Advanced Motion Correction and Image Reconstruction for Cardiac Magnetic Resonance

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Abstract

Cardiovascular magnetic resonance is a noninvasive imaging tool that provides high-resolution anatomical and functional images without exposure to ionizing radiation. The unique ability to manipulate contrast and encode functional information into the imaging signal allows for a broad range of clinical application to assess morphological and hemodynamic disorders. With coronary artery disease being the leading cause of death in Western societies, the diagnosis of stenosis in coronary arteries and their hemodynamic relevance play an important role in therapeutic decisions. Long scan duration and artifacts from physiological motion, however, are still major obstacles for the transition into clinical practice.

In the present thesis, new technical developments are presented for scan acceleration and artifact removal in whole-heart coronary magnetic resonance angiography, three-dimensional first-pass myocardial perfusion and cine imaging.

In the first study, a retrospective motion correction scheme is proposed for whole-heart coronary scans with interleaved acquisition of motion information. A 3D nonrigid motion model is derived from 2D motion scouts acquired interleaved with the coronary scan without imposing a scan time penalty. Image reconstruction and motion correction were performed simultaneously by inversion of a forward model describing the transformation from the motion-free image to corrupted k-space data. In a study with ten healthy volunteers, the retrospective nonrigid correction scheme allowed for respiratory gate-free acquisition and hence a reduction in scan time by a factor of two compared to the conventional respiratory gating and acquisition at end-expiration.

Three-dimensional first-pass perfusion imaging is often impaired by respiratory motion artifacts. An iterative k-t principal component analysis reconstruction with nonrigid correction of frame-to-frame respiratory motion is proposed in the second part. Motion information was extracted using shape-constrained image registration of the composite of
training and k-t undersampled data. The validity of the approach was tested for 10-fold k-t undersampling using simulation data and in-vivo measurements.

The third study presents a novel reconstruction technique employing nonlinear transform domains for image reconstruction of undersampled k-space data. The nonlinear mapping from the image domain into a high-dimensional feature space is performed implicitly by kernel principal component analysis. Thereby, corrupted data are projected onto the main principal components in the dot product feature space. The principal components are derived from the surrounding of image blocks. Image reconstruction is performed iteratively with interleaved steps for nonlinear projection and gradient updates to ensure consistency with acquired k-space data. The algorithm was evaluated using undersampled simulation data and in vivo two-dimensional cine and three-dimensional whole-heart coronary data and allows for higher acceleration factors compared to standard compressed sensing reconstruction.

In conclusion, the presented methodological improvements described in this thesis allow for scan time efficient compensation of respiratory motion artifacts in relevant cardiovascular imaging applications including 3D coronary and first-pass myocardial perfusion imaging. Dedicated image reconstruction algorithms have been proposed to push further scan acceleration by exploiting data correlations in both linear and nonlinear transform domain.
Zusammenfassung


In der vorliegenden Arbeit werden neue technische Entwicklungen zur beschleunigten Aufnahme und Unterdrückung von Bildartefakten für die koronare Magnetresonanzangiographie, die dreidimensionale myokardiale Perfusionsbildgebung und für die zeitlich aufgelöste Bildgebung der Herzbewegung vorgestellt.

In der ersten Studie wird eine Methode zur retrospektiven Bewegungskorrektur bei Ganzherzaufnahmen, wie sie zur Darstellung der Herzkranzgefäße benötigt werden, vorgestellt. Hierbei wird durch eine verschachtelte Aufnahme von 2D Bewegungsinformation ein elastisches 3D Bewegungsmodell zur Bewegungskorrektur erstellt, ohne dabei die Messzeit zu erhöhen. Die Bildrekonstruktion und die Bewegungskorrektur wurden simultan durch die Inversion einer Vorwärtsgleichung durchgeführt, die die Transformation vom bewegungsfreien Bild zu den deformierten k-Raumdaten beschreibt. In einer Studie mit zehn gesunden Probanden ermöglichte das Verfahren eine uneingeschränkte Aufnahme während der Atembewegung und damit eine
Reduktion der Messzeit um den Faktor zwei, verglichen mit konventionellen Aufnahmen im ausgeatmeten Zustand.


Zusammenfassend lässt sich festhalten, dass die methodischen Verbesserungen, die in dieser Dissertation beschrieben sind, eine erfolgreiche Korrektur von Bewegungsartefakten für 3D Aufnahmen des gesamten Herzens ermöglichen. Darüber hinaus wurden neue Bildrekonstruktionsalgorithmen entwickelt, die neben linearen auch nichtlineare Korrelationen für beschleunigte Bilaufnahmeverfahren ausnutzen.
1 Introduction

1.1 Cardiovascular Magnetic Resonance for Ischemic Heart Disease

Cardiovascular magnetic resonance (CMR) is increasingly applied for the assessment of patients with known or suspected ischemic heart disease (IHD) (von Knobelsdorff-Brenkenhoff and Schulz-Menger 2012). The unique versatility of CMR to obtain anatomical and functional images allows for the diagnosis of right or left ventricular impairment and helps in guiding therapeutic decisions. In a multi-national study with 11,040 patients (Bruder et al. 2009), CMR was found to provide sufficient diagnostic image quality in 98% of the subjects and a significant impact on patient management was reported in two-thirds of the cases. CMR is an attractive alternative and valuable complement to other techniques such as transthoracic echocardiography (TTE), cardiac catheterization, computed tomography (CT), and single-photon emission computed tomography (SPECT). For example, while invasive coronary catheterization remains gold standard for assessing the degree of anatomic stenosis, CMR stress perfusion allows assessing the hemodynamic consequence of the obstruction (von Knobelsdorff-Brenkenhoff and Schulz-Menger 2012). The following sections briefly introduce the clinically most relevant CMR techniques.

Cine imaging

Cine MR images are acquired in long- and short-axis views using a high-resolution steady-state free precession sequence, which provides high contrast between myocardium and blood pool. The segmentation of the right and left ventricular blood pools allows for determination of systolic and diastolic ventricular volumes, stroke volumes, ejection fraction, and myocardial mass with high reproducibility (Karamitsos et al. 2007). Cardiac wall motion analysis is performed under pharmacological stress, typically by an intravenously administered dosage of dobutamine. Under stress, a relevant coronary stenosis causes
shortage of oxygen supply resulting in wall motion abnormalities (Figure 1.1). In comparison with the continuous acquisition of stress TTE, CMR acquires images only every few minutes. While the accuracy of echocardiography is dependent on the proficiency of the operator to a large degree, the diagnostic accuracy and the image quality of dobutamine CMR is reported to have higher reproducibility and lower inter-observer variability (Syed et al. 2005; Paetsch et al. 2006).

![Systole and Diastole Images](image)

**Figure 1.1** Cine CMR images acquired in systole (left) and diastole (right). The white arrow indicates a wall motion defect.

### Perfusion MRI
Myocardial perfusion CMR imaging captures the first passage of a gadolinium-based contrast agent through ventricles and myocardium in stress and rest condition. The MR image acquisition is performed with a series of ECG-gated T1-weighted images, e.g. using a gradient echo sequence. Demands for high spatial and temporal resolution as well as sufficient cardiac coverage make scan acceleration techniques necessary (P Kellman et al. 2004; Plein et al. 2005; Plein et al. 2007; Manka et al. 2010). Under pharmacological stress, the blood flow in normal coronary arteries is 3- to 5-fold increased whereas no or minimal change is found in severely diseased arteries (Wilson et al. 1990). The segments with a perfusion defect are identifiable by the decreased signal intensity and delayed uptake of the contrast agent as compared to normal myocardium (Figure 1.2). The same sequence is performed at rest after a delay of at least 10 minutes to allow for contrast agent washout. Since the severity of coronary stenosis does not always correlate with its hemodynamic relevance (Gould 2009), a more adequate gold standard for comparison with stress perfusion CMR is the pressure wire derived fractional flow reserve (FFR) (Costa et al. 2007).
Figure 1.2 First-pass myocardial perfusion imaging. A central slice of a 3D myocardial perfusion examination at three time points for peak right-ventricular (RV), peak left-ventricular (LV) and peak myocardial enhancement is shown. A perfusion defect is indicated by the white arrow.

Despite the progress in CMR perfusion imaging methodology, the procedure remains challenging in standard clinical protocols given long breathhold durations, the limited cardiac coverage and dark rim artifacts in phase-encode direction at the boundary of blood pool and myocardium originating from Gibbs ringing and partial volume effects due to the limited number of k-space profiles and the high signal intensity differences between myocardium and blood pool (P Kellman and Arai 2007).

Late gadolinium enhancement
Late gadolinium enhancement (LGE), also referred to as delayed enhancement, offers a way to detect and characterize myocardial infarction. In an area of scarring or fibrosis, the washout time of contrast agents is abnormally prolonged (Figure 1.3) owing to the decreased capillary density in irreversibly injured myocardium (Rehwald 2002). For maximum contrast between infarcted and non-infarcted tissue, a T1-weighted inversion-recovery gradient echo sequence is performed approximately 10 minutes after intravenous administration of gadolinium-based contrast (Simonetti et al. 2001).
Figure 1.3 Late gadolinium enhancement in infarcted tissue. The white arrow indicates infarcted tissue of the left ventricle.

**T2 weighted edema imaging**

Myocardial edema, i.e. increased myocardial water content, is a feature of acute ischemia even if the myocardium is not irreversibly damaged (Abdel-Aty et al. 2009). T2-weighted CMR imaging (Figure 1.4) can detect regional or global increase in myocardial water content as an early stage indicator for irreversible myocardial injury (Friedrich 2010). The development of myocardial edema is linked to the disruption of the energy-dependent ionic transport mechanisms across the cell membrane. Using a spin echo acquisition with long repetition time and echo times of 60 to 64 ms, free water is the most significant contributor to the imaging signal in muscle tissue leading to a relative enhancement of the edema in the image.

Figure 1.4 T2 weighted edema imaging of a healthy subject. Edema in the myocardial muscle would appear brighter than normal tissue.
MR coronary angiography

Coronary arteries have a diameter of few millimeters to submilimeter range and move up to 1 cm during the cardiac cycle (Al-Kwif et al. 2006). Coronary angiography is typically performed in mid-diastole in a window of minimal cardiac motion with a respiratory navigator on the diaphragm to compensate for respiratory motion (Figure 1.5). With a spatial resolution of about 1mm isotropic, MR coronary angiography is still inferior compared to X-ray coronary angiography which provides spatial resolutions down to 0.4 mm (D. a Bluemke et al. 2008).

![Right coronary artery](image1.png) ![Left coronary artery](image2.png)

**Figure 1.5** MR coronary angiography of a healthy subject. A 3D whole-heart scan was reformatted to show the right and the left coronary artery.

1.2 Outline

A brief overview of the principles of Magnetic Resonance from signal generation to spatial encoding is presented in Chapter 2.

Chapter 3 starts with methods for signal-to-noise optimal combination of receive channels in image domain and k-space. Four basic undersampling schemes are presented for scan acceleration. Image reconstruction techniques are introduced to resolve undersampling artifacts by exploiting redundancies in k-space (partial Fourier imaging, parallel imaging) and image space (compressed sensing, k-t methods).
Cardiac and especially respiratory motion and motion correction is covered in Chapter 4. Prospective and retrospective motion correction techniques are introduced and current methods for motion estimations are reviewed.

Chapter 5 deals with acceleration of free-breathing coronary whole-heart scans by nonrigid respiratory motion correction and continuous acquisition during the respiratory cycle.

An iterative implementation for the k-t principal component analysis (k-t PCA) reconstruction technique is presented in Chapter 6 providing improved image quality and suppression of artifacts for frame-to-frame respiratory motion in first-pass 3D myocardial perfusion.

A novel reconstruction technique exploiting nonlinear image correlations in a high-dimensional kernel feature space is presented in Chapter 7.

1.3 Contribution of the Thesis

In the present work, it is demonstrated that whole-heart coronary CMR angiography can be accelerated by at least a factor of two using large respiratory gating windows, if nonrigid respiratory motion correction is employed in image reconstruction. Nonrigid motion correction was implemented based on patient-specific 3D motion models derived from additional data acquired during idle periods of the measurement sequence. The effectiveness of the approach relative to conventionally gated CMR acquisitions is shown using in-vivo measurements in healthy volunteers.

Clinical first-pass myocardial perfusion imaging is often compromised by respiratory motion artifacts in a clinical setting. To address this shortcoming, an iterative algorithm is proposed to correct for frame-to-frame respiratory motion in 3D myocardial perfusion imaging. Data-driven motion estimation is based on low-resolution training data acquired interleaved with k-t undersampling. The approach is validated for 10-fold k-t undersampling using computer simulations and in vivo data sets corrupted by respiratory motion artifacts. Results obtained in healthy subjects and patients demonstrate the value of the method in comparison to breath-held reference data. Using the method a major step forward is made to enable free-breathing whole-heart perfusion imaging.
A novel technique for image reconstruction of undersampled data is proposed which exploits nonlinear transform domains to separate image content from noise and undersampling artifacts. Image reconstruction is performed iteratively with interleaved steps for nonlinear projection and gradient updates to ensure consistency with acquired k-space data. The algorithm is evaluated using undersampled simulation data and in vivo two-dimensional cine and three-dimensional whole-heart coronary data and shown to be superior to compressed sensing reconstruction.
2 Principles of Magnetic Resonance Imaging

2.1 Magnetic Resonance

Applying a magnetic field to matter causes a magnetic response. The induced macroscopic net magnetization $\mathbf{M}$ can be characterized by the volumetric density of magnetic moments due to electric currents (any charged particle with angular momentum has a magnetic dipole moment) and spin, a quantum mechanical property of elementary particles. The magnetic dipole moment $\mu$ is proportional to the angular momentum:

$$\mu = \gamma J$$

where the angular momentum $J$ is the sum of orbital angular momentum $L$ and intrinsic spin $S$. The gyromagnetic ratio $\gamma$ is given by the electric charge $q$, mass $m$, and the quantum mechanical g-factor $g$ ($= 1$ for classical particles):

$$\gamma = g \frac{q}{2m} .$$

The magnetic moment $\mu$ in an external field $B$ has a potential energy defined as the work needed for re-alignment

$$E = -\mu \cdot B .$$

If the magnetic moment is not fully aligned with the magnetic field, it precesses around the direction of the magnetic field with an angular frequency known as Larmor frequency

$$\omega = -\gamma B .$$

Upon irradiation with radiofrequency pulses at the Larmor frequency, the magnetization can be rotated into the transversal plane. The rotating transversal component induces a voltage in receive coils which generates the MR signal.
2.2 Time Evolution

An external magnetic field $B$ exerts a torque on a magnetic moment $\mu$. The time-dependence of the resulting precession is given by the Larmor equation:

$$\frac{d\mu}{dt} = \gamma (\mu \times B)$$  \[II.5\]

For a macroscopic magnetic moment $M = (M_x, M_y, M_z)$, Bloch extended the Larmor equation to include phenomenological relaxation terms $T_1$ and $T_2$. For an equilibrium magnetization $M_0 = (0,0,M_0)$ and an external magnetic field $B(t) = \Delta B(t) + (0,0,B_0)$ the Bloch equations read

$$\frac{dM_x(t)}{dt} = \gamma (M(t) \times B(t))_x - \frac{M_x(t)}{T_2}$$
$$\frac{dM_y(t)}{dt} = \gamma (M(t) \times B(t))_y - \frac{M_y(t)}{T_2}$$
$$\frac{dM_z(t)}{dt} = \gamma (M(t) \times B(t))_z - \frac{M_z(t) - M_0}{T_1}$$  \[II.6\]

The spin-lattice decay time $T_1$ is the characteristic time for relaxation along the longitudinal $z$ direction back to the equilibrium magnetization $M_z$. The spin-spin relaxation time $T_2$ describes the decay of the transversal magnetization perpendicular to the static magnetic field.

2.3 Microscopic Picture

Microscopic magnetic moments of particles originate from quantum mechanical spin, an intrinsic angular momentum which is the consequence of a relativistic extension of the Schroedinger equation. Quantum mechanical systems are described by probability wavefunctions. The spin wavefunctions are commonly expressed as linear combinations of energy eigenstates of the magnetic energy [II.3]. Energy eigenstates of the time-independent magnetic energy are stationary states implying that the probability density and all observable quantities are constant in time, i.e. magnetic moments do not rotate or precess around the magnetic field as frequently stated. For a spin-\(\frac{1}{2}\) system as used in magnetic resonance imaging, there are exactly two distinct eigenstates (“spin-up” and “spin-down”) whose resonance frequency is given by the classical Larmor frequency [II.4]. In MR
experiments, the spin-$\frac{1}{2}$ system is only partially polarized such that the difference in population probability of both states is of the order of $10^{-6}$ (Figure 2.1). Although the superposition of both eigenstates has a phase distribution which precesses with the Larmor frequency around the magnetic field, the mean phase distribution of a spin ensemble is static. This is a consequence of the weak coupling between individual spin systems yielding only a very small number of spins which are coherently entangled (Braunstein et al. 1999). Upon irradiation with radiofrequency pulses, the polarization direction can be changed. If the radiofrequency pulse has magnetic field components $B_i$ perpendicular to the external $B_0$ field, which are in resonance with the Larmor frequency, the spin system rotates around $B_i$ with an angular frequency of $-\gamma B_i$. Incident radio-frequency pulses do not change the coherence or entanglement of multiple spin systems (Hanson 2008). The classical Larmor equation and Bloch equations for the expectation value of the spin can be derived by solving the von Neumann equation with the appropriate Hamiltonian (Fano 1957).

**Figure 2.1 Microscopic picture of spin dynamics in an external field.** Each of both energy eigenstates of a spin-$\frac{1}{2}$ system form conical spin orbitals (a). Both are stationary states i.e. all observables are constant in time. In particular, they do not rotate or precess around the magnetic field. At room temperature, the spin-$\frac{1}{2}$ system is only partially polarized and is described by a linear combination of both energy eigenstates (b). The superposition has a time-dependent phase distribution precessing around the magnetic field but owing to the weak coupling between individual spin systems, the mean phase distribution of a spin ensemble is static. The arrow indicates the expectation value of the spin components in space which is the best analogy to the classical magnetization vector. Its $z$ component is proportional to the difference in the population probability. Radio-frequency pulses with a magnetic field components being in resonance with the Larmor frequency of the spin system can be used to rotate the polarization direction (c).
2.4 MR Image Reconstruction as Inversion Problem

The acquired MR data $d$ is given by the proton density distribution $\rho$ of the excited imaging volume $V$:

$$d = \int_V \rho(x) \, dx.$$  \hfill [II.7]

The MR signal is complex-valued comprising magnitude and phase of the transversal magnetization. As the rotation frequency depends on the magnetic field, the phase of the acquired data can be manipulated by switching additional magnetic fields. For spatially linear magnetic gradient fields, the total accumulated phase from excitation to acquisition is proportional to the location and the magnetic gradient

$$\Phi(x, t) = \gamma \int_0^t B(x, t) \, dt = \gamma \Delta B_x t + \gamma \int_0^t G(t) \, dt.$$  \hfill [II.7]

In the k-space formulation of magnetic resonance imaging, the time integral of the gradient is denoted $k = \gamma \int_0^t G(t) \, dt$ and the MR signal can be written as Fourier transform of the imaged object

$$d(k) = \int_V \rho(x) e^{-ik \cdot x} \, dx.$$  \hfill [II.8]

After sampling an appropriate amount of k-space data, a discretized image can be reconstructed using the inverse Fourier transform. In realistic experiments, the acquired signal is weighted with the receive coil sensitivity $c$ and corrupted by noise

$$d(k) = \int_V c(x) \rho(x) e^{-ik \cdot x} \, dx + n.$$

The encoding typically includes further weighting terms such as $T_1$ and $T_2$ relaxation responsible for tissue contrast, bipolar gradients for velocity or diffusion encoding, background phases, and errors terms due to inhomogeneous magnet fields and gradient imperfections.

Since linear transformations can be conveniently expressed in matrix formulation, the integral form of the encoding equation can be discretized and written in matrix equation

$$d = E \cdot i + n$$  \hfill [II.10]

where $E$ is the encoding matrix comprising the coil sensitivity weighting and the Fourier sampling including under- and non-Cartesian sampling. Vector $d$ stacks the acquired data, $i$ is the discretized representation of the object, and $n$ the measurement noise.
3 Image Reconstruction

MR reconstruction is an inversion problem of a linear system of equations $d = El + n$ where a discretized image $i$ is to be found by balancing the trade-off between consistency with the acquired data $\|EI - d\| < \epsilon$ and suppression of measurement artifacts such as undersampling aliases, motion, and noise. In the most basic case, the encoding and reconstruction matrices are given by the forward and inverse Fourier transform, respectively. For more complex encoding matrices including multiple receive channels, undersampling, and motion, the inverse can be found employing the Moore-Penrose pseudoinverse $E^\dagger = (E^\dagger E + \lambda I)^{-1}E^\dagger$ or solving the normal equation, respectively,

$$(E^\dagger E + \lambda I)I = E^\dagger d.$$  \[\text{III.1}\]

The regularization parameter $\lambda$ ensures the invertibility of $E^\dagger$ and is typically chosen to match the noise level. Prior knowledge such as low resolution estimates or the image support can be incorporated by replacing identity matrix $I$ with appropriate data. Iterative inversion can also be written as minimization problem

$$\arg\min_i \|EI - d\|^2 + \lambda \|I\|^2.$$  \[\text{III.2}\]

As the gradient at a minimum is zero, the linear system of equations [III.1] is found by setting the derivative of [III.2] to zero. The minimization approach allows incorporating nonlinear reconstruction terms and non-Euclidian norms.

The following sections give a more detailed overview of signal-to-noise optimal image reconstruction from data obtained with multiple receive coils and undersampling techniques exploiting redundancy in $k$-space (partial Fourier imaging, parallel imaging) and image space ($k$-$t$ undersampling, compressed sensing).
3.1 Coil Combination

If a coil array with multiple receive channels is used, the encoding equation is an overdetermined linear system of equations. This means that the encoding matrix $E$ is not square but a rectangular, tall matrix $E = F \otimes s \in \mathbb{C}^{\cdot \times \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \cdot \
computational load considerably. The coil array compression algorithm presented in (Buehrer et al. 2007) combines k-space data to a reduced set of virtual coils which is optimized to retain a maximum of signal-to-noise in a region-of-interest.

3.2 Partial Fourier Imaging

Partial Fourier reconstruction exploits the Hermitian symmetry of real valued signals in Fourier space

\[ d(k) = \int d(x) e^{-ik \cdot x} \, dx = d(-k)^*, \forall \rho(x) \in \mathbb{R} \]  

[III.7]

Under the assumption of a spatially slowly varying image phase, just more than half of k-space has to be acquired using the low resolution k-space center as phase estimate during reconstruction. Feinberg (Feinberg et al. 1986) proposed a direct conjugate replacement upon using the low resolution estimate for rotating the complex image to real values. Gibbs ringing artifacts can be reduced by a homodyne detection (Noll, Nishimura, and Macovski 1991) which filters the k-space with a ramp filter (Figure 3.1).

![Ramp filter in homodyne reconstruction](image)

**Figure 3.1 Ramp filter in homodyne reconstruction.** In a homodyne reconstruction, the complex image is rotated to real values using the symmetrically sampled k-space center. Afterwards, the asymmetrically sampled k-space is weighted twice to account for the missing signal power in the outer k-space.

Improved reconstruction results can be achieved by using iterative projection onto convex sets (POCS) (Haacke, Lindskogj, and Lin 1991), finite impulse response (FIR) filters (McGibney et al. 1993) or iterative reconstruction by penalizing the imaginary components after phase correction (Bydder and Robson 2005; Michael Lustig, Donoho, and Pauly 2007).
3.3 Parallel Imaging

The redundancy in k-space data when acquiring with multiple receive coils can be used for undersampling. By adding a k-space sampling operator $\Xi$ to the encoding matrix $\mathbf{E} \rightarrow \Xi \mathbf{E}$, an image can be reconstructed by solving the normal equation [III.1] (Pruessmann et al. 2001). The reconstruction performance is again limited by the invertibility of $\mathbf{E}^\dagger \mathbf{E}$. For linear independent coil sensitivity maps and if the measurement noise is reasonably low, the achievable undersampling factor scales with the number of coils. Owing to geometrical constraints and the associated linear dependence of realistic receive coil sensitivity maps, reasonable undersampling factors are typically between 2 and 4 in Cartesian imaging if a single phase-encode dimension is undersampled (Wiesinger, Boesiger, and Pruessmann 2004).

For Cartesian undersampling with distinct Nyquist ghosts, the unfolding can also be written as pixel-wise unfolding in the image domain. Upon transformation of the encoding equation using an inverse Fourier transform, the folded image is represented by

$$f = \mathcal{F}^{-1} \Xi \mathcal{F} s_l.$$  

[III.8]

The system matrix is given by the multiplication of the point-spread function $\mathcal{F}^{-1} \Xi \mathcal{F}$ with the sensitivity maps. Assuming a two-fold regular undersampling, a folded pixel acquired in two coils can be written as (Pruessmann et al. 1999)

$$\begin{pmatrix} f_{1,1} \\ f_{1,2} \end{pmatrix} = \begin{pmatrix} s_{1,1,1} & s_{1,2,1} \\ s_{2,1,1} & s_{2,2,1} \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix}. $$  

[III.9]

Denoting the folded sensitivities with $\hat{s} = \mathcal{F}^{-1} \Xi \mathcal{F} s$, the unfolded pixels can be derived by multiplication with the pseudoinverse $\hat{\mathbf{S}}^\dagger = (\hat{\mathbf{S}}^\dagger \hat{\mathbf{S}})^{-1} \hat{\mathbf{S}}^\dagger$. 

$$\mathbf{f} = \hat{\mathbf{S}}^\dagger \hat{\mathbf{s}}.$$  

[III.10]
Acquiring less data decreases the signal-to-noise ratio with the inverse square root of the reduction factor \( r \), denoting the relative reduction in the number of acquired profiles. In addition, the noise in unfolded images is governed by the condition number of the sensitivity matrix, which defines how orthogonal (in the information theoretic sense) the k-space data is acquired. For the folded sensitivities \( \hat{s} \), the additional under-sampling noise at pixel \( p \) in image domain induced by the point-spread function is given by the geometry factor (“g-factor”) \( g_p = \sqrt{(\hat{S}^H \hat{S})_{p,p}^{-1}(\hat{S}^H \hat{S})_{p,p}} \). The total noise penalty of undersampling is, thereby, \( \frac{\text{SNR}_{\text{red}}}{\text{SNR}_{\text{full}}} = \frac{\text{SNR}_{\text{full}}}{g_p \sqrt{r}} \).

**Figure 3.2 Sensitivity encoding.** Two-fold undersampling results in Nyquist ghosts (left). If sensitivity maps vary between receivers in a coil array, the folded images in each coil contain different information (right) which can be used to derive a single image without folding artifacts.

Alternative implementations of parallel imaging aim to reconstruct missing profiles directly in k-space using a weighted sum of neighboring profiles as in SMASH (Sodickson and Manning 1997) or in an autocalibrated, SNR optimal way using multiple profiles from a neighborhood as in GRAPPA (Griswold et al. 2002). Recently, the GRAPPA approach was extended by estimating an optimal correlation and weighting of acquired and reconstructed k-space profiles during reconstruction, called SPIRiT (Michael Lustig and Pauly 2010).
Figure 3.3 **Parallel imaging reconstruction in k-space.** VD-Auto-SMASH reconstructs k-space data for the combined image data by linear combination across coils for a given profile. In GRAPPA, the combination is performed using acquired k-space data within a certain distance and each coil is reconstructed separately. SPIRiT imposes calibration consistency of acquired and reconstructed k-space data. All three techniques use autocalibration profiles in the k-space center to calculate the weights for linear combination. Figure adapted from (Griswold et al. 2002) and (Michael Lustig and Pauly 2010).

### 3.4 Compressed Sensing

Compressed sensing exploits implicit redundancy in the image domain to restore missing k-space profiles. Undersampling patterns required for compressed sensing are incoherent as already proposed by (Marseille et al. 1996). Accordingly, “noise-like” artifacts are introduced in the Fourier reconstructed image which are then resolved by nonlinear denoising in a sparse transform domain. Upon transformation with a nearly orthogonal transform into a sparse domain, the signal is represented by a small set of significant coefficients where incoherent, noise-like data remains dispersed across all coefficients. Owing to the norm preserving properties of orthogonal transforms, data coefficients have a high signal strength as compared to those containing noise and undersampling artifacts. Noise and undersampling artifacts can be removed by iterative thresholding or minimization in the transform domain. The original formulation of compressed sensing requires the sparsifying transform $\Phi$ to fulfill the restricted isometry property (RIP) upon transformation of signal data $x$ (E.J. Candes and Tao 2005)

\[
(1 - \delta) \|x\|^2 \leq \|\Phi x\|^2 \leq (1 + \delta) \|x\|^2
\]

[III.10]
for small constant $\delta$. There are, however, also formulations with weaker requirements (Emmanuel J. Candes and Plan 2011; Calderbank, Howard, and Jafarpour 2010).

In MRI, compressed sensing is usually formulated as optimization problem

$$\arg \min_i \| \Phi i \|_{1, \delta \leq \epsilon}$$

[III.11]

The $l_1$ norm promotes sparsity of image $i$ upon transformation $\phi$ (Chen, Donoho, and Saunders 1998). Consistency with the acquired k-space data is enforced by the second term with $\epsilon$ being usually defined by the noise level. For static images, the transform $\phi$ is typically a wavelet transform or a finite-differences transform. Image reconstruction can be performed iteratively by solving the regularized $l_1$ minimization problem with nonlinear conjugate gradients (Michael Lustig, Donoho, and Pauly 2007) or iterative soft (Daubechies 2004) or hard (Blumensath and Davies 2008) thresholding. The nonlinear conjugate gradient approach minimizes the cost function

$$\arg \min_i 0.5 \| E i - d \|_2^2 + \lambda \| \Phi i \|_{1, \delta \leq \epsilon}$$

[III.12]

where a line-search is performed in the conjugate gradient direction of the derived cost function. For an orthogonal transform $\phi$, iterative thresholding algorithms have an iterative update according to

$$i_{n+1} = \phi^H \hat{\mathcal{P}}(i_n - \mu E^H (E i_n - d))$$

[III.13]

Equivalent notations denote the image estimate $\hat{i} = \phi \hat{i}$ in the sparse transform domain and use an encoding matrix $\hat{E} = E \phi^H$ to map from the transform domain to k-space. The iteration steps are thus

$$\hat{i}_{n+1} = \mathcal{P}(\hat{i}_n - \mu \hat{E}^H (\hat{E} \hat{i}_n - d)) .$$

[III.14]

$\mathcal{P}$ denotes thresholding of the image data and is given by

$$\mathcal{P}_{\text{hard}}^{\text{hard}}(x) = \begin{cases} x, & |x| \geq \text{th} \\ 0, & |x| < \text{th} \end{cases}$$

[III.15]

$$\mathcal{P}_{\text{soft}}^{\text{soft}}(x) = \begin{cases} \frac{x}{|x|} x, & |x| \geq \text{th} \\ 0, & |x| < \text{th} \end{cases}$$
Reduction factors can be increased by nonlocal filtering and patch based denoising, for example with non-local means filtering (Buades, Coll, and Morel 2005; Adluru et al. 2010) and collaborative filtering of image volumes (Dabov et al. 2007; Akçakaya et al. 2011).

**Figure 3.4 Compressed sensing.** The upper row shows a numerical phantom and its representation in the wavelet domain. The noise-like, incoherent undersampling artifacts in the lower row spread across many wavelet coefficients with small signal strength.
3.5 Dynamic Imaging

In dynamic imaging, an imaging volume is acquired consecutively over time to form an image series. Examples in CMR include cine imaging and first-pass myocardial perfusion imaging. The additional redundancy in repeatedly acquired imaging volumes allows for higher undersampling factors by exploiting spatiotemporal correlations. As for static images, there are two general undersampling schemes.

3.5.1 Reconstruction of Incoherently Undersampled Data

If the sampling pattern is incoherent in space and time, the compressed sensing scheme can be extended to the time domain to achieve higher transform domain sparsity. Image reconstruction is performed as for static images by solving, for example, equation [III.12]. Sparse transforms of the time domain include the temporal Fourier transform (M Lustig et al. 2006; H Jung et al. 2009), temporal gradients (Adluru, Whitaker, and Dibella 2007), time-frame reordering (Adluru and Dibella 2008) and, principal component transformations along time (Feng et al. 2011; H Jung et al. 2009). More recently, a low-rank penalty was enforced implicitly (Zhao et al. 2010; Sajan Goud Lingala et al. 2011) and explicitly by decomposing the time series into a low-rank and a sparse component \(i = L + S\) using robust principal component analysis (Candès et al. 2011; Otazo 2013) in each iteration step. The sparse component \(S\) is then additionally transformed into the temporal Fourier domain and thresholded for denoising.

3.5.2 Reconstruction of k-space Data on a Lattice Pattern: k-t Undersampling

If regular undersampling is performed on a sheared grid in k-space and time such that the pattern is shifted each time frame, undersampling artifacts appear as flickering with high temporal frequency. Unfolding can then be performed by low-pass filtering in the temporal frequency domain which is also known as UNFOLD reconstruction (Madore, Glover, and Pelc 1999). The method was independently studied by Willis and Bresler (Willis, Bresler, and Member 1997). The undersampling pattern is also called k-t undersampling (Tsao, Boesiger, and Pruessmann 2003) as the undersampling lattice is defined in k-space and time domain, the k-t space. The reciprocal reconstruction domain for UNFOLD and derived methods is referred to as x-f space.
The temporal Fourier transform serves two purposes. It acts as sparsifying transform and it separates undersampling replicas in temporal frequency direction. The latter is explained by the Fourier shift theorem. By adding offsets to the undersampling lattice for each time frame, a phase-ramp in image domain is imposed giving each Fourier alias a distinct phase. Since the pattern is shifted every time frame, each signal replica has a phase ramp over time. Upon transformation into the temporal Fourier domain, the replicas get separated in frequency domain as each alias is shifted by a different amount. The point-spread function is thus no longer given by distinct points on a column in image domain but on a diagonal in temporal frequency with maximal spacing in between the replicas (Figure 3.5). Exact reconstruction is only possible if the signal replicas do not overlap in temporal Fourier domain, thus limiting the maximal acceleration to about a factor of 2.

![Diagram of undersampling](image)

**Figure 3.5 k-t undersampling.** If a regular undersampling pattern is shifted (a), the aliases in the point-spread function obtain a phase offset (b) which is then reflected in the folding of the image aliases (c). If the pattern is shifted each time frame, the folding aliases in (c) are summed each time frame with a different phase (constructively or destructively), resulting in temporal flickering of the undersampling artifacts. Upon transformation into the temporal Fourier domain (d,e), each replica is shifted according to the Fourier shift theorem. If the Nyquist aliases do not overlap in x-f domain, hard-thresholding can be employed for unfolding. Signal overlaps in x-f domain may be treated by additional regularization or soft-thresholding. Figure adapted from (Madore, Glover, and Pelc 1999) and (Tsao, Boesiger, and Pruessmann 2003).
k-t BLAST/SENSE

K-t BLAST and k-t SENSE (Tsao, Boesiger, and Pruessmann 2003) use lattice undersampling, also referred to as k-t undersampling, but acquire additional low-resolution training data for a weighted filtering in the spatiotemporal frequency domain, the x-f space. The weighting allows unfolding of overlapping aliases at the expense of increased noise. While k-t BLAST is used for one coil, k-t SENSE takes into account coil sensitivities for improved unfolding performance. To perform the unfolding in the x-f domain, an additional temporal Fourier transform is used in the encoding matrix: $E' = E F_{t ightarrow f}$. By including the low-resolution training data $\tilde{e}^{-i M}$ in the x-f domain as prior knowledge in the generic normal equation for reconstruction [III.1], the image in x-f space can be reconstructed by solving

$$ (E^{\ast} E + \lambda \tilde{e}^{-i M}) i^{' -1} = E^{\ast} d. \quad [III.16] $$

For analytically invertible matrices, the reconstruction formula can be written as

$$ i^{' -1} = (E^{\ast} E + \lambda \tilde{e}^{-i M})^{-1} E^{\ast} d. \quad [III.17] $$

If the number of coils is smaller than the reduction factor, an analytical equivalent but numerically more stable inversion can be performed by solving

$$ i^{' -1} = \tilde{e}^{-i M} E^{\ast} (E^{\ast} + \lambda \tilde{e}^{-i M} + \tilde{e}^{-i M} E^{\ast} d. \quad [III.18] $$

If the whole image series has to be reconstructed at once, the linear system of equations of [III.1] can be inverted by conjugate gradient algorithms or by minimizing

$$ \arg \min_{i^{' -1}} \| E i^{' -1} - d \|^2 + \lambda \| i^{' -1} M^{-1} i^{' -1} \|^2. \quad [III.19] $$

This formulation describes conjugate gradient descent in x-f space. By inserting the identity matrix $I = F_{f ightarrow t} F_{f ightarrow t}$, the cost function can be minimized in the x-t domain

$$ \arg \min_{i} \| E i - d \|^2 + \lambda \| i^{' -1} M^{-1} F_{f ightarrow t} i^{' -1} \|^2. \quad [III.20] $$

While analytically equivalent, the numerical properties are different. Convergence rates and accuracy of gradient descent methods are better if the variables are normalized to have similar finite differences and small standard deviations which is not the case in an x-f representation.
The nominal acceleration factors in cardiac imaging are up to factor 5 for cine imaging, perfusion and phase-contrast measurements (Kozerke et al. 2004; Baltes et al. 2005; Plein et al. 2007). The effective undersampling factor including acquisition of the training data is smaller. Higher undersampling factors typically result in temporal smoothing of dynamic image features.

**k-t PCA**

The Fourier transform is well suited to sparsify periodic signal changes but fails to represent abrupt and strong intensity variations over time efficiently. Accordingly, signal replicas in x-f domain remain spread out and overlap strongly such that only small undersampling factors are achievable. If the image series has, however, low rank and the time evolution can be described by a few basis functions, a principal component analysis can be employed for a basis transformation. The first principal component describes the largest variance of the data and subsequent components the largest variance orthogonal to the previous components. The basis transformation can be determined from training data in the x-f domain, for example. In such a scheme, unfolding is performed in x-pc space and, accordingly, the encoding process modifies to $E' = \mathbf{E} \mapsto \mathcal{F} \mapsto \mathbf{B} \mapsto f$ (Henrik Pedersen et al. 2009).
4 Motion Correction

Patient motion is a major source of artifacts in MR images (Scott, Keegan, and Firmin 2009). In image reconstruction, however, it is frequently assumed that encoding inconsistency due to motion during the measurement is negligible. This chapter gives an overview of the effects of bulk tissue and macroscopic physiological motion and how motion correction can be incorporated into MR image reconstruction. Motion on time scales smaller than the MR repetition time, i.e. motion occurring between excitation and acquisition of a k-space profile also called intra-view motion (Korin et al. 1989) is not considered here.

4.1 Motion Types

Motion in thoracic imaging is predominantly due to cardiac and respiratory induced movement of the object of interest. The heart contracts 50 to 100 times per minute with a relatively heart-rate invariant systolic phase of 400 ms (Weissler, Harris, and Schoenfeld 1968) which is mainly characterized by the contraction of the heart and ejection of blood. The remainder of the cardiac cycle is referred to as diastole. The motion of the left ventricle has been extensively studied and consists of three major components: longitudinal shortening, radial contraction, and opposite relative rotation of the apex and the base of the heart (Scott, Keegan, and Firmin 2009). During the cardiac cycle, the apex remains relatively stationary and the total heart volume including blood pool and muscle remains almost invariant (Hoffman and Ritman 1985). The maximum displacement of coronary arteries during the cardiac cycle is one the order of 1 cm (Al-Kwifi et al. 2006) with peak vessel velocities in early to mid-systole and early diastole (Hofman, Wickline, and Lorenz 1998) and stationary periods in end diastole (Y. Wang, Vidan, and Bergman 1999) and end systole (Jahnke et al. 2005).
Figure 4.1 Cardiac motion. Left: Thorax in short-axis view depicting right and left ventricle. Right: y-t profile plot for profile through the left ventricle (stippled line left) during the cardiac cycle.

The respiratory cycle has a high variability among subjects. The respiratory period was reported to be 4.3 sec ± 1.1 in healthy subjects (Taylor et al. 1997). Respiratory motion was found to be predominantly a translation of organs in superior-inferior direction and the movement of the chest wall in anterior-posterior direction (Y. Wang, Riederer, and Ehman 1995). The translation of the heart was measured as 18.1 ± 9.1 mm in feet-head direction and 2.4 ± 1.5 mm in antero-posterior direction. A linear correlation between feet-head motion of the heart and the diaphragm displacement was found with a slope of 0.6 ± 0.2. The high standard deviation and further studies suggest that the linear correlation is only valid for small displacements (P. G. Danias et al. 1999). For large motion, the high variability between subjects (McLeish et al. 2002; Keegan et al. 2002) prompts for patient specific model (Taylor et al. 1999). Furthermore, respiratory motion describes a hysteresis loop where inspiration and expiration follow different paths (Figure 4.2 (K Nehrke et al. 2001)).
Motion Types

Figure 4.2 Hysteresis of respiratory motion. The feet-head translation curves of the heart and the diaphragm follow a counter-clockwise hysteresis curve for inspiration versus expiration. Qualitative adaptation from (K Nehrke et al. 2001).

Inspiratory and expiratory breathhold positions do not generally match the exhaled and inhaled positions during free-breathing (Keegan et al. 2002). Breathing can be performed by chest breathing or abdominal breathing where tidal breathing typically involves both (Scott, Keegan, and Firmin 2009). Accordingly, a range of respiratory motion models have been developed for multiple modalities and fields of application (McClelland et al. 2013). The breathing motion of a healthy volunteer is illustrated by a plot over time for a profile in feet-head direction through the liver in Figure 4.3.

Figure 4.3 Breathing motion of internal organs. The image depicts a single profile through the liver and the right lobe of the lung during multiple breathing cycles.
4.2 Effects of Motion

Motion corrupted k-space profiles affect every pixel in the image domain. Accordingly, motion during any time of the acquisition can distort the entire image. The effects of affine motion have an analytical expression in k-space. Consider each voxel position $x$ in the imaging volume to be transformed according to $Ax + \delta x$. Upon substitution $u = Ax + \delta x$, the transformed encoding equation can be written as

$$d_{Ax+\delta x}(k) = \int \rho(Ax + \delta x)e^{-ik^T x} d\ x = \int \rho(u)e^{-ik^T u} d\ u \ e^{ik^T \delta x}$$

$$= \int \rho(u)e^{-i(A^{-1})^T k^T u} d\ u \ e^{ik^T \delta x}$$

$$d(k) \rightarrow e^{-k^T \delta x} \rightarrow d((A^{-1})^T k) e^{ik^T \delta x}$$

yielding the following relation between motion in image domain and its effect in k-space:

<table>
<thead>
<tr>
<th>Image domain</th>
<th>k-space</th>
</tr>
</thead>
<tbody>
<tr>
<td>Translation</td>
<td>Phase ramp</td>
</tr>
<tr>
<td>Rotation</td>
<td>Rotation</td>
</tr>
<tr>
<td>Compression/expansion</td>
<td>Expansion/compression</td>
</tr>
</tbody>
</table>

Nonrigid motion has no analytical representation in k-space but can be approximated on small scales by localized affine motion (Little, Hill, and Hawkes 1996; Christian Buerger, Schaeffter, and King 2011) and its k-space can be described by the summation over individually transformed subvolumes.

Typical distortions due to periodic motion are ghosting artifacts and image blurring (Wood 1985). Moving objects appear blurred along the direction of motion while Nyquist replicas induced by the sequential sampling show up in phase-encode direction.

4.3 Motion Compensation Techniques

There are three general approaches to address motion during acquisition. Combinations thereof are frequently applied.
**Fast imaging**

Optimized pulse sequences and accelerated image acquisition are employed to reduce data acquisition periods in time such that motion becomes negligible. By acquiring k-space data faster than the typical time scale of motion, artifacts can be reduced to a minimum. Undersampling techniques for scan acceleration are covered in Chapter 3. If the scan cannot be acquired in real-time (Uecker, Zhang, and Frahm 2010), additional pro- or retrospective motion correction schemes have to be incorporated.

**Prospective motion correction**

In prospective motion correction real-time motion estimation is used to minimize motion artifacts in the acquired data.

Cardiac scans are typically synchronized with the cardiac cycle in a segmented acquisition using an electrocardiogram (ECG). To account for the natural variability of the heart rate, only up to 80-90% of the cardiac cycle are acquired while in the remaining time, the system waits for the next R-wave (D. A. Bluemke et al. 1997). Retrospective gating allows coverage of the full cardiac cycle by performing a continuous measurement where profiles may be acquired multiple times in each segment and the R-wave is used to switch between segments. If an ECG is not applicable or erroneous, cardiac self-gating techniques can derive an ECG-like signal from cardiac induced MR signal variation in a repeatedly acquired k-space segment (Crowe et al. 2004; Larson et al. 2004; Buehrer et al. 2008).

While healthy subjects are able to hold their breath for 20 to 30 seconds, scanning in patients is typically restricted to 10-15 second breathhold periods. However, the breathhold position may still drift and breathholding was reported to be unsuitable in 33% of patients for high-resolution imaging (Jahnke et al. 2006). For long acquisitions or if breathholds are not feasible, respiratory motion can be compensated in a gated free-breathing acquisition (Sachs et al. 1994; Y. Wang, Rossman, et al. 1996). Thereby, the motion is continuously monitored during the scan and evaluated in real-time to determine whether the currently acquired data is accepted or rejected and scheduled for re-acquisition (Figure 4.4). Motion detection using a pencil beam navigator placed on the diaphragm outperforms gating with an external respiratory bellow (McConnell et al. 1997). A typical respiratory gating window width for a navigator placed on the right hemidiaphragm is 5 mm (Stuber et al. 1999).
Figure 4.4 Prospective motion correction by ECG-triggering and respiratory motion gating.

A cardiac sequence is typically synchronized to the cardiac motion with an ECG. Respiratory motion is compensated by restricting the acquisition to a small window within the respiratory cycle, e.g. the exhaled state.

The improved image quality of respiratory gating comes at the expense of prolonged scan duration. Typical respiratory gating efficiencies for a 5 mm gate are between 30 and 50% which makes larger gating windows preferable. For large gating windows, the linear dependence between diaphragm and heart motion is no longer valid (P. G. Danias et al. 1999). Since effects of motion during the acquisition of central k-space profiles are more pronounced in the image, respiratory motion artifacts can be reduced by k-space reordering (Bailes et al. 1985) and combined with navigator gating windows (Weiger et al. 1997). Slice and volume tracking has been proposed to relax gating conditions to some extent (P. Danias et al. 1997). However, the assumption of rigidity of the heart is limited to small respiratory induced displacements only (K Nehrke et al. 2001). Motion of coronary arteries could be modeled with affine models for respiratory gating windows of up to 20 mm (Manke et al. 2002) with mean model errors between 0.7 mm (left coronary artery) and 1 mm (right coronary artery) with a high inter-subject variability. Whole-heart images were prospectively corrected for affine motion by inverting its effects on k-space sampling (equation [IV.1]) using a patient specific, pre-calibrated motion model (Manke, Nehrke, and Börnert 2003). Due to its optimization on a volume of interest, blurring outside the volume of interest and ghosting artifacts throughout the image originating from tissue with different motion characteristics can degrade image quality (Kay Nehrke and Börnert 2005).

Retrospective motion correction

Retrospective motion compensation algorithms are designed to suppress artifacts in motion corrupted data. Affine motion correction can be performed similarly to prospective
Motion Compensation Techniques

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correction by updating the k-space position according to [IV.1]. Linear motion is accounted for by using a phase ramp in k-space (Korin et al. 1989), image rotation by rotation of profiles in k-space (David Atkinson and Hill 2003; Maas, deB. Frederick, and Renshaw 1997) and scaling by the appropriate inverse scaling of the profile data. Retrospective motion correction is thus a reordering of k-space data from the acquired regular grid to a distorted grid which matches the static image. As a consequence, it is limited to a reasonable amount of motion within the field-of-view. Through-plane motion and very large motion has to be accounted for by additional models and reconstruction algorithms for undersampled data.

If sufficiently many k-space profiles are acquired per motion state, image based motion correction can be performed after reconstructing images from the partially acquired k-space in each motion state. The periodicity of the respiratory motion can be exploited to gradually fill k-space by binning acquired profiles according to their respiratory phase. Spiral interleaves can be matched to breathhold reference interleaves by cross-correlation to guide image shifting and adaptive averaging (C J Hardy et al. 2000). Respiratory-phase resolved images obtained using 3D radial imaging (Bhat et al. 2011) or Cartesian sampling with spiral phase ordering (Henningsson et al. 2013) may be averaged after correction for affine motion to obtain a high-resolution whole-heart image with 100% gating efficiency.

A general framework to correct for arbitrary motion can be modeled by setting up a forward equation from the ideal object to corrupted k-space data (Batchelor et al. 2005). Using matrix descriptions, motion is modeled as linear mapping and motion correction is reduced to an inverse problem for a generalized encoding matrix including MR encoding and motion related spatial transformations. Accordingly, for a multi-shot acquisition, the encoding matrix is composed of a sum of transformation matrices as given by

\[
d = \sum E T \cdot E^{'} I .
\]

where \(T\) are spatial transformations warping the image from a reference position to the motion state during the acquisition of the profiles given by the selection matrix \(E\). The generalized encoding matrix \(E\) can be used with reconstruction algorithms for parallel imaging (Odille, Cîndea, et al. 2008), compressed sensing (Muhammad Usman et al. 2013) and dynamic imaging as described in Chapter 6 (Schmidt et al. 2013). For frame-by-frame motion correction in dynamic imaging (Asif et al. 2012; Schmidt et al. 2013), the motion
correction can also be reinterpreted as additional sparsifier for improved undersampling artifact removal.

4.4 Motion Estimation

External sensors

The cardiac cycle is typically monitored with an electrocardiogram (ECG). The peak of the R-wave is used for triggering or gating MR sequences. For high field strengths and fast gradient switching which degrade the electrical ECG signal detection, an acoustic detection of an ECG signal can be preferable (Frauenrath et al. 2009). Respiratory motion can be externally monitored with belts across the patient (R. L. Ehman et al. 1984), amplitude demodulation of the ECG signal (Felblinger and Boesch 1997) and bellows (Y. Wang et al. 1995). Respiratory gating has shown improved image quality with MR based navigator techniques (McConnell et al. 1997).

MR navigators

Navigators may be categorized into explicit and implicit navigators. Using explicit navigators, a dedicated MR sequence is interlaced with the acquisition of the imaging data. The navigator data are, however, not included in the imaging data. In contrast, implicit navigators are derived directly from the imaging sequence and can be reused to enhance the signal-to-noise ratio or perform additional regularization in image reconstruction.

A commonly used explicit navigator is the pencil beam sequence (Liu et al. 1993) which excites a localized column of tissue. The acquired signal is then processed to obtain 1D motion information (Y. Wang, Grimm, et al. 1996). In cardiac imaging, the pencil beam navigator is typically placed on the right hemidiaphragm to detect the movement of the lung/liver interface (Figure 4.5).
Figure 4.5 Pencil beam navigators for estimation of translational motion. The pencil beam navigator is typically placed on the right hemidiaphragm (top left image). Navigators placed directly on the heart (top right) may interfere with the imaging sequence and do not provide better detection of the respiratory phase. A navigator placed on the chest wall can be used for estimation of antero-posterior motion.

Orbital (Ward et al. 2000) or spherical (Welch et al. 2002) navigators can detect rotation and scaling motion parameters but superimposition of the moving heart and static tissue from the chest wall and spine can deteriorate the navigator signal (Lai et al. 2008). Alternatively, the acquisition of low-resolution images for motion estimation is possible. In some applications, the idle time during the MR scan can be used to acquire low-resolution 2D images for detecting feet-head and antero-posterior translation of the heart (Gurney and Yang 2007; Wu et al. 2013). Fat-selective spiral sequences were used for low-resolution imaging of the epicardial fat for 3D translational correction of the heart (Keegan et al. 2007). Two-dimensional image navigators have also been used to identify respiratory phases (von Siebenthal et al. 2007) and as predictor for 3D respiratory motion models (King et al. 2012). Image navigators with higher resolution and multiple dimensions can be obtained by...
segmented acquisition and binning of navigator data using the respiratory phase as identified using a pencil-beam navigator on the diaphragm (Schmidt et al. 2011). To derive displacement vector fields of motion, image navigators are processed using various image registration algorithms (Klein et al. 2010; Andronache, Cattin, and Székely 2005; Christian Buerger, Schaeffter, and King 2011).

Implicit navigators are based on repetitive sampling of k-space regions using the imaging sequence. In spiral and radial acquisitions (Figure 4.6), the densely sampled k-space center has been used for motion detection in fMRI (Glover and Lai 1998), respiratory gating (Pipe 1999; C J Hardy et al. 2000) and cardiac self-gating (Larson et al. 2004; Crowe et al. 2004). Radial profiles were used for translational and rotational motion estimation (Maas, deB. Frederick, and Renshaw 1997). Interlaced acquisition of free induction decays has permitted prospective cardiac and respiratory gating (Buehrer et al. 2008). Alternatively, repetitive sampling of a single central k-space profiles may be used for gating purposes (Uribe et al. 2007). Care has to be taken to suppress the strong signal form the chest wall. To this end, two additional profiles and intensity modulation in antero-posterior direction using phase encoding gradients has been proposed (Lai et al. 2008). The startup cycles of balanced steady state free-precession sequences can be used for the acquisition of a low-resolution image in 2D (Henningsson et al. 2012) and 3D (Moghari et al. 2013; Henningsson et al. 2013).

**Figure 4.6 MRI self-gating acquisition for implicit motion estimation.** The repeatedly acquired central k-space in radial and spiral can be used for estimation of the cardiac and the respiratory phase.

In dynamic imaging, Cartesian and Golden angle sampling for the acquisition of low-resolution imaging data as navigators has been proposed for retrospective motion correction (Hansen et al. 2012). Additional binning of Golden angle data into respiratory bins for enhanced spatial resolution was used (Muhammad Usman et al. 2013). The algorithm described in Chapter 6 (Schmidt et al. 2013) is based on fully sampled training data acquired interleaved with k-t undersampling.
If additional sensor data is obtained from additional sensors like ECG and multiple breathing belts, the motion can be approximated to be piece-wise constant and optimized in coupled linear systems of equations for cardiac and respiratory motion compensation (Odille, Vuissoz, et al. 2008).
5 Nonrigid Retrospective Respiratory Motion Correction in Whole-Heart Coronary MRA

5.1 Introduction

Motion is a major source of artifacts in MR imaging. Respiratory motion, in particular, remains a challenge in many cardiac applications (Scott, Keegan, and Firmin 2009). Restricting data acquisition to quiescent phases in the respiratory cycle by using gating or triggering methods (Y. Wang, Rossman, et al. 1996) can be used to reduce motion-related artifacts. However, these accept/reject approaches do prolong measurement times significantly and hence can cause patient discomfort with increasing risks for drifts and changes in respiratory patterns (Taylor et al. 1997). Accordingly, methods to prospectively correct for respiratory-induced motion of the heart have been devised (Y. Wang, Rossman, et al. 1996). By approximating the heart as a rigid body, the image slice or volume position can be adjusted to compensate for respiratory related shifts. However, practical difficulties in deriving displacement information of the heart directly have made it necessary to rely on remote motion detection either by using respiratory belts (Runge et al. 1984) or navigators positioned on the diaphragm (R. Ehman and Felmlee 1989). Correction factors to account for the non-rigidity of diaphragm and cardiac displacements had to be introduced (Y. Wang, Riederer, and Ehman 1995). Slice or volume tracking techniques have primarily been used to relax gating conditions for increased gating efficiencies (P. Danias et al. 1997). Further work followed and indicated that a rigid motion model cannot fully account for deformation occurring in the heart (K Nehrke et al. 2001). An affine motion model including patient-specific calibration was proposed and demonstrated for whole-heart imaging (Manke, Nehrke, and Börnert 2003). The affine model including translational, rotational and shear

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components has been shown to reduce errors in estimating the motion of the heart significantly. However, the model remains limited in that it only allows for nine degrees of freedom which are updated from a single or very few navigator measurements during the scan. Furthermore, due to its optimization for a target region like the heart and since affine motion correction is performed globally, image quality may get compromised by ghosting artifacts from static tissue outside the region of interest (Kay Nehrke and Börnert 2005). Another potential shortcoming relates to model calibration which is done prior to the actual scan. Inconsistencies between the calibrated model and the actual motion of the heart may occur during lengthy scans as breathing patterns may change and hence can compromise motion correction. To this end, self-gating approaches using the FID signal (Crowe et al. 2004), k-space profiles (Uribe et al. 2007), and low-resolution images (C J Hardy et al. 2000; Christopher J Hardy et al. 2003; Larson et al. 2005) have been described to collect motion related information interleaved or simultaneously with the actual data acquisition. Self-gating signals have been used to prospectively or retrospectively gate data acquisition. However, non-rigid image correction has been difficult to achieve as point-by-point quantitative displacement information is typically not available from self-gating signals. Retrospective correction of translational motion was successfully demonstrated using image based self-gating (Keegan et al. 2007). Auto-focus approaches may be applied if dedicated self-gating signals or images are not available. By using image quality criteria the effect of trial motions are evaluated to find the unknown deformation field (D Atkinson et al. 1999). However, since non-rigid motion during the MR encoding process can cause non-uniform sampling in k-space (Bammer, Aksoy, and Liu 2007; David Atkinson and Hill 2003), additional encoding information is required.

Coronary artery imaging has been one of the most challenging applications of cardiac MR given the size and motion of coronary vessels. Using pencil beam navigators in conjunction with slice tracking excellent image quality can be obtained using targeted volumes (Botnar et al. 1999; W. Y. Kim et al. 2001) or whole-heart approaches (Weber, Martin, and Higgins 2003). The main disadvantage of prospective accept/reject gating approaches in coronary imaging is, however, the low gating efficiency, which typically ranges between 40-60%. This leads to lengthy exams easily exceeding 15 min if the entire heart is to be imaged at high resolution without parallel imaging.
Recently, a framework that includes arbitrary motion in the forward encoding model of MR was introduced (Batchelor et al. 2005). Under the assumption that the motion field is known the method permits retrospective correction of non-rigid motion effects. In brief, the model formulates the transformation from the motion-free image to the acquired motion-distorted k-space profiles as matrix equation. If the entries of the transformation matrix are known, standard numerical matrix inversion algorithms can be used to reconstruct a motion-free image. A key element of the method, however, is the knowledge of the deformation fields. Several approaches have been demonstrated including auto-calibration methods (Odille, Vuissoz, et al. 2008), calibration by reference scans for 2D motion (Odille, Cîndea, et al. 2008), navigators and data driven methods for rigid motion (Bammer, Aksoy, and Liu 2007).

In the present work a method to acquire a full 3D motion model interleaved to the actual scan is proposed. By exploiting the quasi-periodicity of respiratory motion, a low resolution 2D imaging slice is obtained interleaved with the segmented 3D whole-heart coronary scan in every cardiac cycle. The slice location is cycled after each acquisition to cover the whole heart over an entire respiratory cycle. Non-rigid deformation fields can then be extracted by image registration and used to populate a spatial transformation matrix for iterative image reconstruction. It is demonstrated that the method allows doubling the gating efficiency in whole-coronary MR without or only little penalty in image quality.

### 5.2 Methods

#### Theory

It has been shown that image distortions due to known arbitrary motion can be retrospectively corrected for by a linear reconstruction framework (Batchelor et al. 2005). A general matrix equation describes the process from an ideal image to the motion distorted k-space data. Numerical inversion algorithms such as conjugate gradient methods can be used to invert this linear system of equation to recover the ideal image from the motion corrupted data. Without motion the equation simply represents MR encoding:

\[
d = \mathbf{E} \circ \mathbf{a},
\]

[V.1]

with \( \mathbf{a} \) being the imaged object, \( d \) the acquired data and \( \mathbf{E} \) the MR encoding matrix, usually consisting of coil sensitivities and Fourier transform. To account for motion in the image
domain, an image warping operator $\tau_i$ is applied to the motion-free image $o$ which warps the image from the reference position to the $i$-th position of all possible motion states. All associated k-space profiles acquired at this motion state are selected by the sampling operator $w_i$. The k-space is populated by summing over all motion states:

$$d = \sum_i w_i E T \tau_i o.$$  \[V.2\]

Several k-space profiles may have similar spatial transformations. In particular, intra-shot data can be assumed to have identical warping operators $\tau_i$. Please note that intra-view motion which means motion during a repetition time (Korin et al. 1989) is not considered here.

Denoting $E' = \sum_i w_i E T \tau_i$ for the generalized motion sensitive encoding matrix the same line of argument as in (Pruessmann et al. 1999) is used to obtain an SNR optimal solution for coil array data:

$$o_{min} = (E'^* \Psi^{-1} E')^{-1} E'^* \Psi^{-1} d,$$  \[V.3\]

where $\Psi$ is the noise covariance matrix and $o_{min}$ gives a minimum norm solution to the least squares problem $\|E' o - d\|$. Rewriting Eq. [V.3] as linear system of equations and including the noise covariance matrix in $E'$ and $d$ (see Appendix A), the normal equation is obtained:

$$E'^* E' o = E'^* d.$$  \[V.4\]

$E'^* E'$ is symmetric and positive-semidefinite and therefore lends itself to fast and memory efficient conjugate gradient algorithms for iterative inversion to calculate $o$. Since only $E' u$ and $E'^* v$ need to be calculated on image domain vectors $u$ and k-space vectors $v$, not every matrix entry of the generalized encoding matrix needs to be known. This allows applying fast Fourier transforms and efficient image warping instead of matrix vector multiplications.

It should be noted, however, that the condition number $\kappa$ is already high by design of the normal equation because $\kappa (E'^* E') = \kappa (E'^*)$. Correcting for motion becomes especially difficult with single coil or only a few coil data. For example, if parts of the object move outside of the field-of-view or rotate (David Atkinson and Hill 2003), k-space will be inconsistently sampled where some k-space points may overlap and others are missing. Therewith, Eq. [V.4] gets underdetermined and has infinitely many solutions. This can be rectified by adding more encoding equations from multiple averages (Odille, Cîndea, et al. 2008) or from
multiple coils with distinct sensitivities (Pruessmann et al. 1999). In addition regularization and preconditioning (Pruessmann et al. 2001) can be used. The latter should further modify the right-hand side of equation [V.4] to speed up the inversion with a better initial guess of the solution.

**Numerical implementation**

The linear system in Eq. [V.4] was preconditioned with intensity correction (Pruessmann et al. 2001):

\[
(PE^o E P)(P^o o) = PE^o d ,
\]

where the preconditioner \( P \) is defined by one over the root sum of squares of the coil sensitivities. The overall reconstruction scheme was implemented in Matlab (Mathworks, Natick, MA) as illustrated in Figure 5.1 using the LSQR algorithm (Paige and Saunders 1982).

The spatial transformations \( \tau_i \) were defined by a mapping from the coordinate systems of the input image to the output. To avoid holes and overlaps in resampling the warped output, inverse mapping, a common technique in digital image warping (George 1990), was implemented as follows. An inverse deformation field pointing from the regular grid of the output image to an irregular grid on the input image was used to “pull” interpolated pixel values from the input to the output image. To ensure constant intensity after warping, images were pre-weighted with the deformation field density. The transpose \( \tau_i^T \) was defined by warping backwards along the deformation lines (see Appendix B), where the fields were re-gridded by tri-linear interpolation. The Fourier transform \( \mathcal{F} \) was implemented using the fast Fourier transform for Cartesian data and an additional gridding and inverse gridding steps (Pruessmann et al. 2001; Rasche et al. 1999) for undersampled data.
Figure 5.1 Flow chart of image reconstruction including non-rigid motion correction. For clarity, the additional paths for multiple coils have been collapsed into a single path with coil number γ for the second and all following respiratory positions.

Computer simulations

The performance of non-rigid motion correction was evaluated using a numerical phantom which was generated based on motion-free in-vivo 3D whole-heart coronary images. The model was distorted using in-vivo motion data and a five channel coil array with orthogonal sensitivity maps was composed to simulate multi-coil acquisition. The motion distorted model data were subsequently reconstructed using the known motion fields for the original five channel coil array data and data compressed to a reduced set of virtual coils using the coil array compression method as described in (Pruessmann et al. 2001) (see Appendix C). The root-mean-square error (RMSE) of the corrected data relative to the motion-free reference was calculated to assess the dependency of non-rigid motion correction
performance on the number of independent coil elements used in reconstruction. Another set of simulations was performed to test the consistency of the image registration algorithm (Andronache, Cattin, and Székely 2005). To this end, ten motion-free whole-heart scans were warped by motion vector fields and corrupted with noise matching various signal-to-noise ratios. The resulting image volumes were subsequently registered using the image registration method. The root mean squared deviation between known and the newly obtained motion vector fields was calculated as a function of signal-to-noise ratio.

**Data acquisition**

A conventional navigator gated segmented balanced SSFP 3D coronary whole-heart scan with fat suppression and T2 preparation pre-pulses was set up (Weber, Martin, and Higgins 2003). The sequence was extended to acquire a low-resolution 2D motion scout slice per heart beat interleaved with the segmented 3D acquisition. The motion scout imaging slice location was cyclically permuted with each cardiac cycle to cover the entire volume defined by the 3D whole-heart scan (Figure 5.2). A pencil beam navigator was integrated into the motion scout to determine the respiratory phase. Both the imaging data and the motion scout were acquired in sagittal orientation with the frequency-encoding direction set along the feet-head direction.

![Figure 5.2 Pulse sequence diagram including a standard 3D balanced SSFP sequence triggered to mid-diastole extended with a 2D motion scout acquired during early systole.](image)

Data were acquired in 10 healthy volunteers after informed consent was obtained according to the institutional guidelines. All experiments were carried out on a whole body 1.5T MRI system (Achieva, Philips Healthcare, The Netherlands) using a five channel cardiac array coil. Sequence parameters for the 3D image were as follows: isotropic spatial resolution: 1.33 mm, field-of-view: 256x256x144 mm³, acquisition matrix: 192x192x108, TR/TE: 4.6/2.3 ms, flip
angle: 110°, acquisition window: 74 ms. Data acquisition was triggered to mid-diastole using a look-up table implemented on the scanner. Respiratory gating with a gating window of 5 mm was used with continuous updates of the gating window position to account for drifts of the mean diaphragm position during the scan. Rejected data were stored along accepted profiles to permit retrospective use of larger or infinite gating windows in conjunction with the proposed non-rigid retrospective motion correction. The single-shot 2D balanced SSFP motion scout data (TR/TE: 2.6/1.3 ms) were acquired interleaved with 4x4 mm$^2$ in-plane resolution at 256x256 mm$^2$ field-of-view and 4 mm slice thickness. Accordingly, at least 36 heart-beats were required to cover the volume defined by the 3D whole-heart scan. In image reconstruction motion scout images were compounded according to their slice position and respiratory phase to create respiratory-phase resolved imaging volumes (Figure 5.3).

**Figure 5.3 Schematics of the motion scout acquisitions consisting of cycled single-shot 2D images.**
Using respiratory phase information as derived by a navigator the 2D slices are compounded to form respiratory-phase resolved volume data for motion compensation.
Image reconstruction

Three types of images were reconstructed from the acquired data: a) for reference, data acquired during respiratory phases within a 5 mm gating window were reconstructed using Roemer reconstruction (Roemer et al. 1990), b) consecutive data without any gating were collected and reconstructed using Roemer reconstruction and, c) consecutive data without any gating were reconstructed using the motion compensation strategy proposed in this work. For the latter, the corresponding sub-set of motion scout data acquired along with the whole-heart data were distributed across four respiratory phase related bins using a respiratory phase histogram. Accordingly, four different respiratory phase related volumes were reconstructed. Missing slices were linearly interpolated. Three-dimensional deformation fields were calculated relative to the end-expiratory reference using hierarchical image registration based on local affine transformations and a cross-correlation based similarity measure (Andronache, Cattin, and Székely 2005). In a top down approach, affine registration and sub-division into smaller image sub-volumes was repetitively performed as long as enough structural information was present in the sub-volumes. Thin-plate splines were used to interpolate the displacement of individual voxels. Image registration took about 2 minutes on standard PC hardware. Upon registration the resulting motion model was tri-linearly inter- and extrapolated composing a quasi-continuous set of data covering the entire respiratory cycle with respiratory frames of 0.5 mm width. The motion model was subsequently used to populate the spatial warping operators $\tau$, in equation [V.2]. Image reconstruction was performed on standard PC hardware where each iteration step was scheduled in parallel for different motion states. Reconstruction times were less than one minute per iteration resulting in overall reconstruction times of about 6 min for 6 iterations.

Data analysis

The in vivo images of the 5 mm gated reference, the motion distorted and the motion corrected scan were reformatted to present slices of the right coronary artery (RCA), the left anterior descending artery (LAD) and the left circumflex artery (LCX).

Vessel centerlines were extracted and profiles perpendicular to the vessel axes were interpolated whose maximum gradient was used to determine the boundaries of each vessel. The edge strength was calculated using a 3D Canny edge filter (Canny 1986) and served as
quality measure for sharpness of the vessel boundaries and local edge entropy which was evaluated within a box of 5 pixel edge length.

Averaged values of edge entropy and sharpness for each volunteer were taken over the minimal vessel length of reference, motion distorted and motion corrected data. Averaged results for edge entropy and sharpness were normalized to the data of the reference scan. A paired Student’s t-test was used for statistical analysis. Visual scores were given by two independent observers blinded to the respiratory correction method. The image quality of each coronary artery was graded on a scale from 1 to 4 where a grade of 1 indicates a poor or uninterpretable image (coronary artery is visible but with markedly blurred borders); a grade of 2 implies good artery visibility (coronary artery is visible with moderately blurred borders); a grade of 3 implies very good artery visibility (coronary artery is visible with mildly blurred borders); and a grade of 4 implies excellent artery visibility (coronary artery is visible with sharply defined borders) (Jahnke et al. 2004). Statistical analysis was done using Wilcoxon signed rank tests.

5.3 Results

Numerical Phantom

Figure 5.4 illustrates the dependency of non-rigid motion correction performance on the number of coil elements used if the motion field is exactly known. While macroscopic ghosting artifacts by the applied respiratory motion could be removed, non-uniform noise is present in phase-encode direction (horizontal). When using five independent channels, lowest reconstruction error is achieved while considerable error results if only single element data is used.
Figure 5.4 The motion free numerical phantom and a motion distorted copy. The lower rows show motion corrected images and their difference to the original image. The insets indicate the root mean square deviation of the motion corrected image to the undistorted data set.

Figure 5.5 shows boxplots of the root mean squared deviation between known motion fields and registration results from accordingly transformed images for a range of signal-to-noise ratios. The deviation increases strongly for single-digit signal-to-noise ratios.

Figure 5.5 Boxplots for the root mean deviation between 10 known deformation fields and vector fields estimated from images warped according to the motion field. SNR is defined as the mean signal over the heart divided by the standard deviation of the added noise.
In Vivo Experiments

The mean gating efficiency of the 5 mm gated reference was 51% ± 11% at a respiratory range of the diaphragm of 261 mm ± 104 mm. Figure 5.6 shows example images of the main coronary arteries for the 5 mm gated reference, the gate-free scan and the motion corrected scan. In the gate-free scan, motion artifacts impair vessel delineation and entail a shorter visible vessel length. Motion corrected images show a perceived image quality comparable to the gated scan.

![Example images of the main coronary arteries.](image)

**Figure 5.6 Example images of the main coronary arteries.** The first and second row show standard reconstructions of the 5 mm gated reference and the gate-free scan. Images in the lower row were reconstructed using the non-rigid motion correction scheme using the gate-free data.

A quantitative comparison of all ten volunteers is given in Figure 5.7 summarizing normalized mean and standard deviation for vessel sharpness, local edge entropy and vessel length. Statistical analysis using a Student’s t-test revealed that for all criteria, the gate-free reconstruction without motion correction showed a significant difference (p < 0.05) to the 5 mm gated reference. After non-rigid motion correction, there was no statistical difference found comparing the image quality of the left coronary arteries LCX and LAD with the 5 mm gated reconstruction. For the right coronary artery lower vessel sharpness and edge entropy was detected with P-values of 0.04 (vessel sharpness) and 0.02 (edge entropy).
Figure 5.7 Comparison of image quality parameters of the gate-free data with and without non-rigid motion correction relative to the 5 mm gated reference in ten volunteers. Columns marked with (*) differ significantly (p < 0.05, paired Student’s t-test) from the 5mm gated reference.

The normalized image quality scores from two independent observers are shown in Figure 5.8 for each coronary artery. A degraded image quality for all coronary arteries was found for the gate-free reconstruction without motion correction. The statistical significance was determined with a paired Wilcoxon test and resulted P-values of 0.013 (RCA), 0.014 (LCX), and 0.013 (LAD). Motion corrected reconstruction restored image quality. The mean vessel visibility was found to be a little lower for the RCA but without significant difference to the reference with a P-value of 0.4. For LCX and LAD, P-values were 0.82 and 0.89, respectively.
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Figure 5.8 Mean image quality scores for vessel visibility on a scale from 1 (poor/uninterpretable) to 4 (excellent vessel visibility) in ten volunteers. Columns marked with (*) differ significantly ($p < 0.05$, paired Wilcoxon test) from the 5 mm gated reference.

5.4 Discussion

In this work non-rigid motion correction for whole-heart coronary MRA has been proposed and implemented. Using image based respiratory motion related displacement information of the entire imaging volume it has become possible to obtain high-quality whole-heart scans without applying respiratory gating. Accordingly, scan times were reduced by more than a factor of two relative to conventional scans using a 5 mm gating window with typical gating efficiencies on the order of 45%.

The proposed interleaved acquisition of motion scout data does not impose any scan time penalty and efficiently exploits the dead time present in coronary protocols. Motion information itself is derived from compounded 2D motion scout data exploiting the periodicity of the underlying respiratory motion. Such a scheme demands a minimum number of cardiac cycles to fully populate the motion model. With the current protocol and based on the respiratory patterns of the volunteers in this study, the minimum number of cardiac cycles required is approximately 400-500 and hence the minimum hypothetical scan time achievable would be 6 to 7 minutes. The minimum number of cardiac cycles may increase for large drifts or abrupt changes in the respiratory pattern. This limitation may be addressed by modifying the motion scout sequence to acquire multiple slices per cardiac
cycle in conjunction with parallel imaging (Pruessmann et al. 1999) or compressed sensing (Michael Lustig, Donoho, and Pauly 2007) approaches. Also, by immediate evaluation of respiratory positions as recorded by the diaphragm navigators, the slice position of the motion scout may be adapted in real-time to efficiently cover the volume across the respiratory range and respiratory states insufficiently covered by the motion model can be handled by re-acquisition of the specific imaging profiles or acquisition of additional motion information at the end of the scan. To this end, respiratory hysteresis can also be incorporated and may further improve the data presented here. Although the motion estimation benefits from a sagittal orientation of motion scout imaging slices, no preferred orientation for the coronary acquisition is implied by the proposed respiratory motion correction method.

Non-rigid motion correction using a generalized notation of the MR encoding process relies on a spatial transform matrix describing displacement of each individual tissue point as a function of respiratory motion. In computer simulations it was demonstrated that image based registration of the compounded motion scout data provides sufficient accuracy for motion correction in this application. Furthermore the impact of independent coil channels on the reconstruction accuracy was investigated by compressing the physical coil channels into virtual coils. This part of work has demonstrated that coil encoding is clearly beneficial in the inverse problem. For the current work only a five channel array was available and it remains to be shown if larger coil arrays can improve reconstruction accuracy further.

Matrix inversion associated with non-rigid motion correction is computationally demanding. In the current implementation in Matlab the total data reconstruction time for a 192x192x108 acquisition matrix is below 10 minutes. By code implementation using compiled languages and using commodity graphics cards (Hansen, Atkinson, and Sorensen 2008; Strzodka, Droske, and Rumpf 2004) this drawback can be well addressed.

Based on the image quality criteria evaluated in this work non-rigid motion correction was found to provide equal or even better data quality relative to the 5 mm gated reference for the left coronary system. Image quality of the right coronary artery was found to be slightly inferior, however still showed significant improvement over the non-gated reference scan. We attribute the lower quality of the right coronary artery to the subdivision of the image for hierarchical image registration without attention to interfaces between structures with
different motion characteristics. Accordingly, the large differences in motion between chest wall and heart may not be fully accounted for by the registration approach. This drawback may be overcome by guiding volume subdivision based on anatomical information for chest wall and inner organs available from the low-resolution data.

Overall, scan times normalized to 60 beats/min heart rate were 8 min on average in the non-gated acquisition comparing to 16 min for the 5 mm gated data in the study population.

The motion correction algorithm is by design compatible with image based parallel imaging as it generalizes the work presented in (Pruessmann et al. 2001). Parallel imaging performance, though, depends now additionally on the patient motion as coil sensitivity information is needed for re-population of undersampled data and filling local k-space gaps introduced by non-shape-preserving motion. Compressed sensing has been demonstrated to work for coronary MRA (Akcakaya et al. 2010) and does not require sensitivity information to unfold undersampled data but should be applied after motion correction as it non-linearly mixes k-space data.

5.5 Conclusion

Non-rigid retrospective motion correction permits efficient correction of respiratory motion related image artifacts in whole-heart coronary MRA acquired without respiratory gating. Accordingly, scan times can be reduced by more than a factor of two relative to navigator gated acquisitions with comparable image quality. The method hence holds promise to speed up whole-heart imaging protocols and larger studies in patient populations are warranted to demonstrate the benefit in a clinical setting.
5.6 Appendix

Appendix A

Elimination of the Noise Matrix

The sample noise matrix was introduced to minimize noise in the final image when coil arrays are used. We proceed as in (Pruessmann et al. 2001) by assuming time-independent noise defined by

\[ \Psi_{\gamma,i,j} = \eta_{\gamma,i} \eta_{\gamma,j} \]  \hspace{1cm} \text{[V.6]}

where \( \eta_{\gamma,i} \) is the noise output of the \( \gamma \)-th channel. Cholesky decomposition of \( \Psi \) leads to

\[ \Psi = LL^H. \]  \hspace{1cm} \text{[V.7]}

Let \( \nu \) be the direct product of the vector spaces \( \nu_i \) for the two or three spatial dimensions and \( \nu_c \) for the coil dimension: \( \nu = \nu_i \otimes \nu_c \). As the spatial transformation \( T_i \) only operates on \( \nu_i \) and the noise matrix and its decomposition in \( L \) only on \( \nu_c \), the \( L \) and \( T \) matrices commute and \( LL^H \) can be pre-multiplied on k-space sample data \( d \) and sensitivities \( S \) as in (Pruessmann et al. 2001):

\[ d_{\gamma,i}^{\text{decorr}} = \sum_j (L^{-1})_{\gamma,i,j} d_{\gamma,j} \]  \hspace{1cm} \text{[V.8]}

\[ s_{\gamma,i}^{\text{decorr}}(r) = \sum_j (L^{-1})_{\gamma,i,j} s_{\gamma,j}(r) \]  \hspace{1cm} \text{[V.9]}

Appendix B

Transpose of spatial transformation operator

Let \( \sigma_{i \rightarrow j} \) be an atomic deformation where just one pixel is moved from position \( i \) and added to the pixel at position \( j \). \( \sigma_{i \rightarrow j} \) can be written as a matrix which is identity except for entries \( ii \) and \( ij \), which are permuted, i.e. 1 at position \( ij \) and 0 at \( ii \). Its transpose is \( \sigma_{j \rightarrow i} \) which is identity except for indices \( ii \) and \( ji \). This is equivalent to copying a pixel from position \( j \) to position \( i \). Please note that due to this copying the transposed spatial transformation doesn’t necessarily preserve global image intensity in the case of compression of pixels.
Appendix C

Array compression of coil arrays for extended encoding equations

Array compression combines coil channels to a subset of virtual coils to reduce the amount of data which needs to be processed. This is done by a linear combination along the coil dimension to a smaller subset of virtual coils. The same reasoning as in Appendix A can be used to prove the applicability for motion sensitive encoding equations. Let $A$ be the linear mapping from the full coil vector space to coil vector space of lower dimensionality, $A : \mathbb{V}_c \rightarrow \mathbb{V}_c'$. The coil compression is a left-multiplication with the linear combination $A$:

$$A d = A \sum_i W_i F_i T_i o .$$ \hfill [V.10]

Let, again, $\mathbb{V}$ be the direct product of the vector spaces $\mathbb{V}_i$ for the spatial dimensions and $\mathbb{V}_c$ for the coil dimension: $\mathbb{V} = \mathbb{V}_i \otimes \mathbb{V}_c$. $W, F, \text{ and } T$ operate only on $\mathbb{V}_i$ and the sensitivities $S$ only in coil dimension $\mathbb{V}_c$. $A$, therefore, is commuting with $W, F, \text{ and } T$, and operates directly on the coil data $d$ and the sensitivities $S$, such that:

$$d_{c, x}^{\text{compress}} = \sum_{t'} A_{x, t'} d_{x, t'},$$ \hfill [V.11]

$$S_{x}^{\text{compress}}(r) = \sum_{t'} A_{x, t'} S_{x, t}(r).$$ \hfill [V.12]

The noise covariance matrix transforms accordingly to:

$$\Psi^{\text{compress}} = A \Psi A^\top .$$ \hfill [V.13]
6 Iterative k-t Principal Component Analysis with Nonrigid Motion Correction for Dynamic Three-dimensional Cardiac Perfusion Imaging

6.1 Introduction

The detection and quantification of myocardial perfusion plays an important role in characterizing coronary artery and ischemic heart disease (Al-Saadi et al. 2000; Schwitter and Arai 2011; Manka et al. 2011). In cardiac MR, perfusion information is commonly imaged by detecting dynamic changes in myocardial signal intensity during the first passage of a contrast agent. Demands for high spatial and temporal resolution as well as sufficient cardiac coverage make scan acceleration techniques necessary (P Kellman et al. 2004; Plein et al. 2005; Plein et al. 2007; Manka et al. 2010). Besides optimized and fast pulse sequences (PKellman and Arai 2007), k-space acquisition can be undersampled to reduce acquisition time and increase coverage in image space. Parallel imaging techniques (Sodickson and Manning 1997; Pruessmann et al. 1999; Griswold et al. 2000; Griswold et al. 2002) allow reconstructing undersampled data on a frame-by-frame basis with acceleration rates of 2-3 and acquisition of 2-4 slices within a single cardiac cycle (PKellman and Arai 2007). Shifting the undersampling pattern from frame to frame permits temporal filtering approaches (Madore, Glover, and Pelc 1999; Di Bella et al. 2003) which can be combined with parallel imaging to reduce image artifacts at similar acceleration rates (PKellman et al. 2004). Substantially higher acceleration factors from 5 in 2D to 10 in 3D perfusion imaging (Plein et al. 2007; Vitanis et al. 2011; Shin et al. 2013) can be achieved by acquiring additional fully sampled low-resolution training data to adaptively control image reconstruction in the x-t domain (k-t

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SENSE (Tsao, Boesiger, and Pruessmann 2003)) or principal component x-pc domain (k-t PCA (Henrik Pedersen et al. 2009)).

Three-dimensional cardiac perfusion imaging provides the necessary large coverage of the left ventricle (Manka et al. 2012; Jogiya et al. 2012) and inherently avoids misregistration problems potentially compromising multi-slice approaches. However, the sensitivity to respiratory motion in highly accelerated k-t PCA scans remains challenging (Vitanis et al. 2011). Respiratory induced nonrigid organ deformation smears out signal replicas in the x-pc domain and can lead to insufficient unfolding, especially for large and abrupt motion caused by incomplete breathholding. Navigator based prospective respiratory motion compensation as in accept/reject algorithms is not applicable as the bolus passage needs to be sampled in real-time without interruption. Prospective slice tracking gives significant improvement over free-breathing data but nonrigid motion components may still compromise data reconstruction (H Pedersen et al. 2009).

General motion correction methods can correct for nonrigid motion if the relative organ deformation is known for each acquired k-space subset (Batchelor et al. 2005). The necessary motion information can either be obtained from an additional fully sampled acquisition of k-space concurrent to actual image acquisition (Schmidt et al. 2011), from the data itself using inversion of coupled systems driven by external sensors (Odille, Vuissoz, et al. 2008), iteratively interleaved reconstruction and motion estimation (Hong Jung et al. 2010), or reconstruction of partial k-space data sorted in respiratory bins derived from self-gating signals (C Buerger et al. 2012).

In the present work, a nonrigid respiratory motion correction method for k-t undersampled 3D cardiac perfusion imaging is presented. The k-t PCA approach is extended to perform iterative regularization with training data in a motion corrected x-pc domain where each time frame is warped to a reference respiratory state. Motion information is extracted from the low-resolution k-t training data using shape constrained nonrigid image registration. It is demonstrated that the method allows for robust image quality in subjects with incomplete breathholds or under free-breathing condition.
6.2 Methods

**k-t PCA**

In k-t accelerated scans, the acquisition of a series of dynamic images is undersampled using a sheared grid in k-t space where the k-space sampling pattern is shifted in every time frame in a predetermined way. In accordance to the Fourier shift theorem, the alternating k-t pattern imposes a frame dependent phase ramp in the point-spread function in x-t domain which results in Nyquist replica specific shifts in the temporal frequency domain upon transformation into the reciprocal x-f space. A further reduction of signal overlaps from different aliases can be achieved by orthogonalisation using principal component analysis (PCA) and basis transformation from the x-f to x-pc space such that the first principal component describes the largest variance of the data and subsequent components the largest variance orthogonal to the previous. The unaliased object signal is then selected by regularization with a fully sampled, low-resolution training data set.

The closed-form reconstruction equation as given in (Henrik Pedersen et al. 2009) may be rewritten as a regularized system of linear equations according to:

$$\text{arg min}_i \| E i - d \|_2^2 + \lambda \| (\text{PC} \cdot M)^{-1} B f_{\rightarrow \text{pc}} F f_{\rightarrow \text{pc}} i \|_2^2.$$  \[VI.1\]

where the first term ensures data consistency between the measured k-space data \(d\) and the image estimate \(i\) transformed with encoding matrix \(E\). \(E\) describes coil sensitivity information, spatial Fourier transform and sampling in k-space. The second term in Eq. [VI.1] represents regularization with the training data in x-pc space, where \(f_{\rightarrow \text{pc}}\) denotes the Fourier transform along the time domain and \(B_{\text{pc}}\) the PCA basis transformation from x-f to x-pc space. With \(\rho_{tr}\) being the fully sampled training data, the signal covariance matrix \(M^2\) in x-pc domain reads:

$$i \cdot \rho_{tr} = B f_{\rightarrow \text{pc}} F f_{\rightarrow \text{pc}} \rho_{tr} (B f_{\rightarrow \text{pc}} F f_{\rightarrow \text{pc}} \rho_{tr})^T = \iota \rho_{tr} \cdot \iota \rho_{tr} \cdot \iota \rho_{tr}.$$

\[VI.2\]

For numerical stability and to prevent noise enhancement, the off-diagonal elements of \(M^2\) are usually set to zero (Vitanis et al. 2011). The weighting matrix \(M\) in Eq. [VI.1] is then defined by a diagonal matrix whose elements are given by the magnitude of the training data in the x-pc domain. Otherwise \(M\) can be calculated by Cholesky decomposition of positive semidefinite \(M^2\). Residual artifacts in the reconstructed images typically come from
insufficiently separated replicas in the x-pc domain. Therefore, overall reconstruction quality benefits from dynamic image series with only a few significant principal components for best separation of replicas in x-pc space. However, large and abrupt breathing motion significantly spreads the signal across the x-pc domain (Vitanis et al. 2011) and hence inherently compromises reconstruction quality.

**Iterative k-t PCA with motion correction**

To reduce the aliasing and ghosting artifacts due to breathing motion, training data regularization may be performed in a coordinate system compensated for breathing motion. If \( \mathbf{T} \) denotes the spatial transformation which warps all dynamic frames to a reference breathing state, therewith compressing the signal in x-pc domain, the sparsified regularization can be expressed as:

\[
\lambda^2 \| (\mathbf{r}_{t \rightarrow p} \mathbf{M})^{-1} \mathbf{B}_{f \rightarrow t, f} \mathbf{F}_{t, l} \mathbf{M}^{\top} \|^2.
\]  

[VI.3]

where \( \mathbf{r}_{t \rightarrow p} \mathbf{M} \) is calculated using the motion corrected training data:

\[
\mathbf{r}_{t} \mathbf{\rho}_{n} = \mathbf{T} \mathbf{\rho}_{n}.
\]  

[VI.4]

Operator \( \mathbf{T} \) may be considered a sparsifying operation and hence motion estimation is not required to be exact as long as image warping provides a sufficient approximation of a particular frame relative to the reference motion state.

**Implementation**

The algorithm was implemented in Matlab (Mathworks, Natick, MA) using the LSQR algorithm for minimization (Paige and Saunders 1982). Similar to (Hansen et al. 2006), the problem was preconditioned with a diagonal preconditioner:

\[
\mathbf{P} = \frac{1}{\sqrt{\mathbf{E}^\top \mathbf{E} + \lambda^2 \text{diag}(\mathbf{b}^2)}}
\]  

[VI.5]

(see Appendix A for preconditioned minimization). Image warping was implemented by back mapping (Schmidt et al. 2011) i.e. the warped image was resampled with tri-linear interpolation from the original image by mapping voxel locations of the deformed image onto the original image space. A cubic spline interpolation was performed for the final image warping after reconstruction. A pre-whitening of the k-space data using the measured noise
covariance matrix enforces a signal-to-noise optimal reconstruction (Pruessmann et al. 2001). Memory load was reduced by linear combination of the physical coils to form an array of 10 virtual coils (Buehrer et al. 2007). The k-space data was rescaled to a standard deviation of 0.1 allowing for a fixed regularization parameter $\lambda^2 = 1 \times 10^{-2}$. Images were reconstructed using a fixed number of 60 iterations. To speed up the reconstruction, the first 20 iterations were performed with only the first six principal components, while all principal components were used in the remaining 40 iterations, resulting in a total reconstruction time of below 20 minutes and a total memory load of less than 3 GB. Partial Fourier acquisition was accounted for after reconstruction using a homodyne filter (Noll, Nishimura, and Macovski 1991).

### Computer simulations

To test the reconstruction performance of the algorithm, a numerical phantom was generated from a segmented 3D in vivo data set with 160x147x10 voxels. The signal intensities of right and left ventricular blood pools, myocardium, liver, stomach, and arteries were adapted according to first-pass contrast enhanced perfusion data obtained in-vivo. An additional data set was created to simulate the free-breathing condition by applying elastic motion with a maximum amplitude of 1.7 and 0.5 cm in feet-head and antero-posterior directions. A coil array of 28 symmetric receive coils was modeled and data were sampled with 10-fold k-t undersampling including an elliptically fully sampled k-space center as training data with semi-axes of 11 and 7, respectively. Gaussian white noise was added to obtain a signal-to-noise ratio of 30 for heart and liver at peak contrast enhancement. Data were reconstructed with standard k-t PCA and iterative k-t PCA with motion correction using the exact motion vector field as was imposed to simulate motion, using -40\% to +40\% underestimated and overestimated motion vector fields and using a ±20\% randomly distorted motion vector field as input.

### Data acquisition

Three-dimensional perfusion data were acquired in 10 volunteers upon informed consent according to institutional guidelines was obtained. Experiments were carried out on a Philips 3T Ingenia system (Philips Healthcare, Best, The Netherlands) using a 28-channel phased array coil. In all subjects, a saturation-recovery gradient echo sequence was used with a WET saturation pulse and the following typical imaging parameters: TR: 2 – 2.2ms, TE: 0.9-1ms,
flip angle: 15°, spatial resolution: 2.3x2.3x10mm³, 10 slices, 30 dynamics, acquisition window: 205 - 225ms, saturation delay: 140ms. Data were undersampled by a factor of 10. Training profiles were acquired interleaved with the undersampled acquisition providing a fully sampled ellipse with half axes of 11 and 7 profiles in kᵣ and kₓ directions, respectively. An elliptical k-space shutter and partial Fourier acquisition with 62.5% coverage in frequency-encode direction and 75% in the two phase-encode directions was applied (Figure 6.1) resulting in a total k-space coverage of approximately 5% relative to a fully sampled Cartesian matrix. A total of 104 to 107 phase encodes were acquired per time frame of which 45 comprised the fully sampled, elliptical k-space center. During the exams, five volunteers were asked to start breathing half-way through the scan to simulate incomplete breathholding. For the remaining five volunteers, the scan was performed during free-breathing. The protocol in each subject included a breathhold 3D perfusion scan, which served as reference, and the motion-corrupted perfusion scan acquired afterwards. A contrast bolus of 0.05 mmol/kg b.w. of gadolinium (Gadovist, Bayer Schering, Berlin, Germany) was applied in both scans. A waiting period of 20 min was inserted in-between scans to allow for contrast agent washout. As part of the preparation phase for each scan, noise samples were acquired for all coils to calculate the noise covariance matrix. A breathhold coil calibration scan was acquired to determine coil sensitivity maps. The survey scan used to plan slice orientation and position for 3D perfusion imaging was exported for automatic segmentation and motion estimation.
**Methods**

Figure 6.1 a: Dynamic k-t undersampling pattern in \( k_y-k_z \) space and overall sequence timing (a). Partial Fourier acquisition of 75% in \( k_y \) and \( k_z \) is included. An elliptical, fully sampled region is sampled in k-space to provide training information for every dynamic frame. Perfusion data is acquired at peak systole. 

b: Acquisition pattern at a given time frame showing a 10-fold undersampled grid pattern (light gray dots) and an elliptical k-space center with half axes of 11 and 7 profiles in \( k_y \) and \( k_z \) directions (dark gray).

**Shape constrained nonrigid motion estimation**

Relative deformation vector fields were derived from the composite of training data and k-t undersampled data to populate the spatial transformation matrix \( T \). The composite data was reconstructed using TSENSE (Peter Kellman, Epstein, and McVeigh 2001) and spatially low-pass filtered using a Hamming window. Image registration was performed with the ITK based elastix (Klein et al. 2010) toolbox using a multi-resolution registration approach. Accordingly, results of a coarse registration step on low-resolution data were used as initial deformation for a finer registration with higher resolution. Three iterations were performed with resolution downsampling by factors of 4, 2, and 1. For nonrigid registration, a b-spline transformation model was chosen with the grid-spacing varying between 136x136x160 mm\(^3\).
and 34x34x40 mm$^3$ according to the different resolution levels. The transformation parameters were optimized based on advanced Mattes mutual information (Klein, Staring, and Pluim 2007) as image similarity measure and an additional transform rigidity penalty (Staring, Klein, and Pluim 2007) which favors affine motion for image regions specified by binary masks. The total cost function was the weighted sum of both metrics. Separate image regions assumed to be governed by affine motion were defined for the chest wall, back, heart and liver using automatic segmentation. The reference masks were generated based on manual segmentation of a multi-slice cardiac survey scan covering the whole thorax for robust inter-subject registration. The segmentation was obtained in one representative subject and adapted to the survey scans acquired in each individual subject by registration and corresponding warping of the segmentation masks. Finally, the binary masks were reformatted to the short-axis geometry of the perfusion scans, overlapping pixels were removed and all masks combined into a single rigidity mask image as required by elastix (Figure 6.2).
Figure 6.2 Shape constrained motion estimation from k-t undersampled data. Using TSENSE, the composites of training and undersampled data are reconstructed and spatially filtered to form input data for image registration. Anatomical compartments are defined on the survey scan obtained in each individual subject using a reference segmentation. Each compartment is allowed to undergo affine motion in the subsequent image registration step.

Image reconstruction and post-processing
Two image series were reconstructed from each acquired data set using (1) standard k-t PCA and (2) iterative k-t PCA with motion correction (k-t PCA\textsuperscript{mc}). Standard k-t PCA was implemented according to (Vitanis et al. 2011). Upon reconstruction using iterative k-t PCA\textsuperscript{mc}
and k-t PCA, a homodyne k-space filter was applied as final post-processing step on a frame-by-frame basis (Vitanis et al. 2011). Thereby, the complex image data is rotated to real values using the negative phase of the fully sampled k-space center to exploit the complex symmetry in k-space of real valued signals: \[ \rho(x) = \int \rho(x)e^{i\omega}dx = d(-k), \forall \rho(x) \in \mathbb{R}^\mathbb{Y}. \] Acquired and reconstructed k-space data within the elliptical shutter as defined by the time average of the k-t sampling pattern were used for frame-by-frame Hermitian conjugate replacement using a k-space filter to weigh the asymmetrically k-space portion twice while suppressing conjugate k-space data (Noll, Nishimura, and Macovski 1991). For evaluation, the previously estimated breathing motion was used for warping the dynamic series to one reference breathing state.

**Data analysis**

Reconstruction accuracy was compared visually and semi-quantitatively based on signal intensity curves of the ventricles and myocardium. A six-sector model per slice was used including baseline correction to account for differences in residual contrast agent concentration prior to each scan. Signal upslopes were compared relative to the breathheld reference. To assess motion induced fluctuations of signal intensity curves, the variance of signal intensity over time relative to temporally median-filtered data was calculated. The mean and standard deviation of this variance was calculated for free-breathing and interrupted breathhold data sets.

**6.3 Results**

**Computer simulations**

Figure 6.3a compares mid-ventricular slices obtained with standard k-t PCA and motion corrected k-t PCA (k-t PCA\textsuperscript{mc}) using the exact, 30% underestimated, and ±20% randomly distorted motion vector fields. In all cases, k-t PCA\textsuperscript{mc} was found to outperform standard k-t PCA. Difference images of k-t PCA\textsuperscript{mc} to ground truth are shown in Figure 6.3b for reconstruction with under- and overestimated deformation fields. Residual aliasing was found for image reconstruction with systematic errors greater or equal to 30% in the motion vector fields.
Results

Figure 6.3 Computer simulations. a: Comparison of standard k-t PCA and motion corrected k-t PCA $^{mc}$ for known deformation vector fields, 30% underestimated motion and ± 20% randomly distorted motion vector fields. b: Difference image of k-t PCA $^{mc}$ reconstructed images to ground truth for various degrees of under- and overestimation of deformation fields.

Figure 6.4 shows x-t profiles of the reconstructed images and their difference to ground truth. The differences to ground truth seen in Figure 6.3 and Figure 6.4 are largest at residual ghosting artifacts and at positions of large intensity changes in space, i.e. at the interface of chest wall to air and the boundary of the ventricles during contrast bolus passage. Signal intensity curves are plotted in Figure 6.5 for three sectors of the myocardium (inferoseptal, inferolateral, and anterior) in three slices (basal, mid-ventricular, and apical). Errors in myocardial signal intensity curves of images reconstructed with distorted motion vector...
fields (Figure 6.5) were found to be largest for the inferoseptal wall compared to the thicker inferolateral and anterior sector.

**Figure 6.4** Computer simulations. Comparison of x-t profiles and their differences to ground truth. The top-left inset indicates the profile position in space.
Figure 6.5 Computer simulations. **a**: Signal intensity curves reconstructed with standard k-t PCA without motion correction (top left), motion corrected k-t PCA \( \text{mc} \) for known deformation (top right), 30% underestimated motion (bottom left) and ± 20% randomly distorted motion vector fields (bottom right). Dotted lines are from an infero-septal sector, dashed lines from infero-lateral and solid lines from an anterior sector. The intensity curves are extracted from three slices, basal (light grey), mid-ventricular (grey), and apical (black). Root mean squared differences to ground truth are given in the lower right of each graph. **b**: Signal intensity curves of the left ventricular blood pool for all reconstructed images. **c**: Temporal profile plots on a log scale for two locations in the myocardium indicated by I and II in the phantom image.
In-vivo experiments

In-vivo images reconstructed with standard k-t PCA and k-t PCA\textsuperscript{mc} are shown in Figure 6.6 for data acquired during an interrupted breathhold (Figure 6.6a,b) and during free-breathing of the subject (Figure 6.6d,e). Images reconstructed from data acquired during complete breathholds are given for reference. Using k-t PCA\textsuperscript{mc} motion artifacts and residual ghosting artifacts were significantly reduced relative to the standard k-t PCA reconstruction for both interrupted breathhold and free breathing. Signal intensity curves are plotted for three mid-ventricular myocardial sectors and the left ventricular blood pool in Figure 6.7. Incomplete unfolding and ghosting artifacts are present upon standard k-t PCA reconstruction compromising signal intensity curves. Image reconstruction using k-t PCA\textsuperscript{mc} resolves the residual aliasing and yields signal intensity curves close to those extracted from the breathheld reference.
Figure 6.6 In-vivo experiments. Image slices for a single time frame as well as x-t slices reconstructed with standard k-t PCA and motion corrected k-t PCA relative to the k-t PCA breathhold reference for interrupted breathhold (a,b) and free-breathing data sets (d,e). All dynamics were warped to a respiratory reference position using the estimated deformation vector fields. For b) and e), the motion before registration of the training data and residual motion is given in (c,f).
**Figure 6.7** In-vivo experiments. a: Signal intensity curves for two subjects based on data reconstructed with standard k-t PCA (upper row), motion corrected k-t PCA\textsuperscript{mc} (middle row) and breathhold reference scans (lower row). Dotted lines are from an inferoseptal sector, dashed lines from and inferolateral and solid lines from an anterior sector. The intensity curves are extracted from the basal (light grey), mid-ventricular (grey), and apical (black) slice. Root mean squared differences relative to the breathhold signal intensity curves are given in the lower right of the graphs. b: Signal intensity curves of the left ventricular blood pool for all reconstructed images.
Figure 6.8 Error! Reference source not found. and Figure 6.9 Error! Reference source not found. show bullseye plots of the upslopes of signal intensity curves of the entire ventricle as well as bullseye plots of the variance of the differences of intensity curves relative to the median filtered signal intensity curves. Using k-t PCA\textsuperscript{mc} upslopes were found to be more homogeneous in space (up to variations of 10-15%). Error! Reference source not found. gives an overview over all 10 subjects including respiratory range and mean and standard deviation for the given variance measure.

Figure 6.8 In-vivo experiments. Bull's eye plots of myocardial perfusion upslopes (upper row) for a k-t undersampled data set with interrupted breathhold, reconstructed with standard k-t PCA (left) and k-t PCA\textsuperscript{mc} (middle) from one subject. The right plot shows a breathhold reference data set. The lower row shows the variance after subtracting a median filtered curve as measure for the waviness of the signal intensity curves. White patches indicate that not enough myocardium was visible for extracting signal intensity curves.
Figure 6.9 In-vivo experiments. Bull’s eye plots of myocardial perfusion up-slopes (upper row) for a free-breathing k-t undersampled data set reconstructed with standard k-t PCA (left) and k-t \( \text{PCA}^{mc} \) (middle) from one subject. The right plot shows the breathhold reference data set. The lower row shows the variance relative to the median filtered signal intensity curve. White patches indicate that not enough myocardium was visible for extracting signal intensity curves.
In this work iterative k-t PCA with nonrigid motion correction has been presented and implemented for dynamic 3D cardiac perfusion imaging. Using computer simulations and in-vivo data it has been demonstrated that respiratory motion artifacts from free-breathing and interrupted breathhold 3D cardiac perfusion data sets can be corrected for to a large extent. Perceived image quality, signal intensity curves and signal intensity upslpes of free-breathing data sets were found to be comparable with data acquired during complete

<table>
<thead>
<tr>
<th>Subject</th>
<th>Standard k-t PCA</th>
<th>Motion corrected k-t PCA</th>
<th>Breathhold k-t PCA reference</th>
<th>Maximal heart motion in feet-head direction [mm]</th>
<th>Chest wall motion next to the heart in antero-posterior direction [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free-breathing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#1</td>
<td>0.38 ± 0.70</td>
<td>0.06 ± 0.11</td>
<td>0.02 ± 0.03</td>
<td>7</td>
<td>0.6</td>
</tr>
<tr>
<td>#2</td>
<td>0.31 ± 0.61</td>
<td>0.09 ± 0.11</td>
<td>0.20 ± 1.03</td>
<td>8.8</td>
<td>1.1</td>
</tr>
<tr>
<td>#3</td>
<td>0.34 ± 0.94</td>
<td>0.02 ± 0.02</td>
<td>0.01 ± 0.02</td>
<td>3.5</td>
<td>0.2</td>
</tr>
<tr>
<td>#4</td>
<td>0.59 ± 0.47</td>
<td>0.06 ± 0.09</td>
<td>0.08 ± 0.11</td>
<td>6.8</td>
<td>1</td>
</tr>
<tr>
<td>#5</td>
<td>0.60 ± 0.91</td>
<td>0.03 ± 0.07</td>
<td>0.03 ± 0.05</td>
<td>11</td>
<td>1.7</td>
</tr>
<tr>
<td>Interrupted breathhold</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#6</td>
<td>0.54 ± 0.87</td>
<td>0.13 ± 0.28</td>
<td>0.01 ± 0.02</td>
<td>12.7</td>
<td>2.5</td>
</tr>
<tr>
<td>#7</td>
<td>0.83 ± 1.04</td>
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<td>0.03 ± 0.05</td>
<td>14.7</td>
<td>6</td>
</tr>
<tr>
<td>#8</td>
<td>1.1 ± 1.3</td>
<td>0.27 ± 0.27</td>
<td>0.05 ± 0.07</td>
<td>21</td>
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</tr>
<tr>
<td>#9</td>
<td>1.1 ± 1.4</td>
<td>0.12 ± 0.18</td>
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<td>2.2</td>
</tr>
<tr>
<td>#10</td>
<td>0.58 ± 0.53</td>
<td>0.07 ± 0.05</td>
<td>0.04 ± 0.06</td>
<td>14.1</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Table 6.1 Mean and standard deviation of the variance of signal intensity curves relative to the median filtered curves. Respiratory induced displacement of the heart and chest wall are quoted for each subject.

6.4 Discussion

In this work iterative k-t PCA with nonrigid motion correction has been presented and implemented for dynamic 3D cardiac perfusion imaging. Using computer simulations and in-vivo data it has been demonstrated that respiratory motion artifacts from free-breathing and interrupted breathhold 3D cardiac perfusion data sets can be corrected for to a large extent. Perceived image quality, signal intensity curves and signal intensity upslpes of free-breathing data sets were found to be comparable with data acquired during complete
breathholding of the subject. Artifacts due to abrupt and large breathing motion could be largely suppressed but further studies are warranted to indicate the minimal amount of k-space data necessary for fully suppressing image artifacts caused by strong and irregular breathing motion.

The method relies on pixel-wise deformation vector field information for each dynamic scan relative to a reference respiratory state. This information was obtained using image registration of composite data constructed from the fully sampled training and the undersampled data acquired with k-t PCA. Registration accuracy is limited by high contrast changes during first-pass bolus passage, the resolution of the composite data used as input and the small field-of-view in feet-head direction. To avoid misregistration of, for example, the left ventricle at peak contrast to the right ventricle at peak contrast, the transformation model of the registration was constrained to penalize fully nonrigid motion for the heart, liver, chest wall, and back. The required anatomic segmentation was based on a single manually segmented cardiac survey covering the whole thorax and adapted by inter-subject registration to the individual subject. In the present work the accuracy of image registration was estimated to be on the order of 3 mm near the heart. To this end, computer simulations were used to demonstrate that image reconstruction works sufficiently well even if motion information is under-/overestimated or randomly distorted up to a certain degree.

In-vivo, k-t PCA was able to restore image quality from data corrupted by respiratory motion. Semi-quantitative evaluation based on signal intensity curves revealed consistent improvement relative to standard k-t PCA reconstruction. It remains to be investigated if the improvements are also reflected in improved accuracy of myocardial blood flow values if absolute quantification is performed.

The method presented here is completely data driven and works for already acquired k-t undersampled perfusion data sets as long as the survey images are stored for shape constrained nonrigid image registration along with the perfusion data. For data sets without survey, the rigidity masks may be segmented manually.

In order to improve the accuracy of image registration, higher resolution input is required. This may be achieved by acquiring undersampled instead of fully sampled training data. Parallel imaging (Pruessmann et al. 1999) or compressed sensing (Michael Lustig, Donoho, and Pauly 2007) reconstruction can be employed to recover unfolded, high-resolution
training data at the expense of increased image noise. In addition, external sensors may be used to record physiological data during the scan (Filipovic et al. 2011) in addition to image based displacement information to improve the accuracy of motion estimation. More robust organ segmentation for constrained nonrigid image registration may be obtained from a segmentation atlas based on multiple subjects.

Image registration of all frames to a single respiratory state may imply large local and non-rigid deformations per frame depending on the respiratory pattern. The image deformations result in complex k-space distortions which in turn may lead to local undersampling greater than the nominal undersampling rate. This is a general limitation of retrospective motion correction approaches. It is subject to further studies whether radial sampling or additional spatial compression can mitigate these effects.

Reconstruction itself may be further improved by using compartments for PCA basis generation as in (Vitanis et al. 2011) given accurate registration of the training data. Partial Fourier acquisition may be incorporated into reconstruction as a regularization term (Bydder and Robson 2005).

6.5 Conclusion

Iterative k-t PCA with nonrigid motion correction enables correction of respiratory motion artifacts in dynamic 3D myocardial perfusion imaging. The method is applicable to both exams acquired during incomplete breathholds and during free-breathing of the subject. While data obtained during regular breathing results in image quality comparable to breathheld exams, irregular and abrupt breathing motion remains a challenge and requires further investigation.
7 MR Image Reconstruction Exploiting Nonlinear Transforms

7.1 Introduction

Undersampling and truncation of k-space acquisition allows for accelerated MR exams. Aliasing artifacts introduced by sampling below the Nyquist rate can be minimized by exploiting redundancy in k-space (partial Fourier (Noll, Nishimura, and Macovsk 1991), parallel imaging (Sodickson and Manning 1997; Pruessmann et al. 1999; Griswold et al. 2002)) or image domain (k-t methods (Madore, Glover, and Pelc 1999; Tsao, Boesiger, and Pruessmann 2003), compressed sensing (Michael Lustig and Pauly 2010)). While physical constraints exist for parallel imaging as to how orthogonal data can be acquired, reconstruction techniques exploiting implicit redundancy depend on the information content in the image data. These algorithms usually take advantage of transform properties of correlated image data. By introducing artifacts with different transformation characteristics, artifacts and noise may be removed using filter approaches in appropriate transform domains.

If a dynamic image series is acquired using a k-t lattice sampling pattern (Willis, Bresler, and Member 1997) undersampling artifacts are moved to the band edge in the temporal frequency domain and hence can be removed by temporal low-pass filtering (Madore, Glover, and Pelc 1999). If the image series itself contains high temporal frequencies, the reconstruction accuracy can be improved by incorporating a low spatial resolution estimate of the image for weighting in the spatial-temporal frequency domain (Tsao, Boesiger, and Pruessmann 2003). Additional transformation of spatiotemporal signals using principal component analysis has been proposed to further improve reconstruction accuracy (Henrik Pedersen et al. 2009; Liang 2007).
Compressed sensing reconstruction techniques require incoherent undersampling which introduces noise like artifacts (Michael Lustig, Donoho, and Pauly 2007). Suppressing undersampling artifacts is effectively done by nonlinear image denoising while enforcing data consistency with the acquired k-space data. Denoising is to be performed in a sparse transform domain. With the image signal being constrained to only a few coefficients, undersampling artifacts are suppressed by penalizing or thresholding noise-only coefficients. Several sparse transformations have been proposed for image reconstruction including wavelets and image gradients for spatial denoising (Michael Lustig, Donoho, and Pauly 2007; Block, Uecker, and Frahm 2007), temporal Fourier transform (M Lustig et al. 2006; H Jung et al. 2009), temporal gradients (Adluru, Whitaker, and Dibella 2007), time-frame reordering (Adluru and Dibella 2008), low-rank or principal component transformations along time (Zhao et al. 2010; Feng et al. 2011; H Jung et al. 2009) and combinations thereof (Sajan G Lingala et al. 2011). In addition, data-dependent transformations can be informed and optimized during reconstruction by dictionary learning (Elad and Aharon 2006; Doneva et al. 2010) and blind compressed sensing (Gleichman and Eldar 2011; Sajan Goud Lingala and Jacob 2013). Sparsity can also be enforced using image patches for sparse representation in spatial (Akçakaya et al. 2011) and temporal (H Jung et al. 2009; M Usman et al. 2011; Asif et al. 2012) directions.

The reconstruction schemes described above employ linear transformations to represent the full image by a reduced set of coefficients while distributing artifacts across the remaining set of coefficients. Compressed sensing theory guarantees convergence for linear transformations which fulfil the restricted isometry property (E.J. Candes and Tao 2005), i.e. which are nearly orthogonal. Upon orthogonal transformation into a sparse transform domain, the image signal can be efficiently described by a few coefficients and separated from noise, which is incoherently spread over all components. The sparsest linear transform also yields the best separation of the image signal from noise-like artifacts.

In contrast, nonlinear transformations can compress data arbitrarily efficient by encoding nonlinear prior information into basis functions. At the same time the general property of noise separation is compromised. The sparsest nonlinear coordinate transformation is a basis function connecting each data point, representing all image signals including undersampling
artifacts and noise along a single dimension. Consequently, non-linear transformations have to be adapted carefully to separate noise from valid image data.

In the present work, incoherent undersampling artifacts are suppressed in nonlinear transform domains. This is achieved by implicitly defining a nonlinear mapping into a high-dimensional kernel feature space based on the corrupted data themselves using kernel principal component analysis (kernel PCA). The transformed data are projected onto a reduced set of principal components separating artifacts from image data followed by back-mapping into the image domain. MR image reconstruction is performed iteratively by interleaved steps of gradient updates for data consistency and projection onto nonlinear principal components. The efficacy of the reconstruction is evaluated on a two-dimensional phantom and on two-dimensional and three-dimensional in-vivo data of the heart.

7.2 Theory

Linear and nonlinear data representation

Image redundancy can be exploited to approximate spatial and temporal variations with fewer coefficients. Especially on short spatial scales, a linear dependence is apparent when plotting an image profile as a function of an adjacent profile (Figure 7.1). Accordingly, image data can be efficiently represented upon transformation into gradient domains, if images are piece-wise constant, or into wavelet domains, if variations are localized in image and frequency domains (Michael Lustig, Donoho, and Pauly 2007). The sparsity present in the transform domain determines the maximum achievable undersampling rate. Long-range correlations, however, are increasingly nonlinear and require a significantly larger set of linear coefficients for their representation hence limiting the undersampling rates. In the wavelet domain, long distance correlations are represented by high-level wavelet coefficients, which also correspond to a low-resolution representation of the image. The decreased sparsity at high wavelet levels (Figure 7.1) hence requires a dense sampling of the k-space center. Data dependent nonlinear basis functions can model long-range correlations arbitarily efficient by encoding prior knowledge into basis functions. As nonlinear correlations are a priori unknown, the nonlinear basis functions have to be estimated from a set of training samples. Contrary to linear basis functions, sparsity is not the measure of
choice to determine the maximum undersampling factor as a single component would be sufficient to describe the data but at the same time will also approximate artifacts. To prevent incorporating artifacts into basis functions, which is often referred to as overfitting, regularization has to be employed.

**Figure 7.1** The graphs in the middle show plots of the profiles with circles (profile 1) and crosses (2) against the profile on the solid line (3). Changes between adjacent lines are predominantly linear and can be described by a few linear coefficients in wavelet or gradient domains (upper graph). Correlations to more distant lines are more complex. The image in wavelet domain (right) exemplifies the large amount of significant wavelet coefficients for high wavelet levels (top left in the image).

**Kernel PCA**

Kernel principal component analysis (kernel PCA) is a nonlinear extension to PCA where information is separated from artifacts in a high-dimensional feature space. It comprises of a three step process including (1) data mapping into feature space $\mathcal{F}$ where data is linearly separable; (2) a conventional linear PCA to project data onto the first $n$ eigenvectors, and (3) back-mapping of data points from feature space to input space by numerical inversion of the implicit transformation.

**Nonlinear transformation into the kernel feature space**

The nonlinear mapping $\Phi : \mathcal{X} \to \mathcal{F}$ from training input space $\mathcal{X}$ to the high-dimensional feature space $\mathcal{F}$ is not calculated explicitly (Figure 7.2). Instead, kernel PCA reformulates standard principal component analysis to operate on scalar products of function values $\Phi(x)\Phi(y)$. The dot products are evaluated directly in input space by means of Mercer’s
theorem, which states that any positive-definite, symmetric, and continuous kernel function

\[ k : \mathcal{X} \times \mathcal{X} \rightarrow \mathbb{R} \]

can be written as an inner product

\[ k(x, y) = \Phi(x)^T \Phi(y). \] [VII.1]

where the nonlinear mapping \( \Phi : \mathcal{X} \rightarrow \mathcal{F} \) and the feature space \( \mathcal{F} \) are defined by the kernel input data (Boser, Guyon, and Vapnik 1992; Vapnik 2000). Throughout this paper, a Gaussian kernel

\[ k(x, y) = \exp(-0.5 \|x - y\|^2 / \sigma^2) \]

is used. The kernel width \( \sigma \) controls the degree of nonlinearity of mapping (Rasmussen et al. 2012). In the nonlinear limit of overfitting where \( \sigma \ll \|x - y\| \), the kernel matrix approaches the identity matrix. The eigenvectors are then derived from the training data i.e. image features and noise are both interpreted as valid data. In the linear limit of a very large \( \sigma \), the kernel matrix comprises only of ones and noise becomes indistinguishable from data. Accordingly, the kernel width should match the scale of the structure which should be denoised (Braun, Buhmann, and Müller 2008). As the Euclidian distance \( \|x - y\| \) scales with the square root of the dimension \( N \) of the input space \( \mathcal{X} \), i.e. length of the vectors \( x \) and \( y \), the parameter \( \sigma \) can be normalized with respect to the dimensionality as \( \sigma = \sqrt{N} \sigma \) (Mika et al. 1998).

![Kernel PCA transformation](image)

Figure 7.2 Kernel PCA deduces an implicit transformation from training data (light grey/green circles) into a high-dimensional feature space where linear algorithms can be employed to separate image data from artifacts (dark grey/red circles).

**PCA projection in a dot product space**

Given a set of M samples as training data which are centered in the feature space, i.e. \( \sum_i \Phi(x_i) = 0 \), PCA diagonalizes the signal covariance matrix. Since all eigenvectors have to be in the span of the \( \phi \)-images of the training data, it can equivalently be written as an
eigenvalue problem of the $M \times M$ dimensional kernel matrix $K$ (Schölkopf, Smola, and Müller 1998) with matrix elements $K_{ij} = k(x_i, x_j)$

$$M \hat{a} = K a$$ \[VII.2\]

The projections of a test vector $\phi(x)$ onto the n’th principal component in feature space spanned by the training data \{$\phi(x_i)$\} is then given by $\beta_k = \sum_i \alpha_i \gamma_i k(x_i, x)$ (Mika et al. 1998).

Please note that the implicit function $\phi$ maps into an infinite dimensional feature space if Gaussian kernel functions are used and kernel PCA will return a projection $P_q \Phi(x)$ onto the first $q < M$ largest principal components. As a result the condition known from linear PCA is met i.e. the squared error $\sum_k \|P_q \Phi(x_i) - \Phi(x_i)\|^2$ is minimum and the variance in feature space is maximum.

**Back-mapping of the projected data: The pre-image problem**

The data-dependent inverse mapping of $\phi$ is unknown and does not exist as $\phi$ is typically neither injective nor surjective. Approximate solutions can be found by mapping an estimate $z$ in input space to feature space and update it by optimizing a cost function for the best fit to the projected test value $P_q \Phi(x)$ (Figure 7.3). Throughout this study, an iterative pre-image algorithm (Mika et al. 1998) is used which minimizes the Euclidian distance in feature space $\|\Phi(z) - P_q \Phi(x)\|$ with a fixed-point iteration scheme. For any kernel of the form $k(x, y) = k(\|x - y\|)$ as given for Gaussian kernels, the iteration steps can be written as

$$z_{t+1} = \frac{\sum_i \gamma_i k(z_t, x_i) x_i}{\sum_i \gamma_i k(z_t, x_i)}$$ \[VII.3\]

The scalar value $\gamma_i = \sum_k \beta_i \alpha_i^k$ comprises $\beta_i$, being the projection of test vector $x$ onto the k’th principal component as defined above and $\alpha_i$, the i’th eigenvector of the training kernel matrix.
Figure 7.3 Image data $x$ is transformed into feature space by transformation $\Phi$ and projected onto the first $q$ eigenvectors by $P_q$. Backmapping of the projected data is done by finding a so called pre-image $z$ in image space which minimizes the Euclidian distance between $\Phi(z)$ and $P_q\Phi(x)$.

**Training samples and denoising with nonlinear transformations**

Data-dependent transformations need to be trained on a set of samples to determine the mapping parameters. The training samples should correlate with the image data. In image reconstruction techniques employing linear PCA, low-rank dynamic data series can efficiently be compressed along the temporal direction. Thereby, the time profile of each voxel is effectively approximated by linear combinations of the principal component basis functions which are either estimated from low-resolution data (Henrik Pedersen et al. 2009; H Jung et al. 2009) or by singular value shrinkage (Sajan Goud Lingala et al. 2011).

To exploit arbitrary correlations in multi-dimensional data, the use of image blocks has proven successful in image processing, MR data denoising and linear sparse representations (Wiest-Daesslé et al. 2008; Adluru et al. 2010; Akçakaya et al. 2011). For kernel PCA, a set of image blocks can be stacked to vectors and used as training input space $\mathcal{X}$. Although correlation and artifact removal may be performed for all image blocks at once, subdivision into smaller chunks is preferable as the kernel matrix size scales with the square and the computational complexity with the cube of the sample size.

In the present work, each image block is denoised separately using a training sample set containing image blocks centered on neighboring pixels. The pixels of each block are stacked to vectors $\mathbf{x}_i$ such that the dimension of the input space is given by the numbers of pixels per block (Figure 7.4). A kernel matrix using a Gaussian kernel function is then populated with data from the surrounding of each patch. Each image patch is finally projected onto the first
few principal components in the features space spanned by the training patches from neighboring pixels and subsequently transformed to the input space using a fixed-point iteration scheme of equation [VII.3]. To restore images from the overlapping image blocks, a triangular weighted reprojection is performed to minimize ringing and step artifacts (Salmon and Strozecki 2012). For very large sample sets, the number of samples can be reduced by clustering the samples and replacing each cluster by a cluster prototype. In this study, clusters are replaced by a weighted sum using a Gaussian distance function to the cluster mean as weighting (Figure 7.5).

Figure 7.4 Workflow for artifact removal in a nonlinear transform domain employing kernel PCA.
Figure 7.5 The total number of samples are aggregated according to their Euclidean distance to form a maximal number of $k$ clusters. The samples of each cluster are replaced by a distance weighted mean (cross).

Projected MR reconstruction for nonlinear transform domains

MR reconstruction inverts a linear encoding equation $d = \mathbf{E} \mathbf{m}$ where $d$ are the acquired $k$-space data, $\mathbf{E}$ the encoding matrix including Fourier sampling, and $\mathbf{m}$ the image to be reconstructed. Image reconstruction is constrained by a projected Landweber iteration scheme as in iterative shrinkage and thresholding algorithms (Chambolle et al. 1998; Daubechies 2004). The update rule is given by

$$m_{k+1} = P_{k} (m_k - \mathbf{E}^H (\mathbf{E} m_k - d))$$  \[VII.4\]

where $P_{k}$ is the kernel PCA feature extraction, i.e. the projection onto the span of the training data in feature space. For data from multiple receive coils, the gradient update $\partial \mathbf{m}_k$ can be optimized with SENSE iterations

$$\mathbf{m}_{k} = P_{k} (\mathbf{m}_k + \partial \mathbf{m}_k)$$  \[VII.5\]

$$(\mathbf{E}^H \mathbf{E}) \partial \mathbf{m}_k = \mathbf{E}^H (d - \mathbf{E} \mathbf{m}_k)$$  \[VII.6\]

Low-order phase corrections can be either incorporated into the encoding matrix as in (Michael Lustig, Donoho, and Pauly 2007) or can be accounted for by explicit projection of the data to the low-order phase estimate in equation [VII.5].
7.3 Methods

Simulations
To evaluate reconstruction performance, a two-dimensional in vivo image in short-axis view was simulated and retrospectively undersampled along one direction using a Cartesian pseudo-random undersampling pattern (Michael Lustig, Donoho, and Pauly 2007). Artificial noise following a normal distribution was added to obtain an average signal-to-noise ratio of 20. The 192x192 image matrix was sampled with 97, 65, 49, and 39 k-space profiles, corresponding to acceleration factors of 2, 3, 4 and 5, respectively.

In vivo data
A fully sampled two-dimensional data set in short axis view of the heart was acquired on a 3 T scanner (Ingenia, Philips Healthcare, The Netherlands) with a 28-channel coil array and compressed to 4 virtual coils (Buehrer et al. 2007). The scan parameters of the balanced SSFP sequence included a field-of-view of 270x270 mm², slice thickness: 8 mm, TR/TE: 3.8/1.84 ms, voxel size: 1.4x1.4 mm², flip angle = 45°, acquisition matrix: 192x190. K-space data was compressed to 4 virtual coils and K-space profiles were retrospectively discarded for reduction factors from 2 to 5. In addition, two whole-heart scans were acquired on a 1.5 T system (Achieva, Philips Healthcare, The Netherlands) with a 5-channel cardiac coil in the end-diastolic rest period with a balanced SSFP sequence and scan parameters including a field-of-view of 256x256x144 mm³, acquisition matrix: 192x192x108, voxel size: 1.33x1.33x1.33 mm³, TR/TE: 4.6/2.3 ms, flip angle 110°, acquisition window: 74 ms. Eight-fold pseudo-random undersampling was used. All data were acquired in healthy subjects after written consent was obtained according to institutional guidelines.

Data reconstruction
Each data set was reconstructed with Lustig’s sparse MRI code (Michael Lustig, Donoho, and Pauly 2007) and with the algorithm proposed here. Both approaches were implemented in MATLAB (Mathworks, Natick, MA). Lustig’s code was extended to support three dimensions and to include coil sensitivity information. The regularization parameters for
compressed sensing reconstruction were found by an exhaustive search starting from noise level.

The reconstruction approach employing nonlinear transforms proposed here included two steps. To remove large and potentially correlated undersampling artifacts, 15 iterations were performed using the first principal component while decreasing the normalized kernel width from twice the noise level to half the noise level. Thereby the most dominant image features were retained while small structures and noise were smoothed or completely removed. Detailed image structures were then reconstructed in a second step using 40 iterations with a fixed kernel width and taking into account all principal components above the noise level. The noise level was determined based on the cumulated energy in the principal components (Braun et al. 2008). The image blocks used for correlation were 5 pixels wide in each direction with search window width of 15 pixels.

Computation time for kernel PCA artifact removal of a single image block was on the order of 100 msec using standard PC hardware. Accordingly, image reconstruction times of the 2D data was 10 min.

7.4 Results

Simulations

Results comparing zero-filling, compressed sensing with wavelet transform and total variation, and the proposed projection in nonlinear feature space are shown in Figure 7.6 for undersampling factors from 2 to 5 for the simulated data. In comparison to the linear wavelet and gradient transforms, reconstruction using the kernel methods based nonlinear transform was found to yield improved image fidelity and reduced noise. This is particularly apparent at undersampling rates of 4 and 5. Figure 7.7 depicts the full field-of-view for the proposed algorithm for all undersampling factors tested.
Figure 7.6 Simulation data. The upper row depicts the ground truth and reconstruction results for zero-filling, compressed sensing with wavelet and total variation constraints and the proposed algorithm with kernel PCA projections. The zoomed images below show reconstruction results and their difference to the ground truth multiplied by 5 for undersampling factors of 2 to 5. Root mean squared errors are indicated.
Results

**Figure 7.7** Simulation data. Reconstructed image for the proposed algorithm for undersampling factors 2 to 5.

**In vivo data**

Figure 7.8 compares zero-filling, compressed sensing, and the projection in nonlinear feature space for retrospectively undersampled two-dimensional cardiac data. It is seen that wavelet and total variation based compressed sensing results in a loss of resolution for increasing undersampling factors. Using proposed nonlinear transforms, the overall structure and sharpness was well preserved for all undersampling factors. The difference images in Figure 7.8 reveal that compressed sensing reconstruction compromises image structures especially at higher undersampling factors while the proposed reconstruction scheme introduces mainly uncorrelated noise as compared to the fully sampled reference.
**Figure 7.8** In vivo data. The upper row depicts the fully sampled image, zero-filled Fourier transform and the reconstruction results for compressed sensing and the proposed algorithm for 4x undersampled data. The zoomed images below show reconstruction results and their difference to the fully sampled image multiplied by 5 for undersampling factors of 2 to 5. Root mean squared errors are indicated.

Reformatted images showing the right coronary artery reconstructed from eight-fold undersampled three-dimensional whole heart scans obtained in two subjects are compared in Figure 7.9. In contrast to compressed sensing reconstruction, contrast and vessel sharpness were found to be comparable to the reference when using a nonlinear feature space.
Discussion

Figure 7.9 Whole-heart in vivo data. Reformatted coronary images showing the right coronary artery in two volunteers as reconstructed from 8-fold undersampled MR data using zero-filling, $l_1$ compressed sensing and the proposed projection in a nonlinear feature space.

7.5 Discussion

In this work, an algorithm for image reconstruction from undersampled MR data exploiting nonlinear transform domains has been proposed and implemented. Images were reconstructed iteratively by interleaved gradient updates using the acquired k-space data and projections onto a reduced set of principal components in a high dimensional kernel feature space. Undersampling artifacts in two- and three-dimensional phantom and in vivo data were successfully removed and results compared favorably relative to those obtained with compressed sensing reconstruction.

The requirements for optimal reconstruction with a nonlinear transform are different from standard compressed sensing using orthogonal linear transforms. In compressed sensing, the maximum achievable undersampling factor is related to sparsity which determines the number of significant coefficients in the transform domain while incoherent undersampling artifacts are dispersed across all coefficients. In nonlinear transform domains, noise-like artifacts can accumulate in specific coefficients if nonlinear basis function also capture noise
and generate a pseudo-signal. Data dependent nonlinear transforms, hence, need to employ regularization as trade-off between efficient data representation and artifact separation.

Most common data dependent nonlinear transformation are extensions of standard PCA, as for example Kramer’s nonlinear PCA (NLPCA), which is based on auto-associative neural networks (Kramer 1991), and kernel PCA. NLPCA trains a neural network to find a sparse representation of training data. NLPCA has the advantage of having an explicit back-mapping to the training input space which allows for alternative MR reconstruction schemes such as II-minimization, if appropriate gradient functions for the nonlinear mapping can be calculated. Training the neural network scales linearly with sample size, but is generally a time-consuming optimization procedure with non-deterministic results as the cost-function usually contains local minima. The restriction in sample size of kernel PCA resulting from the cubic dependency on the sample size was solved by correlation of image blocks with their vicinity and reducing the number of samples by clustering. For image series, the correlation can also be performed in the time-domain as already used in post-processing and noise removal of fMRI data sets (Rasmussen et al. 2012).

The performance of artifact removal with kernel PCA is controlled by the kernel width and the number of retained principal components. Efficient separation of image data from artifacts is only achieved if the kernel width is on the scale of the structure in the image. A fixed kernel width can be used if noise and artifacts are on the same intensity level. Owing to the large intensity differences in undersampled MR images, the kernel width in the present work was chosen adaptively for the first few iterations to remove artifacts from different intensity levels while image signal was recovered by the gradient update in the next iteration.

Principal component analysis in feature space is based on a L2 loss function which is sensitive to outliers. Especially for high reduction factors, large and correlated undersampling artifacts can deviate already the first few principal components from the desired ones. Pre-filtering training data and employing statistically robust linear feature selection in feature space (Alzate and Suykens 2008) could further improve artifact removal and simplify the selection of kernel width and number of principal components.
In kernel PCA, the Euclidean norm as distance measure is used in the kernel input space. More advanced dissimilarity measures, e.g. based on structural similarity (Z. Wang et al. 2004) may allow for higher undersampling factors.

Reconstruction times were on the order of 10 min per image with the present implementation as the projection step was applied to each image block independently. Potential improvements in reconstruction speed can be achieved by correlating multiple image blocks at once and employing iterative kernel PCA schemes such as a kernel Hebbian algorithm (K. I. Kim, Franz, and Schölkopf 2005) which also scales linearly with the sample size. The use of many computer nodes in parallel as for example on graphics cards could further reduce reconstruction times. The convergence rate of the reconstruction could be increased by modifying the gradient updates with prior knowledge or gradient directions from previous iteration steps (Donoho, Maleki, and Montanari 2009; Engl 1987).

7.6 Conclusion

Image reconstruction from undersampled data exploiting nonlinear transform domains and kernel methods is feasible and outperforms compressed sensing reconstruction. The method holds considerable potential to allow for higher acceleration factors relative to compressed sensing for a range of applications including cardiovascular imaging.
8 Discussion and Outlook

In this thesis, methodological developments have been presented for the suppression of respiratory motion and undersampling artifacts.

Nonrigid motion correction for whole-heart coronary magnetic resonance angiography has been proposed and implemented. Interleaving the coronary scan with the acquisition of image-based navigators, a patient-specific 3D nonrigid motion model was derived without imposing any scan time penalty. The nonrigid respiratory motion correction has enabled a gate-free acquisition of whole-heart scans and thus a scan time reduction of a factor of two. The concurrent acquisition of the motion model is applicable to MR exams with sequence pauses during the cardiac cycle to acquire 2D motion scouts. In its current implementation, a single fully-sampled 2D imaging slice is obtained once per heartbeat. Accordingly, a minimum of ~400-500 heart cycles is required for a full 3D model. This can be addressed by acquiring multiple slices in conjunction with k-space undersampling.

The proposed implementation of an iterative of k-t PCA algorithm with training regularization in a motion compensated transform domain has enabled correction of respiratory motion artifacts in 3D first-pass myocardial perfusion imaging. Reconstruction performance of data acquired during regular breathing results in image quality comparable to breathheld exams, but abrupt and strong motion amplitudes remain challenging. To address the low resolution and the varying contrast over time, motion information was obtained using a shape-constrained image registration of the composite of training and undersampled data. Thereby, the transformation model was restricted to approximately affine motion for chest wall, heart, and spine. Additional undersampling of the training data and reconstruction with higher resolution reduces partial volume effects in areas where the displacement fields have high spatial variation, e.g. between chest wall and inner organs, and can thus improve the fidelity of the motion corrected PCA basis.

Image reconstruction using nonlinear projections can be used for effective removal of undersampling artifacts. Long-range correlations which cannot be sparsely modeled with
wavelet and finite-differences transforms can be approximated by nonlinear basis functions allowing for higher undersampling factors relative to standard compressed sensing. The current implementation of image reconstruction in nonlinear transform domains has a high computational load. Since every image block is processed separately, vastly parallel processing as in graphical processing units can improve speed considerably. For very large image dimensions, iterative kernel PCA alternatives like kernel Hebbian algorithms are preferable due to the linear dependence on the sample size.

**Outlook**

**Motion Correction:**

Besides gating, advanced motion compensation techniques are typically either prospective or retrospective. Both are limited in handling very large motion amplitudes. In prospective approaches, wrongly corrected static tissue introduces blurring and ghosting artifacts. By using retrospective methods, k-space is distorted and gaps are introduced upon transformation into the static reference frame of the object. A combined approach using partially prospective adaption of encoding gradients and retrospective correction of remaining motion and artifacts introduced by the prospective adjustments should mitigate the effects of large motion.

If scan time in dynamic perfusion imaging is not an issue, the free-breathing image acquisition can be prolonged to fill each respiratory motion state with enough k-space data for image reconstruction and perform motion compensation in the image domain. For k-t undersampling, the pattern should be updated in real-time according to the respiratory state to ensure optimal separation of the Nyquist replicas in the x-pc space. Assumptions on slow signal changes over time do not hold in this case due to the non-uniform temporal spacing of the time frames in each motion state.

**Motion Estimation:**

If MR navigators are limited in the dimensionality, e.g. as for the 1D respiratory navigators for self-gating, static tissue and the strong fat signal from the chest wall compromise the
obtained motion information. Besides the intensity modulation in antero-posterior direction proposed in (Lai et al. 2008), spatially selective 2D and 3D radiofrequency pulses can be employed for reduction of the field-of-view to suppress signal from the chest wall and static tissue from the spine. Multi-channel transmit systems are beneficial for optimized radiofrequency pulses.

Magnetic field probes can be used to measure tissue magnetization. The magnetization decreases with the inverse-square of the distance to the tissue. Consequently, any tissue motion changes the signal in the field probes. Because of the sparse measurement of the spatial distribution of the magnetization, detailed motion information can only be inferred upon after calibration with an estimation of the magnetization at several motion states.

The shape-constrained image registration as proposed in Chapter 6 can be improved by increasing the sample size for the reference segmentation, for example by using a segmentation atlas.

**Accelerated Imaging:**

Various approaches exist for combinations of parallel imaging and compressed sensing. Considering the performance of encoding with coil sensitivities with a few distinct aliases, a point-spread function with distinct peaks and incoherent aliases in-between provides a trade-off between sampling requirements for both reconstruction schemes. Coherent undersampling in the k-space center has been proposed with various approaches for the higher k-space coefficients (Hutter et al. 2013; Sung and Hargreaves 2013). An additional shift of the undersampling pattern along time is beneficial for dynamic imaging.

The sampling pattern for compressed sensing is typically optimized in advance for a point-spread function with minimum side lobes. But for images with spatially varying intensities, the actual aliasing strength in image domain depends on the object too. Optimizing the sampling pattern using an image estimate can reduce residual aliasing.

In conclusion, significant methodological advances to accelerate MR scans and suppress artifacts from respiratory motion and k-space undersampling have been achieved in this work. Based on in vivo studies the effectiveness of the proposed methods towards their potential implementation in clinical practice has been demonstrated.


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**List of Publications**

**Journal Articles**


**Conference Abstracts and Proceedings**


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