

Respiratory Motion of the Heart:
Implications for Magnetic Resonance
Coronary Angiography

Guy Shechter

A dissertation submitted to the Johns Hopkins University in conformity with the
requirements for the degree of Doctor of Philosophy.

Baltimore, Maryland

2004

Copyright © 2003 by Guy Shechter,
All rights reserved.

Abstract

Magnetic resonance (MR) coronary imaging is susceptible to artifacts caused by motion of the heart. The purpose of this thesis was to study the respiratory motion of the coronary arteries and to use the results to develop strategies for improved MR imaging.

The first section of the thesis describes an MR motion correction technique for objects undergoing a 3D affine transformation. The remainder of the thesis focuses on measuring the respiratory motion of the heart from free breathing X-ray angiograms.

Stereo reconstruction methods are used to generate 3D models of the arteries from biplane angiograms. A method for tracking the motion of the arteries in a sequence of biplane images is presented next. The algorithm uses 3D regularizing constraints on the length changes of the arteries and on the spatial regularity of their motion. The algorithm was validated using a deforming vascular phantom. RMS 3D distance errors were measured between centerline models tracked in the x-ray images and gold-standard models derived from a gated 3D MR acquisition. The mean error was 0.69 ± 0.06 mm for four different orientations of the x-ray system.

The motion field recovered from free breathing angiograms is a combination of the cardiac contraction and respiratory motion of the heart. A cardiac respiratory parametric model is formulated to decompose the field into independent cardiac and respiratory components. Results are presented for ten patients imaged during spontaneous tidal breathing. For all patients, the heart translated caudally (mean, 4.9 ± 1.9 mm) and rotated in a cranio-dorsal direction (mean, $1.5^\circ \pm 0.9^\circ$) during inspiration. In eight patients, the heart also translated anteriorly (mean, 1.3 ± 1.8 mm) and rotated in a caudo-dextral direction (mean, $1.2^\circ \pm 1.3^\circ$).

Anatomic landmarks were used to compare results across patients. Three dimensional displacements and velocities were compared, and quiescent periods in the

PhD Thesis © 2003 by Guy Shechter.

respiratory and cardiac cycles were measured. Finally, respiratory motion was analyzed using three linear motion models that correspond to available MR motion correction techniques: translation, rigid body, and affine. Calculations indicate that a two-to-four fold increase in scan efficiency is attainable, resulting in reduced scan times while maintaining image quality.

Advisor: Elliot R. McVeigh, Ph.D.

Contents

List of Figures	vii
List of Tables	xv
1 Background	3
1.1 Coronary Artery Disease	3
1.2 Clinical Imaging of Atherosclerosis	4
1.3 Magnetic Resonance Coronary Angiography	5
1.4 Motion Correction for MRI	7
1.5 Respiratory Motion of the Heart	9
1.6 Specific Aims	11
2 MR Motion Correction of 3D Affine Deformations	12
2.1 Theory	13
2.1.1 3D Affine Transformation	13
2.1.2 Space-Frequency Duality of 3D Affine Transformations	14
2.2 Computer Simulation: Prospective Correction	16
2.2.1 Method	16
2.2.2 Results	18
2.3 Discussion	21
2.4 Conclusion	25
3 Reconstructing 3D Arterial Trees from X-ray Angiograms	26
3.1 X-ray Angiography	26
3.1.1 Hardware	27
3.1.2 The Imaging Equation	27
3.2 Methods	31
3.2.1 Geometric Distortion Correction	31
3.2.2 Imaging System Calibration	40
3.2.3 Stereo Reconstruction of 3D Curves	43
3.3 Results	50
3.4 Discussion	55

3.5	Conclusion	57
4	Motion Tracking of Arteries in Biplane Cineangiograms	58
4.1	Description of Algorithm	60
4.1.1	Motion Models	60
4.1.2	Energy Minimization	62
4.2	Experimental Validation: Phantom	67
4.2.1	Method	67
4.2.2	Results	69
4.3	Experimental Validation: Clinical Angiograms	71
4.3.1	Method	71
4.3.2	Results	72
4.4	Discussion	78
4.5	Conclusion	81
5	Respiratory Motion of the Heart from Free Breathing Coronary Angiograms	82
5.1	Methods	83
5.1.1	Coordinate Systems	83
5.1.2	Imaging protocol	83
5.1.3	Cardiac Respiratory Phase Plane	84
5.1.4	Motion Tracking in Biplane Cineangiograms	84
5.1.5	Respiratory motion: Translation, Rigid Body, Affine, or More?	88
5.1.6	Cardiac and Respiratory Parametric Model (CRPM)	89
5.1.7	Measuring Respiratory Motion Parameters	94
5.2	Results	94
5.2.1	Translation, Rigid Body, Affine, or More?	95
5.2.2	Cardiac Respiratory Parametric Modeling	99
5.3	Discussion	103
5.4	Conclusion	106
6	Cardiac and Respiratory Motion of the Coronary Arteries	107
6.1	Method	108
6.1.1	Imaging Protocol	108
6.1.2	Motion Reconstruction	109
6.1.3	Data Evaluation	110
6.2	Results: Cardiac Motion	114
6.2.1	Displacement	114
6.2.2	Velocity	118
6.2.3	Rest Period	124
6.3	Results : Respiratory Motion	130
6.3.1	Displacement	130

6.3.2	Velocity	134
6.3.3	Rest Period	138
6.4	Discussion	144
6.4.1	Comparison with Previous Studies: Cardiac Motion	145
6.4.2	Comparison with Previous Studies: Respiratory Motion	147
6.4.3	Implications for MR Coronary Imaging	149
6.5	Conclusion	157
	Bibliography	159
A	The Fourier Transform and 3D Affine Deformations	174

List of Figures

2.1	The space–frequency duality of 3D affine transformations. A spatial 3D affine deformation of an object, is equivalent to a 3D affine deformation, with a phase and amplitude modulation of the object’s frequency representation (k –space). The space and frequency affine transformations are related by Eqs. (2.5) and (2.7).	15
2.2	(a) The discrete 3D heart phantom constructed using the implicit algebraic equation $(x^2 + 2y^2 + z^2 - 1)^3 - z^3(x^2 + 0.1y^2) < 0$. (b) A 3D affine deformation of the phantom.	17
2.3	Flow diagram for prospective 3D affine motion correction.	19
2.4	Three orthogonal slices through the imaging volume. Columns I and II show the binary phantom in the undeformed (see Figure 2.2) and maximally deformed states, respectively. A simulated 3D spin-warp acquisition of the periodically deforming phantom results in significant ghosting artifacts (III). Correction for the known 3D translation, rotation, and scaling components of the 3D affine deformation improves the quality of the images (column IV), but artifacts due to uncompensated shearing remains. In column V, images obtained with 3D affine motion correction for a known deformation.	20
2.5	Flow diagram for retrospective 3D affine motion correction.	24
3.1	X-ray coronary angiography is performed by selectively injecting the arteries with a bolus of iodinated contrast.	28
3.2	Diagram of an x-ray imaging system. An x-ray source and image intensifier are arranged on a C-arm gantry. The isocenter is defined as the point of rotation of the imaging arm. The SOD, or source to object distance, is measured to the isocenter, where the imaged object is typically placed. SID is the source to image intensifier distance, and IS is the intensifier size. The figure is adapted from the Series 9800 Mobile C-Arm Operator’s Guide (OEC Medical Systems Inc).	29

3.3	The primary angle (PA) and secondary angle (SA) define the geometric orientation of the imaging system with respect to the patient. Zero degree primary and secondary angles correspond to an anterior-posterior projection. The primary angle diagram is viewed from the patient's feet.	29
3.4	The coordinate system of the imaging C-arm. For the mathematical description of the imaging process, different projections of the patient are obtained by rotating the patient in the camera's fixed frame of reference.	30
3.5	Geometric distortion of a rectangular grid of radio-opaque beads spaced at 1cm intervals. The image was acquired with a 0° LAO/RAO, 0° Cranial/Caudal, and a source intensifier distance of 1058 mm.	33
3.6	Morphological dilation of the background improves the result of threshold segmentation, which is particularly noisy at the image intensifier boundary. Result of threshold segmentation in (a), followed by morphological dilation in (b).	35
3.7	The undistorted bead positions are generated using the parametric model defined in Equation (3.2.1). The vector (u,v) describes the fundamental separation between two neighboring beads.	35
3.8	Shapes of four different size neighborhoods used to compute the undistorted bead positions. The neighborhood sizes are (a) 49, (b) 25, (c) 9, and (d) 5 beads.	36
3.9	Undistorted beads(+) calculated from, and superimposed on the distorted image of Figure 3.5.	37
3.10	Screen-shot of <i>gcoro</i> . The software enables the user to segment artery centerlines on an image, while being constrained by the multiscale response map. <i>gcoro</i> was written by Arnaud Contes and provided courtesy of the Chir group at INRIA-Sophia Antipolis.	44
3.11	(a) LAO cranial projection of the left coronary artery tree. Results of the vessel detection filter are shown in (b)-(e) for different values of σ . This second derivative based method enhances rectilinear structures, such as vessels. (f) The multiscale response map stores the best response among the different σ values at each pixel.	46
3.12	Three dimensional reconstruction of curves is complicated by the need to define correspondence between points in the two projections. In this example, the bifurcations are well defined point matches. Along the length of the curve, the matching is more ambiguous.	48
3.13	The epipolar constraint is used to identify matching points between two curve projections. The plane $P_1S_1S_2$, defined by the two x-ray sources and a point in the first image plane, intersects the second image plane along a line. The epipolar constraint states that the matching point P_2 is on this line.	48

3.14	(a) The correspondence matrix represents all possible point matches between a curve's two projections. Each possible match has an associated cost, or error metric, and is defined as the distance of one point to the epipolar line generated from the other point (b). The minimum cost path through the correspondence matrix (white line) represents the optimal matching between the two curves. Figure (b) is adapted with permission from [73].	49
3.15	RMS errors of dewarping polynomials as a function of polynomial degree for different imaging orientations (a)-(e). The RMS error of the horizontal and vertical polynomials are plotted independently as solid lines, and the norm distance RMS error is plotted as a dashed line. The maximum displacement error from each of the fits (a)-(e) is plotted in (f) as a function of polynomial degree.	51
3.16	Correction of the geometric distortion found in the image shown in Figure 3.5 using fifth degree bi-polynomials.	52
3.17	A bead phantom was reconstructed from a group of projection images, and the 3D reconstruction was projected onto these images. (a) No calibration was performed. (b) In-plane rotation, (α), of each image was optimized. (c) In-plane rotation, (α), and translation (t_x, t_y) of each image was optimized.	54
3.18	RAO (a) and LAO (b) projections of the left coronary tree at end diastole. In (c), a wide-eyed stereogram of the reconstructed arteries, where the vessel diameters reflect the scale with the largest response in the artery detection step.	56
4.1	RAO (a) and LAO (b) projections of the vascular phantom. In (c), one slice of the 3D MRI volume of the phantom, and in (d) a maximum intensity projection of the MR images.	68
4.2	The vascular phantom was reconstructed and tracked through seven pairs of biplane x-ray images. The solid line shows the 3D RMS error between the tracked vascular phantom and the gold standard centerline models obtained from MR imaging at each motion phase. As a baseline error level (dashed line), the 3D RMS error between the untracked x-ray reconstruction, and the deforming gold standard MR reconstructions was computed. The lines represent the mean (and one standard deviation) of results obtained in four independent acquisitions obtained with different biplane angular separations.	70

4.3	Convergence plots for five interframe motion tracking steps in the clinical coronary angiogram dataset of one patient. Two circular marks on each curve indicate the transition between the rigid and affine motion tracking, and between the affine and B-solid motion tracking steps. The energy increases observed at the transitions between the different motion models is due to the larger spatial smoothing used for the initial recovery phase of each motion model as part of the multiresolution tracking strategy.	75
4.4	The RMS reprojection errors following tracking through one cardiac cycle in five patient data sets.	75
4.5	In one patient, the mean 3D displacement (dashed line) from end-diastole of points on the coronary tree are shown in comparison to the measured RMS reprojection error (solid line). Error bars show one standard deviation of the 3D displacements. The first image frame represents end-diastole, and the 14 frames span one cardiac cycle. . .	76
4.6	Tracking results for one patient over one cardiac cycle. The biplane image pairs correspond to atrial contraction (top row), systole (middle row) and end-diastole (bottom row).	77
5.1	(a) Respiratory phase is measured by tracking the displacement of the diaphragm along a profile in the angiogram images. (b) The displacement of the lung-diaphragm interface is shown as a function of image number for the profile shown in (a).	85
5.2	(a) Cardiac Respiratory Phase Plane (CRPP). (b) The CRPP representation corresponding to the data of Fig. 5.1 is shown. Because the tree is not fully opacified at the start and end of the injection, only images which can be used for tracking the motion of the heart are shown. The label “Im N” represents the N-th image of the angiogram sequence. The sampling density on this plane depends on the frame rate, heart rate, respiratory rate, and the duration of the contrast injection. . .	86
5.3	A right coronary artery is shown in relation to its B-solid. The B-solid deforms the space and the arteries within, such that the projected motion of the arteries is consistent with the biplane angiogram images. The x , y , and z displacements of one B-solid control point are shown as a function of the angiogram image number. The plots show four cardiac cycles and a slower respiratory drift spanning 100 images (3.3 seconds). The CRPP representation of the data is shown in Fig. 5.2b.	90
5.4	The CRPM is applied to each B-solid control point independently. The results of the model fit (solid line) are shown with respect to the original data (dots) from Fig. 5.3.	96

5.5	Biplane images of patient P2 at tidal end expiration and end inspiration. The images show the heart in diastasis. The white lines represent the projection of a 3D coronary tree model onto the imaging planes. The 3D deformation of the coronary tree is calculated automatically using a motion tracking algorithm.	96
5.6	Three orthogonal projections of patient P2's coronary arteries at tidal end expiration (solid model) and end inspiration (dotted lines). The arteries are shown at a mid-diastolic (diastasis) cardiac phase. Clockwise from top left: RL projection; AP projection; SI projection. . . .	97
5.7	Tidal end inspiration images for patient P2. The white lines represent the projection of a 3D coronary tree onto the images. The first column shows the ability of a 3D translation motion model to register the coronary tree reconstructed at end expiration to these end inspiration images. The second and third columns show a rigid and affine motion model respectively. An improvement in the fit is seen from left to right, but there is evidence of residual local deformation.	98
5.8	Residual errors of three motion models used to characterize the tidal respiratory motion of the left coronary tree for nine patients. e_{3D} is a baseline 3D RMS distance between the coronary tree at the respiratory extremes. e_T , e_R , and e_A are the residual 3D RMS distance after registration using, respectively, a 3D translation, 3D rigid body, and 3D affine transformation.	100
5.9	Residual errors of three motion models used to characterize the tidal respiratory motion of the right coronary artery for four patients. e_{3D} is a baseline 3D RMS distance between the coronary tree at the respiratory extremes. e_T , e_R , and e_A are the residual 3D RMS distance after registration using, respectively, a 3D translation, 3D rigid body, and 3D affine transformation.	100
5.10	Validation results for the CRPM in Patient P9. The 3D RMS error, $e_{3D}(\Upsilon_t, \widehat{\Upsilon}_t)$, is calculated between the coronary tree Υ recovered from the images, and the coronary tree $\widehat{\Upsilon}$ generated by the parametric CRPM. e_{3D} as plotted as a function of (a) image number, (b) cardiac phase, and (c) respiratory phase. In this patient, a higher variability in RMS error is coincident with the QRS complex (b) and with the tidal end-expiration and end-inspiration respiratory phases (c). . . .	102
5.11	Rigid body motion parameters of the heart as a function of diaphragmatic displacement in patient P8.	104
6.1	Landmarks on the right and left coronary artery trees were selected using the reporting system of Austen <i>et al.</i> [112]. (Figures borrowed from the original publication.)	111

Acknowledgements

I am grateful to my advisor, Elliot McVeigh, who provided me with guidance and support from beginning to end. I admire how he encourages his students to pursue their own scientific and personal interests. I credit his style of management with helping me to develop into an independent researcher. He was keenly aware of my perfectionist tendencies and knew just when to encourage me to get the job done. He has shown me how to balance work and play and that one can have fun on the road to being successful.

My undergraduate advisor, Robert Phair, mentored me during my early Johns Hopkins years. He took me into his lab and guided me through the process of independent research. I admire his excitement for science and his sense of idealism. I thank him for encouraging me to pursue a doctoral degree.

Ever since Richard Johns interviewed me for the PhD program, he has remained involved in my journey. As I remember his socializing with students at the Friday pre-seminar lunches, I thank him for being involved with the next generation of scientists. I am in awe (and afraid) of his ability to ask just the right question that leaves you speechless and in doubt of your entire direction of research.

I extend my sincere gratitude to Evelyn McCann, the PhD program's administrator. She made the graduate school experience a pleasant one. I can't even begin to understand how she maintains an unwavering kindness and desire to help while having to work with so many students and professors.

As I prepare to start a post-doctoral fellowship, I am reminded of Cengizhan Ozturk and Jerome Declerck, who were post-docs in the lab at Johns Hopkins when I was a young graduate student. Cengizhan and Jerome are libraries of technical information and are always willing to share their knowledge. Cengizhan taught me all about splines and the art of scientific self-deprecation. Jerome introduced me to the world of mathematical formalism and the mentality of the French.

Jerome was responsible for introducing me to his colleague, Eve Coste-Maniere. As leader of the Chir Equipe at INRIA, the French Institute for Computer Science and Automation, Eve invited me to the Cote d'Azur to work on common research

interests. The nine months I spent in Sophia Antipolis were an unbelievably fantastic experience - and scientifically rewarding, too! (Thank you, Elliot, for encouraging me not to miss this opportunity.) I thank the entire Chir team for making my stay enjoyable, for forcing me to learn French, and for helping me settle into a new place.

Frederic Devernay mentored me through my scientific renaissance. He taught me the way of computer vision and guided me in the application of those methods to the field of medical imaging. My perspective on society and government has been forever changed by our social democracy vs. capitalism polemics. I am lucky to have shared my office with Christophe Blondel, who made every day at INRIA fun. I admire his mathematical prowess and his willingness to work together to solve problems that plagued both of us. I am thankful to Christophe and Marion Mastantuono for their friendship and for making sure I fully experienced the French lifestyle.

I am also grateful to Laurent Zenouda and Valerie Serban for opening their home to me, their downstairs neighbor. They made the small village of Valbonne feel even cozier over Friday night dinners and countless bottles of wine.

When I returned to Hopkins/NIH, I was fortunate to meet Jon Resar. He made my experiments happen. I truly appreciate the time Jon took to explain the world of interventional cardiology to me, and I admire the kind manner in which he interacts with others.

I extend a warm thank you to all my friends and colleagues at Johns Hopkins and the National Institutes of Health. Special mention goes to Christopher Yeung, Luis Gutierrez, Patrick Helm, and Daniel Ennis, who often found themselves as my sounding boards. Luis also served as copy editor for many of my writings. I am very appreciative that Luis, Daniel Herzka, and Patricia Codina took me in as a roommate, which made the last stretch of my Ph.D. adventure pure fun.

I want to thank members of my family: my parents Ruth and Zvi for encouraging me to stick with the program, and for learning to stop asking when I would be finished; my brother Barak for technical discussions and assistance; my grandparents Cili and Moshe Eichel, and Milka and Menachem Shechter for their love and support; my Texas family Alona, Lea, and Yitzchak Eichel for their encouragement; and Gili and Henry Charrabe for fun weekend diversions in New York City.

Chapter 1

Background

1.1 Coronary Artery Disease

Atherosclerotic coronary artery disease (CAD) is a pathology of the arteries that supply blood to the heart. The development of atherosclerosis is a gradual process involving deposition of lipids, macrophages, lymphocytes and proliferation of smooth muscle cells in the artery wall [1]. Plaques may occupy nearly 40% of the internal elastic lamina of a coronary before the lumen begins to narrow [2]. Decreased blood flow and oxygenation to downstream tissues may go unnoticed for years, or may present clinically as angina in more severe cases. *Unstable* plaques can undergo acute changes, including the rupture of the plaque's thin fibrous cap, causing a thrombosis-mediated stenosis of the lumen, resulting in a myocardial infarction, or "heart attack" [3]. However, only 20% of coronary attacks are preceded by long standing angina [4].

CAD is the single largest killer of Americans, responsible for more than five hundred thousand deaths in the United States in 1999. Almost one quarter of a million deaths were caused by a sudden cardiac arrest, and more than half of the individuals who died suddenly of CAD were previously asymptomatic [4]. The development of a non-invasive screening tool for CAD could be valuable. Biochemical characterization and earlier detection of unstable plaques could stimulate delivery of stabilization therapy [5] to reduce future acute coronary events [6, 7]. Moreover, knowledge of the functional sequelae of identified stenoses could influence therapy in a more meaningful way than pure morphological measurements of the size of coronary stenoses.

1.2 Clinical Imaging of Atherosclerosis

Different imaging modalities are used to study atherosclerotic disease, including x-ray angiography (XA), intravascular ultrasound (IVUS), angioscopy, and ultrafast computed tomography (CT) [8]. X-ray coronary angiography is the clinical gold standard for defining coronary anatomy and the degree of luminal obstruction of the coronary arteries [9]. High temporal (15–30 frames/second) and spatial (1.0–3.3 line pairs/mm [10]) resolution projection images are acquired as a bolus of iodinated contrast agent is injected directly into a coronary artery. However, the invasive procedure has a 0.23% risk of death, myocardial infarct, or stroke [11]. Because XA images the coronary lumen, only advanced plaques which affect the lumen diameter are detectable.

IVUS is a new approach for visualizing the artery wall with resolution between 100–250 μm using a catheter based ultrasound probe. Nissen *et al.* [12] demonstrated the ability to separate plaques into three categories: 1) calcified tissue; 2) fibrosis or microcalcifications; and 3) thrombotic or lipid rich tissue. Invasive optical visualization of the arterial wall is called angioscopy. Uchida *et al.* [13] demonstrated a correlation between the color and glistening characteristics of plaques, and the occurrence of acute coronary syndromes in a 12 month follow-up period. Plaque surface disruptions and thrombi can also be directly visualized. These procedures are more invasive than XA, in that the catheter must be advanced to the site of suspected plaques. Moreover, coronary blood flow must be interrupted for angioscopy.

The recent development of multi-slice (or multi-detector) computed tomography (MSCT) has spurred interest in CT coronary angiography. Rapid imaging allows a stack of sub-1 mm slices covering the entire heart to be acquired during a breath-hold, but the temporal resolution is about 125–250 ms. Increasing the temporal resolution to reduce motion artifacts requires longer scan times, which will require improved respiratory motion gating and correction methods. A clinical study of 44 patients concluded that the sensitivity of MSCT angiography for detecting stenoses $\geq 50\%$ was 78% (39/50 lesions), but that visualization of vessels of less than 2 mm in diameters was limited by the spatial resolution [14]. A similar study obtained sensitivity and

specificity values of 82% and 93% (51 lesions with $\geq 50\%$ occlusion) [15]. These systems also have the ability to quantify the amount of calcium, but the usefulness of this measurement is still being debated [16, 17, 18, 19]. Ultimately, coronary imaging with MSCT exposes the patient to contrast and x-ray radiation. Administration of β blockers or other negative chronotropic drugs may be required to stabilize and reduce the heart rate for reduction of motion artifacts [14, 20].

1.3 Magnetic Resonance Coronary Angiography

Magnetic resonance has the potential to combine the imaging modalities currently used to study atherosclerosis and provide a complete picture of CAD during a single non-invasive examination. Magnetic resonance coronary angiography (MRCA) could be a non-invasive alternative to XA for coronary lumen imaging. In presenting the state of the art in MRCA, we reference developments in coronary wall imaging which suffers from similar technical limitations.

Initial results with cardiac gated 2D imaging during a breath-hold were variable and unreproducible [21, 22, 23]. These 2D methods are limited by motion during a breath-hold [24], inadequate resolution, small signals and low SNR, flow artifacts, and the difficulty of capturing tortuous vessels in the imaging plane, which is complicated by misregistration of neighboring slices due to breath-hold inconsistency [25]. Improved visualization of the lumen and arterial wall, with a reduction of flow artifacts, was demonstrated with black blood imaging techniques. Fayad *et al.* [26] measured a difference in coronary wall thickness between volunteers (0.75 ± 0.17 mm) and CAD patients (4.38 ± 0.71 mm) with breath-hold 2D black blood, fat saturated images transverse to the axis of the right coronary artery (RCA) and left anterior descending (LAD). Stuber *et al.* [27] combined black blood imaging with navigator echoes [28], fast 1D images used to measure the motion of internal organs, to acquire images during free breathing. The superior-inferior motion of the diaphragm, as measured by the navigator echo, is used to translate the position of the imaged slice during the acquisition. Using this technique, Botnar *et al.* [29] demonstrated increased vessel wall thickness (1.5 ± 0.2 versus 1.0 ± 0.2 mm) and reduced lumen area

($7.0 \pm 2.3 \text{ mm}^2$ versus $9.3 \pm 1.9 \text{ mm}^2$) in the proximal RCA of patients with known CAD. The scan time for acquiring one 2D slice during free breathing was between 4.5–6.8 minutes. These studies also demonstrate the shortcomings of 2D imaging. Thick slices (3–5 mm) and an in-plane spatial resolution of between 0.5–1.0 mm can lead to partial volume effects and signal averaging when visualizing sub-millimeter pathologies. Measurements of lumen area and wall thickness could be distorted by oblique sectioning of the artery.

Three dimensional (3D) MRCA can provide higher resolution, higher SNR, isotropic volumetric images. However, imaging times longer than possible breath-holding durations require a robust motion compensation strategy. A comparison of different respiratory suppression techniques concluded that in patients, only free breathing methods work well [30]. Post *et al.* showed that navigator echoes placed on the diaphragm could be used to retrospectively gate a 3D free breathing MRCA [31]. Acquisition of a $256 \times 128 \times 31$ matrix with a spatial resolution of $1.2 \times 2.3 \times 2.1 \text{ mm}$, achieving a coverage of 6.5 cm, required 11 minutes. Sensitivity and specificity for detection of $\geq 50\%$ stenoses was 38% and 95%. A similar study by van Geuns *et al.* achieved sensitivity and specificity values of 50% and 91% [32].

The current state of MRCA is best represented by the results of a recently published seven center clinical trial [33]. A navigator gated 3D MRCA imaging sequence was chosen for its ease of use and standardization for a large number of patients. Despite good visualization of the coronary arteries, MRCA could only be used to reliably identify three-vessel disease. Specificity and sensitivity for detection of a focal stenosis of greater than 50% were low, ranging between 53-93% and 52-90% respectively, depending on the imaged artery. Total scan times were long (mean, 70 minutes) and highly variable (range, 33-145 minutes).

Increases in image resolution and SNR, and reduced imaging time are required for MRCA to develop into a clinically usable modality for reliable diagnosis and staging of focal coronary pathologies. Better motion compensation is one way to reduce imaging times and obtain these improvements.

1.4 Motion Correction for MRI

Fourier transform imaging is the most common technique for generating magnetic resonance (MR) images [34, 35]. As data are acquired, they fill a Fourier space, or k -space [36], matrix which is then Fourier transformed to obtain the image. Since each part of k -space contributes to the reconstruction of the entire image, any incoherence between (inter-view), or within (intra-view), k -space lines, can lead to blurring and ghosting artifacts in the images [37, 38]. Fast hardware has provided readout times of 1-2 ms [39, 40], leaving inter-view physiologic motion as the most common cause of motion related artifacts.

Different methods, including signal averaging, gating, phase reordering, and ghost positioning, have been proposed for reduction of artifacts due to periodic motion [41, 42, 43, 44, 45]. Of these different methods, gating can provide the best image quality and contrast, at the expense of longer imaging times. Data are acquired during short temporal windows during which the object is assumed to be motionless. This method allows data for an image to be acquired at the same motion phase during multiple cycles of the motion; for example, in cardiac imaging, one image can be composed from the same phase of the cardiac cycle during successive heartbeats. In general, for a desired image resolution and contrast, there is an inverse relationship between the temporal width of the data acquisition window, and the total scan duration.

In practice, cardiac [42] and respiratory [41] gating techniques are routinely used to “freeze” the motion of organs for thoracic imaging. However, when gating both of these motions concurrently, a low imaging duty cycle leads to long imaging times. Physiologic changes over time [46], patient non-compliance and discomfort [24], and economic factors make the case for shorter imaging times, which can be achieved by increasing the duration of the data acquisition window around the gating signal. However, this may introduce motion which would degrade image quality.

Special motion correction techniques can be used to compensate for certain types of motion. Korin *et al.* described a post-processing phase correction method for compensating for in-plane translation of a phantom during the acquisition of an MR image [47]. Navigator echoes [28], fast one dimensional images interleaved with the

MR data acquisition, were introduced to quantify motion *in vivo*, and were used first to retrospectively correct for superior–inferior respiratory motion in the abdomen based on the motion of the diaphragm [48]. Retrospective correction for through–plane translation of the imaging slice has been described in [49, 50]. Alternatively, motion information derived from navigator echos can be applied prospectively to track the translational motion of slices [51] and volumes [52, 53].

Motion correction for rigid body rotation in a 2D imaging plane was described by Korin *et al.* [54]. Fiducial markers were used to quantify motion of the head *in vivo*, and correction was applied retrospectively. Combining rotation with translation, and making the transition to 3D, Derbyshire *et al.* implemented a real–time system for prospectively modifying the scan plane and demonstrated the method for human brain imaging [55]. The use of spherical navigator echoes has been recently presented for measuring 3D rigid body motion *in vivo* [56].

Unfortunately, physiologic motion of soft tissues can rarely be described completely by rigid body transformations. Haacke and Patrick described the effect of spatial scaling on k –space, and proposed a linear expansion correction method [43]. They demonstrated improvement of abdominal imaging during free breathing by monitoring the movement of the abdominal wall, and by changing the imaging gradients prospectively to compensate for anterior–posterior expansion and compression of the abdomen. Atalar and Onural extended this concept, and presented a retrospective correction method for removing artifacts caused by 2D in–plane translation and scaling [57].

Motion correction techniques with more degrees of freedom need to be explored. By increasing the amount of physiologic motion that is correctable, the imaging duty cycle would be increased, and the total imaging time reduced.

1.5 Respiratory Motion of the Heart

The motion of the heart due to respiration is not understood well. More than 30 years ago, Dougherty studied the effects of respiration on the electrocardiogram, and noted that Einthoven had concluded in 1913 that the heart undergoes anatomic rotation in the frontal plane with respiration [58, 59]. Motivated by the development of computer tomography and its potential uses for thoracic imaging, Bogren provided the first quantitative study of the respiratory motion of the heart from x-ray cineangiograms [60]. He observed that the superior–inferior (SI) motion at the valve planes was approximately half as much as the SI motion of the diaphragm, which averaged 15 mm (range=10-19mm) during normal respiration. The existence of an anatomic rotation of the heart during respiration was substantiated using contours of the cardiac silhouette, and from heterogeneous measurements of displacement along the length of the right coronary artery (RCA) in a projection image.

Nearly twenty years later, and driven by respiratory limitations in cardiac MR imaging, the problem resurfaced. Wang used 2D MR images at multiple breath–hold levels to conclude that the primary motion of the heart was translation in the superior–inferior (SI) direction, and that SI motion of the heart at the level of the coronary ostia was between 0.6–0.7 times the SI displacement of the diaphragm [61]. Another report of 12 volunteers using real–time 2D MR imaging during free breathing validated this mean ratio, but reported high variability both between subjects and within each individual [62]. However, these studies were limited by the study of in–plane motion only. Additionally, the landmark seen in a given imaging plane is not guaranteed to be the same material point observed in the plane at a later time due to through–plane motion.

A 3D rigid body analysis of the motion of the heart was presented by McLeish [63]. Three dimensional MR datasets of the whole heart were obtained at multiple breath–hold levels, and registered using an image intensity method. Rotations and translations were reported between maximum expiratory and inspiratory positions for nine patients and eight volunteers, and additional local deformations were studied. The use of a 6 mm imaging slice thickness, and breath–hold imaging limits the use of this

method for studying the free breathing motion of the coronary arteries. A 180 ms temporal resolution is insufficient for isolating the effects of cardiac motion from the respiratory analysis.

Manke studied the motion of the coronary arteries by reconstructing 3D slabs at three respiratory phases during a free breathing MR acquisition [64]. Template matching of 3D volumes was used to register the LAD and RCA between the end-expiratory images, and the two inspiratory datasets. Limitations of this study include the use of a small number of landmarks for registration, a small number of respiratory samples, and a 3 mm slice resolution. The acquisition of each 3D volume was acquired over multiple breaths, introducing the possibility of temporal averaging, or low pass filtering of the true motion.

Since MR cannot yet provide high spatial and temporal resolution images of the coronary arteries, measuring their motion and deformation with this imaging modality is of limited utility. It would be more informative to study the coronary arteries using x-ray angiography, a high spatial and temporal resolution modality.

1.6 Specific Aims

Magnetic resonance coronary imaging could be improved with more accurate modeling and compensation of respiratory motion. A high spatial resolution description of the respiratory motion of large segments of coronary trees has not yet been presented. The most significant limitation has been the lack of a suitable method for recovering the 3D motion and deformation of the coronary arteries *in vivo*.

The goal of this work is to study the respiratory motion of the heart, and to use this information to develop strategies for improving MRCA. The following specific aims were completed:

1. Describe a motion correction technique which compensates for a 3D affine transformation of the imaging volume during an MR acquisition.
2. Develop an automatic method for quantifying the motion and deformation of the coronary arteries using standard biplane X-ray cineangiograms.
3. Quantify the effects of tidal respiration on the orientation and shape of the coronary tree.
4. Identify optimal MRCA imaging strategies, using measured respiratory motion models and available MR motion correction techniques.

This work addresses the following hypotheses:

1. The *in vivo* motion and deformation of the coronary arteries can be recovered from high temporal and spatial resolution biplane x-ray cineangiograms.
2. Rotational motion and respiratory induced deformation of the coronary arteries render translation-only respiratory motion models of the heart inadequate for applications requiring accuracy comparable to the vessel diameters.
3. The motion and deformation of the coronary arteries during portions of the respiratory cycle are well modeled by a 3D affine transformation, and are therefore suited for targeted motion correction strategies during free breathing MRCA.