the heart.

**Outlook and further developments**

The motion data obtained by the evaluation of MR tagged images allows to compute the local mechanical tissue properties of the myocardium (stress/strain). However, presently there exist two major limitations: First, the spatial resolution in the images has to be further improved with stronger gradient systems and/or technically supported feed-back to the patient allowing to achieve a reproducible exhaled state. Second, the muscle tissue is highly anisotropic. This means that the trajectory of any arbitrary point on the
4.1 Discussion

Myocardium has not only to be known in its 2D projection as it is the case at the moment. Dynamic 3D information is needed for finite element modeling. Assessment of locally and temporally resolved 3D heartwall motion can either be achieved by combination of orthogonal stacks of images, by a direct 3D grid tagging with subsequent 3D acquisition or by encoding through plane velocity into the MR signal phase. In combination with ultra-fast imaging techniques, scanning time becomes reasonable for such techniques. Identically to the 2D case, quantitative 3D motion data has to be extracted from the images. This requires even more complex image evaluation strategies with robust automated procedures. Finally, the extraction and the visualization of the relevant information has to be ensured, too.

Clinically, it still has to be further investigated in what respect MR myocardial tagging provides new and unique diagnostic information when compared to gold standard techniques in cardiology. First results obtained in an ongoing study - heart transplant patients with rejection - have already shown very promising preliminary results. Eventually, MR myocardial tagging will become a real alternative for biopsy during therapy and follow-up in these patients.

The studies concerning real-time imaging are very promising. They allow to compare local heartwall motion at rest and under physiologically induced stress conditions. For the first time, consequences of arrhythmias on the heart wall dynamics can carefully be investigated. Real-time imaging of the heart would also help to quantify the influence of breathing on the bulk motion of the heart. The accuracy and the functionality of any device for measuring the breathing level during MR studies can be investigated. Potentially, instantaneous imaging of the heart could also be applied for interactive, time efficient plan scanning. In combination with tissue tagging, real-time imaging of the heart might be applied for monitoring purposes since beat-to-beat variations, local hypokinesis or non concentric regional contraction can be detected. Thus, real-time cardiac imaging provides additional information which evidently improves the value of conventional cardiac MR.
APPENDIX A

A.1 Slice Following Cardiac Imaging

Abstract

Conventional MR imaging techniques generally acquire spatially fixed slices with respect to the scanner coordinate system. In a quantity of cardiac applications, where time resolved short axis images are acquired, this leads to unreliable results: During systole, the heart performs a radial contraction with respect to the short axis which is accompanied by a long axis contraction where the base moves towards the apex. This long axis contraction results in through plane motion in short axis acquisitions. Therefore, not always the same tissue is imaged in different heart phase images. This leads to interpretation errors with subsequently falsified results of the analysis. A MRI imaging technique that allows to compensate for through plane motion is proposed in the present paper. First, the theoretical background based on the mathematical analysis is discussed. Subsequently, the resulting slice following MRI sequence which was implemented and tested on a Philips Gyroscan ACS II System is presented. For the documentation of potential effects associated to through plane motion, a volunteer study is added in a second part. Functional parameters derived from examinations with a slice following sequence are compared to those from a conventional technique which does not take through plane motion into account.
Introduction

It had been pointed out for years, that MR studies tend to overestimate wall thicknesses of the myocardium when compared to gold standard methods for measuring the wall thickness (1). On the one hand, this overestimation may be caused by the fact, that the heartwall is not imaged perpendicularly. In this case, MR images fail to show the shortest transmural distance and hence, wall thickness is obviously overestimated (Fig. 1).

![Fig. 1. Overestimation of the wall thickness due to non-perpendicular projection.](image)

On the other hand, it is not so easy to evaluate the endocardial borders due to geometrical irregularities caused by e.g. papillary muscles. In the present paper we want to document, that additionally to these two mentioned effects, through plane motion phenomenons are also responsible for a misregistration of end systolic wall thicknesses when compared to end diastole and hence, an overestimation of wall thickening results. During systole, a long axis contraction of the myocardium is observed where the base of the heart moves towards the apex. This contraction amounts up to 2 cm for the left (1), and even more for the right ventricle and depends on the myocardial segment and its position with respect to the long axis (2, 5, 6). In contrast, the slice thickness for the imaged short axis section of the myocardium should be restricted to a few millimeters. This means, that the selected tissue of the myocardium moves through a spatially fixed
Appendix A

imaging plane during the cardiac cycle. Thus, the amount of this through plane motion considerably exceeds the thickness of the selected slice. Motion perpendicular to the imaging plane results in images acquired at different myocardial levels. Therefore, there is no possibility to compare measurements from the same myocardial tissue throughout the cardiac cycle. This misregistration means that regional functional analysis is either highly inaccurate or fails completely. Accurate quantification of functional cardiac parameters such as wall thickness, wall thickening and ejection ratio derived from multiple heartphase short axis images provides the possibility to compare the same tissue of the myocardium at different time points during the cardiac cycle.

There exist several approaches to solve this problem (1-3, 7-9). But techniques like 'Tagging and Slice Isolation' (1) suffer from image contamination of adjacent tissue with different $T_1$ and are hardly multi heartphase capable because the desired tissue can only be imaged at one specified time point and not throughout the entire cardiac cycle. A further strategy (7), based on 3D phase contrast method, determines the place of the initially selected tissue by a time integration of the 3D velocity map of several slices of the myocardium. This integration may lead to a systematic error for the estimation of the position of the desired slice which strongly depends on the temporal resolution and the placement of the acquired slices (9). Alternative approaches (2) try to involve a priori knowledge: Based on images acquired perpendicular to the desired slice the amount of through plane motion can be estimated and the results finally can be corrected. These techniques may fail to take regional variations of through plane motion into account (4), because a too great series of assumptions has to be made. A promising approach to solve the problem of the through plane motion was the application of a STEAM-based slice following sequence (10-12), where STEAM-preparation is only applied to the desired tissue. In subsequent readouts including STEAM-demodulation, only signal from the originally STEAM-prepared slice would be derived for different heartphases. But this technique has shown to suffer from limitations resulting in signal loss if the tissue of the desired slice is deformed or tilted during the heart contraction (12).

A new method for the assessment of cardiac parameters using a slice following technique which is based on a subtraction method is presented: Immediately after the detection of the R-wave of the ECG, a thin slice of 6-8mm is labelled by the inversion of the magnetization. Subsequently, multiple heartphase images are acquired using a
multi heartphase imaging technique. Hereby, a thick slice which encompasses the potential extent of the selected tissue is imaged. This procedure including labelling and imaging is performed twice, whereby the sign of the labelling function is inverted for the second experiment. The subtraction of these two sets of acquisitions finally results in multiple heartphase images of only the initially labelled tissue.

In the present paper, the theoretical background of this sequence is discussed. Based on this theoretical part, a series of improvements concerning the signal to noise ratio are proposed. This technical consideration is followed by a volunteer study, in which 10 healthy volunteers were investigated with a conventional imaging technique (C). In order to get comparable results for functional parameters like wall thickness (WT) and wall thickening (dWT) and for the quantification of inaccuracies resulting from through plane motion, all volunteers were investigated additionally by the application of the described slice following method (SF). Finally the so obtained quantitative parameters are discussed.
Methods and Materials

Slice following principle

Immediately after the detection of the R-wave of the ECG \((t = t_0)\), a thin slice of 6-8 mm \((-dz, \text{Fig. 2})\) is labelled by the inversion of the magnetization. Subsequently, multiple heartphase images are acquired using a multi heartphase imaging technique.

Hereby, a thick slice \((=ds, \text{Fig. 2})\) which encompasses the potential extent of the selected tissue \((-\text{distorted, dark slice, Fig. 2})\) is imaged. This experiment including labelling and imaging is performed twice, whereby the sign of the labelling function is inverted for the second time. The subtraction of these two sets of acquisitions finally results in multiple heartphase images of only the initially labelled tissue. As a prerequisite for such an approach, the labelled tissue always has to stay within the imaged volume (Fig. 2). The slice following capable pulse sequence which bases on the theoretical considerations (following detailed in the next paragraph) is presented in Fig. 3. This sequence consists of two preparation phases (Fig. 3; a & c) preceeding two multi heartphase imaging parts (Fig. 3; b). In order to obtain maximum labeling efficiency in terms of relative signal level, the magnetization within the thin slice has to be set to +1 for the first and -1 for the second experiment, respectively. For this purpose, the

Fig. 2. Through plane motion principle: The initially selected slice \((t = t_0)\) at the position \(z_0 \pm dz\) moves and distorts during the cardiac cycle with respect to its initial state. \(dz = \text{thickness of the initially selected slice}; ds = \text{thickness of imaged volume}; \tau = \text{time delay between slice selection and imaging.} \)
magnetization of the thin slice is inverted due to the slice selective 180° RF pulse (Fig. 3; a) and is uninfluenced or set to +1 for the second experiment (Fig. 3; c). In the acquisitional part of the sequence, a volume which is large enough to encompass the extend of the initially selected tissue (Fig. 2, ds) is imaged.

**Theoretical background**

As documented in Fig. 2, the initially selected slice \((t = t_0)\) at the position \(z_0\) moves and distorts during the cardiac cycle with respect to its initial state. The object to be imaged is supposed to be at thermal equilibrium before any MR experiment has been started. The spatially dependent equilibrium magnetization can be written as \(M_0(x,y,z)\), or \(M_0\) for simplicity. The magnetization of a thin slice is modulated or labelled immediately after the R-wave of the ECG. Considering a situation as documented in Fig. 2, the initially selected tissue (prepared slice at \(t = t_0\)) of the myocardium moves towards the apex during systole and moves back again to the initial position during diastole. Therefore, a volume which has to be thick enough to encompass the extend of the previously selected slice is imaged afterwards. In order to describe the contrast behavior during the imaging sequence, we consider a series of \(n\) images acquired by a gradient

---

**Fig. 3.** Slice following pulse sequence. Prior to a standard multiphase imaging sequence (b), a slice selective inversion of the magnetization (a) is applied to the tissue. For the second set of acquisitions, no slice selection (c) precedes the imaging sequence (b). The number of heartphases is denoted as \(n\).
echo multi heartphase imaging sequence as shown in Fig. 3. Denote the steady-state magnetization before the modulation of the magnetization in the thin slice (Fig. 2) at end diastole by $M_{ss}(x, y, z)$ where $z$ is the slice selection direction and $x$ or $y$ is the readout direction. The times indicated in this paper usually refer to the R-wave of the ECG as $t = t_0$.

The $z$-magnetization after the application of a slice selection (Fig. 3, a) immediately after the detection of the R-wave ($t = t_0$) of the ECG is given by

$$M_z(x, y, t = t_0) = m_{ss}(x, y, z) \text{SELECT}(x, y, z) \begin{cases} M_{ss}(x, y, z) \text{SELECT}(x, y, z) & \text{for } z = z_0 \pm \frac{1}{2}dz, \\ M_{vo} & \text{for the rest.} \end{cases}$$

[1]

where the slice selection function describes the spatially dependent modulation of the steady state magnetization. For subsequent considerations, $\text{SELECT}(x, y, z)$ is always -1 or +1 and is influenced by the slice selective inversion of the magnetization (gradient and RF excitation pulse Fig. 3, a). Further, the magnetization outside the selected slice which was not influenced by the application of the selection is denoted as $M_{vo}$. The measured signal is proportional to the transverse magnetization of the entire volume of the thickness $ds$ and can be decomposed in a selected and an unselected part. Due to the longitudinal relaxation described by the relaxation time constant $T_1$, the $z$-magnetization in the selected slice immediately before the first RF imaging excitation pulse (Fig. 3, b) at $t = t_1$ can be written as

$$M_z(x, y, t = t_1) = (M_{ss} \text{SELECT}(x, y, z) - M_0) \exp(-t_1/T_1) + M_0. \quad [2]$$

This $z$-magnetization can now be separated in two different parts $Q_{s1}$ and $Q_{R1}$:

$$M_z(x, y, t = t_1) = Q_{s1} + Q_{R1}, \text{ with} \quad [3]$$

$$Q_{s1} = M_{ss} \text{SELECT}(x, y, z) \exp(-t_1/T_1) \text{ and} \quad [4]$$

$$Q_{R1} = M_0 \left[1 - \exp(-t_1/T_1)\right]. \quad [5]$$

The term $Q_{s1}$ of [4] represents that part of the magnetization which has relaxed in the time period from $t = t_0$ to $t = t_1$. 


A.1 Slice Following

If an RF imaging excitation pulse $\alpha_i$ is applied to the desired slice, the $z$-magnetization of the equations [4] & [5] is scaled by $\cos(\alpha_i)$. Therefore, the two parts of the longitudinal magnetization immediately before the application of the $k^{th}$ RF imaging excitation pulse can be written as

$$Q_{Sk} = M_{ss} \text{SELECT}(x, y, z) \exp(-t_k/T_1) \prod_{i=1}^{k-1} \cos(\alpha_i)$$  \[6\]

for the part containing the information of the selected slice, and recursively

$$Q_{Rk} = (Q_{Rk-1} \cos(\alpha_{k-1}) - M_0) \exp(-\Delta t/T_1) + M_0$$  \[7\]

for the relaxed component of the selected slice. $\Delta t = t_k - t_{k-1}$ is the time period between the RF imaging excitation pulses or simply the heart phase interval. $\Delta t$ is constant for each $k$ since the time period between the RF excitations (Fig. 3, b) is always identical. The relaxed component $Q_{Rk}$ is zero just after the inversion of the magnetization of the slice $dz$ ($Q_{Rk} = 0$ for $t = t_0$, [5]) and increases during the cardiac cycle. The amplitude of the signal $I_k$ after excitation (RF pulse angle $\alpha_k$) at $t = t_k$ which is derived from the two parts $Q_{Sk}$ and $Q_{Rk}$ of the magnetization [6, 7] is proportional to the sum of the transverse part of these magnetizations:

$$I_k \propto (Q_{Rk} + Q_{Sk}) \sin(\alpha_k).$$  \[8\]

Equation [6] documents, that the wanted magnetization of the selected slice i.e. the magnetization containing the labeling information decays due to the longitudinal relaxation with the time constant $T_1$ and additionally due to the repetitive RF excitations of the imaging sequence. In contrast, the relaxed component in equation [7], increases for later heart phases and becomes the more dominant the smaller the time constant $T_1$ is.

The magnetization of the remaining volume which has not been influenced by the labeling procedure (Fig. 3, a) can be recursively written as

$$M_{vk} = (M_{vk-1} \cos(\alpha_{k-1}) - M_0) \exp(-dt/T_1) + M_0$$  \[9\]

for $t = t_k$, where the magnetization $M_{v0}$ at $t = t_0$ is equal to the steady state magnetization $M_{ss}$. Therefore, the sum of the longitudinal magnetizations of the entire volume including the desired thin slice immediately before the $k^{th}$ RF excitation imaging pulse is given by the sum of the components of the equations [6], [7] and [9]:
The signal $I_k$ derived from the transverse component of the resulting magnetization becomes

$$I_k \propto (Q_{Sk} + Q_{Rk} + M_{Vk}) \sin(\alpha_k).$$  \hspace{1cm} [11]$$

Now to achieve a slice following image the signal component $Q_{Sk}$ has to be isolated by a specially designed experimental procedure. The goal of this experiment is the suppression of $Q_{Rk}$ and $M_{Vk}$. Experimentally, this goal can be achieved by the acquisition of two images $A$ and $B$, whereby the selection component $SELECT_A(x,y,z,t_k)$ of image $I_{kA}$ is not equal to $SELECT_B(x,y,z,t_k)$ of image $I_{kB}$. Under this condition, the subtraction of these two images leads to

$$I_{kA} - I_{kB} \propto (Q_{SkA} + Q_{RkA} + M_{VkA}) \sin(\alpha_k) - (Q_{SkB} + Q_{RkB} + M_{VkB}) \sin(\alpha_k)$$

where only the terms $Q_{SkA}$ and $Q_{SkB}$ are different for the two acquisitions $A$ and $B$, and the remaining terms are unchanged:

$$Q_{RkA} = Q_{RkB}$$
$$M_{VkA} = M_{VkB}.$$  \hspace{1cm} [13]$$

Therefore, in consideration of equation [6], the equation [11] can be rewritten as

$$I_{kA} - I_{kB} =$$
$$M_{ss}[SELECT_A(x,y,z,t_k) - SELECT_B(x,y,z,t_k)] \exp(-t_k/T_1) \prod_{i=1}^{k-1} \cos(\alpha_i) \sin(\alpha_k).$$  \hspace{1cm} [14]$$

This equation documents, that the relaxed term $Q_{Rk}$ as well as the term $Q_{ Vk}$ can be eliminated and the selection information is preserved. This means, that the resulting part of this subtraction only contains information about the tissue which was influenced by the slice selection (Fig. 3, a). Maximum signal amplitude can be achieved, if the two selection components $SELECT_A(x,y,z,t_k)$ and $SELECT_B(x,y,z,t_k)$ fulfill the condition

$$SELECT_A(x,y,z,t_k) + SELECT_B(x,y,z,t_k) = 0.$$  \hspace{1cm} [15]$$

By definition, these two components always lie between -1 and +1. In consequence, maximum signal intensity derived from the wanted tissue can be obtained, if $SELECT_A(x,y,z,t_k)$ is set to -1 and $SELECT_B(x,y,z,t_k)$ to +1 or vice versa.
Equation [14] also makes clear, that the labelled information decays under the influence of $T_1$ and is additionally reduced by the consecutive RF excitations. This means that each RF excitation for imaging reduces the amount of the stored information in the $z$-magnetization. However, it should be mentioned that the amplitude of the signal is not linearly related to the reduction of the stored information. This means, that for a signal amplitude of 20%, (with respect to maximum signal $I_{\text{max}} \approx M_0 \cdot \sin(90^\circ) M_z$ and consequently the stored or labelled information is only reduced by 2.1% due to RF excitation.

**Pulse angle optimization**

The image contrast can be optimized by the application of swept RF imaging pulse angles (13). The goal hereby is to choose these angles in such a manner, that the transverse or $xy$-magnetization resulting of the component $Q_{Sk}$ of [6] remains constant for each acquisition. Under the condition that the wanted signal of the selected slice should be distributed equally between the $n$ acquired heartphases, the equation

$$I_{Sk} = I_{Sk+1} \text{ for } k = \{1..n-1\} \quad [16]$$

has to be fulfilled. Based on the equations [14] and [16], the requirement for constant signal amplitude for each heartphase derived from the selected slice can be formulated recursively with the Mansfield formula which has to be extended by the tissue dependent parameter $T_r$ (4):

$$\tan(\alpha_k) \exp(dt/T_1) = \sin(\alpha_{k+1}) \text{ for } k = \{1..n-1\}. \quad [17]$$

In principle, the last pulse angle $\alpha_n$ can be chosen freely. To find constant and maximized signal $I_{Sk}$ in function of $\alpha_n$, a numerical simulation has to be performed. The result is shown in Fig. 4. The dependence of the resulting signal amplitude $I_{Sk}$ on the last RF excitation angle $\alpha_n$ and the parameter $T_r$ is plotted for a heart phase interval of $dt = 80$ ms, $n = 8$ excitations and a $T_r$ of 850 ms (muscle tissue). It is obvious that for shorter repetition times $T_r$, this optimal last RF pulse angle $\alpha_n$ differs significantly from $90^\circ$ for maximized, constant signal intensity.
Signal to noise aspects

Assuming a repetition time of 1000 ms (image acquisition after each R-wave), the iteration of [17] has to be started with an \( \alpha_n \) of 33° (Fig. 4) for a maximized signal amplitude. In contrast, if the image acquisition is performed only after each 4\(^{th}\) R-wave (\( T_r \sim 4000 \text{ ms} \)), optimized signal results with an \( \alpha_n \) of approximately 90°. Considering the maximum possible signal amplitude as \( I_{\text{Max}} = M_{eq} \sin(90°) \), the following signal amplitudes of the two examples above result from the numerical simulation (Fig. 4):

\[
\begin{align*}
I_{Sk(T_r=4000\text{ms})} &= 0.48I_{\text{Max}}; \text{for } k = \{1..n-1\}. \\
I_{Sk(T_r=1000\text{ms})} &= 0.29I_{\text{Max}}.
\end{align*}
\]  

[18]

Due to the reduced recovery phase, the shorter repetition time is reflected in a decreased signal level ([18]). In order to obtain the identical signal to noise ratio (SNR) for both experiments (\( T_r = 1000 \text{ ms} \) and \( T_r = 4000 \text{ ms} \)), multiple signal averages have to be performed for the experiment with a repetition time of 1000 ms. Assuming an identical

![Fig. 4. Numerical simulation of the signal intensity \( I_{sk} \) (k = 1..n) depending on the repetition time \( T_r \), and the last pulse angle \( \alpha_n \) (\( dt = 80 \text{ ms} \); \( T_i = 850 \text{ ms} \); \( n = 8 \) heartphases). For shorter \( T_r \), the last pulse angle \( \alpha_n \) which yields maximized signal amplitude (derived from the wanted slice) differs significantly from 90°. For longer \( T_r (>2000 \text{ ms}) \), \( \alpha_n \) can be defined as 90° without significant signal loss.](image-url)
noise level for the repetition times $T_r = 1000$ ms and $T_r = 4000$ ms, [19] and [20] can be formulated as follows (taking into account that the SNR rises with the square root of the number of signal averages ($= m$)):

$$\frac{SNR}{N} \propto \frac{l_{SNR}}{N}$$  \hspace{1cm} [19]

$$\left(\frac{l_{SNR}}{N}\right)_{T_r=4000\text{ms}} = \sqrt{m} \times \left(\frac{l_{SNR}}{N}\right)_{T_r=1000\text{ms}}.$$  \hspace{1cm} [20]

If [20] is rearranged including the results of [18],

$$m = \left(\frac{l_{SNR}}{N}\right)_{T_r=4000\text{ms}}^2 = \left(\frac{0.49l_{Max}}{N}\right)^2 = 3.$$  \hspace{1cm} [21]

This documents that with a repetition time of $T_r = 1000$ ms, at least $m = 3$ acquisitions or averages have to be performed for reaching the same SNR of one single acquisition with a $T_r$ of 4000 ms. Thus, it is advisable to perform one acquisition every fourth second using the time gap in between the acquisitions for the application of a multi heartphase SF experiment. (n = 8; dt = 80 ms; $T_r = 4000$ ms; $T_l = 850$ ms; $\alpha = 90^\circ$; ds = 20 mm; dz = 6 mm). The signal of each acquisition consists of two unwanted parts $l_{unk}$ (unwanted part of thin slice) and $l_{uk}$ (unwanted part of the imaged volume) and a part $l_{sk}$ which is holding the wanted information. Total signal ($l_k = l_{unk} + l_{uk} + l_{sk}$) is denoted as 100% for each heart phase.

![Signal Composition](image-url)
repetitive breathhold scheme (14) which helps to suppress motion artifacts caused by breathing.

**Optimization of geometrical imaging parameters**

The relative signal amounts coming from $Q_{sk}$, $Q_{rk}$, $M_{vk}$, were computed in a numerical SF experiment. The following parameters served as input: $n = 8$ heartphases; $dt = 80$ ms; $T_i = 4000$ ms; $T_1 = 850$ ms; $ds = 20$ mm; $dz = 6$ mm and $\alpha_q = 90^\circ$ (optimized RF excitation angles according to [17]). In Fig. 5, the relative signal levels of the parts of the magnetization discussed above are plotted for each acquisition of a multi heartphase experiment. The black bars indicate the relative amount (with respect to the total received signal) of the wanted signal component derived from $Q_{sk}$. The white bars show the evolution of the relaxed component $Q_{rk}$ of the selected slice, where the white bars visualize signal coming from the unwanted part of the magnetization $M_{vk}$. The black bars, resulting from the excitation of the thick imaged volume (excluding the thin slice) are scaled with the thickness $ds-dz$. In order to minimize this unwanted signal part, the magnetization $M_{vk}$ should be minimized by choosing a minimized $dz$. As documented in Fig. 1, the thickness of the selected slice ($dz$) and the imaged slice ($ds$) can be chosen freely. However, the ratio for wanted to unwanted signal ($I_{sk}/I_{uk}$) for each acquisition strongly depends on these values:

$$\frac{I_{sk}}{I_{uk}} \propto \frac{dt}{dz} \frac{Q_{sk}}{Q_{rk}+(ds-dz)M_{vk}}.$$  \[22\]

In order to increase the relative amount of wanted signal $I_{sk}$, unwanted signal components which are added to the wanted signal have to be minimized. Then it is obvious, that the term $(ds-dz) \cdot M_{vk}$ in the denominator of [22] should be minimized in order to fulfill this condition. This goal can be achieved by reducing the thickness of the imaged volume ($ds$, Fig. 2, [22]). However, since the selected slice has to stay within the imaged volume ($ds$), this minimization has to be done very carefully by an accurate estimation of the through plane motion at the desired level of the heart (long axis contraction of the myocardium during systole).
**Results**

**Phantom results**

In order to verify the slice following capabilities of the SF sequence, static phantom measurements as indicated in Fig. 6 were performed. Two bottles with different shapes were placed adjacently to each other in the isocenter of the scanner (Fig. 6, a).

![Figure 6](image)

**Fig. 6**. Two bottles with different shapes are placed adjacently to each other. The slice to be selected is positioned only in the bottle closer to the observer (a). The imaged volume encompassed the entire bottle in the foreground and only partly the big bottle in the background. Two experiments with and without initial inversion of the magnetization were performed. (e) shows the reconstructed image of the first of the two acquired data sets in geometrical coincidence to a sagital (b) and a coronal (d) view of the phantom arrangement. This acquisition was performed with the initial 180° inversion of the magnetization within the thin slice. The two images (e) & (f) represent the reconstructed data of the thick imaged volumes, which subtracted finally result in the image (g). It can clearly be visualized that only signal from the initially selected thin slice of the bottle in the foreground remains after subtraction.

The slice to be selected was positioned in the bottle closer to the observer of Fig. 6, a. However, the imaged volume encompassed the entire bottle in the foreground of Fig. 6, a and only partly the big bottle in the background. The selected slice was positionned...
exactly in the isocenter. For triggering the sequence, a simulated ECG signal with an RR interval of 4000 ms was fed to the scanner. The two experiments with and without initial inversion were performed as discussed previously. Fig. 6, c shows the reconstructed image of the first of the two acquired data sets in geometrical coincidence to a sagittal (Fig. 6, b) and a coronal (Fig. 6, d) view of the phantom arrangement. This acquisition was performed with the initial 180° inversion of the magnetization within the thin slice. The two images e & f represent the reconstructed data of the thick imaged volumes, which, subtracted, finally result in the image g of Fig. 6. It can clearly be visualized, that only signal from the initially selected thin slice of the bottle in the foreground remains after subtraction.

Theoretically, fat signal decreases due to the variable RF excitation angles. For verification, the numerical simulation is compared to a SF MR phantom experiment where identical parameters for the simulation and the experiment were used: \( n = 8 \) heartphases; \( \alpha_8 = 90° \); \( ds = 25 \text{ mm} \); \( dz = 6 \text{ mm} \); \( dt = 80 \text{ ms} \); \( Tr = 4000 \text{ ms} \); \( T_{1\text{Muscle}} = 850 \text{ ms} \) and \( T_{1\text{Fat}} = 150 \text{ ms} \).

---

Fig. 7. Comparison of numerical simulation and phantom data. The phantom consists of fat (\( T_1 = 150 \text{ ms} \)) in the upper dark part and of a MnSO₄ - water (\( T_1 = 850 \text{ ms} \)) mixture in the lower bright part. The phantom measurements have been performed with the described multi heartphase capable SF sequence (\( dt = 80 \text{ ms} \); \( T_\ell = 4000 \text{ ms} \); \( n = 8 \); \( \alpha_8 = 90° \)). The numerically simulated as well as the measured signal amplitudes of the phantom experiment are compared. For both cases, the resulting signal amplitude of fat and muscle tissue are presented.
The static phantom of Fig. 7 consists of oil in the upper part \( T_1 = 150 \text{ ms} \) and of a water MnSO\(_4\) mixture in the lower part \( T_1 = 850 \text{ ms} \). The results of the phantom study and the numerical simulation are shown in Fig. 7.

Signal amplitudes are presented for muscle- and fat tissue. For the muscle tissue, the numerical simulation yields a straight line meaning constant signal amplitude from muscle tissue as expected due to the RF pulse angle optimization. The phantom study on the MR system shows minor alteration in the signal derived from muscle tissue. Only for the last acquisition \( n = 8 \) a decreased intensity is observed. This can be explained by an underestimation of \( T_1 \) in the phantom, RF pulse angles slightly too small or due to a non-rectangular slice profile of the initially selected tissue (19). When compared to the simulated data, fat signal in the phantom study slightly decreases faster than the one of the numerical simulation. This phenomenon can as well be explained by the same effects.

**In vivo results**

In Fig. 8, lower part, the two images a and b are the two acquisitions of the imaged volumes at end systole, which, subtracted, yield the image c. Note the black blood within the ventricles and the visibility of the RV. The inner cavities of the ventricles appear black because the initially selected blood within the thin slice moved already out of the thick, imaged area. This means that the labeled spins of the blood within the thin slice moved already out of the thicker imaged volume and therefore don’t contribute any signal to the image. Hence, flowing blood with a through-plane velocity \( v_\phi \) greater than \( ds/t_1 \) appears black which yields a good contrast between muscle and blood.

**Imaging protocol volunteer study**

In order to document that through plane motion may cause errors in the quantification of functional parameters such as wall thicknesses (due to through plane motion), the following volunteer study was performed:

Images were acquired in 10 volunteers aged \( (30 \pm 3 \text{ yr.}) \) without history or physical findings suggesting cardiac diseases. All volunteers underwent the same imaging protocol which included a conventional multi-heartphase FFE imaging method without slice following capabilities and the discussed slice following method in the same session in order to suppress positioning errors of the imaged slice. Double angulated short axis
FIG. 8. Situation at an end systolic timepoint within a cardiac cycle. Left: Subtraction of the large imaged volumes which include the labeled tissue with complementary signs of the magnetization (a and b). The result of this subtraction (c) yields an image containing only information of the initially selected tissue. Signal of the rest of the volume is suppressed due to the subtraction. Right: The same fact as above is demonstrated in an in vivo result. The images a and b are acquisitions of a thick volume (ds = 30 mm) which contains differently labeled thin slices (dz = 6 mm). The result of the subtraction yields an image (c) which preserves only the information of the initially selected thin slice. The here presented images are the fourth acquisition out of eight. The equatorial slice was labeled at end diastole, and images have been acquired 360 ms later at end systole.

view was planned based on two scout scans, whereby the second scout scan was performed in cine mode for being able to estimate the amount of through plane motion (ds, Fig. 2) and hence, to maximize signal derived from the selected, thin slice ([22]).

For both techniques (C & SF), equatorial short axis sections were acquired ECG triggered using a multi heartphase capable gradient echo imaging sequence. The standard FFE imaging sequence involved constant RF excitation angles $\alpha_1$, $\alpha_8 = 45^\circ$. For the slice following sequence, variable optimized pulse angles according to [17] were used. The last pulse angle was set to $90^\circ$ in each case. In order to suppress motion artifacts caused by breathing, a repetitive breathhold scheme (14) was applied with $T_r = 3000..4500$ ms depending on the individual heartbeat rate (Fig. 9). 7 or 8 heartphases were acquired for each volunteer for both techniques. The 3rd or 4th acquisition was usually acquired at the end systolic state of the myocardium. Therefore, the heartphase interval $dt$ varied individually from 55 to 100 ms depending also on the individual heartbeat rate of the volunteer. In plane resolution was $1.4 \times 1.87$ mm for both methods. The thickness of the labeled slices (dz, Fig. 2) was 6 to 8 mm and the thickness of the imaged slice varied from 20 mm to 25 mm and was adjusted to the strength of the long axis contraction of each volunteer. In order to circumvent the influence of non perpendicularly oriented slices with respect to the heartwall as described previously,
equatorial slices of the myocardium were acquired for each volunteer. The equator was defined as mid distance between the apical tip of the inner LV cavity and the aortic root. For the minimization of flow induced artifacts, the signal was acquired in partial echo mode \((T_e = 3.5 \text{ ms})\). The resulting measurement time varied from 8 to 12 minutes depending on the heartbeat rate of the volunteers.

The presented SF sequence was implemented and measurements were performed on a 1.5 T superconductive Philips Gyroscan ACS II whole body system using a cardiac surface-receive coil for signal acquisition.

**Statistics**

All values in the following are given as means ± 1SD. Comparisons between C & SF were performed with a students t-test for paired comparisons. A p-value of less than 0.05 was considered to be statistically significant. For testing whether there exists a linear relation for the parameters measured with the two methods, a least squares fit was performed additionally.
Image evaluation

The multiple heartphase images of C and SF (Fig. 10) have been evaluated with a computer software which was developed at our institute (Alpha AXP workstation, PV Wave). The endocardial as well as the epicardial boundary have been traced manually for each heartphase. With respect to the center of gravity of the mass, the wall thicknesses for each heartphase were then calculated every five degrees starting at the point where the RV leaves LV anteroseptal wall (Fig. 11 c & d). Based on the temporally resolved wall thickness, wall thickening was computed for each individual, too. The locally and temporally resolved data was then stored in ASCII files for further data processing. Since the contrast between muscle and blood is enhanced in late diastolic images when compared to early systolic images (where the blood is still in the imaged volume, Fig. 10), late diastolic images were used for numerical comparison between the two applied methods. The resulting end systolic and end diastolic data are presented in Table 1.

<table>
<thead>
<tr>
<th>Volunteer</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Mean</th>
<th>SD</th>
<th>p</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>WTED\textsubscript{C}</td>
<td>10.1</td>
<td>9.1</td>
<td>8.4</td>
<td>13.7</td>
<td>8</td>
<td>9.6</td>
<td>8.9</td>
<td>10.9</td>
<td>13.4</td>
<td>11.3</td>
<td>10.3</td>
<td>1.6</td>
<td>0.38</td>
<td>0.76</td>
</tr>
<tr>
<td>WTED\textsubscript{SF}</td>
<td>9.4</td>
<td>8.9</td>
<td>6.7</td>
<td>12.2</td>
<td>10.1</td>
<td>9.8</td>
<td>7.6</td>
<td>10.6</td>
<td>10.9</td>
<td>9.8</td>
<td>9.6</td>
<td>1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WTES\textsubscript{C}</td>
<td>16.6</td>
<td>13.7</td>
<td>12.3</td>
<td>16.9</td>
<td>16.8</td>
<td>16</td>
<td>16.5</td>
<td>18.7</td>
<td>19.7</td>
<td>15.3</td>
<td>16.2</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WTES\textsubscript{SF}</td>
<td>14.9</td>
<td>11.7</td>
<td>10.4</td>
<td>15.5</td>
<td>16.8</td>
<td>14</td>
<td>13.4</td>
<td>14.2</td>
<td>17.2</td>
<td>13.8</td>
<td>14.2</td>
<td>1.5</td>
<td>0.04</td>
<td>0.85</td>
</tr>
<tr>
<td>dWT\textsubscript{C}</td>
<td>64</td>
<td>51.1</td>
<td>46.1</td>
<td>23.5</td>
<td>67.8</td>
<td>85.6</td>
<td>71.6</td>
<td>47.1</td>
<td>35.4</td>
<td>60.4</td>
<td>60.4</td>
<td></td>
<td>0.25</td>
<td>0.61</td>
</tr>
<tr>
<td>dWT\textsubscript{SF}</td>
<td>58</td>
<td>31.1</td>
<td>56.8</td>
<td>26.8</td>
<td>65.8</td>
<td>43</td>
<td>76.1</td>
<td>34</td>
<td>58.2</td>
<td>40.7</td>
<td>49</td>
<td>49</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Wall thickness at end diastole and end systole for both methods for each individual. WTED\textsubscript{C}: Wall thickness end diastole C. WTED\textsubscript{SF}: Wall thickness end diastole SF. WTES\textsubscript{C}: Wall thickness end systole C. WTES\textsubscript{SF}: Wall thickness end systole SF. dWT\textsubscript{C}: Wall thickening C. dWT\textsubscript{SF}: Wall thickening SF. Additionally, the mean values including the standard deviations are given (mean, SD). The resulting p-value of the student's t-test and the square root of the coefficient (r) of determination of the least squares analysis are indicated as well.

In late diastole, mean wall thickness of C is only slightly increased in comparison to SF (C: 10.3±1.6 mm; SF: 9.6±1.2 mm; statistically not significant).

This result has been expected, since there is hardly any through plane motion between the selection of the thin slice and late diastole, where the selected thin slice is almost repositioned in its initial state. However, if the end systolic data are compared, an
enhanced wall thickness of C in comparison to SF can be documented in each case (Table 1). The resulting average wall thickness of C yields $16.2 \pm 1.5$ mm. In contrast, the end systolic wall thickness for SF amounts only to $14.2 \pm 1.5$ mm. This means a significantly increased end systolic wall thickness for C ($p < 0.05$). If wall thickening during systole is considered, C indicates a wall thickening of $60.4 \pm 19.7\%$ whereas SF results in $49.0 \pm 13.9\%$. The corresponding p-value of 0.38 indicates only a slight overestimation of wall thickening measured with C which is not statistically significant for the entire collective. However, the individual values are strongly varying which indicates a non-systematic misregistration.
Fig. 12 visualizes the individual wall thickness measurements listed in Table 1. The wall thicknesses of SF and C are compared and visualized in the same graph. In Fig. 12, a, the end diastolic data are presented whereas Fig. 12, b, shows the data derived from the wall thicknesses at end systole. On the x-axis, the wall thickness coming from C is plotted against the values achieved with SF on the y-axis. The dotted line indicates the line of identity, whereas the dashed line results from the linear regression analysis. The corresponding numerical results are indicated, too. It can be clearly seen, that the points are placed slightly below the dashed line at end diastole (Fig. 12, a), which means a relatively small overestimation coming from C. In contrast, for the end systolic timepoint (Fig. 12, b), each datapoint is placed below the line of identity, which yields an increased wall thickness for C. For the late diastolic and the end systolic values of the wall thickness, a relatively good correlation ($r = 0.76$ or $r = 0.85$, respectively) between the results of the two methods can be reported. This indicates that a systematic misregistration of the end diastolic as well as the end systolic wall thickness. However, if wall thickening is considered, the correlation between SF and C decreases ($r = 0.61$), which can also be seen by the scattered datapoints of Fig. 12, c. Hence, the misregistration of the functional parameter wall thickening cannot be considered to be systematically anymore.
Fig. 11. End systolic, equatorial acquisition of a healthy volunteer. In the left column (a & c), conventional images (C) are shown. In the right column (b & d), images acquired with the SF technique are presented. In the lower row (c & d), the measurement of wall thickness is documented. The center of gravity of the left ventricle as well as the separation points of RV and LV serve as reference points of the local coordinate system.

**Discussion and Conclusions**

By the application of a subtraction based slice following technique, imaging of always the same tissue is ensured for different timepoints during the cardiac cycle. The through plane motion induced by systolic long axis contraction perpendicularly to the imaged slice is not anymore a limiting factor. Regardless of the regional variations in the amount of through plane motion, imaging of always the same tissue is guaranteed as long as the labeled slice stays within the imaged volume. Therefore, there's no need for a numerical correction of the data and the sequence can be used for multiple heartphase
experiments. Furthermore, motion of the heartwalls can be tracked directly on robust modulus images without interpolation as it is the case for phase contrast methods. Consequently, an accurate quantification of temporally resolved functional parameters is feasible on all sites and layers of the myocardium. Due to the black-blood characteristics of the sequence, the contrast between the inner cavities and the muscle is optimal for the segmentation of the tissue borders. As a byproduct, even the right ventricle of the myocardium can be tracked (Fig. 10 & 11) - which normally is hardly possible due to through plane motion effects which are very pronounced for the right ventricle (1, 6). Pulse angle optimization leads to a constant signal intensity of muscle tissue and therefore supports computer assisted segmentation. Furthermore, this optimization of the RF angles reduces the intensity of unwanted fat signal, which very often surrounds the myocardium. The appropriate setting of the last RF angle $\alpha_n$ becomes important towards shorter repetition times (e.g. single breathhold methods). From the point of view of SNR, it is advisable to perform one multiple heartphase acquisition every fourth second using the time gap inbetween the acquisitions for the application of a repetitive breathhold scheme which helps to reduce artifacts caused by respiration. Since the here presented slice following method is based on a subtraction technique, irregularities in repositioning of the myocardium between the acquisitions may lead to severe artifacts. Therefore, R-wave detection has to be highly accurate, RR variability has to be taken into consideration and motion irregularities due to breathing have to be suppressed by appropriate strategies like breathholding and/or navigators including patient feedback. The two acquisitions needed for subtraction basically double the required scan time with respect to standard imaging techniques. However, by the combination of this method with fast imaging techniques as discussed in chapter 2.1, this disadvantage becomes relative.
For the experimental part of the study, a significantly increased systematic end systolic wall thickness can be reported if conventional imaging techniques without slice following characteristics are applied. However, the resulting wall thickening during systole shows strong variations if both methods are compared. Even though resulting average values measured with C in comparison to SF are not statistically significant, the individual results of the measurements are severely scattered and yield a non systematic

![Late Diastolic Wall Thickness](image)

\[ y = 0.60x + 3.33 \quad R = 0.76 \]

![End Systolic Wall Thickness](image)

\[ y = 0.82x + 0.85 \quad R = 0.85 \]

![Systolic Wall Thickening](image)

\[ y = 0.39x + 25.26 \quad R = 0.61 \]

Fig. 12. Wall thicknesses measured at late diastole (a) and end systole (b). In (c) the resulting wall thickening is documented. The measurements were performed on images which were acquired with both methods (SF & C). All the graphs are overlaid with the lines of identity and the trendlines of the linear estimation.
misregistration of systolic wall thickening. Therefore, long axis contraction and in consequence through plane motion may lead to misregistrations of functional cardiac parameters which cannot be compensated if conventional imaging techniques are applied.
References


CURRICULUM VITAE

I was born on January 18, 1965, in Biel/Bienne, Switzerland as son of Katharina and Peter Stuber-Hug. In Langenthal, I attended primary, secondary and high school, where I graduated with the Matura Type C (science) degree in autumn 1986.

From 1987 to 1993 I studied electrical engineering at the ETH Zurich. In May 1993 I received my diploma as an eidg. dipl. El. Ing. ETH and started working as a teaching and research assistant at the Institute of Biomedical Engineering and Medical Informatics of the University and ETH Zurich in the magnetic resonance group of Prof. Dr. Peter Boesiger. Here, I worked until April 1997 on the cardio-vascular project, mainly on pulse sequence development for the assessment of heart function, image processing and the coordination of clinical studies in collaboration with the cardiologists of the University Hospital Zurich.

I am married to Franziska Stuber-Wyss since 1994 and we have one daughter, Annina since January 1996.