2010 Research Proposal - Draft

Roy Schestowitz*

December 25, 2010

Abstract

This document groups together papers of interest and highlights those which are potentially relevant to *in vivo* studies of the heart, such as studies that distinguish between a healthy heart and a diseased one based on its different physical attributes. The document then describes an existing line of work where 3-D sets divided by slices are used for tracking motion of the heart.

1 Overview

Analysis of the heart is a problem which is principally associated with biological factors that require knowledge of anatomy, but the problem can be simplified by pre-processing, alternative visualisation paradigms, and occasionally an automated classification of common groups. In this work, the problem gets narrowed down such that only a portion of the heart is dealt with. The key goal is to perform an analysis of human heart images while overcoming its different types of movements which blur tagging and make it increasingly difficult to study the anatomy.

We are attempting to exploit a novel approach whereby an isolated portion of the heart is captured for standalone analysis[1] as the shape of this portion is changed, over time.

DICOM-formatted datasets are to be analysed using calculations of stress (e.g. strain rotation, principal strains, and maximum shear strain), which can be derived by isolating and segmenting the data along the different axes.

*Dr. Roy S. Schestowitz holds a Ph.D. in Medical Biophysics from the Victoria University of Manchester where he specialised in statistical analysis of shape and intensity characterising soft tissue.

[1]The MRI equipment allows new protocols to achieve this selection.

2 Existing Literature

The proposed approach needs to be explored in the context of recent papers including those whose authors choose to work with non-rigid registration (see Isola *et al.* [1] from 2010) and/or simple tagging. Isoda *et al.* [2] have only just published an article which looks at three-dimensional phase-contrast MRI and results include an experiment that deals with the cardiac phase.

Last year's review of shape models for 3-D image segmentation [3] may be worthwhile for extracting the signal from larger images, but given the distinctly dark background captured when isolation is applied at the scanner, there ought to be simpler ways to achieve the same effect and obtain similar segmentation. A paper from Zhuang *et al.* [4] covers cardiac MRI for segmentation of the heart without human intervention. It does not deal with the problem of motion and real-time (or 'off-line') tracking of parts of the heart (4-D), though.

Motion caused by respiration is studied in [5]. Many papers on tracking exist and half a year ago there was a speckle-tracking echocardiographic study into myocardial deformation at the University of Hong Kong [6].

Other authors who had studied myocardial strains over a decade earlier [7] more recently looked at what they described as a "non-invasive method for assessing regional myocardial" [8] (paper from 2003).

Cardiac tagging was done in Johns Hopkins University last year. It was tissue tagging [9] with cardiovascular magnetic resonance (CMR). More experimental work on CMR tagging (from 2008) can be found in [10] where mice hearts are studied. A paper from Wei *et al.* also considered CMR tagging by experimenting on mice [11]. Methods involved "[i]n vivo myocardial function was evaluated by 3D CMR tagging in mdx mice." More material on CMR tagging [12] "introduce[s] a standardized method for calculation of left ventricular torsion by CMR tagging and [determining] the accuracy of torsion analysis in regions using an analytical model." Delling *et al.* [13] looked at CMR and explained: "We sought to assess the correlation between mitral valve characteristics and severity of mitral regurgitation (MR) in subjects with mitral valve prolapse (MVP) undergoing cardiac magnetic resonance (CMR) imaging." Some less relevant papers on the subject may include [14, 15] on CMR tagging.

The problem of tracking parts of the heart is a complicated one and a particular group has proposed "a novel dynamic model, based on the equation of dynamics for elastic materials and on Fourier filtering." [16]

To some groups, robotic "intervention on the beating heart" is said to be a worthwhile route of exploration as well [17]. This one study on pig hearts [18] — like [6] — considers speckle-tracking. There is also lot about HARP, including a paper from last year [19]. Lastly, *Cardiac Imaging* has this broad new survey from 2010 [20].

2.1 Tagging

Qian *et al.* perform a segmentation process of cardiac MRI tagging lines using Gabor filter bank and claim that the method has a better performance than HARP. The group currently looks at more data types than just cardiac [21]. Figure 1 shows how segmentation was done with the aid of deformable snakes sampled along the tags.

2.2 Ideas for Using Tags

Stepping aside from literature, an important problem to overcome will be use of tags or analysis in their absence. One potential way to approach this problem is to assume we get a maximally-spread diamond/square when its furthest two edges are far apart, usually before it gets compressed by movement or localised stress. To demonstrate this point imagine a complete blurring of edges and think of what would happen if you measured the radius of a circle passing through/within (or conversely containing) the diamond. Depending on what corners it passes though, its size can tell us something about the level of localised compression and we have code that calculates this. If put on top of the image a radiologist may be able to assess the level of pressure applied by nearby motion that flattens a diamond. If circles are too messy as annotation, then colour too can be used. We want to explore this idea of visualising a surrogate of stress because we have not seen it in other papers yet.

If a distance or other general measure is used for calculating the stress at one point in the tagged image, a method is still needed for identifying the boundaries of the blocks which tagging yields. Cross-frame analysis is required here and one method for finding a match amid movement is a shuffle transform based on MSD/SSD. Initial tagging is just a grid, which is simple to set up. Having initialised a grid layout (be it diagonal or upright wrt xy), which is essentially just a board of blocks, we can then apply shuffle map wherein two frames (or more) are taken at a time and then for each pixel/voxel (or junction in the tagging, for speed and avoidance of interpolation) searches for a best match after the movement, using available information in all 3 axes (shuffling within a cube of fixed size, where vicinity/neighbourhood is defined and limited by a window size). From this we obtain simple tagging which is quite resistant to blurring or can at least estimate best match when the tagging is blurred. The size of the shuffle window ensures that the grid does not move too far, too fast (although it can be adjusted to explore a wider window in particular areas of the image) and to avoid folding or tearing there can be constraints that need not rely on any splines which are diffeomorphic, such as clamped-plate splines. The merit of this approach is that it uses information in three dimensions without relying on heavy computation (shuffling can be encoded as a

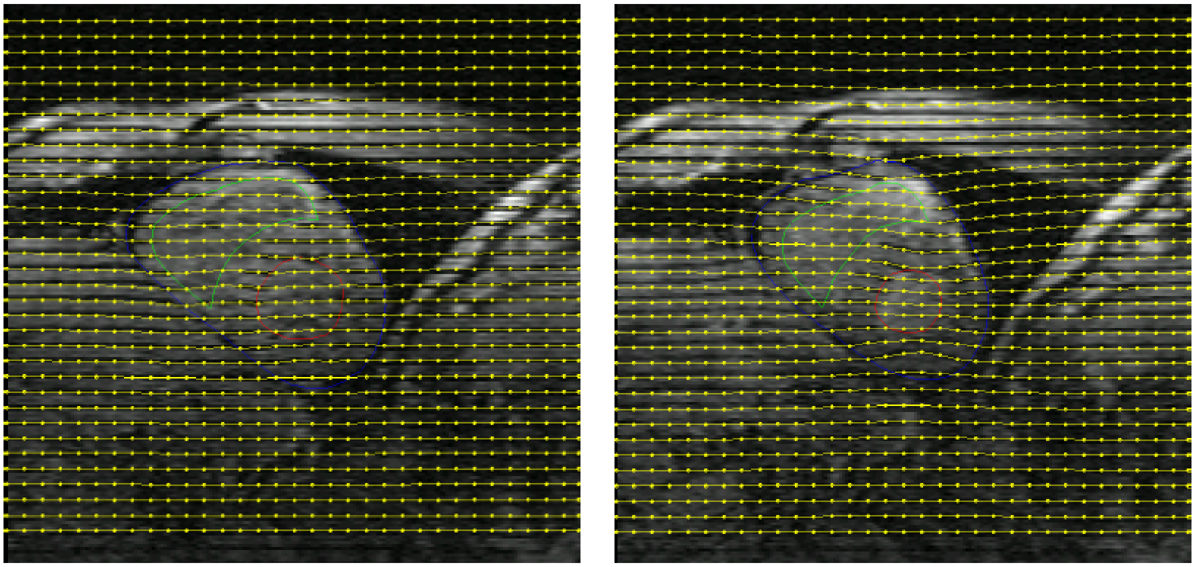

Figure 1: The approach taken by Zhen Qian, who fits snakes to image tagging (image from Qian's Ph.D. thesis)

4^3=64 bit mask), it explores frame correlation, and it is resistant/sensitive to blurring/noise because of a 'best fit' approach. We have begun implementing this for testing on low-resolution data that we got.

We are exploring a way of utilising tagged cardiac data as means of improving segmentation and perhaps – if this goes further – statistical analysis of tags/segmented parts can take place. The nature of the imaged subject/s does not matter to us; it is just that many hours were spent in vain trying to find tagged images and the most/best we found was a single low-resolution (under 300 pixels) sequence of ~10 images. Now, back to the literature.

2.3 Strain-encoded Cardiac Magnetic Imaging

Strain-encoded (SENC) cardiac magnetic imaging is used by numerous groups (e.g. [23, 24]) to detect myocardial dysfunction.

Garot *et al.* [22] performed experiments on five healthy volunteers and nine patients with infarction. They assess performance without tags and to quote the abstract, "Local contractile performance was decreased in infracted myocardium versus that in remote and adjacent myocardium ($P < .01$) and in adjacent versus remote myocardium ($P < .05$)."

The paper says that "[i]n contrast to conventional tagging, strain-encoded MR imaging is a technique that uses tag surfaces that are parallel, not orthogonal, to the image plane, combined with out-of-plane phase-encoding gradients in the perpendicular section-select direction (14). Because local frequency of the tag pattern is related to myocardial strain (15,16), we hypothesized that strain-encoded MR imaging might provide direct myocardial longitudinal strain (Ell) imaging embedded on short-axis images of the LV. This technique may have potential in the online assessment of intrinsic myocardial contractility and may therefore represent a powerful addition to the assessment of myocardial viability by quantifying local function automatically. Thus, the purpose of our study was to prospectively evaluate strain-encoded MR imaging as a method for direct imaging of regional LV function that precludes the need for post-processing and can be used in combi-

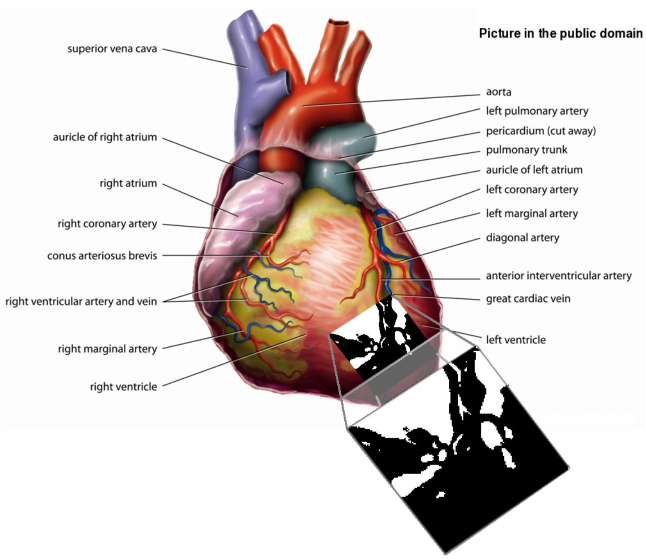

Figure 2: Extraction of a 3-D slice from the heart for strain analysis of the box/cube

nation with contrast material–enhanced MR imaging in the assessment of local myocardial viability."

Mirja Neizel [25, 26, 27] published a series of studies with a group whose study "evaluated the value of systolic and diastolic deformation indexes determined by strain-encoded imaging to predict persistent severe dysfunction at follow-up in patients after reperfused acute myocardial infarction (AMI) in comparison with late gadolinium enhancement (LGE)."

This body of work constitutes a surrogate or replacement for tagging.

3 Data

Experimental data is to be acquired at the hospital using a 3–Tesla (or less) clinical MR system with a specially-tailored protocol that separates a particular region of interest inside the heart (see Figure 2 for illustration). Which cubic region it will be remains to be decided, yet evidently, the acquired data needs to contain several different parts of the heart, e.g. the ventricles. Data is transported in DICOM format and sets can be either temporal or simply different slices taken at a given moment in time, if not analogous phases.

3.1 Tagged Data

Figure 3 shows untagged data, Figure 4 shows tagged data, and Figure 5, which is based on data from Qian, is a low-resolution example which is valuable for proof of concept.

3.2 Synthetic Data

We also generate some synthetic data for the purpose of testing the algorithms on images with known properties. This is beyond the scope of this document.

4 Methods

4.1 Strain analysis

An exploration around strain analysis may be required in order to devise a new algorithm based on a 'triple sandwich' approach, wherein acquisition of images of the human heart have clippings/occlusions in three dimension such that only a small cube is isolated for analysis or some form of tagging.

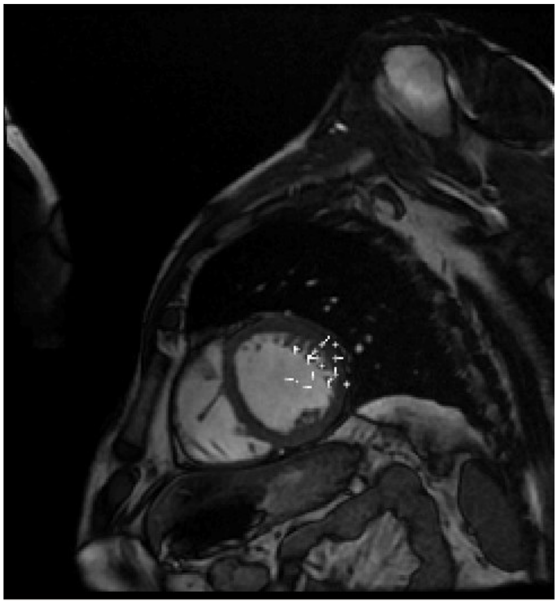

Figure 3: Example of a rectangular grid of points with arrows representing their direction of movement

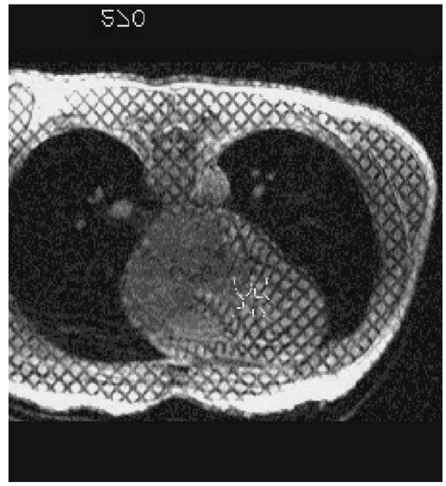

Figure 4: Same as Figure 3, but using another dataset which has tagging

To use a figure from Kurt Gramoll of the University of Oklahoma (Figure 6), for a given element such as the one shown in Figure 2, stresses along the four sides are denoted by subscripts xy and yx (in 2-D). Ways exist for calculating different types of stresses based on different parameters, including angles in some cases.

4.2 Cross-correlation

The current implementation overlays the image sequence with arrows based on a measure similar but not identical to cross-correlation. It can position and initialise points based on several parameters and then show their movement in each frame transition. The next step will be to test this on a synthetic set and refine the algorithm as means of general improvement before validation experiments. This phase of the experiments deals with tracking but not any measurements (e.g. distances, stress) or statistical analysis.

Shown in the figures are some screen snapshots of the arrows put automatically on top of the image sets that are available to us. The next step will be considering the existing literature, then validation experiments with the synthetic data (tagged or not tagged). If within the synthetic dataset the tags are removed, then generating variation based on radii should be easier.

4.3 Algorithm

The existing algorithm, whose corresponding code is available as free/libre software, uses a simple method

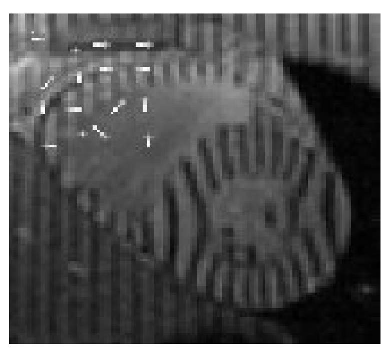

Figure 5: Same as Figure 3, but using the set from Qian

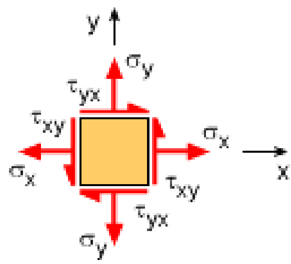

Figure 6: Sign convention for stress element (image from Kurt Gramoll)

to estimate best direction for a set of landmark points to move in. It calculates the shuffle distance within a given window size and then moves any given point in that direction, gradually finding better templates. Initial placement of points can be arranged in a circle and then refined by edge detection or it can be put in a rectangular grid, also with optional rearrangement based on nearby edges. Once all the initial points are in place (loosely connected) the algorithm proceeds frame by frame, modifying the location of points and visualising them while taking stock of directions of movement.

4.4 Visualisation

The remainder of the figures in this document ought to show means of interaction with the data in 3-D.

4.5 Statistical analysis

This is part of the current endeavours. Studying how properties change with or without parameterisation of the data may help acquire knowledge which is not visible to the human eye.

5 Experimental Framework

Within the context of this investigation, no statistical analysis is expected to be required (nor pragmatic) because of the small number of subjects, possibly just one, initially. It is hoped, however, that by looking at several different instances acquired at the same site there will be room for studying the variation in shape of a preselected region and thus a characteristic type of expansion, shearing, tapering, or a more complex combination of factors which strain analysis can account for. Initial code has been written to deal with the raw data itself, yet it remains to be determined which method to use for 3-D segmentation and which calculations to perform on the segmented data. The aim is to decide on measures which are meaningful and distinguishable. Implementation of a prototype is expected to be a trivial task in MATLAB and GNU Octave. Some peripheral tools are written in C and automation coded in Bash (e.g. for data conversions).

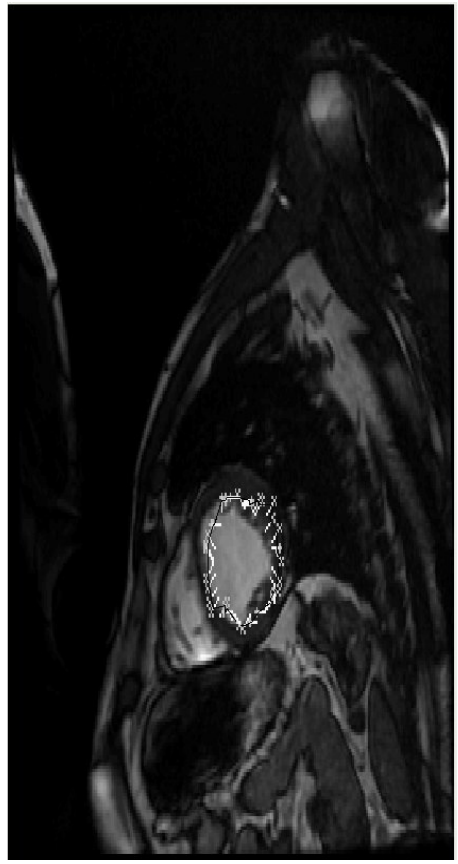

Figure 7: An example image with point directions (movement between 2 frames) and contour connecting them

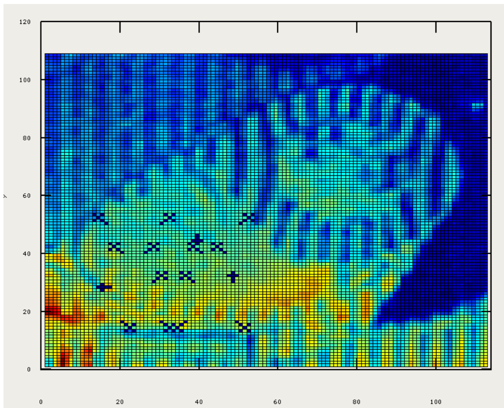

Figure 8: Alternative representation of image intensities with blue arrows indicating point movement

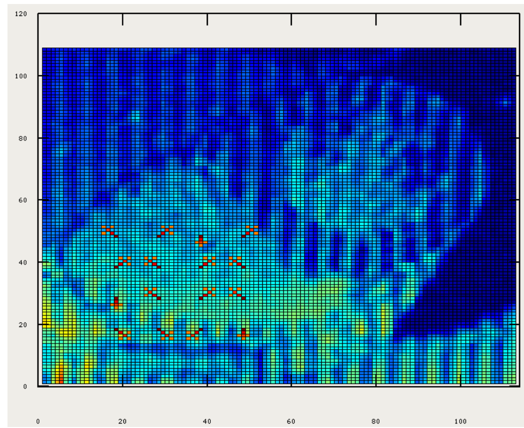

Figure 9: Alternative representation of image intensities with gradient-coloured arrows indicating point movement

6 Timeframe and Possible Extensions

At an existing pace of 50 hours per month, it is expected that a working prototype will be available within a month and further experimentation – including write-ups – possible within two months. There is room for experimental expansion and handling of larger sets of data can be an opportunity for statistical analysis too. This, however, changes the nature of the approach and transforms it into one where strain get parameterised, then dealt with in hyperspace rather than in real space which is easy to perceive and reason about.

References

[1] Alfonso A Isola, Michael Grass, and Wiro J Niessen, "Fully automatic nonrigid registration-based local motion estimation for motion-corrected iterative cardiac CT reconstruction," *Med Phys,* vol. 37, issue 3, pp. 1093-1109, 2010. 1

[2] Haruo Isoda, Yasuhide Ohkura, Takashi Kosugi et al. "In vivo hemodynamic analysis of intracranial aneurysms obtained by magnetic resonance fluid dynamics (MRFD) based on time-resolved three-dimensional phase-contrast MRI," *Neuroradiology,* vol. 52, issue 10, pp. 921-928, 2010. 1

[3] T Heimann and HP Meinzer, "Statistical shape models for 3D medical image segmentation: A review," *Medical Image Analysis,* vol. 13, issue 4, pp. 543-563, 2009. 1

[4] Xiahai Zhuang, Kawal S Rhode, Reza S Razavi et al. "A registration-based propagation framework for automatic whole heart segmentation of cardiac MRI," *IEEE Trans Med Imaging,* vol. 29, issue 9, pp. 1612-1625, 2010. 1

[5] Jason G Parker, Bernard A Mair, and David R Gilland, "Respiratory motion correction in gated cardiac SPECT using quaternion-based, rigid-body registration," *Med Phys,* vol. 36, issue 10, pp. 4742-4754, 2009. 1

[6] Yiu-fai Cheung, Xue-cun Liang, Godfrey Chi-fung Chan, Sophia Jessica Wong, and Shau-yin Ha, "Myocardial deformation in patients with Beta-thalassemia major: a speckle tracking echocardiographic study," *Echocardiography,* vol. 27, issue 3, pp. 253-259, 2010. 1, 2

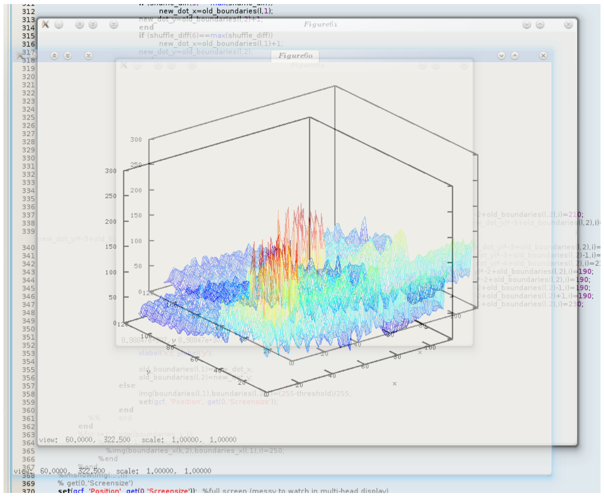

Figure 10: Images shown as a mesh

[7] H Azhari, J L Weiss,and E P Shapiro, "Distribution of myocardial strains: an MRI study," *Adv Exp Med Biol,* vol. 382, pp. 319-328, 1995. 1

[8] Haim Azhari, Daniel K Sodickson, Robert R Edelman, "Rapid MR imaging by sensitivity profile indexing and deconvolution reconstruction (SPID), " *Magn Reson Imaging,* vol. 21, issue 6, pp. 575-584, 2003. 1

[9] Monda L Shehata, Susan Cheng, Nael Nael F Osman, David A Bluemke, and Joao A C Lima, "Myocardial tissue tagging with cardiovascular magnetic resonance," *J Cardiovasc Magn Reson,* vol. 11, pp. 55, 2009. 2

[10] Jia Zhong, Jia Liu, and Xin Yu, "Characterization of three-dimensional myocardial deformation in the mouse heart: an MR tagging study," *J Magn Reson Imaging,* vol. 27, issue 6, pp. 1263-1270, 2008. 2

[11] Wei Li, Wei Liu, Jia Zhong et al. "Early manifestation of alteration in cardiac function in dystrophin deficient mdx mouse using 3D CMR tagging," *J Cardiovasc Magn Reson,* vol. 11, pp. 40, 2009. 2

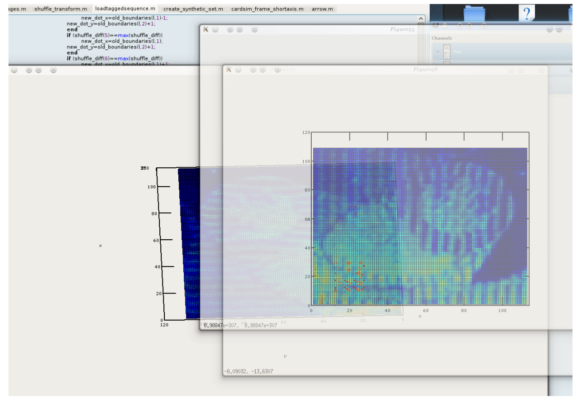

Figure 11: Surface representation of the data

[12] AIris K Russel, Marco J Gotte, Joost P Kuijer, and J Tim Marcus, "Regional assessment of left ventricular torsion by CMR tagging," *J Cardiovasc Magn Reson*, vol. 10, pp. 26, 2008. 2

[13] Lih Lisa Delling, Lih Lisa Kang, Susan B Yeon, et al. "CMR Predictors of Mitral Regurgitation in Mitral Valve Prolapse," *JACC Cardiovasc Imaging,* vol. 3, issue 10, pp. 1037-1045, 2010. 2

[14] Andrea K Rutz, Christoph F Juli, Salome Ryf, et al. "Altered myocardial motion pattern in Fabry patients assessed with CMR-tagging," *J Cardiovasc Magn Reson*, vol. 9, issue 6, pp. 891-898, 2007. 2

[15] Willem G van Dockum, Joost Kuijer, P A Gotte, J W Marco, et al. "Septal ablation in hypertrophic obstructive cardiomyopathy improves systolic myocardial function in the lateral (free) wall: a follow-up study using CMR tissue tagging and 3D strain analysis," *Eur Heart J,* vol. 27, issue 23, pp. 2833-2839, 2006. 2

[16] Joel Schaerer, Christopher Casta, Jerome Pousin, Patrick Clarysse, "A dynamic elastic model for segmentation and tracking of the heart in MR image sequences," *Med Image Anal,* vol. 14, issue 6, pp. 738-749, 2010. 2

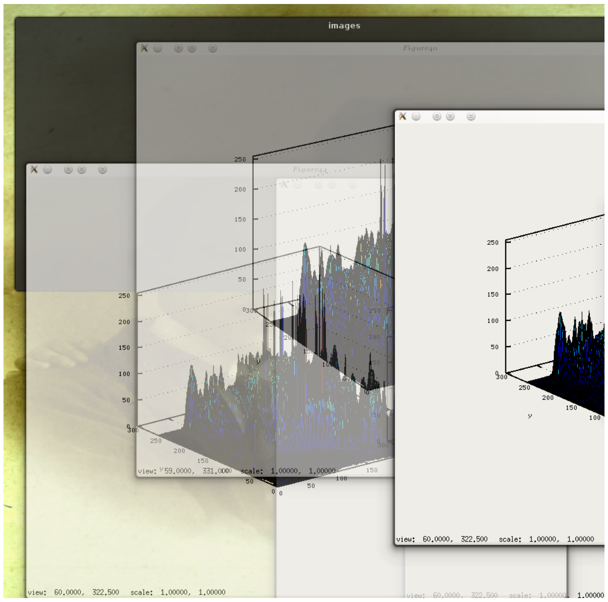

Figure 12: An alternative intensity view handling one 2-D slice

[17] Y Zhou, E Yeniaras, P Tsiamyrtzis, N Tsekos, and I Pavlidis, "Collaborative tracking for MRI-guided robotic intervention on the beating heart", *Med Image Comput Comput Assist Interv,* vol. 13, issue 3, pp. 351-358, 2010. 2

[18] Zhiwen Zhou, Muhammad Ashraf, Dayi Hu, Xiaonan Dai, Yawei Xu, Bill Kenny, Berkley Cameron, Thuan Nguyen, Li Xiong, and David J Sahn, "Three-dimensional speckle-tracking imaging for left ventricular rotation measurement: an in vitro validation study," *J Ultrasound Med,* vol. 29, issue 6, pp. 903-909, 2010. 2

[19] Jia Zhong, Wei Liu, and Xin Yu, "Transmural myocardial strain in mouse: quantification of high-resolution MR tagging using harmonic phase (HARP) analysis," *Magn Reson Med* vol. 61, issue 6, pp. 1368-1373, 2009. 2

[20] Anil K. Attili, Andreas Schuster, Eike Nagel, Johan H. C. Reiber, and Rob J. van der Geest, "Quantification in cardiac MRI: advances in image acquisition and processing," *The International Journal of Cardiovascular Imaging*, vol. 26, supplement 1, pp. 27-40. 2

[21] Z. Qian, S. Rinehart, L. Murrieta, G. Vazquez, P. Battey, and S. Voros, "A novel, dual-contrast in-vivo MR imaging method with principal component analysis reliably quantifies lipid-rich necrotic core and collagen in human carotid atherosclerotic plaques", *Journal of Cardiovascular Magnetic Resonance*, vol. 11(Suppl 1):O45, 2009. 2

[22] J Garot, JA Lima, BL Gerber, S Sampath, KC Wu, DA Bluemke, JL Prince, and NF Osman, "Spatially resolved imaging of myocardial function with strain-encoded MR: comparison with delayed contrast-enhanced MR imaging after myocardial infarction," *Radiology*, 233:596–602, 2004. 3

[23] NF Osman, S Sampath, E Atalar, and JL Prince JL, "Imaging longitudinal cardiac strain on short-axis images using strain-encoded MRI," *Magn Reson Med.*, 46:324-334, 2001. 3

[24] L Pan, M Stuber, DL Kraitchman, DL Fritzges, WD Gilson, and NF Osman, "Real-time imaging of regional myocardial function using fast-SENC," *Magn Reson Med.,* 55:386–395, 2006. 3

[25] M Neizel, G Korosoglou, D Lossnitzer, H Kühl, R Hoffmann, C Ocklenburg, E Giannitsis, NF Osman, HA Katus, and H Steen, "Impact of systolic and diastolic deformation indexes assessed by strain-encoded imaging to predict persistent severe myocardial dysfunction in patients after acute myocardial infarction at follow-up," *J Am Coll Cardiol*, 56:1056-62, 2010. 4

[26] M Neizel, D Lossnitzer, G Korosoglou, T Schäufele, A Lewien, H Steen, HA Katus, NF Osman, and E Giannitsis, "Strain-encoded (SENC) magnetic resonance imaging to evaluate regional heterogeneity of myocardial strain in healthy volunteers: Comparison with conventional tagging," *J Magn Reson Imaging,* 29:99-105, 2009. 4

[27] M Neizel, D Lossnitzer, G Korosoglou, T Schäufele, H Peykarjou, H Steen, C Ocklenburg, E Giannitsis, HA Katus, NF Osman, "Strain-encoded MRI for evaluation of left ventricular function and transmurality in acute myocardial infarction," *Circ Cardiovasc Imaging*, 2:116-22, 2009.

4