JOHN ANDREW SIMS

**DIRECTIONAL ANALYSIS OF CARDIAC LEFT
VENTRICULAR MOTION FROM PET IMAGES**

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IMAGENS DE PET**

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To my family in Brazil. Marta, Rafael, Antonia and Francisco, Marco and Diva, Marcia and Antonio, Gabriel.

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“It is perfectly true, as the philosophers say, that life must be understood backwards. But they forget the other proposition, that it must be lived forwards.”

-- Soren Kierkegaard, Journals and
Papers, 1843

ABSTRACT

Quantification of cardiac left ventricular (LV) motion from medical images provides a non-invasive method for diagnosing cardiovascular disease (CVD). The proposed study continues our group's line of research in quantification of LV motion by applying optical flow (OF) techniques to quantify LV motion in gated Rubidium Chloride- ^{82}Rb (^{82}Rb) and Fluorodeoxyglucose- ^{18}F (FDG) PET image sequences. The following challenges arise from this work: (i) the motion vector field (MVF) should be made as accurate as possible to maximise sensitivity and specificity; (ii) the MVF is large and composed of 3D vectors in 3D space, making visual extraction of information for medical diagnosis difficult by human observers.

Approaches to improve the accuracy of motion quantification were developed. While the volume of interest is the region of the MVF corresponding to the LV myocardium, non-zero values of motion exist outside this volume due to artefacts in the motion detection method or from neighbouring structures, such as the right ventricle. Improvements in accuracy can be obtained by segmenting the LV and setting the MVF to zero outside the LV. The LV myocardium was automatically segmented in short-axis slices using the Hough circle transform to provide an initialisation to the distance regularised level set evolution algorithm. Our segmentation method attained Dice similarity measure of 93.43% when tested over 395 FDG slices, compared with manual segmentation. Strategies for improving OF performance at motion boundaries were investigated using spatially varying averaging filters, applied to synthetic image sequences. Results showed improvements in motion quantification accuracy using these methods.

Kinetic Energy Index (KEf), an indicator of cardiac motility, was used to assess 63 individuals with normal and altered/low cardiac function from a ^{82}Rb PET image database. Sensitivity and specificity tests were performed to evaluate the potential of KEf as a classifier of cardiac function, using LV ejection fraction as gold standard. A receiver operating characteristics curve was constructed, which provided an area under the curve of 0.906.

Analysis of LV motion can be simplified by visualisation of directional motion field components, namely radial, rotational (or circumferential) and linear, obtained through automated decomposition. The Discrete Helmholtz Hodge Decomposition (DHHD) was used to generate these components in an automated manner, with a validation performed using synthetic cardiac motion fields from the Extended Cardiac Torso phantom. Finally, the DHHD was applied to OF fields from gated FDG images, allowing an analysis of directional components from an individual with normal cardiac function and a patient with low function and a pacemaker fitted.

Motion field quantification from PET images allows the development of new indicators to diagnose CVDs. The ability of these motility indicators depends on the accuracy of the quantification of movement, which in turn can be determined by characteristics of the input images, such as noise. Motion analysis provides a promising and unprecedented approach to the diagnosis of CVDs.

RESUMO

A quantificação do movimento cardíaco do ventrículo esquerdo (VE) a partir de imagens médicas fornece um método não invasivo para o diagnóstico de doenças cardiovasculares (DCV). O estudo aqui proposto continua na mesma linha de pesquisa do nosso grupo sobre quantificação do movimento do VE por meio de técnicas de fluxo óptico (FO), aplicando estes métodos para quantificar o movimento do VE em sequências de imagens associadas às substâncias de cloreto de rubídio- ^{82}Rb (^{82}Rb) e fluorodeoxiglucose- ^{18}F (FDG) PET. Com a extração dos campos vetoriais surgiram os seguintes desafios: (i) o campo vetorial de movimento (motion vector field, MVF) deve ser feito da forma mais precisa possível para maximizar a sensibilidade e especificidade; (ii) o MVF é extenso e composto de vetores 3D no espaço 3D, dificultando a análise visual de informações por observadores humanos para o diagnóstico médico.

Foram desenvolvidas abordagens para melhorar a precisão da quantificação de movimento, considerando que o volume de interesse seja a região do MVF correspondente ao miocárdio do VE, em que valores de movimento não nulos existem fora deste volume devido aos artefatos do método de detecção de movimento ou de estruturas vizinhas, como o ventrículo direito. As melhorias na precisão foram obtidas segmentando o VE e ajustando os valores de MVF para zero fora do VE. O miocárdio VE foi segmentado automaticamente em fatias de eixo curto usando a Transformada de Hough na detecção de círculos para fornecer uma inicialização ao algoritmo de curvas de nível, um tipo de modelo deformável. A segmentação automática do VE atingiu 93,43% de medida de similaridade Dice, quando foi testado em 395 fatias de eixo menor de FDG, comparado com a segmentação manual. Estratégias para melhorar o desempenho do algoritmo OF nas bordas de movimento foram investigadas usando spatially varying averaging filters, aplicados em sequências de imagens sintéticas. Os resultados mostraram melhorias na precisão de quantificação de movimento utilizando estes métodos.

O Índice de Energia Cinética (KEf), um indicador de motilidade cardíaca, foi utilizado para avaliar 63 sujeitos com função cardíaca normal e alterada / baixa de uma base de dados de imagens PET de ^{82}Rb . Foram realizados testes de sensibilidade e especificidade para avaliar o potencial de KEf para classificar a função cardíaca, utilizando a fração de ejeção do VE como padrão ouro. Foi construída uma curva ROC, que proporcionou uma área sob a curva de 0,906.

A análise do movimento do VE pode ser simplificada pela visualização de componentes de campo de movimento direcional, ou seja, radial, rotacional (ou circunferencial) e linear, obtidos por decomposição automatizada. A decomposição discreta de Helmholtz Hodge (DHHD) foi utilizada para gerar estes componentes de forma automatizada, com uma validação utilizando campos de movimento cardíaco sintéticos a partir do conjunto Extended Cardiac Torso Phantom. Finalmente, o método DHHD foi aplicado a campos de FO, criado a partir de imagens FDG, permitindo uma análise de componentes direcionais de um indivíduo com função cardíaca normal e um paciente com baixa função e utilizando um marca-passo.

A quantificação do campo de movimento a partir de imagens PET possibilita o desenvolvimento de novos indicadores para diagnosticar DCVs. A capacidade destes indicadores de motilidade depende na precisão da quantificação de movimento que, por sua vez, pode ser determinado por características das imagens de entrada como ruído. A análise de movimento fornece um promissor e sem precedente método para o diagnóstico de DCVs.

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LIST OF ABBREVIATIONS

AAE	Average AE
AEE	Average EE
AE	Angular Error
AIM	Adaptive Intensity Method
AVM	Adaptive Velocity Method
CVD	Cardiovascular Disease
DHHD	Discrete Helmholtz Hodge Decomposition
DRLSE	Distance Regularized Level Set Evolution
ECG	Electrocardiogram
EDV	End-Diastolic Volume
EE	End-point Error
EF	Ejection Fraction
ESV	End-Systolic Volume
FN	False Negatives
FP	False Positives
FWHM	Full Width at Half Maximum
GMRES	Generalized Minimum Residual method
GS	Gold Standard
GT	Ground Truth
HLA	Horizontal Long Axis
KEf	Kinetic Energy Index
LAX	Long Axis
LS	Level Set
LV	Left Ventricle
MVF	Motion Vector Field
NM	Nuclear Medicine
NRMSE	Normalized RMSE
OF	Optical Flow
PET	Positron Emission Tomography
PVE	Partial Volume Effect
RMSE	Root Mean Square Error
RV	Right Ventricle
RWMA	Regional Wall Motion Abnormality
SAX	Short-Axis
SOM	Supervised Observation Method
SPECT	Single Photon Emission Computed Tomography
TN	True Negatives
TP	True Positives
VLA	Vertical Long Axis
XCAT	Extended Cardiac Torso phantom

LIST OF SYMBOLS

u, v, w	Velocity in x,y,z direction (Cartesian coordinates)
u_{GT}	Ground truth velocity field in x direction
E	Image intensity
$\vec{\xi}$	Input vector motion field
α	Weighting parameter in Horn and Schunck optical flow scheme
$\nabla\phi_{ik}$	Gradient of basis function for node i, tetrahedron k.
i, j	indices for principal and secondary node in basis function calculations
k	tetrahedron number
$[S]$	Sparse matrix for calculating curl-free component of motion
$\{D\}$	Piecewise-linear scalar potential field representing the divergence-free part of a motion field
$[T]$	Sparse matrix for calculating divergence-free component of a motion field
$\{\vec{R}\}$	Piecewise-linear vector potential field representing the divergence-free component of a motion field
$ T_k $	Volume of tetrahedron k

1 INTRODUCTION

1.1 Justification and delineation of theme

Cardiovascular diseases (CVDs) represent a significant danger for patients, who are frequently at risk of death. According to data from the World Health Organization, an estimated 17.5 million people died from CVDs in 2012, which is 31% of global deaths¹. DATASUS, the Health Informatics department of the Brazilian Ministry of Health, estimate that these diseases are responsible for 27.3% of deaths in Brazil and 10.5% of hospital admissions.

The study of the cardio-respiratory system is important for improved understanding and diagnosis of CVDs. It is a dynamic system, involving the expansion and contraction of the lungs, motion of the heart, and circulation of blood within vessels, and this inherent movement provides both challenges and possible approaches to diagnosis. The proposed study is based around the theme of quantification of cardiac motion, which leads to approaches for visual representation and extraction of information contained in the motion vector field (MVF) to distinguish between normal and pathological subjects.

The proposed study focusses on the quantification and analysis of the left ventricular MVF, rather than the cardiac MVF in general. The heart is an organ composed of four chambers, the right and left atria (RA, LA) and right and left ventricles (RV, LV). The RV is responsible for sending blood to the lungs while the LV sends blood around the body and is composed of thicker muscle. While diseases of the RV include congenital heart disease and acute or chronic pulmonary hypertension (VITARELLI et al., 2015) and are a valuable subject of study, medical interest in the hospital environment where the proposed study took place was focussed on CVDs

¹ <<http://www.who.int/mediacentre/factsheets/fs317/en/>>

affecting the LV. Further, due to the low spatial resolution of the images used, the thicker muscle of the LV makes a more appropriate subject for motion detection.

CERQUEIRA et al. (2002) recommend nomenclature for describing cardiac anatomy and regions of the LV. Figure 1 shows the plane definitions; the first figure shows the short axis (SAX) view, then the next two figures are a vertical section relative to the short-axis (vertical long axis, VLA) and then a horizontal section (horizontal long-axis, HLA), corresponding to the short-axis, apical 2-chamber, and apical 4-chamber planes traditionally used in 2D echocardiography.

Figure 1: Cardiac plane definition and display for tomographic imaging modalities (CERQUEIRA et al., 2002).

Figure 2 shows an analysis of LV walls based on schematic views, in a parasternal short and long-axis orientation, at three different levels. The figure uses the 17 segment model as suggested by the American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. In the proposed study, the term *frame* is used to refer to a temporal subdivision of images, while *slice* refers to a SAX planar element of a volume image.

The knowledge of the dynamic and structure of cardiac motion is very important to establish efficient diagnostics and effective treatments (LEE et al., 2006). Methods available for quantification of the cardiac MVF vary across imaging modalities, each of which makes use of characteristic image properties. For example, the coherent interference noise in ultrasound,

Figure 2: Representation of the heart, with long axis (LAX) slices (1-3) and short axis (SAX) slices (4-6) at base, mid and apex respectively (LANG et al., 2006).

speckle, can be tracked between frames; the finite decay rate of an applied magnetic field in magnetic resonance can be used to visualise deformation of the myocardium; brightness patterns can be tracked in modalities which produce image sequences of near constant brightness, such as in nuclear emission tomographies, a category of images from Nuclear Medicine (NM) which includes Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT).

Cardiac motion can be understood better through directly studying volume sequences rather than determining the motion based on isolated slices (GUTIERREZ, 1995). Time sequences of 3D volumes are referred to as 4D images, which show the changing position of the myocardial volume through the cardiac cycle. 4D images are routinely acquired in the modern hospital using magnetic resonance imaging (MRI), X-ray computed tomography (CT), ultrasound, PET and SPECT. Manual analysis of these image sequences is a difficult task, which requires the skills of highly qualified specialists to interpret pathological motion caused by circulation problems in coronary arteries, anomalies in the cardiac muscle or disruption in electrical conduction to the ventricles (PUENTES et al., 2000; MURAMATSU; MATSUMOTO; NISHIMURA, 2005), and can lead to various problems, such as inter and intra-operator variability, high financial cost, slow speed of producing results. The proposed study therefore aims to quantify a 4D

cardiac MVF from 4D cardiac images using natively 4D and automated techniques.

Automated computer-aided detection (auto-CAD) and diagnosis algorithms have been applied to a multitude of diseases within medical imaging. The focus of research in the use of these computational techniques is to make relevant information available to clinicians rather than trying to perform direct diagnosis (ARNOLDI et al., 2010; DOI, 2007). Automated analysis can be performed whenever resources and expertise are available.

Although automated motion quantification could be applied to 4D images from the various modalities already mentioned, the proposed study focusses on 4D PET images. MRI has a history of performing motion analysis, with techniques such as cardiovascular magnetic resonance tagging being considered as the reference modality for assessment of regional cardiac function and the most widely evaluated for strain quantification (SHEHATA et al., 2009). However, PET images have the following qualities which make motion quantification an interesting research proposal; more details about PET imaging are provided in Appendix A:

1. The PET image is functional, meaning that it shows metabolic processes through the movement and distribution of a radiopharmaceutical in the body. Parts of the heart with lesions tend to have lower absorption of the radiopharmaceutical. Motion analysis in PET images therefore combines functional information, in terms of absorption of radiopharmaceutical, with cardiac motility, producing a unique result.
2. The acquisition of PET images have a financial cost, besides the cost to the patient in terms of radiation exposure. Although cardiac PET images are generally acquired for other medical purposes in the hospital, such as viability studies, applying motion quantification techniques to the images allows extra benefit of the resource for patients.

Accuracy of motion quantification is determined by attributes of the acquired image sequence and by the approach chosen for computer implementation. For example, the choice of instrumentation and radiopharmaceuticals are factors which affect the noise in the image and limit the temporal resolution of the sequence, strongly influencing the accuracy of motion quantification. The development of improved motion quantification approaches is an important and

ongoing research area in computer vision, not only in medical images, and their use can increase sensitivity and specificity in diagnosis.

One of the challenges of working with patient cardiac 4D images, acquired from the thoracic region, is that they include regions outside the patient's body, non-cardiac structures within the patient, as well as cardiac structures other than the ROI, the LV. An important stage of image processing before motion quantification is to locate and isolate image structures belonging to the LV. If performed manually, this is a time-consuming and operator dependent task, so it is important to develop automated methods.

The information content of the 4D LV MVF is rich in valuable information about the patient, but its analysis presents a challenge since it is large and composed of 3D vectors. Therefore computer methods are of great value for refining, extracting and translating information content into a useful form, possibly providing a statistical summary of the MVF on a regional or global basis. In a clinical context the final form of this information is often a quantitative indicator, which can first be tested for specificity and sensitivity against other indicators and can then provide a basis for assessing the current state of a patient or the progression of disease.

Indicators of cardiac function such as left ventricular ejection fraction (LVEF), a measure of LV volumetric change over the cardiac cycle, have a long history of use and are an established part of medical practice. However, there is currently no indicator in general use for measuring cardiac motility. GUTIERREZ et al. (2003) develop a global measure of motility called kinetic energy index (KE_f) for this purpose, which is calculated directly from the magnitude of the quantified LV MVF, presenting an interesting and important research subject for the proposed study.

BURNS et al. (2008) note that the investigation of the twisting motion present in normal cardiac LV function may provide insights into myocardial dysfunction and help predict response to treatment. The cardiac 4D MVF contains valuable information about cardiac function in its magnitude and direction, and differences in LV rotation between the base and apex give rise to LV torsion. Therefore, automated extraction and analysis of directional information from the

cardiac LV MVF is seen to be important for diagnostic purposes.

1.2 Objectives

1. Propose and evaluate techniques to identify the cardiac muscle in medical images.
2. Research and evaluate methods for quantification of 3D dynamic images in PET from the estimation of velocity carried out at every voxel of the image sequence.
3. Investigate and develop new indicators of cardiac function from MVF estimation.
4. Research and evaluate methods for representation and visualisation of directional information pertaining to the LV, extracted from the 4D cardiac MVF by decomposition into rotation, expansion and contraction.
5. Propose friendly and intuitive schemes for representation and visualisation of information obtained to assist medical teams in diagnosis.

1.3 Organisation

This section provides an overview of the structure of this thesis. Readability was felt to be improved by: (i) placing a description of all materials used in a single chapter; (ii) dividing the research into four chapters, related to stages of work carried out to fulfil the objectives above. Each chapter is self-contained, with methods, results and discussion. The objective relating to the proposal of schemes for representation and visualisation of information was naturally treated together with the fourth objective, where there was considerable interaction between medical teams and the results produced.

The four principal stages of the proposed study are summarised in Figure 3. It can be seen that the study regarding global Kinetic Energy Index as an indicator of cardiac function and directional analysis of left ventricular motion require quantification of left ventricular motion, which in turn requires identification of left ventricular structures.

Figure 3: Stages of the thesis

Chapter 2: **Literature review** situates the proposed study in the area of computer aided diagnosis within the hospital environment, describes some important aspects of PET imaging for the proposed study, and reviews the literature for the stages of the proposed study, presented in Figure 3.

Chapter 3: **Materials** describes the creation of synthetic images and motion fields as well as the acquisition and protocol for selection of PET images used in the proposed study.

Chapter 4: **Identification of left ventricular structures** provides the methodology for locating the LV in the image, cropping the image, and delineating the voxels pertaining to the LV from the cropped image.

Chapter 5: **Quantification of left ventricular motion** investigates techniques for optimising and evaluating the motion detection algorithm.

Chapter 6: **Global Kinetic Energy Index as an indicator of cardiac function** presents a study which evaluates this indicator of cardiac motility, first with images from the Extended Cardiac Torso Phantom (v2.0) (XCAT) images and then with gated Rubidium Chloride- ^{82}Rb PET image sequences, calculated from the quantified MVF, and comparing the results with values of left ventricular ejection fraction.

Chapter 7: **Directional analysis of left ventricular motion** investigates the use of the Discrete Helmholtz Hodge Decomposition (DHHD) for cardiac motion field decomposition. The DHHD is first applied to synthetic motion fields composed of known radial (curl-free) and rotational (divergence-free) motion field components, then validated with synthetic motion

fields generated by the Extended Cardiac Torso (XCAT) phantom (v2.0), and finally applied to the decomposition of gated Fluorodeoxyglucose- ^{18}F (FDG) PET images from a database containing individuals with normal cardiac function and non-compaction cardiomyopathy.

Chapter 8: Presents **conclusions** from the proposed study.

Chapter 9: Lists **original contributions** made to the field.

Annex A: Presents a list of **published articles** during the proposed study.

Annex B: Presents **articles awaiting publication**, submitted during the proposed study.

Annex C: Reproduces the certificate showing **project inclusion by CAPPesq**, liberating the use of PET images for the proposed study.

Appendix A: Outlines basic **principles of nuclear medicine in cardiology**.

Appendix B: Shows the derivation of an analytic expression for computing the **ground truth velocity field for a rotating cylinder**, used in Chapter 5.

Appendix C: Provides an example of the **cluster analysis** that was used, combined with Hough Circle detections, to identify LV structures, as described in Chapter 4.

Appendix D: **DHHD implementation**. Describes specific implementation details of the Discrete Helmholtz Hodge Decomposition, a vector field decomposition algorithm used to extract radial and rotational motion components from the cardiac motion field.

Appendix E: **Volume of tetrahedra resulting from a cubic mesh**. Explores the calculation of tetrahedral volumes, components of the mesh generated to perform the vector field decomposition, as described in Chapter 7.

Appendix F: **DHHD calculations on a mesh from a single cubic space**. Shows example data for 8 motion field vectors, arranged on the vertices of a cube, and resulting DHHD calculations from these data. The calculations were used to test the implementation of the DHHD.

Appendix G: **DHHD: calculation of curl-free potential**. Shows construction of the LHS and RHS of the linear system of equations for calculating the curl-free part of the motion field,

a step for computing the DHHD, with sample data in Appendix F.

Appendix H: **DHHD: calculation of divergence-free potential.** Shows construction of the LHS and RHS of the linear system of equations for calculating the divergence-free part of the motion field, a step for computing the DHHD, with sample data in Appendix F.

Appendix I: **Expressing the vector triple product in matrix form.** Derives an expression to write a vector triple product as a matrix multiplication, a result which is used for construction of the linear system of equations in Appendix H.

Appendix J: Shows **application of boundary conditions to the linear systems** of equations for solving curl-free and divergence-free potentials, a step in vector field decomposition as described in Chapter 7.

2 LITERATURE REVIEW

This chapter provides a general vision of the main project themes, outlining a context in which the main problems, challenges and applications can be expressed. In order to be more accessible, specific details of the review have been divided into sections according to chapters of the methodology.

2.1 Computer aided diagnosis

Early work in automated computer diagnosis in the 1960s were ambitious, and it was believed that automated diagnosis would eventually replace radiologists with computerised systems for detecting abnormalities; this did not come to pass, due to factors such as the unavailability of digital images, limited processing power of computers and lack of advanced image-processing techniques. However, by the 1980s the concept of computer-aided diagnosis (CAD) emerged in which radiologists used computer output as a second opinion, leaving him or her to make the final decision. A synergistic participation was constructed, combining the radiologists competence and the computer's capability (DOI, 2007).

According to SHARMA; AGGARWAL (2010), CAD aims to automate processing so that large numbers of cases can be handled with the same accuracy. This is also advantageous since results are not affected by fatigue, data overload or missing steps. Further, it is possible to achieve fast and accurate results, since high-speed computers are available at modest costs. CAD also supports faster communication, where patient care can be extended to remote areas using information technology. A key advantage of CAD is the ability to quantify parameters that could only have been qualitatively evaluated beforehand. Considering the application of

CAD to cardiology, GARCIA et al. (2007) uses the term *quantitation* to describe the extraction of quantitative parameters. Measures of cardiac function, such as systolic and diastolic global function, regional wall thickening, have been developed; they are robust, readily available to medical staff and reliable estimators, and can therefore assist in diagnosis.

2.2 PET imaging

The modalities comprising nuclear medicine (NM) do not form high resolution images of internal structures, but instead show functional images of physiological processes occurring within the body (WEBB, 1988). The monitoring of any functional changes, anticipating anatomical alterations, can allow early intervention into the processes of disease.

Visualisation of functional processes can be performed using radioactive materials which act as markers within the organism. The agent is chosen depending on the organ or process to be studied, and the distribution of the marker in the body depends on the method of administration and metabolic processes.

Improvements in medical imaging systems can be attributed to advances in instrumentation and methods for extracting information from these images (DEMIRKAYA; ASYALI; SAHOO, 2008). Image quality in NM depends on the choice of radiopharmaceutical, which is composed of a radionuclide, the signal, and the molecular vehicle, determining the biochemical properties (for example binding characteristics, metabolism, elimination rate) (WADSAK; MITTERHAUSER, 2010). The radioactive element is chosen to emit a specific type of detectable radiation with known properties, such as half-life of the radioactive decay.

Technological advances in PET imaging with Fluorodeoxyglucose (FDG) in the late eighties allowed it to become a primary clinical tool in oncology (KITSON et al., 2009). These advances include the availability and use of appropriate radioisotopes, improvements in instrumentation, such as gamma camera technology, the removal of the collimator, and the introduction of time-of-flight (TOF) imaging (MUEHLLEHNER; KARP, 2006). In general, these have resulted in improvements in accuracy, speed and sensitivity. Later cardiac PET emerged as a

useful diagnostic tool to evaluate the vascular condition of the heart (KITSON et al.; BAGCI et al. (2012) according to FOSTER et al. (2014)).

PET is referred to as an emission tomography since the image source is a photon emitted from inside the body, while transmission modalities, such as X-ray computed tomography, measure the attenuation of energy as they pass through the component tissues of the body. PET scans are commonly used in cardiology to diagnose coronary artery disease and assess damage due to a heart attack. Stunned but viable myocardium and dead muscle can be differentiated by performing dual-tracer PET scanning; viable myocardium then appears to have decreased blood flow with normal to increased metabolic activity (LIPTON et al., 2002). Differentiating healthy and damaged heart muscle can show if a patient is suitable for a percutaneous coronary intervention, such as an angiography or coronary bypass surgery; viable (alive) muscle might be saved if blood flow is restored (AMERICAN HEART ASSOCIATION, 2015).

PET has enhanced the understanding of the biochemistry of both normal and abnormal functions within the body, providing the means for imaging the rates of biological processes *in vivo* (BEHLOUL et al., 2001). A great advantage of using PET compared to SPECT is due to the much larger number of elements with low atomic number that undergo positron emission, such as isotopes of Oxygen, Nitrogen, and Fluorine. The disadvantages are the higher cost of the equipment and the short half-lives of the radioisotopes. The convenience of producing a radiopharmaceutical may also vary; while ^{82}Rb can be produced from ^{82}Sr in a generator placed alongside the patient, a cyclotron is necessary for ^{11}C , ^{13}N , and ^{18}F production. Appendix A contains further information about PET imaging, and Table 15 provides details about emission characteristics for some commonly used PET isotopes.

2.3 Identification of the left ventricle

Although segmentation of cardiac PET images may be performed by visual evaluation on a slice by slice basis, this operation is time consuming and suffers from observer bias (BEHLOUL et al., 2001). Automatic, unsupervised image segmentation has an important role to play in

medical imaging, but is a challenging task in PET images due to unpredictable object shapes and inconsistent image quality resulting from noise and sampling artifacts (DEDIC; ALLILI; LECOMTE, 2011). The success of segmentation techniques depends on the envisaged application, imaging modality used and bodily region studied. Clearly, brain segmentation may require different approaches to those of the thorax and artifacts affecting these regions may be different. For example, the partial volume effect is more prominent in brain images, while motion artefacts may be more prominent in the thorax. The selection of segmentation techniques should involve the consideration of specific common problems in PET images, such as the partial volume effect and noise caused by low statistical count (SHARMA; AGGARWAL, 2010).

GUTIERREZ et al. (2003) describe an approach to select the LV cardiac MVF from other structures using a global threshold applied to the MVF; however the approach assumes that LV structures have the highest values of velocity and does not account for artefacts such as the spreading of the MVF over image borders due to regularisation, which is a characteristic of the motion estimation method (HORN; SCHUNCK, 1981).

BEHLOUL et al. (2001) present an approach for myocardium extraction in PET images based on the application of soft computing techniques, while DEDIC; ALLILI; LECOMTE (2011) develop a segmentation method based on a deformable models approach with level sets (LS), where two moving, coupled contours are initialised from inside the left ventricle and outside the heart and deformed to track heart boundaries. The level set (LS) method was initially developed by OSHER; SETHIAN (1988). A curve evolution was implemented in which the level set function (LSF) was evolved on the image from an initial to final value, with the resulting segmentation curve provided by the zero level set. For a 2D image this is a surface in 3D, cut along the zero level to produce a set of contours (XU; PHAM; PRINCE, 2000). The distance regularized level set evolution (DRSLE) (LI et al., 2010) is a successor to the original LS technique, but overcomes problems present in other methods, such as the need for reinitialisation, thereby allowing a more general and efficient LSF initialisation. Results from the LS method depend on both initial positioning of the curve and setting of parameters. LIU et al. (2016) segment the endocardial and epicardial contours of both ventricles from

cine-MRI, using a two-level-set approach based on the DRLSE.

Region boundaries of interest can be defined as curves of a specified shape using the Hough Transform. According to BALLARD (1981), the Hough Transform (HT) was originally applied to the detection of analytic (HOUGH, 1962) and non-analytic curves (DUDA; HART, 1972) in binary edge images, and later extended to the detection of circles by KIMME; BALLARD; SKLANSKY (1975).

With the various constraints imposed by the imaging modality and section of the body imaged, methods for evaluating automated segmentation are important for choosing between techniques and for establishing optimal parameter values. According to CRUM; CAMARA; HILL (2006), the evaluation of segmentation results is difficult where underlying tissue classification is unknown. Possible evaluation approaches include expert manual segmentation, which provide a practical gold standard against which new algorithms may be compared, and use of synthetic data, in which images are constructed from a model where the true structure boundaries are known. ZHANG; FRITTS; GOLDMAN (2008) describe, in a similar manner, that a Supervised Objective Method (SOM) uses a manually-segmented reference image to evaluate the method segmentation.

HARALICK; SHAPIRO (1992), according to BEZDEK et al. (2005), note that in a segmented image, each region should ideally be homogeneous with respect to certain characteristics or features such as grey level or texture, and adjacent regions should have significantly different characteristics or features. However, BEZDEK et al. point out that it is often not easy to determine if a pixel should belong to a region since features used to determine homogeneity may not have sharp transitions at region boundaries; myocardial tissue in gated PET images appears nebulous at myocardial borders due to the partial volume effect, noise characteristics and other effects due to the nature of acquisition. Additional challenges for segmentation may include continuous connection of the LV to neighbouring structures such as the right ventricle and possibly other organs such as the stomach. In order to produce adequate results in this challenging environment, automated algorithms must use sophisticated techniques.

MACEDO et al. (2015) uses a set of six metrics to measure the accuracy of their automated method for 2D lumen segmentation compared to a reference lumen segmentation, being (i) Volume overlap, (ii) Dice Similarity Measure (DSM), (iii) Hausdorff Distance, (iv) RMS Symmetric surface distance, (v) Mean absolute difference of area (MADA), and (vi) Accuracy. Some of these measures rely on the calculation of area, which can be simply translated to a volume calculation, while others are contour measures, which may present a greater challenge for extension to volume calculations, and might be computationally expensive to implement. KARIM et al. (2016) describe a benchmarking evaluation framework for 3D segmentation algorithms, used for detecting and quantifying infarct in cardiac magnetic resonance images of the LV. They employ DSM as their primary measure for the presented approaches and volume difference as a second measure.

2.4 Quantification of left ventricular motion

Techniques for the quantification of myocardial deformation aim to provide a dense MVF consistent with the motion of structured tagging patterns and can be classified into three groups: (i) differential optical flow-based methods coupled with intensity correction schemes, which quantify motion based on the observation of changes of brightness; (ii) phase-based optical flow methods; (iii) methods which determine and track myocardial wall borders; (iv) tracking of induced or anatomical markers, first obtaining sparse motion estimation along tags, and dense motion interpolation over the domain of the image (FABER et al., 1989; FABER et al., 1991; ROUGON et al., 2005).

MEYERING (2002) provides a list of studies, which exemplify the above categories. NAS-TAR; AYACHE (1994) present a method for the analysis of non-rigid motion in 4D cardiac images where the non-rigid motion of the outline of the deformable object is approximated by a deformable surface. BENAYOUN; AYACHE (1995) calculate the MVF using energy minimisation in which one term is related to the differential singularities in the image and the other restricts the singularity of the field. KASS; WITKIN; TERZOPOULOS (1988) develop a method to accompany object motion in a sequence of images, using deformable mod-

els. HORN; SCHUNCK (1981) estimate the MVF in 2D image sequences using optical flow. GUTIERREZ (1995) extends the Horn and Schunck (HS) method to estimate the LV MVF in 4D SPECT images. MEYERING et al. (2002) develop a frequency approach to cardiac motion estimation, performed by the computation of Wigner-Ville and Choi-Williams Distribution.

It is important to evaluate method accuracy in order to determine strengths or failings of a particular method, or situations in which an algorithm might produce superior or desired results. Although qualitative methods may be of some use, quantitative measurements enable a more objective comparison between the estimated motion and the real motion, or ground truth. This allows different algorithms to be compared, based on their results, when applied to the same image, and to explore performance when particular image characteristics are present, such as areas with low texture, large dislocations between frames or occlusions. The importance of measurements of accuracy can be seen in comparisons of 2D OF algorithmic performance by BARRON et al. (1992) and the Middlebury database and evaluation methodology for optical flow, as described in BAKER et al. (2011). This paper lists the error measures used for 2D vector fields, such as average angular error and average end-point error. In a context involving exclusively medical images, TOBON-GOMEZ et al. (2013) describe a benchmarking framework for validating cardiac motion analysis algorithms in magnetic resonance and 3D ultrasound datasets from both phantom and 15 healthy volunteers. This literature review did not find any existing benchmarking frameworks to test and compare PET motion estimation algorithms.

GIBSON (1950) introduce the notion of optical flow (OF) as the apparent motion of pixels in the image plane when there is relative motion between an observer and the objects which compose the image. Estimating the OF field for an image sequence means obtaining a vector field of displacements which map pixels from one frame to the next. From another point of view, the OF calculation attempts to determine the velocity field that corresponds to the real velocity field (SONKA; HLAVAC; BOYLE, 2008).

According to WEDEL; CREMERS (2011) OF approaches can be categorised into feature-based and variational optical flow approaches. Feature-based approaches can produce pixel or sub-pixel accuracy while variational approaches, based on the application of methods from

calculus and regularisation of the solution, can obtain sub-pixel accuracy.

GUTIERREZ (1995) argues that since the image sequence is composed of 3D volume images, the quantification will be more accurate if performed in 3D rather than in simpler 2D projection forms. MCVEIGH (1998) provides an insight into the shortcomings of analysis of isolated 2D image sections, explaining that tissue moves in and out of 2D image planes during the cardiac cycle, so subsequent frames do not correspond to the same tissue.

HORN; SCHUNCK consider image brightness at the point (x,y) in the image plane at time t to be denoted by $E(x,y,t)$ and assume that the brightness of a point in the pattern is constant. Then the brightness constancy of that point is shown by Equation 2.1a. Using a first order Taylor series approximation, they obtain the optical flow equation shown in Equation 2.1b (WEDEL; CREMERS), where u and v are velocities in x and y directions respectively, and E_t, E_x, E_y are partial derivatives of the image intensity.

$$\frac{dE}{dt} = 0 \quad (2.1a)$$

$$0 = E_t + E_x u + E_y v \quad (2.1b)$$

HORN; SCHUNCK note that the OF equation represents an under-determined system and therefore the component at right angles to the brightness gradient cannot be found. Regularisation is used to solve the OF equation, performed by minimisation of the functional shown in Equation 2.2, where $u(\mathbf{x}) \in \mathbb{R}$, and $v(\mathbf{x}) \in \mathbb{R}$ provide the two-dimensional displacement vector of an image pixel $\mathbf{x} \in \mathbb{R}^2$ in the image domain Ω (WEDEL; CREMERS). The accuracy of these subpixel displacements depends on the reliability of the estimator for derivatives.

$$\min_{u(\mathbf{x}), v(\mathbf{x})} \left\{ \alpha^2 \int_{\Omega} (|\nabla u(\mathbf{x})|^2 + |\nabla v(\mathbf{x})|^2) d\Omega + \int_{\Omega} (E_t + E_x u(\mathbf{x}) + E_y v(\mathbf{x}))^2 d\Omega \right\} \quad (2.2)$$

The minimisation produces a system of two coupled differential equations, that can be decoupled and solved using discrete approximations (NESI, 1993). HORN; SCHUNCK suggest

Gauss-Seidel update equations for iterative solution of the linear system.

The value of α^2 in Equation 2.2 is a weight between the data and regularisation terms of the cost function. When an image is noisy, one has less confidence in the data term, and the value of α^2 can be increased to emphasise the smoothness of the solution. In a less noisy environment, increased confidence can be placed in the data term, so reducing α^2 and the smoothness of the solution. HORN; SCHUNCK say that the value of α^2 can be set equal to the expected noise in the estimate of $E_x^2 + E_y^2$.

The Horn and Schunck (HS) method is termed a dense algorithm since regularisation allows calculation of velocity values for every pixel in the image domain. Sparse algorithms, such as the multiconstraint algorithm by NESI (1996), produce OF only for points with special properties. Dense algorithms are required for the proposed study since the cardiac MVF is required for each voxel associated with the LV.

HORN; SCHUNCK consider the difficulties arising from estimation of the MVF; the most relevant implications of these to the proposed study are described in the following:

(i) Textureless regions cannot be tracked without making assumptions based on neighbouring textured regions, although the method produces a velocity field in these regions.

(ii) The aperture problem arises from the difficulty of determining the velocity field with only local knowledge of changes to the MVF (BARRON; THACKER, 2005; WEDEL; CREMERS, 2011). The term aperture indicates that an observer determining the velocity is allowed to view only a small part of the image, as if through a small aperture, which is small enough so that whole objects in the image frame cannot be visualised. Figure 4 shows three versions of the same diagonal displacement of an untextured square within an image, in which three different aperture positions are considered, shown by the circle. The aperture is first placed so that no structural information is visible, the case of a structureless region, leading to ambiguous motion in every direction. Next a single straight edge is included in the aperture, enabling recovery of motion only in the direction perpendicular to the edge. Finally a corner is visible in the image, allowing two dimensional motion estimation due to structural information in

linearly-independent directions. In summary, local motion can only be recovered completely for points with special structural properties but not for points in general. BARRON; THACKER extend the aperture problem to 4D image sequences, where ambiguity can arise from the motion of lines and planes in the images. In this case motion ambiguity is caused by lack structural information in three linearly independent-directions.

Figure 4: Aperture problem in 2D optical flow. The figure on the left shows ambiguity caused by placing the aperture in a region with no structural information. The central figure shows ambiguity caused by structural information in one linearly independent direction. The figure on the right shows an unambiguous situation since the aperture contains structural information in two linearly independent directions (WEDEL; CREMERS, 2011).

(iii) The calculation of OF relies on the motion of brightness patterns, and therefore motion artefacts can arise from changes in illumination levels. In PET images, illumination levels depend on detected gamma photons in the time interval for each gated frame. Possible causes of illumination level variation in PET images are beyond the scope of the proposed study since they require knowledge about PET/CT hardware that is not openly available from the manufacturer.

(iv) Noise reduces accuracy of image derivatives in differential methods, which in turn causes inaccuracies in the MVF.

GUTIERREZ (1995) extends the HS method to 4D images in voxel space by application of a Taylor series expansion and minimisation using the calculus of variations, resulting in Equation 2.3, which is shown in matrix form in Equation 2.4. Here the intensity of a voxel at coordinates x, y, z and time t is expressed as $E(x, y, z, t)$. The algebraic steps for decoupling the equations are shown in an online repository¹, from which Gauss-Seidel update equations in 2.5

¹<http://directionalanalysislmotion.github.io/>

are obtained.

$$\begin{aligned}
E_x^2 u + E_x E_y v + E_x E_z w &= \alpha^2(\bar{u} - u) - E_x E_t \\
E_y E_x u + E_y^2 v + E_y E_z w &= \alpha^2(\bar{v} - v) - E_y E_t \\
E_z E_x u + E_z E_y v + E_z^2 w &= \alpha^2(\bar{w} - w) - E_z E_t
\end{aligned} \tag{2.3}$$

$$\begin{bmatrix} (E_x^2 + \alpha^2) & E_x E_y & E_x E_z \\ E_x E_y & (E_y^2 + \alpha^2) & E_y E_z \\ E_x E_z & E_y E_z & (E_z^2 + \alpha^2) \end{bmatrix} \begin{bmatrix} u \\ v \\ w \end{bmatrix} = \begin{bmatrix} \alpha^2 \bar{u}_{i,j,k} - E_x E_t \\ \alpha^2 \bar{v}_{i,j,k} - E_y E_t \\ \alpha^2 \bar{w}_{i,j,k} - E_z E_t \end{bmatrix} \tag{2.4}$$

$$\begin{aligned}
u^{n+1} &= \bar{u}^n - \frac{E_x(E_x \bar{u}^n + E_y \bar{v}^n + E_z \bar{w}^n + E_t)}{\alpha_m^2 + E_x^2 + E_y^2 + E_z^2} \\
v^{n+1} &= \bar{v}^n - \frac{E_y(E_x \bar{u}^n + E_y \bar{v}^n + E_z \bar{w}^n + E_t)}{\alpha_m^2 + E_x^2 + E_y^2 + E_z^2} \\
w^{n+1} &= \bar{w}^n - \frac{E_z(E_x \bar{u}^n + E_y \bar{v}^n + E_z \bar{w}^n + E_t)}{\alpha_m^2 + E_x^2 + E_y^2 + E_z^2}
\end{aligned} \tag{2.5}$$

The Middlebury Computer Vision Pages website (SCHARSTEIN; SZELISKI, 2014) is a repository for computer vision evaluations and datasets, and includes measures for evaluation of optical flow algorithms. Synthetic image sequences are generated from known or ground truth (GT) displacements, and motion detection algorithms from participating groups are used to obtain a method estimation of the MVF from the image sequences. The accuracy of these algorithms can then be evaluated by comparing method estimated MVFs with GT, using error measures, which are angular error (AE) and endpoint error (EE) in this case.

2.5 Kinetic Energy Index

Left Ventricular Ejection fraction (LVEF) is a fundamental diagnostic and prognostic predictor of coronary artery disease (GERMANO et al., 1995) which is commonly used in cardiology to estimate how much blood the left ventricle pumps out with each contraction. It assesses the variation of the left ventricular cavity volume between end-diastole and end-systole, and can be calculated using Equation 2.6. GERMANO et al. describe an automatic method for quan-

tification of LVEF from gated myocardial perfusion SPECT by estimating end systolic volume (ESV) and end diastolic volume (EDV).

$$LVEF = \frac{EDV - ESV}{EDV} \times 100 \quad (2.6)$$

LVEF can be used in diagnosing and tracking heart failure. For example, an LVEF of 60% means that 60% of the total amount of blood in the left ventricle is pumped out with each heartbeat with 55 to 70% being a value indicative of normal function. LVEF measurements using gated perfusion SPECT are normally volume-based rather than count-based methods, and the time-volume curve allows the identification of end-diastolic (EDV) and end-systolic (ESV) LV cavity volumes (ABIDOV et al.). Figure 5 shows the LV volume curve (black line) created using Cedars-Sinai software (GERMANO et al., 2007) for a routine PET examination.

Figure 5: LV volume (ml) (black line) and filling (ml/s) (magenta line) curves generated by Cedars-Sinai software for ^{82}Rb PET images (DNMMI, Heart Institute, FMUSP)

Although indicators such as LVEF are useful and widely-used for assessing global cardiac function, its value is usually interpreted along with other factors and indicators in diagnosis. For example, LVEF lacks sensitivity for the prediction of sudden death and a reduced LVEF is considered to increase patient risk only when existing in combination with other risk factors (BUXTON et al., 2007); a significant proportion of patients with heart failure also have a normal LVEF at echocardiography during examination. This is because a thickened or stiffened ventricle can hold a lower volume of blood than normal, leading to insufficient supply to

meet the body's needs, resulting in a condition called heart failure with normal ejection fraction (HFNEF) (AMERICAN HEART ASSOCIATION, 2014) ; (WESTERMANN et al., 2008)

Currently, there is no measure of cardiac motility in general clinical use, meaning that motility is assessed subjectively. Kinetic Energy Index (KEf) is such an indicator, calculated directly from the quantified MVF, obtained through optical flow techniques applied to gated SPECT images. First Kinetic energy (KE) is calculated using Equation 2.7a, which creates a 4D scalar field, where u^2, v^2 and w^2 are components of the velocity field in x, y and z directions respectively and m is the voxel mass, which is approximated by the voxel intensity. Next, maximum and minimum KE during the cardiac cycle (KE_{max} and KE_{min} respectively) are used to compute KEf as shown in Equation 2.7b (GUTIERREZ et al.).

$$KE = \frac{1}{2}m(u^2 + v^2 + w^2) \quad (2.7a)$$

$$KEf = \frac{KE_{max} - KE_{min}}{KE_{max}} \quad (2.7b)$$

Figure 6 shows a KE curve for 30 normal individuals and LV volume against frame number with LV volume plotted on the same axes. The KE curve has two clear peaks, corresponding to systole and diastole, with a minimum point between them, corresponding to end systole.

KEf could be used to assist diagnosis of Ischemia, a disease which results in insufficiency of blood supply to the cardiac muscle, leading to possible necrotic regions of cardiac muscle. These regions have hypocapture in PET images and reduced quantified motion due to altered elastic properties. LIPTON et al. (2002), according to ROUGON et al., says that acute and chronic myocardial ischemia can be identified and localized through the detection of kinematic abnormalities, supporting the hypothesis that ischemia could be detected using motility indicators such as KEf.

Figure 6: Mean KE curve (grey line) and LV volume (black line) through the cardiac cycle obtained from 30 normal volunteers (GUTIERREZ et al., 2003).

2.6 Directional analysis of left ventricular motion

Specific medical terminology is used to describe normal or abnormal motion of the LV. Regional wall motion abnormality (RWMA) is a term indicating that the motion of a region of the heart muscle is abnormal. Motion can be reduced (hypokinesia), absent (akinesia) or increased (hyperkinesia). Occasionally it can describe an opposite behaviour (dyskinesia), such as the moving out of a wall in systole rather than moving in. RWMAs can also provide an indication about which coronary arteries are diseased (SAGIV, 2012). These small regional changes in motility can provide a detailed picture of the progress of disease.

The calculation of KE_f simplifies cardiac MVF analysis by discarding vector direction, but directional information provides an important manner to distinguish between, say, dyskinesia and normal motion. In addition to the expansion and contraction of the ventricle, which results in volumetric changes, torsion is found to be present in normal cardiac motion resulting from the difference in rotation between LV apex and base. BURNS et al. (2008) measure torsion using speckle tracking imaging, finding basal and apical clockwise rotation in early systole, and clockwise apical and anticlockwise basal rotation in late systole, as shown in Figure 7(a). The normal rotation is summarised in Table 1. They conclude that measurement of LV torsion may

Table 1: Normal LV rotation of apex and base of LV in systole and diastole (adapted from BURNS et al. (2008)).

	apex	base
Early systole	anticlockwise	anticlockwise
Late systole	anticlockwise	clockwise overcompensating
Diastole	clockwise	anticlockwise

provide insights into myocardial function and help predict response to treatment.

Figure 7: LV apical and basal rotation and LV torsion versus time from speckle tracking imaging. (a) Torsion versus time plot for a healthy adult male at rest with anticlockwise rotation arbitrarily defined as positive and time normalised to percentage duration of systole (100% is end systole defined by cessation of Doppler left ventricular outflow tract flow). During early systole (point A), both apex (green) and base (red) rotate anticlockwise (as represented by blue arrows in the left figure of Subfigure (b)) whereas later in systole (B), the apex rotates anticlockwise and the base rotates clockwise (yellow arrow) creating the torsion. Torsion (orange) is derived by subtracting the basal rotation from the apical rotation. (b) Representation of apical and basal rotation in early and late systole, as referred to by subfigure (a) (BURNS et al., 2008)

BUCKBERG (2004), according to NOTOMI et al. (2005), notes that recent research in clinical cardiac mechanics has moved away from SAX and LAX ventricular function and LVEF to three-dimensional ventricular deformation studies, which include investigations of LV torsion. There is a significant correlation between LV twist and LVEF, and increasing evidence shows that LV twist is superior to LVEF in characterising hemodynamic aberrations in patients with heart failure. LV twist is an index of systolic myocardial deformation, while LVEF reflects LV volume reduction during systole (BERTINI et al., 2009). SENGUPTA; KHANDHERIA; NARULA (2008) investigate LV twist mechanics, describing the cause of the twist and sum-

Figure 8: LV fibre orientation is a right-handed helix in the subendocardium and a left-handed helix in the subepicardium (A). During isovolumic contraction (IVC), the phase of the cardiac cycle after closure of the aortic valve and before the onset of mitral valve filling, circumferential forces are generated by endocardial fibre shortening, rotating the LV about the long axis clockwise as viewed from the apex (B). During the ejection phase, shortening of subepicardial fibres wrapped in an opposite, left-handed helix rotates the LV anticlockwise (C) (BERTINI et al., 2009).

marising clinical applications of LV twist for diagnosis of specific diseases, including coronary artery disease, valvular heart disease and hypertrophic cardiomyopathy. The arrangement of cardiac myocytes forms axial tracts that interconnect to form a three dimensional network. Fibres begin at the LV apex, spiralling upwards to the base. The subendocardial and subepicardial fibres ascend as a right and left-hand helix, respectively, with the midwall fibres aligned along the LAX, as shown in Figure 8.

Diagnosis of other diseases may be improved using an analysis of LV torsion. The LV of individuals with Non Compaction Cardiomyopathy (NCC), a rare and inherited congenital disease that probably first appears in the embryo, can display rigid-body rotation, where the apex and base have synchronised rotational motion; therefore the quantification of LV torsion could be used as an objective, quantitative and reproducible criterion for diagnosis (VAN DALEN et al., 2011; VAN DALEN; GELEIJNSE, 2013).

LV torsion measurements are obtained from rotational components in the MVF, and these in turn can be quantified using a variety of imaging modalities and diverse techniques. However, MVF quantification produces velocity components in Cartesian coordinates, meaning that an approach is required to extract rotational motion from the velocity field. The MVF of the LV is complex, including simultaneous contraction and expansion of the other walls, so the isolation of LV torsion from other motion is not trivial. ROUGON et al. suggest that transformation to

a cylindrical polar coordinate system is often used to obtain radial and rotational components, where the origin is placed at the centre of gravity of the LV and orientated along the long axis. The radial velocity can then be extracted as the component towards the origin and rotational velocity perpendicular to the origin, as shown in Figure 9.

Figure 9: Relevant orientations for deformation assessment in (a) SAX and (b) LAX views. For the LV, a cylindrical coordinate system is often used with origin at the LV gravity center and along the long-axis (ROUGON et al., 2005).

REBELO et al. (2010) develop a similar scheme for representing the MVF produced using OF techniques from SPECT images in patients with LV dyssynchrony. The cardiac MVF is decomposed into contraction, expansion and rotation based on a conversion from Cartesian to spherical coordinates, and the results are displayed in slices to show rotation and radial motion. Colour coding is introduced to assist visualisation of motion; the component of the movement is indicated with positive or negative values mapping to red and blue, with the colour intensity representing the magnitude of the velocity vector. The following scheme is used: (i) radial expansion is positive, contraction negative; (ii) horizontal rotation clockwise is negative, anticlockwise is positive; (iii) vertical rotation downwards is positive, upwards is negative, as shown in Figure 10.

Modelling the motion of the LV as a cylinder or sphere raises the following problems: (i) manual placement of the origin may be required, which introduces operator-induced error and variability (REBELO et al.); (ii) there is an inherent assumption that radial and rotational motion

Figure 10: Results of visualisation software for representation of directional components by conversion to spherical coordinates. Velocity images are shown for a subject with normal cardiac function in a slice from the midcavity portion of the LV. Row 1 presents diastolic images and row 2 presents systolic images. Subfigures (a) and (b) show radial components, (c) and (d) show horizontal rotational components, and (e) and (f) show vertical rotational components (REBELO et al., 2010).

can be modelled as towards a single point or around a single axis in the coordinate system, which could lead to large distortions; (iii) decomposition into geometrically based components assumes that the LV has a quasi-spherical or cylindrical geometry, whereas the shape of the LV is closer to a truncated ellipsoid (FRANGI; NIESSEN; VIERGEVER, 2001) and pathological LVs may deviate greatly from this geometry.

In order to analyse the rotational part of the dense and three-dimensional cardiac MVF, radial and linear components of the motion must first be removed. Feature-based vector field decomposition techniques allow a means for separating the rotational component while also determining areas or points which characterise the vector field. These critical points are the most important features in the flow (POLTHIER; PREUSS, 2003), and are composed of attractors, repellers and saddles, which are considered to define the structure of the flow. A critical point where some of the streamlines are straight is called a node, which can be repelling or attracting. Points around which streamlines are all curved are called spirals, and the direction of rotation may be clockwise or anti-clockwise and they may be repellers or attractors (WIEBEL, 2004).

PALIT (2005) presents a review of techniques to detect critical points in a vector field.

Phase portrait was introduced by RAO; JAIN (1992) as a means of visualising the flow of a 2D field by making local approximations of the field using linear differential equations. A similar analysis by FORD; STRICKLAND (1995)) determined critical points by an eigenvalue analysis. COHEN; HERLIN (1999) developed the Poincaré index, while NOGAWA et al. (1997) used the Cauchy residue theorem to detect vortices. The discrete Helmholtz Hodge decomposition (DHHD) was introduced by POLTHIER; PREUSS (2000) and is a technique which extends the continuous Helmholtz Hodge decomposition to discrete 2D vector fields, performing the decomposition on polyhedral surfaces. TONG et al. (2003) notes that the DHHD is a variational algorithm, and therefore less sensitive to noise than techniques that rely on local estimates, such as those using the Jacobian. TONG et al. extend the 2D vector decomposition to 3D fields on arbitrary tetrahedral grids, producing a full multiscale decomposition of a vector field into divergence-free (DF), curl-free (CF) and harmonic remainder (HR) parts. In some literature, DF and CF components are termed incompressible and irrotational fields.

GUO; GUO; MANDAL; LI; GUO et al. (2003, 2005, 2006) apply the 2D DHHD as defined by POLTHIER; PREUSS to analysing cardiac electrical patterns in animal hearts, based on the assumption that the electric action potential of fibrillated hearts contain sources, sinks, and rotational patterns. Figure 11 shows detected features in the curl-free (CF) and divergence-free (DF) MVF components, resulting from decomposition of an input field estimated using optical flow. The critical points are represented by symbols and placed over the detected centres of radial and rotational motion. BHATIA; MEMBER; NORGARD (2013) provides a review of literature in the area of the Helmholtz-Hodge Decomposition, including a discussion of boundary conditions relating to flow analysis and visualisation.

Figure 11: Application of 2D DHHD to cardiac video analysis, showing critical points in the flow: (a) Detected sources and sinks, $\circ$ and $*$ symbols, marked on curl-free (CF) component of optical flow; (b) Detected clockwise and anti-clockwise rotation, $\diamond$ and $\square$ symbols, marked on divergence-free (DF) component of optical flow; (c) Critical points superimposed on image from a single video frame (GUO, 2003).

3 MATERIALS

This chapter describes the materials used in the proposed study, including image sequences and MVFs, and also the protocols used for the selection of PET image sequences. The study took place in a hospital environment, at the Heart Institute (InCor), São Paulo, Brazil, which is a teaching hospital (Medical Faculty of the University of São Paulo, FMUSP). Hospital resources, particularly from the Informatics Division and Department of Nuclear Medicine and Molecular Imaging (DNMMI) were made available, including liaison with medical teams, use of computing resources and hospital PACS, software used in Cardiology, and the use of images acquired using modern instrumentation.

The images and MVFs used in the proposed study can be divided into the following categories: (i) computer-generated synthetic; and (ii) from living individuals for research purposes. Synthetic data can be generated with a corresponding ground truth, enabling assessment of motion quantification methodology when used in conjunction with appropriate error measures. Synthetic image sequences and MVFs of the following types were generated for the proposed study: (i) geometrically determined phantoms, such as moving blocks or cylinders; (ii) sophisticated phantoms, namely the cardiac image sequence and MVF generated by the the 4D extended (NURBS-based) Cardiac-Torso phantom software, or XCAT phantom (version 2) (SEGARS et al., 2010; THE JOHNS HOPKINS UNIVERSITY, THE JOHNS HOPKINS HOSPITAL, AND THE JOHNS HOPKINS HEALTH SYSTEM, 2016). Synthetic MVFs from geometrical and XCAT phantoms were also used. The XCAT phantom is presented in more detail in Section 3.2. PET images were acquired in the DNMMI at the Heart Institute and consist of images using two different radioisotopes: (i) Rubidium-82, with a temporal resolution of 8 frames per

RR; (ii) Fluorodeoxyglucose (FDG), with resolution 16 frames per RR, where RR means the interval of time as shown by the electrocardiogram from the peak of one QRS complex to the peak of the next, i.e. one cardiac cycle. The use of medical images for this project were liberated by decision of the Ethical commission for analysis of research projects (CAPPesq) by formal inclusion of the proposed study in Project 0030/11, and the issued certificate is reproduced in Annex C.

The following sections describe the preparation or acquisition of the images and MVFs used throughout this work, first the synthetic images and MVFs followed by PET images.

3.1 Generation of synthetic textured cylinder images

A solid textured cylinder was created with radius of 28 voxels and height 5 voxels against a non-textured background of intensity zero. The texture was created using Equation 3.1 with the constant term for the texture equal to 0.5 and sinusoidal amplitude 0.25, resulting in a texture which varies between zero and one. A rendered version of the generated cylinder is shown in Figure 12. Further details about image generation can be found in GUTIERREZ et al. (2003).

$$E(x, y, z) = \alpha + \beta[\sin(\omega_1 x) + \sin(\omega_2 y)] \quad (3.1)$$

Figure 12: Rendered textured cylinder, used for quantification of error in motion detection algorithms. (SIMS; FURUIE; GUTIERREZ, 2014)

Five sequences of the cylinder in rotation and translation in the xy plane were generated with rotational velocity of 1° , 2° , 5° per frame, and translation of $(u,v,w) = (1,0,0)$ and $(1,1,0)$ pixel per frame, as shown in Table 2. Accompanying ground truth MVFs were created for the translation sequence by giving all voxels inside the volume a constant velocity and zero outside, while the values of rotational velocity were determined using Equation B.1 in Appendix B, similarly with zero values outside.

Sequence	Description
1	rotation of 1° per frame
2	rotation of 2° per frame
3	rotation of 5° per frame
4	translation $(u,v,w) = (1,0,0)$
5	translation $(u,v,w) = (1,1,0)$

Table 2: Image sequences for cylinder in rotation and translation

3.2 Generation of XCAT image sequences and motion fields

XCAT phantom image data and MVF data were prepared. The XCAT phantom consists of a whole body model containing a high level of anatomical detail and is suitable for application in imaging modalities such as CT, MRI, and PET. The phantom enables realistic simulation of cardiac deformation. The XCAT phantom is capable of generating both 4D images and the corresponding vector positions of the voxels throughout the sequence.

XCAT images are generated by running a licensed program with an input parameter file (.par), providing specific configuration details. A sample parameter file is included in a github repository ¹.

The parameter file was set to generate 4D distribution emission radionuclide activity of the heart, simulating images from NM. XCAT was run in a mode to generate images (mode 0) and a mode to generate position vectors (mode 4). Sequences with 16 and 64 frames were generated with image volumes of size 128 slices of 128 by 100 voxels. The energy of the photons was set to 140keV, pixel size to 0.3125cm and slice depth of 0.3125cm, typical values for NM.

¹ <http://directionalanalysislmotion.github.io/>

The startslice and endslice values were set from 360 to 459 to include the region of the body containing the heart.

The following subsections provide further details about generation and reading of image data and position vectors.

3.2.1 Extraction of XCAT image data

The coordinate system of the XCAT images is shown in Figure 13. The origin of the Z axis is at the toe ($Z=0$), increasing towards the head. Y runs from anterior ($Y=0$) to posterior (maximum Y) and X from right ($X = \text{zero}$) to left (maximum X), in patient-oriented coordinates. The cardiac images generated by XCAT pre-align the patient's transverse plane with the cardiac SAX. Generated images are separate binary files corresponding to each frame. Due to configurations specified in the parameter file, the binary stream starts with the voxel at the coordinate origin (0,0,360), incrementing in X, then Y, then Z until (127, 127, 459). Slices begin closest to the feet, increasing towards the head.

Figure 13: Representation of coordinate axis system definition for XCAT phantom images, adapted from WIKIPEDIA (2015).

Software was written to read XCAT image data and produce 4D binary data archives suitable for use with MATLAB. Figure 14 shows a single XCAT SAX slice of the input image sequence and a 3D rendered image of the XCAT heart. The left ventricle is present as a thick ring of muscle in the centre of the image. Other structures visible are the right ventricle (RV),

ribs, vertebrae and sections through the arms. Figure 15 shows slices through horizontal and vertical long axis (HLA and VLA) and SAX, cropped to show the LV in more detail. The figure has been annotated to indicate the position of the LV, RV, the atria, and the base and apex, in the three orthogonal views.

Figure 14: XCAT phantom images. (a) Short axis slice through torso for a single frame of XCAT image sequence; arms, chest cavity, ribs, spine, breasts and heart are clearly visible; (b) 3D rendered side view of XCAT heart.

Figure 15: Cropped XCAT phantom images of atria and ventricles in the three perpendicular aspects, with right and left atria and ventricles (RA, LA, RV, LV) and base and apex marked.

3.2.2 Calculation of synthetic cardiac XCAT phantom motion field

Organisation of the data in text files: Software was written to create a synthetic cardiac XCAT phantom MVF from generated position vectors, extracted from text files. These are

named according to the frame of data contained, from 2 to the total number of frames.

Text files begin with header information followed by a list of position vectors. An example position vector is shown in Listing 3-1, which shows positions in frame 2 of a 16 frame sequence. Integer position (x,y,z) in frame 1 are specified first, followed by the frame 2 position as three floating point numbers. This entry can be interpreted as saying that the voxel, defined by position (66,60,17) in frame 1, moves to (65.852495 59.981924 16.994149) in frame 2. The voxel list contains only a subset of all image voxels, and those absent are at the frame 1 position. For the purposes of this text, let the position in frame f be represented by the vector $\vec{p}_f = (x_f, y_f, z_f)$.

Listing 3-1: XCAT position vector showing a single voxel displacement in frame 2

```
known_vector_dias_lv_4 frame1 66 60 17 frame2 65.852495 59.981924 16.994149
```

Some of the vectors listed in the text files are labelled `interpolated vector` and others as `known vector`. The known vectors are reliable values of position, whereas interpolated vectors are calculated from the known vectors and do not necessarily coincide with the structures of the LV and other organs. Only `known vectors` were selected for generation of the XCAT MVF.

Creation of 4D position vector array: The first task was to convert the position information in the text files into a matrix form to facilitate later velocity calculations. An empty 4D array of size nx, ny, nz, nf was allocated, capable of containing a 3D displacement vector $\vec{p}_f$ at each element of the array, where nx, ny, nz are dimension of the XCAT image and nf the number of frames. Each spatial 3D volume of the array, of size nx, ny, nz , was initialised to the frame 1 volume position. For example, the vector at coordinates (13,14,17) in all frames was set to contain $\vec{p}_f = (13, 14, 17)$. Next the text files were read line by line, extracting the position in frame 1, (i, j, k) , the frame number, f , and the voxel location $\vec{p}_f$ for that frame. Finally the position matrix $\vec{p}_f$ was updated with the value contained in the text files. When all displaced (listed) voxel positions in all the files had been placed into $\vec{p}$, any undisplaced voxels would be

left with the position from initialisation.

Calculation of XCAT motion field: The XCAT MVF was estimated from the position array, $\vec{p}$. Figure 16(a) shows the data as represented in the 4D array, read from text files, with position vectors relative to location in frame 1 while (b) shows the required output for vector velocity, calculated using a forward differences scheme.

Figure 16: 2D representation of position vectors (a) as produced by the XCAT phantom (b) displacement over a single frame

Centred and forward finite differences schemes were implemented for calculation of the ground truth velocity field from the position vectors as shown in Equation 3.2a and 3.2b respectively, where f is the frame number, i, j, k are integer voxel positions, $v_{i,j,k}^f$ is the velocity at frame f for the voxel at (i, j, k) , and δt is the time interval between frames, which was set to one. In this case velocity is measured in units of voxels per frame.

$$v_{i,j,k}^f = \frac{(p_{i,j,k}^{f+1} - p_{i,j,k}^{f-1})}{2\delta t} \quad (3.2a)$$

$$v_{i,j,k}^f = \frac{(p_{i,j,k}^{f+1} - p_{i,j,k}^f)}{\delta t} \quad (3.2b)$$

To illustrate the velocity field calculation using forward differences, consider a 2D vector field consisting of four vectors in a 2 by 2 grid, with the displacement expressed at frame 2. Imagine that XCAT outputs the vector data shown in Listing 3-2:

Listing 3-2: XCAT position vector showing a single voxel displacement in frame 2

```
known vector frame 1: (1,0) frame 2: (1.04 , 0.01 )
known vector frame 1: (0,1) frame 2: (0.05 , 0.99 )
```

Pixels (0,0) and (1,1) are not included in the listing, and are at frame 1 positions. Construct a 3D (2D + time) array to contain all position values:

$$\text{Frame 1: } \begin{pmatrix} (0,0) & (0,1) \\ (1,0) & (1,1) \end{pmatrix}, \text{ frame 2: } \begin{pmatrix} (0,0) & (0.05,0.99) \\ (1.04,0.01) & (1,1) \end{pmatrix}$$

Now calculate velocity field. Use forward differences, as in Equation 3.2b, modified for the 2D + time case, $v_{i,j}^f = \frac{(p_{i,j}^{f+1} - p_{i,j}^f)}{\delta t}$ where $\delta t = 1$. Then velocity in frame 1 is given by:

$$\begin{pmatrix} v_{0,0}^1 & v_{0,1}^1 \\ v_{1,0}^1 & v_{1,1}^1 \end{pmatrix} = \begin{pmatrix} (0,0) & (0.05, -0.01) \\ (0.04, 0.01) & (0,0) \end{pmatrix}$$

The first row of Figure 17 shows the x component of velocity (u) in SAX, HLA and VLA slices using centred differences. The difficulty of visualising three orthogonal MVF components in a single image slice can be overcome through using different colours to represent each orthogonal velocity component, as shown in the second row of Figure 17. The SAX figure shows that the LV is contracting. Quiver plots of short axis slices through the XCAT MVF at apex and base are shown in Figure 18 for frame 3.

Figure 17: XCAT motion field computed from known vectors in three orthogonal planes, calculated using centred differences. Row 1 shows the x component of velocity (see key for velocity to colour mappings) and row 2 shows each velocity component, u, v, w , represented as red, blue and green respectively, with velocity magnitude related to colour saturation.

Figure 18: XCAT velocity field, represented in quiver plots in the SAX plane, computed from known vectors: (a) apical; (b) basal slices.

3.3 Creation of synthetic motion field from Gaussian potentials

The DHHD is used in this work for decomposition of an input MVF into rotation, radial motion, and linear translation. This section considers the creation of synthetic input fields from superposition of rotational components, F_{ROT} , radial components, F_{RAD} , and linear components in order to test and perform experiments on this algorithm. MVF components and input fields were created on a grid of size $55 \times 55 \times 55$, chosen to be large enough to allow a reasonably smooth MVF, while being small enough to allow convenient run time and memory usage.

F_{RAD} , was created by forming a 3D Gaussian scalar potential, ϕ , according to Equation 3.3a, then applying the gradient operator and normalising as shown in Equation 3.3b. The values of x , y and z in Equation 3.3a refer to positions on the integer grid, with x_c , y_c , z_c defining the centre of the potential, and σ , the standard deviation, defining the smoothness and extent of the MVF in the domain. Sinks or sources were created by applying the gradient operator to a positive or negative potential respectively. F_{ROT} , rotational components around an axis parallel to the z -axis, was formed using a vector potential, $(0, 0, \phi)$, then applying the curl operator and normalising as shown in Equation 3.3c. Anti-clockwise or clockwise rotations in the xy plane, as seen from above, were created from positive or negative potential respectively. Example plots of F_{RAD} and F_{ROT} are shown in Figure 19. The following subsections, describe the creation of two types of distinct complex fields using these radial and rotational components.

Figure 19: 3D plot showing example 3D radial and rotational motion field components, F_{RAD} (sink, left) and F_{ROT} (anti-clockwise rotation as seen from above, right).

$$\phi = e^{-\frac{1}{2\sigma^2}[(x-x_c)^2+(y-y_c)^2+(z-z_c)^2]} \quad (3.3a)$$

$$F_{RAD} = \frac{\nabla\phi}{\max(|\nabla\phi|)} \quad (3.3b)$$

$$F_{ROT} = \frac{\nabla \times (0, 0, \phi)}{\max(|\nabla \times (0, 0, \phi)|)} \quad (3.3c)$$

3.3.1 Creation of the complex field for qualitative analysis

A complex synthetic 3D input MVF was created for qualitative analysis of the DHHD. Four MVF components were created with $\phi = 5.0$, superposed, and motion centres placed as follows: (i) sink at (20,20,28); (ii) source at (34,34,28); (iii) clockwise rotation in xy plane at (20,34,28); (iv) anti-clockwise rotation in xy plane at (34,20,28), each with the input harmonic component, $F_H = 0$. A slice through the MVF at $z = 28$ is shown in Figure 20, where the field is shown as viewed from above (decreasing z).

Figure 20: Slice through the complex input motion field for the DHHD at $z = 28$ with $\sigma = 5.0$. Components are a sink, a source, a clockwise rotation and an anti-clockwise rotation, each of which has been enlarged.

3.3.2 Creation of the complex fields for quantitative analysis

A single anti-clockwise rotation and a single sink were created to quantify the accuracy of the decomposition. Both components were centred at $(28,28,28)$, and summed. σ was given values of 1.250, 1.768, 2.500, 3.536, 5.000, 7.071, 9.129, 12.910 for both F_{RAD} and F_{ROT} , creating 8 MVF variations.

Figure 21: Synthetic input field and radial and rotations components, formed from Gaussian potentials with $\sigma = 7.071$: (a) F_{RAD} (b) F_{ROT} (c) Synthetic input field, ξ , resulting from summation of (a) and (b).

3.4 PET images

This section describes the acquisition and protocol for selection of PET images, using the radiopharmaceuticals Rubidium Chloride- ^{82}Rb and Fluorodeoxyglucose- ^{18}F . The proposed study uses shortened names, such as ^{82}Rb and FDG. The description of acquisition of ^{82}Rb images was adapted from FALCÃO et al. (2015).

3.4.1 Acquisition of Rubidium Chloride - Rb-82 PET images

The Department of Nuclear Medicine and Molecular Imaging (DNMMI) at the Heart Institute, University of Sao Paulo Medical School, made an image database available for the use of the proposed study, containing more than 660 acquisitions with ^{82}Rb PET image sequences. Acquisitions were performed by personnel from the DNMMI using a Philips Gemini PET/CT scanner². The CT image is used for registration and to perform attenuation correction during the process of image formation, and the image is gated using the signal from the ECG, which is only available for the PET/CT's internal routines. Appendix A.3 contains more information about acquisition of gated images.

The dataset includes gated PET acquisitions from individuals with altered and normal cardiac function, and accompanying information from clinical patient records, such as the commonly used cardiac index, LV Ejection Fraction (LVEF). Figure 22 shows the structure of the ^{82}Rb image database, where each acquisition is composed of a rest and stress examination. Gated images composed of eight frames were created, a low temporal resolution, due to the limited radioactive count produced by the ^{82}Rb isotope. It was found that forming sixteen gated frames produced images with an unacceptable level of noise.

Individuals underwent rest-dipyridamole stress ^{82}Rb -PET with absolute quantitative flow measurements using Cedars-Sinai software (mL/min/g). Acquisition of rest images was performed using a 3-D listmode acquisition over 8 min, following square wave intravenous injec-

²Philips Gemini TF 64 TOF, Series number 7535, Manufactured Jan 2012 by Philips Medical Systems (Cleveland) Inc., Cleveland, Ohio, USA, Identification code NM 0183, HC 147938

Figure 22: Structure of Rubidium-82 image database

tion of Rubidium Chloride- ^{82}Rb (10 MBq/Kg; Jubilant DraxImage³) over 60-seconds. Emission images from the first 2 minutes of acquisition were binned to form input arterial data, and the last 6 minutes to form myocardial uptake data.

Dipyridamole was infused intravenously (0.56 mg/Kg) over four minutes to induce pharmacologically-induced cardiac stress followed by the same dose of ^{82}Rb . Stress images were acquired and processed as above. Two low-dose CT-based attenuation corrections for PET transmission scans were performed before ^{82}Rb administration (120 kV; 115 mAs; 33 mA and 0.435 pitch). Reconstruction used a 3D Ramla iterative algorithm. LVEF was calculated from both rest and stress images using 4D QGS software (GERMANO et al., 2007), version 2012.2. The pixel size was 4mm.

The electrocardiogram (ECG) signal is acquired simultaneously with the image and used to construct a sequence of image volumes from detected photon events collected over several hundred RR intervals. The length of RR intervals vary constantly during the examination as the cardiac frequency of the individual changes.

Images were manually reoriented to align the LAX with the coordinate system. HLA, VLA and SAX slices of a Rubidium cardiac image are shown in Figure 23 for the eight gated frames.

3.4.2 Selection protocol for Rubidium Chloride - Rb-82 Chloride PET image sequences

63 images were selected from the Rubidium-82 image database, consisting of: (i) 30 individuals with normal cardiac function (NCF) group; and (ii) 33 individuals with low/ altered

³Jubilant DraxImage Inc. 16751 TransCanada Highway, Kirkland, Quebec, Canada, H9H 4J4

Figure 23: Eight gated frames of Rb-82 image sequence in HLA, VLA, SAX slices. Representative ECG signal adapted from REMOTEa LTD (2016).

cardiac function (LACF). Criteria for inclusion in the NCF group was LVEF > 50 and for the LACF group LVEF < 50 , both being determined by the result of the stress examination using Cedars-Sinai software. Rest images were exclusively used for the study.

3.4.3 Acquisition of FDG-F-18 PET images

The DNMMI made an FDG- ^{18}F image database available for the proposed study, containing 31 gated acquisitions and using the same PET/CT scanner as for the Rb image acquisition.

The dataset includes acquisitions from individuals with normal cardiac function and non-compaction cardiomyopathy (NCC). The database contains a single acquisition for each individual and a time resolution of 16 gated image frames per cardiac cycle. Time resolution was decided by DNMMI personnel after acquisition due to adequate radioactive count produced by the FDG.

Images acquisition used a 3-D listmode over 20 min, after a square wave intravenous injection of FDG over a 120-second interval followed by 38 min in a supine position and 40 minutes uptake.

After a normal end-expiration and before FDG administration, one low-dose CT-based attenuation correction for PET transmission scans was performed (120 kV; 115 mAs; 33 mA and 0.435 pitch).

Images were reconstructed using an iterative algorithm (3D Ramla). LVEF was calculated from rest images using 4D QGS software (GERMANO et al., 2007), version 2012.2. The pixel size was 4mm. Images were manually reoriented to align the LAX with the coordinate system.

The electrocardiogram (ECG) signal was acquired for the same purpose as in Rb images. The resulting HLA, VLA and SAX slices of a FDG cardiac image are shown in Figure 24 for the sixteen gated frames, while orthogonal sections through a rendered FDG volume image of the LV are presented in Figure 25.

Figure 24: Sixteen gated frames of FDG image sequence in HLA, VLA, SAX slices.

Figure 25: HLA, VLA and SAX slices and rendered LV for single frame of FDG image.

3.4.4 Selection protocol for segmentation of FDG PET image sequences

Selection of images for the testing of segmentation algorithms (Chapter 4) was performed as follows. From the complete set of images, 4 image sequences were randomly chosen, and from each of these, 4 frames were randomly selected. This provided a total of 16 image volumes, comprising 395 SAX slices.

3.4.5 Selection protocol for decomposition of FDG PET image sequences

Selection of images for motion decomposition using the DHHD (Chapter 7) was performed as follows. An expert cardiologist selected a single control image from the 31 available, based on visual assessment of cardiac motion and considerations from other tests performed at the time of imaging. This is referred to as image N, a female, aged 34 years old at the time of the examination, without previous incidence of cardiac disease. In order to provide a comparison with image N, an image from an patient with low cardiac function, referred to as image L, was also selected, aged 46 years old at the time of the examination, presenting NCC, heart failure and with an artificial pacemaker implanted.

3.4.6 Noise characteristics and degradation of PET images

Comparing Figures 23 and 24 shows that Rb-82 PET images contain higher levels of noise, visible in the form of nebulous structures around the LV, and originating principally from low radioactive count. This noise generally degrades the results for the various phases of the pro-

posed study. Low count is also the reason why the temporal resolution of the Rb images is lower than for FDG, as has already been described.

Factors leading to high noise in ^{82}Rb , are represented graphically in Figure 26. ^{82}Rb tends to form high concentrations in the myocardium, whereas FDG becomes more distributed in the body, so to avoid saturating the PET/CT scanner the dose administered to the patient must be low. The low dose combined with the very short half-life of ^{82}Rb leads to a lower statistic and therefore high image noise, as seen in Table 15 in Appendix A. A consideration specific to the acquisition made in the DNMMI is that the primary purpose of the Rb-82 image acquisition was to investigate coronary flow reserve (CFR), but the same listmode acquisition data were used for CFR studies and formation of gated frames. Figure 27, generated using PMOD v3.4 (PMOD TECHNOLOGIES LLC, 2016), shows the variation of radioactive count for one of the ^{82}Rb acquisitions over 8 minutes. The full 8 minutes of this listmode data was used for the CFR study, whereas the gated frames used only the data from 2 until 8 minutes, where the acquisition had stabilised (seen as a stable decaying slope in the figure). The starting activity for the gated frames (at 2 minutes) was therefore around 0.5 of the peak activity, again limiting the ^{82}Rb statistic. Table 15 shows that the positron range (PR) for ^{82}Rb is a mean distance of 5.9mm in water compared with 0.6mm for FDG, which also limits the resolution of the ^{82}Rb images.

Figure 26: Factors leading to high noise levels in ^{82}Rb PET images.

Figure 27: Example of variation of count over acquisition of ^{82}Rb PET images (provided by DNMMI, Incor, FMUSP), with list-mode data from 2 to 8 minutes being used to construct gated frames.

4 IDENTIFICATION OF LEFT VENTRICULAR STRUCTURES

4.1 Methodology

UDUPA et al. (2006) define image segmentation as the process of identifying and delineating objects in images. Recognition is the high-level process concerned with the approximate location of the object of interest in the image, whereas delineation is the low-level process of determining its precise spatial extent. Steps for identification of the LV have been divided into these stages, and Figure 28 shows how they are implemented to interact with motion quantification.

Figure 28: Overview for identification of LV structures.

1. **Recognise and limit LV:** The 4D DICOM images are limited to the ROI. The FDG images are $128 \times 128 \times 128$ voxels with 16 frames, which results in 33.6×10^6 voxels, whereas the ROI is approximately 0.6×10^6 voxels, assuming it to be a cube with sides of 35 voxels (14cm). Determining the ROI enables cropping of the LV, which in turn allows an image sequence of reduced size to be passed to motion quantification algorithms, resulting in savings of storage and processing time. Since the motion detection algorithm described in Chapter 5 produces artefacts at the image limits, it is desirable to crop the image slightly larger than the LV.

2. **Motion quantification:** The MVF is calculated, containing regions with non-zero velocity outside the LV which should be eliminated for improved accuracy.
3. **Delineate LV:** The voxels pertaining to the LV are delineated and a segmentation mask created.
4. **MVF delineation:** The segmentation mask is applied to the MVF to LV myocardium, setting velocity vectors to zero outside the mask.

4.1.1 Materials

FDG image sequences were utilised for validation and testing of cropping and segmentation routines, and their selection is described in Section 3.4.4. Evaluation of the delineation was performed by comparison with manual segmentation of the 16 randomly selected frames from 4 image sequences, a total of 395 SAX slices, using software described in Subsection 4.1.3.1. ^{63}Rb image sequences were also used for testing the cropping routines, whose selection is described in Section 3.4.2.

4.1.2 Automated LV location and crop

The aim of this procedure is to extract the ROI from the PET image sequences prior to further processing, and is composed of the following stages: (i) LV detection and crop of LV in SAX slices; (ii) Determination of LV extent in LAX direction and crop.

4.1.2.1 LV detection and crop of LV in SAX slices

This phase detects the LV in SAX image slices, making the following *a priori* assumptions:

1. The midsection of the LV appears as rings of muscle, the edges of which have the form of two concentric circles.
2. The centres of circles fitted to the LV move little through subsequent slices. Maximum deviation of the centre was determined empirically as approximately 2 pixels (0.8cm)

through the SAX slices. It is assumed that manual reorientation of the PET images to align the long axis of the LV with the coordinate system was performed adequately by personnel from the DNMMI.

3. Detected radii of inner and outer circles, which approximate slices through inner and outer surfaces of LV myocardium, have maximum diameter of less than 20cm, which is equal to a circle of radius 25 pixels, with pixel width of 4mm. STOLZMANN et al. (2008) finds End-diastolic LV inner diameter to be 5.0 ± 0.8 cm and End-diastolic septal wall thickness to be 0.9 ± 0.2 and End-diastolic posterior wall thickness to be 0.9 ± 0.2 using CT and based on measurements from 100 patients. This gives an approximate outer diameter of 6.8cm. With a resolution of 4mm per pixel, expected circle diameters are approximately 17 pixels PET images respectively. The largest circles admitted using the proposed methodology therefore admit circle diameters of approximately three times this average value, sufficient to allow detection of the outer border of the LV in all individuals, including those with pathological conditions such as hypertrophy.

Given the validity of the above assumptions, the Hough Circle Transform (HCT) may be used to identify LV borders in the unstructured image. A brief introduction to the transform is provided in Appendix C.1. HCT parameters were chosen based on *a priori* knowledge of LV dimensions, as mentioned above.

The image processing scheme, presented in Figure 29, encompasses image processing stages on the level of the slice, the frame and the sequence and analysis on the frame and sequence level. The descriptions below detail each stage of the processing, organised by the level of data they are applied to (slice, frame or sequence).

Slice level processing:

1. **Edge detection:** An edge image was created by applying a Canny edge detector, with default settings, to the 2D SAX slices.
2. **Hough circle transform:** Circles in each slice were detected using the transform. The

Figure 29: Summary of processing stages to crop image volumes in the SAX plane, adapted from SIMS; GUTIERREZ (2016)

radius detected was between 4 and 25 pixels, with the lower limit chosen to reject small circles, which were often found to be the product of noise or non-cardiac structures. The selected circles, corresponding to the ten highest peaks from the Hough accumulator, were stored for analysis. A threshold on the accumulator was set to 5.0, a value established to reject poor quality circles.

3. **Circle cluster analysis:** A cluster analysis was performed on the saved circles using hierarchical clustering functions. Agglomerative methods were used, whereby a dendrogram is created by forming a series of partitions, starting from all circle centres as single member clusters, and terminating with a single group containing all individuals. Euclidean distance between pairs of circle centres was used as a similarity measure. Specifically, the agglomeration is performed at each step as follows: (i) find the distance between closest pairs of individuals in existing groups; (ii) select the minimum distance, and; (iii) combine elements of both groups at the minimum distance (EVERITT et al., 2011). Once the dendrogram had been formed, clusters were chosen based on the cut-off distance of 2 voxels (0.8cm) between centres, previously described in the *a priori* assumptions. Standard deviation of radius, r_{sd} was used within each cluster to identify the cluster belonging to the LV, as shown in Equation 4.1, where p is the complete set of circles detected, k are circles belonging to the cluster, r_k is the set of radii for the cluster, r_{mean} is the mean

radius of the cluster, n_k is the number of circles in the cluster. Appendix C.2 provides further description of the cluster analysis in the form of an example.

$$r_{sd} = \sqrt{\frac{\sum_{k \in p} (r_k - r_{mean})^2}{n_k}} \quad (4.1)$$

4. **Select greatest radius:** The circle with the largest radius was selected from the cluster with the largest standard deviation of radius (r_{sd}). Circle centre coordinates and radius were passed back to the calling function for a frame level analysis.

Frame level processing: The input to the routines at frame level was the set of greatest circles, each selected from a different slice.

1. **(Frame level) Cluster analysis:** The purpose of this phase is to discard detected greatest circles not corresponding to the LV. A cluster analysis was performed using the set of greatest circle centres, with clusters determined by a maximum distance of two pixels. A histogram was used to determine the cluster containing the largest number of greatest circles, which was assumed to be circles corresponding to the LV. The circles corresponding to this cluster were retained and the rest excluded.
2. **Define LV limits:** the selected cluster of circles were used to define the image limits, L_{xmin} , L_{xmax} , L_{ymin} , L_{ymax} , according to Equations 4.2 and represented in Figure 30.

$$L_{minx} = x_{min} - r_{max} - c \quad (4.2a)$$

$$L_{maxx} = x_{max} + r_{max} + c \quad (4.2b)$$

$$L_{miny} = y_{min} - r_{max} - c \quad (4.2c)$$

$$L_{maxy} = y_{max} + r_{max} + c \quad (4.2d)$$

where x_{min} , x_{max} , y_{min} , y_{max} , r_{max} are the maximum and minimum values of x and y for the centres of greatest circles found in the the selected cluster of slices, c is a constant

added to allow extra clearance between the outer part of the left ventricle myocardium and the edge of the image; c was set to 3 pixels, determined by experiment to reduce motion artefacts in motion quantification.

Figure 30: Quantities required for definition of boundary box. Two circles are shown, representing the extremes of circle centre through the frames, with maximum and minimum values of circle centre in x and y directions. Limits of the outer box are determined using the largest value of radius from the sequence, r , and an additional clearance constant, c .

Image sequence level processing: Each frame has defined limits, and the largest of these is taken to crop the image sequence.

1. **Define global image limits:** a global boundary box for the image sequence was determined by taking the maxima and minima of the frame level boundary boxes throughout the image sequence.
2. **Crop image sequence:** The global boundary box was applied to crop the image sequence in the xy plane.

4.1.2.2 Determination of LV extent in LAX direction and crop

In this phase the set of slices containing the LV are determined, allowing cropping perpendicular to the SAX. Two approaches were tested: (i) identify apex and base through HCT detections; (ii) identify the slice containing the circle with the largest radius and crop the image a determined number of slices above and below this point, sufficient to leave the base and apex far from image borders over the whole image set.

4.1.3 Automated LV segmentation

The purpose of segmentation is to delineate the LV myocardium from surrounding regions, which include cardiac structures such as the RV and atria. The proposed method follows in the line of research presented in DEDIC; ALLILI; LECOMTE (2011), but employs the Distance Regularized Level Set Evolution (DRLSE) algorithm (LI et al., 2010; LIU et al., 2014; LIU et al., 2016) to approximate outer edges of the LV in SAX slices. Circle detection data is used for initialising the segmentation routines, and since image limitation excludes many structures which cause false circle detections, reapplying the circle detection routine produces a more reliable result than reusing data from the cropping stage. So circle detection routines were applied to the cropped image, greatest circles on the slice level were obtained, and false detections eliminated by cluster analysis. The resulting data was saved for later use. The procedure for creating reference and method segmentations are described in the following sections, and applied to FDG images.

4.1.3.1 Reference segmentation

Software with a graphical user interface was developed to perform, view and evaluate segmentations, allowing a mask to be created by application of a threshold to a single SAX slice, followed by the definition of a ROI by drawing a polygon. The mask can then be modified by adding or removing pixels, and finally saved. Similarly, an existing mask can be loaded, modified and resaved. Figure 31 shows the definition of the outer edge of the LV; in Subfigure (a), a polygon is drawn to define the outer edge of the LV; in (b) the polygon is closed and the software marks selected pixels as red; and (c) shows a screenshot from the GUI, with the polygon on the left and the segmented image on the right.

4.1.3.2 Automated segmentation

The delineation of the outer LV edge uses a prior from HCT detections. The DRLSE algorithm was applied to SAX 2D slices throughout the image sequence. The segmentation in each frame commenced with the slice containing the largest circle radius as determined by

Figure 31: Screenshots showing software for manual segmentation of FDG images: (a) definition of outside edge of LV with polygon (b) definition of LV with overlaid red dots (c) final view of original image (left), with segmentation marked by dots, and (right) segmented region.

the HCT. The initial level set was determined as -2 within this circle and $+2$ outside, and the LS evolved. Upon convergence, the final level set function was used to initialise the slices immediately above and below. The evolved contours were used to successively initialise other slices, towards the base and apex. The stopping condition for the segmentation was when the LS contour vanished, ideally close to base or apex. The final level set function was stored at each step, and the segmentation of the outer LV border obtained by selecting all pixels in the slice with negative LS values. Optimum parameters of the DRLSE were determined by experiment in Section 4.1.3.3.

Having established the outer border of the LV, the inner surface was defined by application of a global threshold. The optimum value was established by experiment in Section 4.1.3.3.

4.1.3.3 Experiments

Evolution of the DRLSE depends on minimisation of energy defined by the following terms: (i) distance regularisation term; (ii) edge term, minimised when the zero LS is located at object boundaries; (iii) a weighted area term, which was introduced to accelerate motion of the zero level contour. Each term has a weight, being μ , λ and α respectively. The weighted area and edge terms are approximated by Dirac delta and Heaviside functions, with width defined by a coefficient, ϵ . In addition, σ defines the width of a Gaussian function for pre-smoothing (LI et al., 2010).

These weights and coefficients were optimised for use on the FDG PET image set. Ref-

erence and automatic segmentations were performed for the selected 16 frames. Automatic segmentations varied LS parameters $\lambda, \alpha, \epsilon$ as shown in Table 3, and for each variation the error was measured between the reference and method segmentation using the Dice Similarity Measure (DSM) (DICE, 1945; KARIM et al., 2016). The DSM is shown in Equation 4.3, extended to volume images, where V_R and V_M are the resulting reference and method image volumes from the segmentation, respectively.

Table 3: Values of DRLSE parameters which were varied in method segmentation

λ	α	ϵ
0.06, 0.08, 0.1	0.003, 0.005, 0.008	0.7, 0.9, 1.1

$$DSM = 2 \cdot \frac{V_M \cap V_R}{V_M + V_R} \cdot 100\% \quad (4.3)$$

A total of 108 automatic method segmentations were obtained from the permutations of parameters and with thresholds 0.8, 0.1, 0.12 and 0.14 to exclude voxels inside the blood pool. $\sigma = 0.8$ and $\mu = 0.01$ were held constant for all tests. Mean and standard deviation of DSM were obtained for each method segmentation and the optimum combination of LS parameters and threshold was determined by maximum DSM.

4.2 Results

4.2.1 Automated LV location and crop

4.2.1.1 LV detection and crop of LV in SAX slices

Figures 33 and 32 show circle detections at slices for a mid section SAX slice with FDG and ^{82}Rb PET images. The images have been manually zoomed to the ROI to facilitate visualisation. The edge detection was applied to the initial slice, then circles detected from the image edge map. Subfigure (a) shows the original slice, with the LV seen as a ring of muscle close to the centre, while (b) shows a manually zoomed section of the slice, for the convenience of the reader. Subfigure (c) shows the corresponding edge map for the zoomed section and (d) shows

detected circles for the edge map, with the circumference and centres of circles shown in yellow and green respectively.

Figure 32: Hough circle detections in mid-region of LV from ^{82}Rb images: (a) original slice (b) manual zoom to ROI (c) edge image (d) detected circles (yellow) with centres marked (green).

Figure 33: Hough circle detections in mid-region of LV from FDG PET images: (a) original slice; (b) manual zoom to ROI; (c) edge image; (d) detected circles (yellow) with centres marked (green) (SIMS; GUTIERREZ, 2016).

The results of the automatic cropping with 63 ^{82}Rb images and 16 frames of FDG PET images were evaluated by inspection and found to be provide adequate results since there was invariably a space of several pixels between the LV and image boundary, while the crop greatly reduced the volume required for processing. Figure 34 shows images resulting from limitation in the SAX plane for ^{82}Rb and FDG images.

4.2.1.2 Determination of LV extent in LAX direction and crop

Figure 35b shows a plot of variation of greatest circle radius in each slice against slice number, an example of the variation used to determine LV limits along the LAX. The following filtering was performed on the circle detections before plotting the variation: (i) determine the mean circle centre for circles comprising the supposed LV cluster; (ii) remove circle detections

Figure 34: Result of cropping ^{82}Rb and FDG PET images in SAX plane.

with a centre more than 3 pixels away from the mean circle centre. Figure 35a shows the corresponding HLA slice for the variation plot.

In Figure 35a the tip of the apex occurs at approximately slice 12, and the end of the base at approximately slice 39. However, in 35b the apex appears to be at slice 14 and the base at slice 35. The maximum radius of 11.5 pixels is found at slice 29, which is confirmed from Figure 35a. Locating the apex and base from HCT detections was found to be challenging in general, whereas the maximum radius was found with much greater certainty. After evaluating the two methods tested for performing the LAX crop, method (i) (identify apex and base through HCT detections) was discarded since the results were unpredictable and inaccurate, whereas method (ii) (identify the slice containing the circle with the largest radius and crop the image a determined number of slices above and below this point) was seen to be much more robust. A value of 27 pixels above and below the slice containing the greatest circle was found by running the algorithm over the entire dataset and increasing the value as necessary.

Figure 36 shows the results of cropping the image in the SAX plane and LAX direction; it

Figure 35: Variation of circle radius with slice number for a single FDG frame (a) HLA slice through FDG frame (b) Variation of greatest circle radius in each slice by slice number.

can be seen that the LV is adequately central in all images, with the best results for FDG, which has lower noise. However, in the HLA and VLA views, it can be seen that the crop has left an unnecessary amount of space above the base and below the apex.

4.2.2 Automated LV segmentation

Figure 37 shows the final position of the level set function (LSF) after being evolved on a single slice of the LV using the DRLSE. The LSF maximum and minimum are 2 (outside the contour) and -2 (inside).

The largest value of DSM, 93.43%, was found with the parameter set corresponding to $\lambda = 0.06$, $\alpha = 0.003$, $\epsilon = 0.7$ and with the threshold set at 0.12, averaged over the 16 frames in the study. Table 4 shows the percentage DSM values from each of the 16 frames which contribute to this best value, which have a standard deviation, $\sigma_D = 0.0215$. The worst result for DSM was 89.76% , obtained with $\lambda = 0.1$, $\alpha = 0.008$, $\epsilon = 1.1$ and with threshold 0.14. These results are consistent with values in the literature for cardiac segmentation from magnetic resonance imaging, with CONSTANTINIDES et al. (2012) obtaining $91\% \pm 3\%$ DREI-JER; HERBST; PREEZ (2013) $93\% \pm 2\%$, and TRAN (2016) $96\% \pm 1\%$ DSM for automated

Figure 36: Result of cropping a ^{82}Rb PET image in SAX and LAX planes.

epicardial segmentation.

Table 4: Results of segmentation produced using optimum set of DRLSE parameters and thresholds, calculated by comparison of method and manual segmentations using percentage DSM, applied to 4 frames from 4 individuals. Frame numbers are shown in parentheses (SIMS; GUTIERREZ, 2016).

Individual 1	Individual 2	Individual 3	Individual 4
90.97%(1)	92.64%(3)	94.97%(1)	94.20%(4)
92.94%(5)	95.83%(11)	94.59%(2)	93.72%(10)
92.01%(6)	94.18%(13)	93.11%(8)	93.74%(14)
92.22%(14)	97.52%(15)	94.39%(12)	87.89%(16)

Figure 38 shows three final LS contours for the optimum and worst sets of parameters for the outer LV border segmentation. The optimum set of parameters is seen to create a segmentation which is slightly more contacted around the outer LV contour.

Figure 37: 3D surface of final LSF, resulting from application of DRLSE to a single SAX slice. The zero LS contour is marked with a red line (partially visible)

$(\lambda, \alpha, \epsilon)$	Apical	Mid	Basal
$\begin{pmatrix} 0.06 \\ 0.003 \\ 0.7 \end{pmatrix}^T$			
$\begin{pmatrix} 0.1 \\ 0.008 \\ 1.1 \end{pmatrix}^T$			

Figure 38: Final level set contours for optimum (upper row) and worst performing (lower row) sets of parameters for the same FDG frame in apical, mid and basal slices.

4.3 Discussion

4.3.1 Automated LV location and crop

Satisfactory results were obtained for the automatic cropping of the LV over the data set tested. Adequate cropping was identified in images from individuals with abnormalities, such as hypertrophic LV, demonstrating a certain robustness. However, it is possible that images presenting hypocapture, which have a lower radioactive count in certain regions, could present challenge for the circle detection, leading to failure of the algorithms. In this case, two solutions

may be investigated: (i) adjust edge detection so that the algorithm finds an edge between a region of hypocapture and the background; (ii) detections produced around only part of the circle perimeter will create a lower number of votes than the full perimeter, therefore the threshold of the circle detection algorithm may be lowered to admit these partial circles. More detailed testing could be performed by creating a set of challenging images, allowing tuning of parameters for these cases.

Values of parameters for automatic cropping were determined empirically by repeated evaluation of the results until adequate results were obtained, which is a laborious and inexact approach. A better approach to evaluating parameters for circle fitting could involve the creation of a gold standard image, with circles manually fitted over SAX slices by an expert in order to quantify the performance of the automatic method. Slices representing difficult cases could also be included, such as those with hypocapture, as mentioned previously.

While cropping in the SAX plane was felt to be accurate enough for the task of reducing image size, the LAX crop left excessive space beyond the apex and base. It was seen in Figure 35 that the slice containing apex and base was not found accurately with circle detections, and instead the largest slice was determined more robustly; however, this has the disadvantage of leaving the excessive space. In general, the performance of the cropping algorithm was found to be lower with ^{82}Rb than FDG due to its increased noise.

The methodology made use of the HCT for interaction with the edge image. The results show that the SAX slices could be detected fairly robustly as approximate circles. Future work could use ellipse detection to improve results, however the extra dimension in the accumulator, with radius replaced by major and minor axes, would increase processing times and might make the cluster analysis more complex and less efficient.

4.3.2 Automated LV segmentation

In the proposed methodology, DSM was used to determine optimum parameters and thresholds over the entire dataset of 395 SAX slices, and these optimum parameters used for quantita-

tive evaluation of the resulting segmentation. This evaluation methodology could be criticised for having introducing a bias into the results, and future tests could be conducted using a set of randomly chosen frames for optimisation of parameters (image set 1) and a different set of randomly chosen frames (image set 2) for evaluating these parameters, as shown in Figure 39.

Figure 39: Revised methodology for segmentation evaluation, in which the 108 method segmentations of image set 1 are compared with corresponding reference segmentations to determine optimum parameters. Then image set 2 is segmented using the optimum parameters, and compared with its corresponding reference segmentations to determine DSM.

The methodology used a single volume-based error measure, DSM, to perform the optimisation; perhaps additional error measures, such as the contour-based Hausdorff distance, could be used to enhance the analysis.

Original versions of the methodology used two LS contours to define the inner and outer borders in a similar manner to DEDIC; ALLILI; LECOMTE (2011). While finding the outer edge border is possible for any SAX slice, the inner border disappears towards the apex, and at the base the septal wall is not present and the muscle has a crescent shape. The proposed methodology, where a threshold is applied after definition of the outer contour, eliminates potential problems arising from the inner LS contour.

Figure 38 shows that there is little visual difference between the segmentations from the optimum and worst case scenarios. The optimum contour can be seen to remove a little more structure from around the LV, such as the RV, and thereby achieves a higher value of DSM. However, the definition of the reference contour depends on expert judgement, since the PET images are quite diffuse at the edges, attributed to the Partial Volume Effect (PVE) (Appendix A.2). Figure 40 shows a zoomed section of an FDG PET image; it can be seen that there are various border pixels which are grey and could be included or excluded from manual segmen-

tation. It may be possible to reduce the PVE in PET images to provide a truer segmentation, using techniques such as image deconvolution; however the consideration of these topics are considered outside the scope of this thesis.

Figure 40: Zoomed region of FDG PET image, showing blurring of LV border.

Although no similar studies were found for direct comparison of segmentation results, the approach taken in KARIM et al. (2016) is to compare state-of-the-art segmentation methods in magnetic resonance images with simpler methods, such as thresholding. In this way, the sophisticated techniques used to perform the segmentation could be justified in terms of their complexity and longer processing times. For the proposed study, the comparison of the image segmentation could be made with the methodology used in GUTIERREZ et al. (2003), where the voxels pertaining to the LV are selected by applying a threshold to the MVF estimated by optical flow.

The relatively small set of images used in the segmentation does not provide confidence for the segmentation method to be applied to a group containing various types of abnormalities. Further, the FDG patient profiles contained only individuals with normal function and NCC, so the algorithms should be tested over a wider range of abnormality. However, the extension of the dataset for larger numbers of images is very time-consuming, since the full dataset must be manually segmented. In future work the segmentation methodology could be evaluated with ^{82}Rb images, which would be expected to produce poorer performance owing to higher noise.

The routines developed use 2D slices to perform 3D segmentation. FABER et al. (1991) suggest that segmenting image volumes using natively 3D techniques can provide improved results, since information about shape, smoothness, and connectivity in the 3D image can be taken into account. Future work could compare the proposed methodology with a direct 3D segmentation.

5 QUANTIFICATION OF LEFT VENTRICULAR MOTION

5.1 Methodology

Following GUTIERREZ (1995), quantification of LV motion was performed using the Horn and Schunck (HS) optical flow (OF) method (HORN; SCHUNCK, 1981). This chapter investigates approaches to improve LV quantification using HS, and evaluated their performance.

5.1.1 Improving optical flow accuracy with spatially varying averaging filters

Texture in PET images is provided by local variations in detected radioactive emission. PET images are diffuse and the myocardium lacks specific markers for sparse feature tracking which may be available in other modalities or techniques. Further, images are low resolution, noisy, and corrupted by the PVE, which make segmentation-based approaches unattractive. A viable approach, however, is to use OF techniques.

The HS method relies on quadratic regularisation of the velocity field in order to find unique solutions of velocity and produce a dense MVF. While this motion model assumes the velocity field to be smooth throughout the image domain, the heart moves relative to a predominantly static and textureless background, meaning that different regions of the image have distinct velocities, with discontinuities in velocities occurring at the surfaces of the cardiac tissue.

The Gauss-Seidel update equations require average velocity to be calculated in every iteration of the HS algorithm, which is implemented by using fixed-weights (HORN; SCHUNCK). EL-FEGHALI; MITICHE (2000) point out that these filters are responsible for inaccuracy in

2D images, particularly at the motion boundaries between objects, and suggest that accuracy can be improved by using spatially varying averaging filters (SVFs).

Further gains in accuracy of the HS scheme can be made by optimising model parameters, shown in Equation 2.5, which can be accomplished by using error measures to determine the difference between method and ground truth (GT) MVFs. Synthetic sequences of cylinders in rotation and translation with their corresponding GT MVFs were used for this purpose; their preparation is described in Section 3.1.

5.1.1.1 Approaches for estimating mean velocity

As shown in Equation 2.3, the HS method requires average velocity to be calculated throughout the image sequence, for every iteration. HORN; SCHUNCK and GUTIERREZ use fixed filter coefficients to calculate the average velocity for pixels and voxels. Since the averaging scheme is applied iteratively in the update equations, mixing of velocity regions across the motion boundary occurs.

To illustrate this point, Figure 41a shows a cylinder moving through a stationary medium with uniform velocity. There are large regions inside and outside of the cylinder volume that have uniform velocity. The motion boundaries correspond to the surfaces of the cylinder, where there is a discontinuity in the value of velocity. Figure 41b shows a slice through the cylinder, and marks three positions for the estimation of average velocity. An averaging filter is applied to current velocity estimates to calculate the average velocity field. The filter has finite size, here represented by a 3×3 grid of pixels, although it might be a cube of $3 \times 3 \times 3$ voxels in a 4D implementation. Outside the cylinder and away from the motion boundaries, the average velocity filter is in a smooth region, where the velocity is expected to be zero. Inside the cylinder volume and away from the motion boundaries, the surfaces of the cylinder, the filter is also in a smooth region. However, when the averaging filter is used over a discontinuous velocity region, it forms an average from both regions, blurring the velocity field.

MITICHE; AGGARWAL (2014); EL-FEGHALI; MITICHE (2000) replace the fixed filter

Figure 41: Cylinder with constant velocity moving in a stationary medium, showing difficulty in velocity estimation at cylinder surfaces: (a) 3D representation of motion through stationary medium; (b) Single slice through cylinder in YX plane

coefficients with spatially varying averaging filters (SVFs) to improve performance at motion boundaries; the SVF attempts to calculate average values using only pixels on the same side of the motion boundary as the central pixel. MITICHE; AGGARWAL present two implementations of SVFs: (i) average intensity method (AIM), which uses spatially varying filters defined by image intensity to identify motion boundaries, and (ii) average velocity method (AVM), which uses SVFs defined by current estimates of velocity to identify motion boundaries. The HS fixed-weight non-adaptive method (NAM), applied to voxel space and using fixed filter coefficients, can be used to compare performance of AIM and AVM.

The concept of 4-neighbourhood and 8-neighbourhood connectivity in 2D images can be extended to 3D voxel space, where 6-neighbourhood voxel connectivity is with face neighbours, 18-neighbourhood with face and edge neighbours 26-neighbourhood with face, edge and corner voxels (GONZALEZ; WOODS, 2008; UDUPA; HERMAN, 2000).

Equation 5.1 describes an 18-neighbourhood fixed filter coefficient scheme, where face

voxels are given a weight $\frac{1}{9}$ and edge voxels $\frac{1}{36}$.

$$\begin{aligned}\bar{u}_{i,j,k} = & \frac{1}{9}(u_{i+1,j,k} + u_{i-1,j,k} + u_{i,j+1,k} + u_{i,j-1,k} + u_{i,j,k+1} + u_{i,j,k-1}) \\ & + \frac{1}{36}(u_{i+1,j+1,k} + u_{i-1,j+1,k} + u_{i+1,j-1,k} + u_{i-1,j-1,k} + u_{i+1,j,k+1} + u_{i+1,j,k-1} \\ & + u_{i-1,j,k+1} + u_{i-1,j,k-1} + u_{i,j+1,k+1} + u_{i,j-1,k+1} + u_{i,j+1,k-1} + u_{i,j-1,k-1})\end{aligned}\quad (5.1)$$

Both AIM and AVM define a smoothing filter, ϕ_I , which estimates each component of average velocity between the central pixel, i , and each member of its 26 voxel neighbourhood, j , as shown in Equation 5.2, where N_i is the neighbourhood of i . γ_j^i is the coefficient of the SVF, calculated according to the descriptions below, which replaces the fixed filtering coefficient, and μ_j is one of the velocity components u_j, v_j, w_j .

$$\phi_I = \sum_{j \in N_i} \gamma_j^i \mu_j \quad (5.2)$$

AIM weighs filter coefficients according to differences in intensity. The model assumes that different regions have distinct velocity, which can be distinguished by differences in voxel intensity. Coefficients of the filter, γ_j^i , are calculated using Equation 5.3, where E_i is the intensity of the central voxel, E_j the intensity of the j th voxel, and k iterates over the voxel neighbourhood of i . The coefficient γ_j^i is calculated for voxel j , a neighbour of the central voxel, i , and the denominator normalises the coefficients.

$$\gamma_j = \frac{\frac{1}{1+|E_j-E_i|}}{\sum_{k \in N_i} \frac{1}{1+|E_k-E_i|}} \quad (5.3)$$

AVM forms filter coefficients, γ_j^i , by assuming that motion boundaries are represented by differences in the evolving velocity, i.e. it assumes that distinct objects with relative motion, can be distinguished by different values of evolving velocity. These coefficients are calculated according to Equation 5.4, which includes an exponent, $\beta > 1$, accounting for small differences in velocity values, and where μ_i, μ_j represent the central and neighbouring voxel velocity for

one of the velocity components u , v , or w . Further details can be found in SIMS; FURUIE; GUTIERREZ (2014)

$$\gamma_j^i = \frac{\left(\frac{1}{1+|\mu_j-\mu_i|}\right)^\beta}{\sum_{k \in N_i} \left(\frac{1}{1+|\mu_k-\mu_i|}\right)^\beta} \quad (5.4)$$

The three algorithms were implemented using time domain convolution, but there is a difference in the intensity of calculation required for each, depending on the convolution kernel. NAM uses the same kernel for each voxel and iteration, whereas AIM uses a different kernel for each voxel, defined from the image, which is invariant, meaning that these kernels are constant over successive iterations. Finally AVM has a kernel which requires calculation for each voxel and which changes in each iteration. Subsequently, the cost of processing is highest with AVM, then AIM, with NAM being the lowest. However, in the implementation defined herein, AIM was implemented in the same way as AVM, where it recalculated the kernel for each iteration.

5.1.1.2 Schemes for estimating partial derivatives

The HS method requires estimates of partial derivatives from the image sequence. The following approaches provide alternatives for this estimation:

1. Centred differences, can be implemented by convolution with a kernel $[-0.5, 0, 0.5]$ in x , y , z , t . This was denominated as simple kernel (SK).
2. Simoncelli matched balanced (MB) kernel derivatives uses convolution kernels, represented in Figure 42 for the calculation of the partial derivative in x , E_x . After initially blurring the image with kernel $b = [0.25, 0.5, 0.25]$, it is averaged using kernel $p5 = [0.036, 0.249, 0.431, 0.249, 0.036]$ in 3 dimensions to reduce noise, then differentiated in the remaining dimension using kernel $d5 = [-0.108, -0.283, 0.0, 0.283, 0.108]$ (BARRON; THACKER, 2005).

Figure 42: Calculation of partial derivative in x , E_x , with Simoncelli's matched balanced filters.

5.1.1.3 Experiments performed

First, synthetic MVFs were created from image sequences using different schemes and model parameters, and then they were evaluated to find the best combinations by comparing estimated MVFs with ground truth fields. Three schemes for calculating average velocity were the two SVFs, AIM and AVM, and the fixed weight filters, NAM. The values $\beta = 5, 6, 7$ were used in testing, creating three variants of the AVM methods referred to as AVM5, AVM6, AVM7. Two schemes for estimating partial derivatives, described in Subsection 5.1.1.2, were tested. Three values of number of iterations (50, 100, 150) and four values of α^2 were used. A total of 120 method MVFs were generated, using combinations of the above, per image sequence. Results were produced for 5 image sequences described in Section 3.1.

An overview of the processing scheme is shown in Figure 43. Inputs are the synthetic images, the corresponding GT velocity field, and model parameters. Image derivatives are first calculated and then velocity is estimated iteratively. In the last step final velocity estimates are compared with the ground truth velocity using error measures to establish their accuracy.

Angular error (AE) and endpoint error (EE) measures were extended from BAKER et al. (2011) for use in 4D images as shown in Equations 5.5a and 5.5b, where u_{GT}, v_{GT}, w_{GT} are GT velocities in x, y, z directions. For the calculation of AE, the value of 1.0 as the z -component was replaced with the velocity, w , and a lower-limit threshold of 0.0001 placed to avoid zero values in the denominator.

Figure 43: Scheme for quantification of motion field and error calculation with synthetic cylinder images. Generated images are passed to the optical flow routine, partial derivatives of image intensity are calculated from the generated cylinder images, and a system of linear equations is solved. Finally, the quantified field is compared with a ground truth field to quantify method error.

$$AE = \cos^{-1} \left(\frac{u \cdot u_{GT} + v \cdot v_{GT} + w \cdot w_{GT}}{\sqrt{u_{GT}^2 + v_{GT}^2 + w_{GT}^2} \sqrt{u^2 + v^2 + w^2}} \right) \quad (5.5a)$$

$$EE = \sqrt{(u - u_{GT})^2 + (v - v_{GT})^2 + (w - w_{GT})^2} \quad (5.5b)$$

$$RMSE = \sqrt{\frac{\sum_{i,j,k=1}^{I,J,K} (u - u_{GT})^2 + (v - v_{GT})^2 + (w - w_{GT})^2}{IJK}} \quad (5.5c)$$

$$NRMSE = 100\% \cdot \sqrt{\frac{\sum_{i,j,k=1}^{I,J,K} (u - u_{GT})^2 + (v - v_{GT})^2 + (w - w_{GT})^2}{\sum_{i,j,k=1}^{I,J,K} (u_{GT})^2 + (v_{GT})^2 + (w_{GT})^2}} \quad (5.5d)$$

Values were calculated per voxel using average AE (AAE) and average EE (AEE). Global error measures of root mean square error (RMSE) and Normalised RMSE (NRMSE) were also used, as shown in Equations 5.5c and 5.5d. NRMSE is expressed as a percentage, whereas RMSE is a value per voxel and I, J, K are image dimensions.

5.1.2 Approaches for solving the HS linear system

HORN; SCHUNCK (1981) suggest Gauss-Seidel (GS) update equations to solve OF equations. This subsection describes a methodology for comparing the accuracy of the velocity

field produced by GS equations with that produced by a sparse matrix solution employing Generalized Minimum Residuals (GMRES) (THE MATHWORKS INC., 2014; GOLUB; LOAN, 1996).

5.1.2.1 Implementing the sparse matrix solution

Equation 2.4 shows the linear equations for the HS method. The following rearrangements were performed to assist understanding and implementation.

Each of the 9 submatrices in the left hand side of this equation are of dimension n^2 , where n is the number of voxels in the image. The submatrices are sparse, with only the leading diagonal being non-zero.

The equation is of the form $A\vec{x} = \vec{b} + C\vec{x}$; the right hand side consists of a vector, $\vec{b}$ and a term $C\vec{x}$, where $[C]$ is a matrix consisting of coefficients which form the average velocities.

Let $[D]$ be a coefficient submatrix for calculating the average values. $[D]$ is identical for each of u , v , w in a fixed filter averaging scheme and allows Equation 2.4 to be written as Equation 5.6.

$$\begin{bmatrix} E_x^2 + \alpha^2(1 + D) & E_x E_y & E_x E_z \\ E_x E_y & E_y^2 + \alpha^2(1 + D) & E_y E_z \\ E_x E_z & E_y E_z & E_z^2 + \alpha^2(1 + D) \end{bmatrix} \begin{bmatrix} u \\ v \\ w \end{bmatrix} = - \begin{bmatrix} E_x E_t \\ E_y E_t \\ E_z E_t \end{bmatrix} \quad (5.6)$$

The rows of $[D]$ represent the central voxels, i , and columns represent the relationship of i with every possible neighbouring voxel. In the fixed filter scheme, NAM, there are a total of 18 neighbouring voxels, j , and all other elements have zero values. To construct the matrix, face and edge neighbours for each central voxel are given the corresponding fixed filter coefficients from Equation 5.1.

5.1.2.2 Experiments performed

4D image sequences of cylinders in translation and rotation (1 voxel per frame translation and 1° , 2° , 5° per frame rotation), detailed in Table 5, were used to measure the accuracy in optical flow for GS update equations and sparse matrix solution. Both methods were supplied with the same derivatives, calculated using centred differences (SK), as described in subsection 5.1.1.1. Slice 3 of frame 5 of the cylinder was used in the analysis to calculate values of NRMSE.

Experiments were performed with all image sequences taking values of $\alpha^2 = (0.1, 0.15, 0.2)$ for the GS and GMRES solutions, and GS was run for different values of the iteration index (20, 50, 100, 200). The GMRES algorithm was given the following settings: number of restarts = 10, tolerance = 10^{-14} and maximum iterations = 500.

Table 5: Image sequences used to test spatially varying averaging filters (SIMS; FURUIE; GUTIERREZ, 2014)

Sequence 1	rotation of 1° per frame
Sequence 2	rotation of 2° per frame
Sequence 3	rotation of 5° per frame
Sequence 4	translation of $(u,v,w) = (1,0,0)$ pixels per frame

5.2 Results

5.2.1 Improving optical flow accuracy with spatially varying averaging filters

Figure 44 shows the YX plane of the rotating cylinder, sequence 1 (1° rotation per frame), for slice 3, with the optical flow field calculated using the non-adaptive method (NAM), and with SK derivatives, $\alpha^2 = 0.5$, and 50 iterations. There are two zoomed sections to allow clearer visualisation of the quantified MVF, at the centre and at the cylinder surface, where the motion discontinuity occurs.

A qualitative analysis of the MVF finds the detected velocity vectors in the correct sense (clockwise, as seen from above), with velocity close to zero at the centre, increasing towards

Figure 44: Quantified motion field for slice 3 of rotating cylinder, in the YX plane, resulting from using NAM, SK, $\alpha^2 = 0.5$, and 50 iterations.

the border. The velocity appears to reach its maximum value about four pixels from the border, decreasing towards the border. The smoothness of the MVF within the cylinder volume seems to be slightly affected by the local variation in spatial gradients created by the checked textured elements. At the border, inaccuracies in direction of rotation can be discerned, with a non-zero velocity field encountered in the region outside the boundary of the cylinder.

Statistics presented in this section were calculated from raw values of OF without smoothing the output velocity field. In order to simplify the analysis, the version of AVM (average velocity method) that produced lowest NRMSE was selected as the best representative of AVM5, AVM6 and AVM7, being subsequently compared with NAM (non-adaptive method, using fixed weight filters) and AIM (average intensity method).

Table 6 shows the best error results obtained for Sequence 1 from application of the four error measures applied to the global image and to the region within the volume of the cylinder.

For SK derivatives, AVM7 provides best global values for NRMSE and RMSE with $\alpha^2 = 0.2$ and with 50 iterations, AEE with $\alpha^2 = 0.5$ and 50 iterations, and AEE with $\alpha^2 = 1.5$ and 150 iterations.

For MB derivatives, best global values of NRMSE, RMSE, AEE are found using NAM, with $\alpha^2 = 0.2$ and 50 iterations. AIM provides the lowest AAE with $\alpha^2 = 0.2$ and 150 iterations.

Table 6: Lowest obtained error values in study for improving optical flow accuracy, for frame 3 of sequence 1 (rotating cylinder at 1° per frame) (SIMS; FURUIE; GUTIERREZ, 2014).

Measure	Method	Global		Within volume	
		SK	MB	SK	MB
NRMSE (%)	NAM	31.1	32.8	17.4	12.3
	AIM	34.0	36.3	16.5	12.1
	AVM7	28.5	33.0	17.0	12.7
RMSE (voxels)	NAM	0.072	0.075	0.040	0.028
	AIM	0.078	0.084	0.038	0.028
	AVM7	0.065	0.076	0.039	0.029
AEE (voxels)	NAM	0.044	0.041	0.021	0.009
	AIM	0.051	0.049	0.021	0.010
	AVM7	0.043	0.043	0.020	0.010
AAE ($^\circ$)	NAM	0.0069	0.0058	0.0069	0.0058
	AIM	0.0060	0.0052	0.0060	0.0052
	AVM7	0.0062	0.0056	0.0062	0.0056

Overall SK produces lower errors than MB.

Figure 45, reproduced from (SIMS; FURUIE; GUTIERREZ, 2014), compares NRMSE for the two derivative schemes. For MB, NAM produces the best results with 50 iterations and $\alpha^2 = 0.2$. AIM produces the highest NRMSE. As α^2 increases, the difference between the algorithms diminishes. For SK, the best results are produced by AVM7 with 50 iterations and $\alpha^2 = 0.2$.

Figure 45: Global percentage NRMSE against α^2 for Sequence 1 with 50 iterations and averaging methods NAM, AIM and AVM7 for (a) MB (b) SK derivatives schemes (SIMS; FURUIE; GUTIERREZ, 2014)

The optimum combination of schemes for each of the 5 image sequences is shown in Table

7, which compares the averaging methods and derivative schemes. Overall, the best derivative scheme is SK, the best value of α^2 is 0.5, with 50 iterations.

Table 7: Optimum combinations of averaging and derivative schemes for all sequences.

Image Sequence	Method	NRMSE α^2 , iter.	RMSE α^2 , iter.	AEE α^2 , iter.	Derivative scheme
1	AVM7	0.2, 50	0.2, 50	0.5, 50	SK
2	AVM7	0.5, 50	0.5, 50	0.5, 50	SK
3	AVM7	0.5, 50	0.5, 50	0.5, 50	SK
4	AVM7	0.5, 50	0.5, 50	0.5, 50	SK
5	AVM5	0.5, 100	0.5, 100	0.5, 100	SK

Programs were run on a micro with 32GB RAM, Intel core I7 3970X, 3.5GHz x 12, running Ubuntu 12.04 64 bit. 50 iterations of the algorithm took 28.25s for NAM, 78.96s for AIM and 167.47s for AVM.

5.2.2 Solving the HS linear system

NRMSE values for the translation sequence are given in Table 8a and for the rotation sequences in Table 8b-d.

The software was run on a Dell I7-XPS8300, with 2600 CPU 3.40GHz and 8GB RAM running Windows7 64-bit. The sparse matrix method with GMRES, averaged over 20 runs, took 20.05 seconds to solve the system, compared with 0.467 seconds for GS update equations. The GMRES algorithm took 5.50 seconds to solve the system with almost all the remaining time taken to construct the sparse matrices.

Table 8: Comparison of methods to solve OF linear system: Global NRMSE (%) for rotational sequences as a function of α^2

(a) translational sequence $(u, v, w) = (1, 0, 0)$ voxels/frame					
α^2	GMRES	Gauss Seidel			
		20	50	100	200
0.1	29.17	28.06	29.09	29.17	29.17
0.15	29.06	28.06	28.98	29.06	29.06
0.2	29.35	28.59	29.28	29.35	29.35

(b) Rotation 1° /frame					
α^2	GMRES	Gauss Seidel			
		20	50	100	200
0.1	28.34	27.73	28.29	28.34	28.34
0.15	27.62	27.06	27.57	27.61	27.62
0.2	27.32	26.94	27.27	27.32	27.32

(c) Rotation 2° /frame					
α^2	GMRES	Gauss Seidel			
		20	50	100	200
0.1	27.61	27.11	27.57	27.61	27.61
0.15	27.38	26.99	27.34	27.38	27.38
0.2	27.79	27.63	27.75	27.78	27.79

(d) Rotation 5° /frame					
α^2	GMRES	Gauss Seidel			
		20	50	100	200
0.1	47.12	47.20	47.11	47.12	47.12
0.15	48.21	48.39	48.21	48.21	48.21
0.2	49.64	49.98	49.64	49.64	49.64

5.3 Discussion

5.3.1 Improving optical flow accuracy with spatially varying averaging filters

Table 7 shows that NRMSE, RMSE and AEE were minimised with 50 iterations for sequence 1 to 4 and 100 iterations for sequence 5, suggesting that a full convergence can produce larger errors than a partial convergence. HORN; SCHUNCK state that in regions where the brightness gradient is zero, velocity estimates are formed from averages of neighbouring estimates and that these values require various iterations to propagate into the region; the process is

similar to the propagation of heat for a uniform plate, where the rate of change of temperature with time is proportional to the Laplacian. The non-textured region outside the cylinder has zero derivatives and the velocity field is propagated from the textured regions of the cylinder. Since the velocity in the non-textured region is zero in the ground-truth, the gradual spreading of velocity from the border causes increasing error as the number of iterations increases.

The choice of derivative scheme is seen to affect measured error, and global measures show that SVFs offer little or no improvement over NAM when using MB derivatives while when using SK they offer a significant improvement in accuracy. This is perhaps due to MB's greater smoothing of the optical flow field and because of its larger neighbourhood of voxels (5x5x5 compared with 3x3x3), both of which reduce performance of the algorithm in the region close to the motion boundary.

The optimum combination of schemes and parameters was achieved using AVM7, SK derivatives, 50 and 100 iterations and α^2 between 0.2 and 0.5.

Figure 45 shows that NRMSE is strongly dependent on the value of α^2 for the rotation sequence. For the MB derivative scheme, the lowest values of NRMSE were obtained when α^2 is 0.2, the lowest value tested. With the SK derivatives, there was a larger performance difference between the averaging methods, but the best performance was again obtained with $\alpha^2 = 0.2$. This is a reasonable result, since a lower value of α^2 reduces the effects of regularisation; at the border region, the flow is discontinuous, so an OF which is less smooth can be a closer approximation to the ground truth.

The reason for longer processing times for AIM and AVM is due to the convolution needed to calculate average velocity. The kernel is recalculated for every pixel position in every iteration as the evolving velocity field changes, whereas NAM uses the same kernel applied throughout the evolving velocity field. Future work could implement the convolution in C++ to reduce processing time.

Although results suggested that AVM7 could provide improved accuracy of results, its longer processing time was felt to make it prohibitive for practical use in the rest of the project.

For this reason, the proposed study used the non adaptive method for motion estimation for quantifying the LV cardiac MVE. Time savings for NAM are, in fact, better than shown in the experiments, since optimised MATLAB routines can be used, producing a decrease in processing time from 28.25 seconds, when implemented as a convolution with a triple loop, to 0.5 seconds, using optimised routines.

5.3.2 Solving the HS linear system

Converged values using the two algorithms give the same results for all test images, providing confidence that the solution of the linear equations is accurate in both cases.

The synthetic image of the cylinders is of size $74 \times 74 \times 5$, totalling 27380 voxels, meaning that the solution is for 82140 equations. A dense matrix to solve the system would require approximately 6.747×10^9 elements. Each line of the matrix has 3 diagonal submatrix elements and 18 for the averaging scheme, giving a total of 21 non-zero elements per line. This gives a total of 1.725×10^6 non-zero elements, approximately 4000 times fewer sparse elements than dense.

The two methods converge to the same value after 100 iterations of the GS algorithm in every case, to two decimal places. However the sparse matrix takes almost 15 seconds to be constructed, independent of the method used to solve it, which is a major drawback of the scheme. For this reason, the GS update equations were chosen for use in the rest of the proposed study.

6 GLOBAL KINETIC ENERGY INDEX AS AN INDICATOR OF CARDIAC FUNCTION

6.1 Methodology

This chapter investigates KE_f as an indicator of motility in gated PET. The 16 frame XCAT image sequence and the 16 frame XCAT ground truth MVF were used for validation, while 63 ^{82}Rb rest perfusion PET images were used for testing, whose acquisition and selection is described in Chapter 3. In addition, values of LVEF, provided by Cedars-Sinai software were also used.

6.1.1 Image processing scheme to calculate Kinetic Energy Index

An automatic software pipeline was written to calculate KE_f , as shown in Figure 46.

Figure 46: Scheme showing processing stages for calculation of KE_f from Rb PET images (SIMS et al., 2015)

In the preprocessing phase, DICOM images were read from the PET image database and processed according to the following stages:

1. **Order DICOM files:** the DICOM files were renamed in a sequential order from the first slice of the first volume to the final slice of the final volume.
2. **Convert images to 4D matrix:** the slices were read into MATLAB and converted to 4D matrix form.
3. **Automatic crop** was performed, with the routines detailed in Section 4.1.2.
4. **Intensity adjustment:** the total count in each cropped volume was adjusted to be constant as described in Subsection 6.1.2.
5. **Low pass filter:** The images were averaged over the 27 neighbourhood of each voxel.

The optical flow routine was implemented using the 4D HS algorithm, using a centred differences derivative scheme, Gauss Seidel update equations and a fixed weight averaging scheme (non adaptive method), as detailed in Chapter 5.

The postprocessing routine was composed of the following routines:

1. **Smooth u, v, w :** the calculated velocity values were smoothed with a median filter, as suggested in SUN; ROTH; BLACK (2010).
2. **Calculate Kinetic Energy (KE) by frame:** Equation 2.7a was applied to all voxels in the cropped image to calculate KE per voxel. KE by frame was calculated by summing these contributions for each frame.
3. **Calculate kinetic energy index:** Equation 2.7b was applied to values of KE by frame for the entire image. The first and last frames were discarded from analysis due to their larger error when estimating temporal derivatives.

6.1.2 Improvement of radioactive count constancy

The brightness of pixels in the PET image are a result of detected radioactive count events in a volume element of the image. After initial tests using the PET data, it became clear that the

total radioactive count of the cropped volume sequence varied between frames. The behaviour of the data is surprising since radioactive decay is a random process and the detected count were expected to be close to constant over the image frames. This is considered to be a limitation in the data since the HS method requires constant brightness of the voxels as they move between frames (Equation 2.1a), and any variation produces errors.

Correction for this variation was attempted by forming a vector B_{total} , whose elements represent the total count in each frame, as described by Equation 6.1, where N is the number of frames in the sequence, X is the total number of voxels in the frame, E is the intensity of the v^{th} voxel. Let f be the frame index, so that the f^{th} volume of B_{total} is B_{total}^f .

$$B_{total} = \left[\sum_{v=1}^X E_v^1, \sum_{v=1}^X E_v^2, \dots, \sum_{v=1}^X E_v^N \right] \quad (6.1)$$

An equalisation module was added to the routine, which performs the following stages: (i) form B_{total} for each volume (frame); (ii) identify the frame number which has maximum B_{total} ; (iii) calculate new intensity using Equation 6.2.

$$E_{new(i,j,k)}^f = E_{(i,j,k)}^f \frac{\max(B_{total})}{B_{total}^f} \quad (6.2)$$

6.1.3 Experiments

6.1.3.1 Validation of Kinetic Energy Index calculation using XCAT images and motion field

The experiments described in this section seek to validate the calculation of KE^f in PET images by comparing values generated using the 16 frame XCAT images and MVF. Generation of the XCAT MVF from position vectors was described in Chapter 3, and the XCAT MVF can also be generated by applying optical flow techniques to the XCAT image sequence.

Processing of the XCAT phantom image was performed according to the following steps:

(i) The XCAT image data was processed using the stages shown in Figure 46, with $\alpha^2 = 1$ and

200 iterations. Since a small variation in brightness was noticed, brightness equalisation was also performed on the image data prior to calculating OF. (ii) XCAT MVF data was processed using known position vectors, which required only the postprocessing phase shown in Figure 46. GT velocities calculated using centred differences were processed and used for comparison. Graphs showing KE per frame (KE curves) were generated for (i) and (ii), from which values of KE_f were obtained.

6.1.3.2 Classification of cardiac function based on global Kinetic Energy Index

The 63 individual Rb PET rest images were used for the following investigation. The value of α^2 in the HS algorithm was set to 10 for the PET images, as determined by experiment. Images were automatically processed according to the scheme, producing KE curves throughout the cycle, and figures showing the variation of radiation count across the cycles, with values of KE_f . KE curves were generated using the equalisation module, and results for KE_f were analysed statistically to study their relationship with LVEF.

In order to investigate the relationship between LVEF and KE_f in rest, linear regression was performed on the pairs of values (KE_f , EF) formed for each individual. In order to evaluate the ability of KE_f as a classifier of cardiac function, sensitivity and specificity tests were performed. Sensitivity was defined as the fraction of individuals with normal function who were correctly classified by KE_f and specificity as the fraction of individuals with low/altered function who were correctly classified by KE_f . A receiver operating characteristic (ROC) curve (FAWCETT, 2006) was generated by varying a KE_f threshold, T , from 0.01 to 1.0 in intervals of 0.01. For each threshold, the number of true positives (TP), false negatives (FN), false positives (FP), and true negatives (TN) were calculated, and from these values true positive rate (TPR), false positive rate (FPR) and Accuracy (A) calculated. Accuracy is the total number of true classifications as a fraction of the total number of patients. The area under the ROC curve (AUC), a measure of overall performance of the classifier, KE_f , was estimated using the trapezoidal rule.

6.2 Results

6.2.1 Validation of global kinetic energy index using XCAT phantom images and motion field

The following results compare the KE curves and values of KE_f generated using the XCAT image sequence and MVF.

Figure 47 shows resulting KE curves from the XCAT phantom; Figure 47a shows the KE curve obtained using OF with a centred differences derivative scheme and non adaptive averaging, while 47b shows the KE curve from the MVF obtained from position vectors, with velocities calculated using centred differences. Qualitatively, the centred differences curve is similar to the curve calculated with OF. Applying Equation 2.7b to the KE curve from OF yields 0.8195, and for the position vectors yields $KE_f = 0.985$.

Figure 47: KE curves for XCAT phantom data: (a) KE curve calculated from the 16 frame XCAT phantom image sequence by optical flow and centred differences; (b) KE curve calculated from the 16 frame XCAT MVF, from position vectors, using centred differences.

6.2.2 Classification of cardiac function based on global Kinetic Energy Index

Figure 48 shows results for an individual with normal cardiac function and resting EF of 74, referred to as individual N, and a patient with low or altered cardiac function, resting EF of 33, referred to as individual L.

For individual N a sharp decrease in count can be observed in frame 8, approximately 15% of the maximum value (Subfigure a). The decrease corresponds to the position of the third peak of the KE curve (Subfigure c), which is seen to disappear after count equalisation (Subfigure e). Similar results are seen for Individual L, where the decrease in total image count is approximately 22% across frames 7 and 8 (Subfigure b). This sharp decrease in count is seen to correspond to the large peak in KE at the end of the cardiac cycle (frame 7) before count equalisation (Subfigure d). The magnitude of this global maximum in KE is much greater than the other peaks. After count equalisation, Subfigure f, the value of KE at frame 7 has been greatly reduced.

For individual N, LVEF at rest was 74%, KE_f before count equalisation was calculated as 87.51%, which reduced to 82.31% after equalisation. Individual L had Rest LVEF of 33%, and the KE_f reduced from 85.69% to 50.15% with count equalisation.

A statistical analysis of the results was subsequently performed. Mean and standard deviation values are shown in Table 9, which also compares results found in this study to those in GUTIERREZ et al. (2003). Figure 49 shows a scatter graph of LVEF against KE_f for the 63 individuals.

Evaluation of KE_f as a classifier of cardiac function was performed by comparison with values obtained from LVEF. ARANGO (2009) describes the use of a confusion matrix for comparing a test to a gold standard, which is shown for this case in Table 10. $LVEF \geq 50$ is considered to be a normal cardiac function and $LVEF < 50$ low or abnormal function. Placing a series thresholds, T , at different values of KE_f at rest allows the determination of true positive (TP), false positive (FP), true negative (TN) and false negative (FN). TP, FP, TN and FN are

Figure 48: Example detected count and KE curves for individuals with normal (N) and low (L) cardiac function. Row 1 shows detected count curves for (a) individual N and (b) L, row 2 shows the KE curves before equalisation for (c) individual N and (d) L, row 3 shows KE curves after count equalisation for (e) individual N and (f) L. (Images for individual L reproduced from SIMS et al. (2015))

Table 9: Comparison of elements of methodology and results from proposed KEf study with that conducted in (GUTIERREZ et al., 2003), showing mean and standard deviation obtained along with the number of individuals.

	Gutierrez (2003)	Present study
Modality:	gated SPECT	gated PET
Equipment	Philips Forte	Philips Gemini
Input images:	16 frames	8 frames
Optical flow:	Multiscale Horn and Schunck	Horn and Schunck
Radiopharmaceutical:	^{99m}Tc -MIBI	^{82}Rb
Results		
Rest:		
normal	0.8582±0.0365 (n=30)	0.5731±0.0899 (n=30)
low	0.4230±0.1169 (n=28)	0.3812±0.1146 (n=33)

defined by the Venn diagrams shown in Figure 50.

Table 10: Confusion matrix, defining true and false positives and negatives for the kinetic energy index study.

		Gold Standard	
		LVEF $\geq$ 50 (+)	LVEF<50(-)
(+)KEf $\geq$ T		TP	FP
(-)KEf<threshold		FN	TN
		$TPR = \frac{TP}{TP+FN}$	$FPR = \frac{FP}{FP+TN}$

A receiver operating characteristics (ROC) curve (FAWCETT, 2006) was created for the 63 individuals in the study, which is shown in Figure 51.

Accuracy, true positive rate (TPR) and false positive rate (FPR) are given by Equation 6.3.

$$TPR = \frac{TP}{TP + FN} \quad (6.3a)$$

$$FPR = \frac{FP}{FP + TN} \quad (6.3b)$$

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \quad (6.3c)$$

To test that the ROC curve had been created correctly, Figure 49 was separated into the two groups of cardiac function and a threshold set, so that the scatter points in each quarter were the TP, FN, TN and FP values. The number of points was counted in each group. Five dotted

Figure 49: Plot of LVEF against KEf for number of 63 individuals, with lines showing threshold placement A,B,C,D,E for statistical analysis (SIMS et al., 2015)

Figure 50: Venn diagrams defining TP, FN, FP and TN counts. U is the set of all individuals in the study, A contains individuals who pass the test $LVEF \geq 50$ and B $KEf \geq T$, where T is the threshold: (a) false negatives (FN) $A \cap B^c = A \text{ AND NOT}(B)$; (b) true positives (TP) $A \cap B = A \text{ AND } B$; (c) false positives (FP) $B \cap A^c = \text{NOT}(A) \text{ AND } B$; (d) true negatives (TN) $(A \cup B)^c = \text{NOT}(A) \text{ AND NOT}(B)$.

vertical lines have been drawn on Figure 49, labelled A, B, C, D, E which are the successive applications of the threshold. TPR and FPR were calculated for each threshold A-E and the results checked on the ROC curve produced, as shown by the arrows labelled A-E in Figure 51, which point to the five data values. Table 11 summarises these calculations. The purple line in Figure 51 shows the expected performance of the classifier (FAWCETT).

The variation of accuracy with the applied threshold is shown in Figure 52a. Accuracy has a peak value of 0.8095 at 44, 46, 47 and 49%. The point (0,1) of the ROC curve represents maximum sensitivity and specificity, so the variation of the distance of coordinates on the ROC

Figure 51: ROC curve for sensitivity and specificity testing for classifying normal cardiac function based on KEf from 63 Rb images (SIMS et al., 2015).

Table 11: Threshold testing of ROC curve calculation in kinetic energy index study (SIMS et al., 2015)

Threshold	TP	FN	FP	TN	TPR	FPR	A
A(0.43)	28	2	23	10	0.933	0.333	0.81
B(0.46)	27	3	9	24	0.9	0.273	0.81
C(0.50)	24	6	7	26	0.8	0.212	0.79
D(0.54)	20	10	3	30	0.667	0.091	0.79
E(0.58)	15	15	0	33	0.5	0.0	0.76

curve to (0,1) was plotted as a function of threshold, as shown in Figure 52b. The largest distance to point (0,1) was 0.2698 at a threshold of 49%.

BRADLEY (1997) and HANLEY; MCNEIL (1982), according to FAWCETT (2006), discuss the area under the ROC curve (AUC) as a method for comparing classifier performance. AUC is equal to the probability that the classifier will rank a positive instance higher than a negative instance, both randomly chosen. AUC ranges from 0.0 to 1.0, with a classifier performance of less than 0.5 meaning that the classifier is worse than a guess (FAWCETT, 2006). Area under the ROC curve (AUC) was calculated as 0.906 using the trapezoidal rule.

Figure 52: Results of ROC analysis for KE_f with $n=63$: (a) accuracy curve against threshold (SIMS et al., 2015); (b) distance from point (0,1) on ROC curve against threshold.

6.3 Discussion

6.3.1 Validation of global kinetic energy index from XCAT phantom images and motion field

Figure 6 shows the expected form of the KE curve from previous studies by GUTIERREZ et al. (2003) in SPECT from a 16 frame image sequence, which has two peaks corresponding to systole and diastole, with the systolic peak higher than the diastolic. The KE curve generated from XCAT phantom images by optical flow is similar to this in form, but the systolic peak is smaller than the diastolic peak, occurring at frame 2 and with a long decay to the local minimum at around frame 8 or 9. The diastolic peak is the global maximum of KE at frame 11. A value of KE_f of nearly 82% was found for the velocity field calculated from XCAT phantom images, which corresponds closely with the mean for normal patients achieved in GUTIERREZ et al. of 0.8582 ± 0.0365 .

The KE curve generated from XCAT position vectors has almost exactly the same form as that generated from images using OF, and yet the values obtained for KE_f is much higher, 0.985, due to the extremely low minimum KE value.

The procedure for calculating KE curves and KE_f is considered to be validated by the above results.

6.3.2 Classification of cardiac function based on Kinetic Energy Index

The form of the KE curve obtained from ^{82}Rb PET images without count equalisation, as seen in Figure 48, was found to be very different from that shown in the XCAT validation, producing three similar sized peaks in the case of Individual N and a very large final peak in the case of Individual L. There was a drop in count in the final frame for Individual N, and over the final two frames for Individual L, which corresponds to the larger than expected values of KE at the end of the cycle. Since the motion detection method requires constant image intensity, the drop in intensity causes motion artefacts, which in turn results in this KE peak. The KE curves after equalisation have a similar form to those in GUTIERREZ et al. and those from the validation with XCAT, although the sequence is 8 frames rather than 16, and the adjusted image sequence produces values of KE_f which are better correlated with LVEF values.

Initial development of the motion detection algorithm exploited periodicity of the LV cycle, but results in the first and last frames were often found to be inconsistent with those in the middle frames, suggesting that the exploitation of periodicity caused the errors. Therefore the derivatives were calculated in a non-periodic and the first and last frame discarded. Later, the changes in total radioactive count over the cardiac cycle were discovered, and equalisation was found to resolve this problem, creating a more consistent velocity estimation, but the non-periodic algorithm was retained. Future work could compare optical flow computed from periodic and non-periodic derivatives with a view to retaining the first and last frames of the cycle after equalisation of radioactive count.

Table 9 shows that the study with SPECT images achieved a much smaller standard deviation for normal individuals and a wider spacing between the mean of the two groups than in the PET study; some possible reasons for these differences are explored here. The table compares the PET and SPECT studies in terms of materials and methodology. There were differences in instrumentation, temporal resolution, radiopharmaceutical, and motion detection algorithm. The SPECT study used gated images with 16 frames per cardiac cycle, whereas the PET study used 8 frames per cardiac cycle, which is thought to be a major factor in the difference between

results; Subsection 3.4.6 explores the reasons why the ^{82}Rb PET images have low temporal resolution. The amount of image noise is also known to be an important factor in degradation of motion detection results; although the SPECT images were unavailable for analysis, meaning that image noise could not be compared directly, the ^{82}Rb images were seen to be very noisy when compared to FDG PET images, as mentioned in Subsection 3.4.6. Future studies could investigate KEf using ^{82}Rb images acquired with higher statistic and 16 frame temporal resolution, and results compared with the two existing studies. GUTIERREZ et al. do not mention any problems arising from variations in total radioactive count per frame during the cardiac cycle.

The value of 0.906 for AUC means that the classifier ranks the cardiac function of an individual with normal cardiac function, chosen at random, higher than an individual with low or altered cardiac function, also chosen at random, 90.6% of the time. This calculation uses LVEF as a gold standard, even though LVEF is not considered alone as an indicator cardiac health in clinical practice.

The measures of accuracy and ROC01 estimate a best threshold for KEf at rest to be approximately 44% to 49%. This value is comparable with LVEF, which has a threshold of around 45% to 50% for normal cardiac function. However, ARANGO (2009) discusses the use of accuracy for determining threshold, pointing out that the measure does not include reference to false positives and negatives and is therefore blind to their relative importance.

7 DIRECTIONAL ANALYSIS OF LEFT VENTRICULAR MOTION

7.1 Methodology

This chapter provides an analysis of directional components in the cardiac LV MVF. The initial part of the methodology provides an overview of the volumetric (3D) DHHD, as shown in TONG et al. (2003), and implementation details described in Appendix D. The functioning of the DHHD was tested as shown in Appendices E,F, G and H. Testing and validation of the methodology was performed with synthetic images before being applied to the LV MVF from PET images.

The following materials were used in this chapter: (i) synthetic MVFs created from Gaussian potentials (Section 3.3); (ii) the XCAT phantom 16 frame MVF (Section 3.2.2) and; (iii) image sequences from the FDG PET dataset (Section 3.4.3).

POLTHIER; PREUSS (2000) suppose the existence of a scalar field, $[D]$, such that $\nabla[D]$ captures the curl-free (CF) part of the input vector field, and a vector field $[\vec{R}]$ such that $\nabla \times [\vec{R}]$ captures the divergence-free (DF) part. The decomposition can then be described as shown in Equation 7.1 (PETRONETTO et al., 2010), where $\vec{\xi}$ is the smooth 3D MVF, $[D]$ is a scalar CF potential field such that $\nabla \times (\nabla[D]) = 0$, $[\vec{R}]$ is a vector DF potential field such that $\nabla \bullet (\nabla \times \vec{R}) = \vec{0}$ and F_H is the harmonic remainder, which represents linear flow. In line with the objective to perform a directional analysis of the 4D cardiac MVF, the DHHD provides an automatic method for computing rotational, radial and harmonic fields.

$$\vec{\xi} = \nabla[D] + \nabla \times [\vec{R}] + F_H \quad (7.1)$$

Implementation of the DHHD requires constructing and solving systems of linear equations for each frame, as shown in Equation 7.2, to estimate the CF and DF potentials, $[D]$ and $[\vec{R}]$, where $\{d\}$ and $\{r\}$ are $[D]$ and $[\vec{R}]$ vectorised, the potentials to be estimated. Calculations are performed on a mesh; given a motion field of size L, M, N vectors, all evenly spaced, the mesh is created so that each vector component forms the vertex of a cubic mesh (size $L-1, M-1, N-1$). More details about formation of the grid can be found in Appendix D. Matrices $[S]$ and $[T]$ depend only on the geometry of the mesh and the vectors $\{b\}$ and $\{c\}$ are calculated from the mesh and MVF. The harmonic field can be estimated from the input, CF and DF fields.

$$[S]\{d\} = \{b\} \quad (7.2a)$$

$$[T]\{r\} = \{c\} \quad (7.2b)$$

A series of computations is required to construct and solve these linear systems; some steps depend only on the mesh geometry, which can be generated from knowing only the dimensions of the MVF, while other steps require the values of the MVF. These steps are therefore categorised as MVF independent and dependent respectively. Since the mesh is the same size for the entire MVF sequence, MVF independent steps can be calculated once at the start, while MVF dependent steps must be repeated for each frame. Further details about the implementation can be found in Appendix D.

Boundary conditions for the 3D DHHD are described in TONG et al. to obtain uniqueness in the decomposition. The gradient of the scalar field, $[D]$, must be normal to the domain boundary, while the curl of the vector field, $[\vec{R}]$, must be tangential to it. While they note that any other constant value at the boundary could be used, sufficient conditions for the decomposition are to select zero scalar and vector zero boundary conditions for all nodes on the domain boundary, i.e. $\nabla[D] = 0$ and $\nabla \times [\vec{R}] = \vec{0}$ (ABRAHAM; MARSDEN; RATIU, 1988). Appendix J provides more details about how the zero boundary conditions were applied to solve the two linear systems of equations.

7.1.1 Testing of the DHHD with Gaussian potential motion fields

7.1.1.1 Qualitative evaluation of the DHHD

The DHHD was applied to the MVF described in Section 3.3.1, CF and DF potentials recovered, and their corresponding vector fields created by application of differential operators grad and curl respectively. The objective of this test is to verify that the DHHD is functioning correctly and to demonstrate quantification of the potentials and generation of MVF components.

7.1.1.2 Quantitative evaluation of the DHHD

Testing was performed using synthetic MVFs described in Section 3.3.2. Estimates of CF and DF fields were obtained using the DHHD. These were compared with ground truth (GT) values (the original radial and rotational fields which were summed to create the input field), and error measures applied to measure performance. The objective of this test was to demonstrate adequate numerical performance of the DHHD, understand the limitations of the DHHD, and determine the error with varying smoothness of the MVF.

Figure 53 shows the processing scheme used to quantify error. CF and DF fields are created from the Gaussian potentials, whose values are stored as GT fields for error analysis. They are combined to form the input vector field to the DHHD, $\vec{\xi}$. The harmonic field, F_H has also been shown for the sake of generality, although in the experiments this component was set to zero. The DHHD was applied to the input field, producing CF and DF potentials, which were used to generate estimated vector components. Errors were found by comparing GT and estimated pairs with error measures. Finally, F_H can be estimated as shown in Equation 7.3, which in this case represents only the error in the numerical process.

$$F_{Hest} = \vec{\xi} - F_{CFest} - F_{DFest} \quad (7.3)$$

Choice of error measure: Error measures used to compare the ground truth field, F_{GT} , with the estimated field, F_{est} were: (i) normalised root mean square error (NRMSE); (ii) maxi-

Figure 53: Scheme for performance evaluation of the DHHD using synthetic motion field components. Curl-free and divergence free fields, F_{CF} and F_{DF} , are obtained by applying differential operators to Gaussian potentials, added together to form the input field $\vec{\xi}$. The CF and DF fields are summed to create the input motion field, $\vec{\xi}$, and the DHHD applied to this field to estimate CF and DF potentials, from which CF and DF motion field components are estimated. Error in the CF and DF components, E_{CF} and E_{DF} , are computed by comparing estimated and ground truth (GT) fields for each component with the NRMSE, maximum error, AAE and WAAE measures, and finally the harmonic field is estimated by subtraction of F_{CF} and F_{DF} from $\vec{\xi}$ (adapted from SIMS; MACEDO; GUTIERREZ (2016)).

mum error; (iii) average angular error (AAE); (iv) weighted AAE (WAAE).

NRMSE can be calculated using Equation 5.5d. Maximum error was obtained by calculating the difference between the estimated and GT MVFs and finding the maximum value. AAE was calculated using Equations 7.4, but cannot be applied to the whole field due to indeterminacy when the magnitude of either estimated or GT vectors are zero. Therefore vectors with magnitude less than a threshold, $\lambda = 0.1$ voxels/frame, were excluded from the measure, a value established by experiment.

$$AE = \begin{cases} \text{acos}\left(\frac{\vec{f}_{GT} \cdot \vec{f}_{est}}{|\vec{f}_{GT}| \cdot |\vec{f}_{est}|}\right) & (|\vec{f}_{GT}|, |\vec{f}_{est}|) \geq \lambda \\ 0 & \text{otherwise} \end{cases} \quad (7.4a)$$

$$AAE = \frac{\sum |AE|}{n} \quad (7.4b)$$

To avoid setting arbitrary and difficult to establish thresholds, formulae for weighted AE (WAE) and weighted AAE (WAAE) were used as shown in Equation 7.5. Zero values still need to be filtered from the calculation of WAE. Weights for velocity vectors at position l, m, n were calculated according to $\mu_{l,m,n} = \sqrt{|u_{GT} \cdot u_{est}| + |v_{GT} \cdot v_{est}| + |w_{GT} \cdot w_{est}|}$, which provides low

weight when either GT or estimated vectors have small magnitude.

$$WAE = \begin{cases} \text{acos}\left(\frac{\vec{f}_{GT} \cdot \vec{f}_{est}}{|\vec{f}_{GT}| \cdot |\vec{f}_{est}|}\right) & (|\vec{f}_{GT}|, |\vec{f}_{est}|) > 0 \\ 0 & \text{otherwise} \end{cases} \quad (7.5a)$$

$$WAAE = \frac{\sum \mu_{l,m,n} |WAE_{l,m,n}|}{\sum \mu_{l,m,n}} \quad (7.5b)$$

7.1.2 Validation of the DHHD with XCAT motion field

A 16 frame XCAT MVF, prepared as described in Subsection 3.2.2, was used as input to the DHHD to produce estimates of F_{CFest} and F_{DFest} . The harmonic field was calculated using Equation 7.3.

F_{CF} and F_{DF} are 3D vector fields and the xy plane (SAX) was chosen for visualisation since rotation of base and apex in the SAX produces LV torsion. However, it is possible that other orientations could contain interesting and useful information, which could be analysed in future studies.

7.1.3 Decomposition of the FDG PET optical flow motion field

Two individuals were selected from the FDG database as described in Section 3.4.5, a single image sequence from the group of individuals with normal cardiac function, referred to as N, and a single image sequence from the patients' group with low cardiac function, referred to as L. These images were processed according to the scheme shown in Figure 54. The images are first cropped (Section 4.1.2), circle detection applied to the image to provide a prior to the level set algorithm in segmentation, count equalised (Section 6.1.2), and the LV segmentation mask determined (Section 4.1.3). Motion estimation is performed using HS OF (Section 5.1) and the DHHD applied to the resulting smoothed velocities. Finally the segmentation mask is applied to the MVF to select the region corresponding to the LV myocardium.

The optical flow routine requires a value of α^2 to be established, which is the regularisation parameter as described in Section 2.4. The value of $\alpha^2 = 0.001$ was found empirically by reducing the value and observing the optical flow field for noise artefacts.

Figure 54: Processing to obtain directional MVF components from 4D FDG images. Input FDG images are first cropped to the region of interest, circles are identified in SAX slices, and count equalised across gated frames. A segmentation mask is generated for each image volume, the MVF quantified and smoothed using a median filter. Finally, the MVF is decomposed using the DHHD and the segmentation mask applied to the components, F_{CF}, F_{DF} and F_H .

Figures of the MVF were produced for peak systole and diastole. The corresponding frames were selected by identifying those with the largest velocity vectors radially from the geometrical centre of the LV in the CF motion component. Apical and basal regions were identified by dividing the LV long axis into approximately equal regions, resulting in apical, mid and basal thirds. Then representative slices for apex and base were chosen from within these two regions. Having found these frames, the rotation at the apex and base were analysed qualitatively from the DF motion component.

Visualisation software was developed for medical staff in the DNMMI to view the resulting decomposition in SAX slices. When the software is started, it loads the appropriate data for the first individual. A GUI appears with appropriate controls for changing the individual, slice and frame, and also showing 5 figures, LAX view marking the current slice and four SAX slices with MVF overlaid (input field and the three components from decomposition). A screen-shot is shown in Figure 59.

7.2 Results

7.2.1 Testing of the DHHD with Gaussian potential motion fields

7.2.1.1 Qualitative evaluation of the DHHD

Figure 55 shows the decomposition of the 3D synthetic input field at slice $z=28$ through the recovered potentials and MVFs. Subfigures (a) and (c) show the estimated CF and DF potentials, which, after application of the gradient and curl operators, respectively, result in the estimated MVF components, shown in Subfigures (b) and (d). Comparing these with Figure 20, the input MVF, shows that only the two radial components are present in F_{CF} , whereas only the two rotational components are present in F_{DF} . Comparison of the input components with those estimated by the DHHD shows that each component has the same central position, direction of motion and diameter.

7.2.1.2 Quantitative evaluation of the DHHD

Table 12 and 13 show error values resulting from applying the DHHD to Gaussian potential MVF with 8 values of σ . Selected results are reproduced in graphical form in Figure 56.

Table 12: Variation of decomposition error in F_{CF} and F_{DF} against standard deviation of Gaussian potential for NRMSE, AAE and WAAE error measures, resulting from applying the DHHD to a synthetic MVF, created from superposition of a single sink and single anti-clockwise rotation.

Test	σ	NRMSE(%)		AAE(°)		WAAE(°)	
		F_{CF}	F_{DF}	F_{CF}	F_{DF}	F_{CF}	F_{DF}
1	1.250	22.23	18.37	7.31	10.08	4.56	6.37
2	1.768	12.41	10.10	5.01	6.38	2.92	4.01
3	2.500	6.56	5.28	2.66	3.53	1.69	2.32
4	3.536	3.37	2.72	1.39	1.88	0.91	1.28
5	5.000	1.71	1.44	0.73	0.94	0.52	0.68
6	7.071	0.87	1.01	0.38	0.48	0.25	0.42
7	9.129	1.75	1.66	1.32	0.79	0.87	0.80
8	12.910	12.29	8.94	9.68	6.53	4.59	2.88

Measured error in the DHHD decreases initially with increasing standard deviation of the Gaussian potential towards a lowest error at $\sigma=7.071$ for all of the error measures. The min-

Figure 55: CF and DF potentials calculated using the DHHD and their resulting velocity fields. All images are slices in the plane $z = 28$: (a) Estimated CF potential; (b) Estimated F_{CF} ; (c) Estimated DF potential; (d) Estimated F_{DF} .

imum RMSE is 0.87% and 1.01% for CF and DF components respectively. For σ larger than 7.071 the error measures increase.

7.2.2 Validation of the DHHD with XCAT motion field

Figures 57 and 58 show quiver plots in the short axis plane resulting from decomposition of the XCAT MVF. Each figure shows systole and diastole respectively in the two columns of figures, and rows show the input MVF to the DHHD, $\vec{\xi}$, followed by the three components resulting from decomposition, F_{CF} , F_{DF} and F_H . The MVF has been overlaid on the approximate location of the myocardium, shown in red scale, which has been estimated as the magnitude of the XCAT velocity field from $\vec{\xi}$. The MVF has been oriented according to an observer looking

Table 13: Variation of decomposition error in F_{CF} and F_{DF} against standard deviation of Gaussian potential for the maximum error measure, resulting from applying the DHHD to a synthetic motion field, created from superposition of a single sink and single anti-clockwise rotation.

Test	σ	Maximum Error CF			Maximum Error DF		
		u	v	w	u	v	w
1	1.250	0.286	0.308	0.307	0.249	0.214	0.042
2	1.768	0.142	0.155	0.155	0.120	0.099	0.025
3	2.500	0.080	0.901	0.899	0.070	0.056	0.015
4	3.536	0.041	0.046	0.046	0.035	0.028	0.008
5	5.000	0.020	0.023	0.023	0.018	0.014	0.004
6	7.071	0.010	0.012	0.012	0.012	0.013	0.004
7	9.129	0.025	0.026	0.026	0.022	0.023	0.010
8	12.910	0.182	0.183	0.183	0.112	0.112	0.038

Figure 56: Results from applying four error measures to the motion field, obtained from Gaussian potentials, showing CF and DF components: (a) percent NRMSE against σ ; (b) average angular error against σ ; (c) weighted average angular error against σ ; (d) Maximum error found for x component (u) of velocity against σ .

from base towards apex.

Frames 4 and 14 of the 16 frame XCAT sequence were chosen to represent systole and diastole respectively, since these frames produce maximum observed velocity for each phase.

Computation statistics: Each frame of the XCAT MVF was $57 \times 57 \times 61$ nodes, providing

Figure 57: Resulting motion fields from applying the DHHD to the XCAT motion field in apical SAX slices. Columns are systole and diastole (frames 4 and 14), rows are $\vec{\xi}$ (input motion field), curl-free field, divergence-free field, harmonic remainder field.

Figure 58: Resulting motion fields from applying the DHHD to the XCAT motion field in basal SAX slices. Columns are systole and diastole (frames 4 and 14), rows are $\vec{\xi}$ (input motion field), curl-free field, divergence-free field, harmonic remainder field.

a total of 1.98×10^5 nodes and a mesh composed of 1.13×10^6 tetrahedra. The size of $[T]$ was 3.5×10^{11} elements, with approximately 2.6×10^7 non-zero elements, giving a sparsity of approximately 7.4×10^{-5} .

The DHHD required a total processing time of 3805 seconds (1.05 hrs) to complete 16 frames of the XCAT MVF, using a micro with 32GB RAM, Intel core I7 3970X, 3.5GHz x 12, running Ubuntu 12.04 64 bit.

7.2.3 Decomposition of the FDG PET optical flow motion field

Visualisation software: Figure 59 shows a screenshot of the GUI software developed for medical teams. The current SAX slice is shown by the horizontal line on the long axis view. A patient can be selected from the patient ID listbox, which has been covered with a yellow box to maintain patient privacy.

Individual with normal cardiac function, N

Figure 60 shows the decomposition of MVF N into CF and DF components. The curl-free components (column 2) contract in systole and expand in diastole, and the centre of global motion seems to be close to the LV centre. All have similar magnitude except for apical diastole, Subfigure (h), whose largest vectors are approximately three times that of the others. Each plot shows a variation of motility over different myocardial regions, for example the anterior region has greatest motility for apical diastole.

Divergence-free components (column 3) have direction of rotation as shown in Table 14 for apical and basal slices in systole and diastole, obtained from a visual inspection of F_{DF} . The overall rotation in the SAX plane has been evaluated as either clockwise (cw) or anti-clockwise (acw). Apical components have a clearly-defined centre which is close to that of the LV, but the basal fields seem to be less uniform in its rotation, perhaps being composed of several combined rotational components. F_{DF} for Apical systole seems to be composed of two opposing rotations. The larger is in the anterolateral region, anti-clockwise, and the smaller is clockwise rotation at the septal region. All components have similar magnitude except for apical diastole, Subfigure

Figure 59: Screenshot of visualisation software developed for evaluation of DHHD results. All figures are short axis slices for frame 3 of slice 33 for the selected individual. The patient ID listbox has been covered with a yellow rectangle: (a) Long axis view of LV (b) input MVF to DHHD, $\vec{\xi}$ (c) Harmonic remainder, F_H (d) CF field, F_{CF} (e) DF field, F_{DF} .

(i), whose largest vectors, in the anterior region, are approximately twice the size of the others.

Individual with low cardiac function, L Figure 61 shows the results of the decomposition for frame 4, which is in systole. Subfigure (a) shows that the displayed slice is between apical and mid regions, (b) shows the input MVF to the DHHD, $\vec{\xi}$, with a scale that shows reduced motility compared to N. The greatest motion is seen in the lateral region, although all regions participate in the contraction. F_{CF} in subfigure (c) shows that this patient with a pacemaker has synchronised contraction between regions of the myocardium, and that these vectors are mostly pointed towards the center of the LV. F_{DF} in (d) contains one small clockwise and two small anti-clockwise rotations in the region of muscle. The rotators are not visible in the input MVF

Figure 60: Application of the DHHD to the motion field from individual N. Rows 1 and 2 show apical and basal systole, and rows 3 and 4 show apical and basal diastole. Column 1 shows the input motion field, $\vec{\xi}$, column 2 and 3 are the curl-free and divergence-free motion fields respectively.

Table 14: Direction of rotation of apex and base in systole and diastole for motion field N. The rotation was determined to be clockwise (cw) or anti-clockwise (acw)

N	Apex	Base
Sys	acw	cw
Dia	cw	acw

Figure 61: Application of the DHHD to frame 4 of motion field L: (a) Long axis view, with horizontal line showing the slice taken; (b) Input motion field, $\vec{\xi}$ calculated using optical flow and overlaid on frame 4 of the image sequence; (c) F_{CF} ; (d) F_{DF} .

since F_{CF} is sufficiently large to mask them. There seems to be no rotation of the LV around its center, as was seen with MVF N.

Further investigation revealed that the rotators extend several slices above and below that shown, and also that the rotators were in similar positions throughout the sequence. Figure 62 shows F_{DF} for the same slice from frames 2 to 10. Frame 2 to 4 have been repeated on the first row, annotated with letters a-i and a symbol used to mark rotational centres. The magnitude of the vectors is small, as shown by the scale. Frame 2 shows the presence of four small vortices (a – d), although there is no observed global rotation of the LV. Frame 3 shows slightly larger velocity components and two clear small vortices, but again no overall rotation. Vortex f is very close to the position of vortex d from Frame 2. In frame 4, there is some overall anti-clockwise

rotation, although the main features are three small vortices, g, h, i , which have similar central positions and senses to vortices a, c, d in Frame 2. Frame 5 has flow centred around a small vortex with similar position to vortex g in Frame 4. Rotational flow is again centred around a small vortex in Frame 6. Frames 7 and 8 have little rotational motion. Frame 9 has a vortex in a similar position to a and g , and another in a similar position to Frame 6. Frame 10 shows clockwise rotation.

Figure 62: F_{DF} , in 9 apical SAX slices for patient L. Frames 2-4 have been duplicated and centres of rotation have been manually marked with the symbol $\otimes$ and labelled with letters a-i.

7.3 Discussion

7.3.1 Testing of the DHHD with Gaussian potential motion fields

7.3.1.1 Qualitative evaluation of the DHHD

The processing of the Gaussian field demonstrates a successful MVF decomposition, correctly separating the radial and rotational MVF components, based on visual inspection. It also provides an example of how the DHHD is used, first forming an input 3D MVF from radial and rotational potentials, extracting CF and DF potentials with the DHHD, and finally computing the CF and DF MVF components. The CF and DF components are seen to be the same as the input radial and rotational inputs.

7.3.1.2 Quantitative evaluation of the DHHD

The variation of NRMSE with standard deviation shows minimum error at $\sigma = 7.071$ with increasing error for σ greater or less than this value. This behaviour can be explained by considering the decreased smoothness of the motion field on the grid for smaller σ and increased errors at the domain boundary for larger σ due to application of boundary conditions.

To explain these points in more depth, it is beneficial to consider the situation in one dimension. Figure 63 shows a representation of Gaussian potentials placed on a one dimensional grid of width $L=55$ with standard deviations 1.250, 7.071 and 12.910. Changing standard deviation from 7.071 to 1.250 produces a corresponding increase in decomposition error as finite element approximations become less valid due to decreased smoothness. As σ increases above 7.071, the gold standard value of potential increases at the boundary, but the estimated value is set to zero by the application of boundary conditions. This disparity causes significant error values.

These results show that for best accuracy of the numerical method, the MVF should be as smooth as possible, but keeping MVF components small at the boundary.

The lowest values of maximum error were obtained for the w component of F_{DF} , since the rotation was in the xy plane with no input component in the z direction.

Figure 63: One dimensional Gaussian potentials with varying values of standard deviation, σ , plotted on a grid of length 55, representing smoothness of Gaussian function and value at the borders (positions 0 and 54), for $\sigma = 1.250$ (red), 7.071 (orange) and 12.910 (blue).

AAE, NRMSE, and WAAE have very similar trends, and produce the same minimum value of standard deviation. AAE and WAAE have a different range (Figures 56b and c), which seems to arise because AAE gives equal weight to all vectors greater than the threshold, while WAAE gives larger weight to larger vectors. In this case, there seems to be little advantage in using both AAE and WAAE.

7.3.2 Validation of the DHHD with XCAT motion field

Figures 57 and 58 show the result of applying the DHHD to the XCAT MVF. The MVF for apical systole and diastole, $\vec{\xi}$, consists of contraction and clockwise rotation in systole and expansion and anti-clockwise rotation in diastole. The CF and DF fields resulting from decomposition show expansion and contraction, and rotation, in a clear manner, with the directions of motion being mainly perpendicular to the midmyocardial line in the case of CF and parallel in the case of DF. It can be seen from the scale of the quiver plot that the DF field is about twice as strong as the CF field in both cases. The harmonic remainder field shows large components at the edges of the LV myocardium and, in the apparent absence of linear components in the MVF, represents error in the decomposition, which occur because of the discontinuous motion boundaries in the XCAT MVF. In future work it might be possible to reduce this error by using a finer mesh at the endocardial and epicardial surfaces.

The basal MVF consists of anti-clockwise rotation in systole, combined with contraction, and clockwise rotation with expansion in diastole, as seen from the CF and DF components. The CF component is of similar magnitude to DF in systole, but about twice as strong in diastole. The DF component is seen to follow the midmyocardial line very closely in both systole and diastole. Again, the harmonic remainder has its largest components at the edges of the LV myocardium.

The expected motion pattern for late systole was anti-clockwise basal rotation and clockwise apical rotation in late systole, and opposite rotations in diastole (see Table 1), producing a LV twist, as described in Section 2.6. This pattern of rotational motion was observed in the results of the XCAT MVF, which shows that the XCAT phantom is generating a realistic field.

The computation statistics show high computational cost in performing the DHHD, which could restrict the future use of the decomposition. Future work could investigate more efficient implementations using parallel computing, or techniques for matrix approximations, such as Fast Multipole.

7.3.3 Decomposition of the FDG PET optical flow motion field

Motion field from individual with normal cardiac function: Table 1 shows the expected rotational direction in systole and diastole. The results in Table 14 show that N follows the pattern for late systole and diastole, but it should be noted that to produce torsion the base and apex need only rotate at different rates, and not necessarily in opposing directions.

Visual inspection of the DF component shows that it does not represent pure rotation of the LV around the LV center, or rotation parallel to the midmyocardial line, and in some instances, the DF component has vectors which are radial from the LV centre. F_{DF} was seen to contain a rotational field that was large in some regions and small in others, and these results seems difficult to justify. The results of MVF decomposition rely on the accuracy of MVF quantification, so the text will now take a critical look at motion detection in PET images.

An important consideration is to determine to what extent the MVF, quantified by optical

flow, is similar to the ground truth LV motion. Due to the difficulty in obtaining a ground truth field, a comparison could be made between the quantified motion fields from PET images and that produced using a different modality, such as that produced from MR tagging or echocardiography; however there is no such field for comparison. A possible manner of evaluating the MVF comes from motion detection with synthetic images; GUTIERREZ (1995) uses rotating and translating cylinders with a strong texture to quantify the motion detection error with HS OF, which varies between 7.66% and 20.27% NRMSE. However, LV motion estimation from PET images has the following disadvantages in comparison with the synthetic cylinder: (i) the PET image has much less texture. In individuals with normal cardiac function, the intensity throughout the myocardium is very uniform close to the midmyocardial line, and large variations in count in this region are indicative of abnormal function; (ii) The PET images are corrupted by the partial volume effect, which tends to blur any variations in pixel intensity and creates the slow decay in voxel intensity from the midmyocardial line towards epi and endocardial borders. The above items mean that there is little texture in the image, and certainly not consistent texture in two independent directions throughout the image, which should be interpreted as a limitation of motion detection and a source of motion detection error. Although the results from motion field decomposition seem to be meaningful, it is clear that their significance should be considered along with other available medical information.

The aperture problem was presented in Section 2.4 and presents limitations for cardiac motion detection. In PET images, clear structural information is most readily available due to the strong contrast between the LV and the background, whereas variation in radioactive count throughout the muscle provides a more limited and weaker texture. Considering short axis slices, which are essentially annular in cross section, we therefore expect the estimate for radial motion to be obtained more reliably than circumferential motion. Figure 64 illustrates this principle with a representation of the LV as a textureless ring of muscle in simultaneous expansion and rotation. The lack of structural information parallel to the LV edge means that rotation is not detected, while radial motion is clearly observable. In this figure, the aperture is represented by a small cyan circle, and a yellow arrow marks the direction of motion that

would be obtained for LV expansion. particular for the DF field, which tends to be parallel to the clearest structural content.

Figure 64: Aperture problem applied to SAX slice of LV. Here the LV is shown as a textureless white ring against a black background and is expanding and rotating clockwise, as shown by cyan arrows. A small region of the image, on the edge of the LV and marked with the cyan circle, is considered as if viewed through an aperture. Structural information is available only in the radial direction, meaning that only radial motion is detectable, as shown by the yellow arrows.

Given this analysis of motion, we can conclude that the optical flow field is certainly representative of LV motion, even if it does not accurately depict the ground truth. As the motion is observed in a cine, we notice the change in LV volume easily as the borders move radially, but the rotation is not as easy to define or characterise. The small amount of structural information within the myocardium in PET images makes circumferential motion field estimation difficult. However, there exist approaches to improve circumferential motion quantification. For example, WANG et al. (2013) use a feature guided approach to improve the accuracy of circumferential motion by tracking features provided by the papillary muscles in PET-simulating XCAT images. The estimate of velocity is used to initialise the velocity field estimates for the Horn and Schunck algorithm, achieving comparable accuracy to the ground truth velocity field.

Cardiac motion and strain analysis can be decomposed into three motion components: radial, circumferential and longitudinal motion (REANT et al., 2008). While the principal focus of the analysis presented is concerned with radial and circumferential motion, the decomposition of the cardiac motion field also enables the longitudinal component to be viewed through the harmonic remainder (HR), which contains both linear flow and numerical errors. Figures 65a and 65b show OF and HR HLA fields for individual N in systole.

The motion of the heart comes about by shortening of the muscle fibres and the arrangement

Figure 65: HLA slice of motion field for individual N in systole: (a) $\vec{\xi}$; (b) F_{HR} .

of these creates the MVF which have been observed, of a mixed rotation and radial motion. Figure 66 shows a schematic representation of muscle fibre arrangement of the LV shown alongside the LV MVF, calculated using optical flow.

Figure 66: Diagram of the muscle fibres of the left ventricle(BENNINGHOFF (1944) in SPALTEHOLZ (1967)) shown alongside a VLA slice of the LV in systole, with corresponding optical flow field overlaid.

The processing scheme for FDG images, as shown in Figure 54, applies the segmentation mask after the DHHD. The rationale for this is that motion estimation produces a smoothed MVF and the DHHD requires a smooth input MVF. In initial experiments, the segmentation

Figure 67: Long axis slices through the cardiac cycle for FDG PET image sequence, showing that the myocardium contained in a particular slice in frame 1 may move to a different slice number in later frames (frames 1, 4, 8, 12, 16 are shown in Subfigures a, b, c, d, e respectively).

mask was applied to the LV MVF before decomposition, but the sharp discontinuities in the MVF created artefacts in the DHHD output.

Analysis of these MVF components by medical teams found temporal analysis to be difficult due to the visualisation of 3D phenomena in 2D slices. Tracking individual slices through multiple frames shows that the same piece of myocardium can change slice number due to contraction and expansion in the long axis direction; hence an apical slice at the start of the sequence may move closer to the base at a later point in the cycle. Figure 67 shows a long axis slice in intervals of approximately 4 frames through the sequence, and shows that the slice number containing the base can vary by as much as 5 over the cardiac cycle.

To diminish the effect of this problem, a proportionality scale could be defined along the long axis with a fractional value that increases from apex to base. A slice could then be chosen according to a fractional value of this distance, allowing a slice, approximately the same as in frame 1, to be chosen and observed through cardiac cycle. Figure 68 shows the possible implementation of the scale for frame 16 and frame 4. It can be seen that the position of the apex is almost constant at these two points in the cycle, while the base has moved around 4 slices. Implementing a scale of this type could also assist in comparing LVs of different sizes. The scale could be created by identifying the apical tip and base throughout the cardiac cycle; Chapter 4 provided a methodology for finding these points in the image, but was found to be challenging

using only results from the Hough Circle Transform. Future work could determine a more robust method for automated identification of these points in order to improve the visualisation of slices through the temporal sequence.

Figure 68: Long axis slices through the cardiac cycle for FDG PET images, showing frames 16 and 1, (a) and (b) respectively, annotated with the proposed proportional scale, which is 0% at apex and 100% at base.

Medical evaluation of LV motion component results could use quantitative or qualitative indicators, describing how the segmented LV wall moves over a number of cases and leading to possible statistical analyses. Qualitative description might be expressed in the form: “the apical region 3 moves towards the LV centre in systole with velocity = high.”

Further work could summarise the LV rotation in apex, mid and base using the DF MVF component. Each of these regions could be assigned a third of the distance between apex and base, and each subdivided, grouping SAX slices together to form thicker slices. Then these circles could be divided into evenly distributed sectors, as shown in Figure 69, where each sector of muscle has a slice depth of 12mm and arc length of 12mm. A statistical summary of each sector could be performed, for example mean and standard deviation of velocity, and these values marked on a representative chart, such as a circle or polar map.

Motion fields from individual with low cardiac function: L was seen to have a lower motility than N, shown by lower magnitudes of the DHHD input MVF, $\vec{\xi}$, at the frame repre-

Figure 69: Representative figures showing the proposed visualisation scheme for the decomposed motion field: (a) various slices of myocardium are combined to approximate a cylinder, which is divided into sectors, and a statistical summary produced for each; and (b) possible graphical representation for each sector in subfigure (a), with a vector showing mean velocity.

sending systole. The CF field shows contraction towards the LV centre, similarly to N. However, the DF field has very low global LV rotation and with three small rotators in the myocardium.

While it is difficult to establish the cause of the rotators from a single individual, some hypotheses are offered. It is possible that the presence of the pacemaker influences the DF MVF, directly or indirectly from the wires or electrodes, perhaps stimulating only certain regions of the ventricle, given that the normal mechanisms of electrical conduction have been altered. Another possibility is that the leads and wires in the CT image cause distortion to the PET image during the process of attenuation correction. Figure 70 shows SAX slices with the position of the electrodes, and the location of the electrode in the right image seems to coincide with that of rotators (d),(f),(i) in Figure 62. However, the electrode in the left image does not coincide directly with any rotators. Further studies could use a larger number of patients with fitted pacemakers to study the position of any small rotators in the myocardium relative to the position of the pacemaker to understand better this phenomenon.

Figure 70: Fused PET/CT image, showing PET in colour superimposed on a CT image. This image was produced using OsirixTM software (OsiriXTM imaging software, Pixmeo, Geneva, Switzerland). Arrows show location of implanted pacemaker electrodes into the LV, in subsequent SAX slices.

8 CONCLUSIONS

Methods were proposed and evaluated for identifying the cardiac muscle in PET images. The approach was composed of two steps, first finding and limiting LV structures in the PET image sequence, and then segmenting the LV myocardium from the cropped images. While both of these stages were performed with FDG images, only the former was performed using ^{82}Rb images. The approach for cropping involved the combined use of edge detection (CANNY, 1986), the Hough Circle Transform (DUDA; HART, 1972) and clustering techniques, with parameters chosen *a priori* to locate the LV in groups of subjects which may include hypertrophy. Cropping the image was found to produce adequate results for both FDG and ^{82}Rb PET image sets, although the method used for cropping in the long axis direction was found to produce an excessive region, extending far beyond the apex and base. For segmentation of FDG PET images, a methodology was developed which combined the Hough Circle Transform and the DRLSE (LI et al., 2010), obtaining a best value of $\text{DSM} = 93.43\%$ with optimum parameters, which is consistent with the literature (CONSTANTINIDES et al., 2012; DREIJER; HERBST; PREEZ, 2013; TRAN, 2016).

The quantification of LV motion from 3D dynamic images used the Horn and Schunck optical flow technique (HORN; SCHUNCK, 1981), a method which results in a dense MVF, or in other words, one which is evaluated at every voxel of the image sequence. The use of spatially varying averaging filters (SVFs) (MITICHE; AGGARWAL, 2014) to reduce motion artefacts in regions of motion discontinuity was investigated; results were evaluated by applying error measures to quantify the difference between method and ground truth MVFs, formed from rotation and translation of synthetic geometrical forms. Model parameters and schemes for calculation

of model quantities were varied. Optimum results were found using the average velocity method spatial filter with $\beta = 7$, using centred differences for estimation of image derivatives, 50 or 100 iterations of the Horn and Schunck algorithm, and with the regularisation parameter, $\alpha^2 = 0.2$. This set of parameters and schemes produced the best NRMSE of 28.5% for cylinder rotation of 1° per frame. In a separate study of the motion quantification, the same synthetic sequences were used to compare methods for solving the linear system of equations; error values were calculated between ground truth and method velocities, first using Gauss-Seidel update equations, as suggested in HORN; SCHUNCK, and then direct construction of the linear system of equation in matrix form and solving using the method of Generalised Minimum Residuals (GMRES) (GOLUB; LOAN, 1996). No difference was encountered between the two methods to measured precision, although the Gauss-Seidel update equations were found to be much more efficient in terms of processing time.

Measures of LV motility can provide important indicators for diagnosis of cardiovascular disease, and can be estimated from the quantified LV MVF. GUTIERREZ et al. (2003) develops Kinetic Energy Index (KE_f), which is an indicator of motility, which has previously been used to classify cardiac function in 58 individuals with normal or low/altered cardiac function from SPECT images, compared against known values of LVEF. The proposed study evaluated 63 individuals with normal and low cardiac function from ^{82}Rb PET images using a similar methodology, with KE_f calculated as 0.5731 ± 0.0899 and 0.3812 ± 0.1146 respectively. KE_f was evaluated as a classifier of cardiac function by computing the area under a ROC curve, found to be 0.906; this represents the probability that the classifier will rank the cardiac function of an individual with normal cardiac function higher than an individual with low/altered function, both chosen at random.

Large variations in total volume image count were encountered in some of the ^{82}Rb PET images over the 8 frames per cardiac cycle; in PET images, the brightness of a voxel is determined by the radioactive count. The motion detection algorithm assumes the brightness of objects in the image to be constant, and a violation of this assumption results in motion artefacts, which cause increased errors in the calculation of KE_f . The reason for the variation in

count is unknown, but similar variations were not mentioned in GUTIERREZ et al. when using SPECT images. However, the variation is known to medical physicists working in the area as a tail drop, where the LV volume curve, used for estimating LVEF, ends on a value lower than it began. This effect was accepted as a limitation of the data, and an approach was developed to reduce the effects of the variation by assuming constant count in image volumes throughout the cardiac cycle. This approach could have the downside of marginally amplifying the noise floor in frames with low count.

Reliable estimates of KEf depend on accurate quantification of motion; however the ^{82}Rb PET images in the study were found to have high noise levels, which degrade motion detection in the following ways: (i) noise affects the motion detection method, which is required to use a higher value of the regularisation parameter, α^2 , relying less on the image data and more on regularisation; (ii) noise in PET images can result from low statistic, which results in gated images of lower temporal resolution. In contrast, it was seen that FDG images have adequate statistic to acquire 16 frames per cardiac cycle, and that the resulting frames still have a larger count, and therefore less noise, than with ^{82}Rb . KEf is a promising measure of cardiac motility, which may prove useful alongside indicators such as ejection fraction in clinical practice, but its benefit can only be shown through further testing. These tests could use a radiopharmaceutical which produces a higher count, providing potentially superior results.

Directional analysis of LV motion in the proposed study used an initial stage of decomposition into rotational and radial components, allowing subsequent separate analysis of these components in a simpler manner. The DHHD was selected for this purpose, and tested initially with radial and rotational components computed from Gaussian potentials. The DHHD was shown to require a smooth input field and to produce large values of error when the input field had large components at the domain boundary since zero boundary conditions were applied at every point along the domain boundary surfaces. For the experiments, performed on a grid of size $55 \times 55 \times 55$, the optimum value of standard deviation for the Gaussian was found to be 7.071, giving NRMSE for curl-free (CF) and divergence-free (DF) fields as 0.87% and 1.01%.

The XCAT MVF, calculated from position vector files, was used to produce a realistic

synthetic cardiac MVF with which to validate the DHHD. A qualitative observation of the decomposed MVF shows clearly separated radial and rotational components in the CF and DF fields, with the DF field clearly following the midmyocardial line. The harmonic field, which contains errors from the numerical process, was seen to have its largest components at the outer surfaces of the myocardium, where the MVF has discontinuous changes in velocity.

The DHHD was used to decompose the optical flow MVF derived from FDG image sequences from an individual with normal cardiac function and a patient with non-compaction cardiomyopathy and a pacemaker fitted. The DF field, which contains the rotational component, was seen to produce a better understanding of LV rotation than from the input MVF, but further processing stages may be required in order to use the vector field for quantification of LV twist. Overall, the DHHD was seen to be a promising tool for cardiac MVF analysis, and could be applied to MVFs derived from other modalities, for example, from speckle tracking echocardiography.

Schemes for representation and visualisation of directional motion field components were developed and made available to medical teams for evaluation. While confirming that the results could be useful for diagnosis, they commented that visualisation could be improved by allowing tracking of the same slice through multiple frames. Also, instead of displaying the MVF for every voxel of a short axis slice, statistics could be calculated for regions of myocardium to allow a qualitative or quantitative study of motion in a style consistent with medical literature.

PET images acquired using different radiopharmaceuticals were found to have different characteristics, which result from their physical properties and image acquisition. The diagnostic value of motility indicators depends on the accuracy of quantified motion, which in turn depends upon these same characteristics, meaning that a radiopharmaceutical such as FDG, which produces a high count, may be preferred over one such as ^{82}Rb , which produced a low count, for future studies.

Quantification of the MVF from PET images allows the development of new indicators to diagnose CVDs and provides a promising and unprecedented approach to the diagnosis of

CVDs.

9 ORIGINAL CONTRIBUTIONS

1. Extension of spatially varying averaging filters to 4D images to improve performance of Horn and Schunck algorithm, quantifying their performance.
2. Development of a method for locating the LV volume in gated PET images from 2D short axis slices using edge detection, the Hough Circle Transform and clustering methods.
3. Development of a method for LV volume segmentation in 2D short axis slices using the Hough Circle Transform and Level Sets.
4. Application of motion quantification techniques to Gated Rb-82 Rubidium Chloride and F-18 Fluorodeoxyglucose PET image sequences.
5. Application of equalisation of radiation count to gated PET images to avoid motion artefacts.
6. Evaluation of kinetic energy index metric for estimating cardiac function in Rb-82 PET images, including statistical comparison of kinetic energy index and LVEF and evaluation of KE_f as an indicator of disease with number of a patients $n=63$.
7. Performance testing of DHHD to determine the error of the DHHD with changing smoothness.
8. Application of the DHHD to perform motion decomposition on a MVF from the XCAT phantom.
9. Application of the DHHD to perform motion decomposition and directional analysis on a cardiac MVF, quantified from PET images using optical flow.

ANNEX A – PUBLISHED ARTICLES

Sims JA, Gutierrez MA. Automatic Left Ventricle Segmentation of FDG PET gated images using Hough Transform and Level Sets. In: XXV Congresso Brasileiro de Engenharia Biomedica. Foz de Iguaçu, PA, 2016. p.1167–1170. Available at: <<http://cbeb.org.br/en/proceedings-and-certificates>>.

Sims JA, Macedo MMG, Gutierrez MA. Directional Analysis of Cardiac Motion Field based on the Discrete Helmholtz Hodge Decomposition. 2016 Computing in Cardiology Conference (CinC), p. 349-352, 2016.

Sims JA, Oliveira MA, Meneghetti JC, Gutierrez MA. Calculation of Cardiac Kinetic Energy Index from PET images. In MEDINFO 2015: eHealth-enabled Health - Proceedings of the 15th World Congress on Health and Biomedical Informatics, São Paulo, Brazil, 19-23 August 2015. 2015; 653-657.

Sims JA, Furuie SS, Gutierrez MA Automatic quantification of Three-dimensional Velocity Field Improved by Spatially Varying Averaging Filters. In XXIV Congresso Brasileiro de Engenharia Biomedica, Uberlandia. Anais do XXIV Congresso Brasileiro de Engenharia Biomedica, 2014; p.1937-1940.

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ANNEX B – ARTICLES AWAITING PUBLICATION

Article awaiting publication in January 2018:

Sims JA, Giorgi MC, Oliveira MA, Meneghetti JC, Gutierrez MA. Directional Analysis of Cardiac Motion Field from Gated Fluorodeoxyglucose PET images using the Discrete Helmholtz Hodge Decomposition. Computerized Medical Imaging and Graphics, Elsevier. Published online: <<https://doi.org/10.1016/j.compmedimag.2017.06.004>>

ANNEX C – PROJECT INCLUSION BY CAPPEsq

SDC: 3568/10/157

Hospital das Clínicas da FMUSP
Comissão de Ética para Análise de Projetos de Pesquisa
CAPPEsq

À
Comissão Científica do InCor

A Comissão de Ética para Análise de Projetos de Pesquisa-CAPPEsq da Diretoria Clínica do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, **APROVOU** na sessão de 25.03.15 a execução do subprojeto intitulado "**Calculation of Kinetic Energy Index from sequences of PET images**", que será tese de doutorado de John Sims sob orientação do Dr. Marco Antonio Gutierrez.

O referido projeto faz parte do **Protocolo de Pesquisa nº 0030/11**, intitulado "**CINTILOGRAFIA DE PERFUSÃO MIOCÁRDICA COM PET: BASES CLÍNICAS PARA ELABORAÇÃO DE GERADOR ESTRÔNCIO/RUBÍDIO-82 NO BRASIL**", aprovado por esta CAPPEsq em 20.04.11.

CAPPEsq, 25 de Março de 2015

Prof. Dr. Alfredo José Mansur
Coordenador
Comissão de Ética para Análise de
Projetos de Pesquisa - CAPPEsq

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APPENDIX A – PRINCIPLES OF NUCLEAR MEDICINE IN CARDIOLOGY

This appendix contains a summary of concepts and principles related to instrumentation, acquisition and formation of images from nuclear medicine (NM) in cardiology. Among imaging techniques belonging to NM in the modern hospital are positron emission tomography (PET) and single photon emission computed tomography (SPECT). The main focus is on the former, although SPECT shares many similarities.

Positron emission tomography (PET) first began to be used in the early 1950s, when it was realized that the high-energy photons produced by the annihilation of the positron-emitting isotopes could be used to describe the physiological distribution of "tagged" chemical compounds in three dimensions. Following around 20 years of technological developments, clinical research activity began following the development of reconstruction algorithms and improvements in detector instrumentation. By the mid-1980s, PET established itself as a tool for medical diagnosis and dynamic studies of human metabolism. From 1975 to 1995, typical values of spatial resolution improved from around 14mm to 4mm, the number of detectors from around 64 to 19,000 and the data generated from around 4 kilobytes to 4 megabytes (NATIONAL RESEARCH COUNCIL AND INSTITUTE OF MEDICINE, 1996).

Isotopes used in PET undergo various types of decay, but the mechanism of primary interest is positron decay. BAILEY et al. (2005) outline two forms of positron production, nuclear transmutation and pair production, of which nuclear transmutation is relevant to the formation of medical images.

Nuclear transmutation is the process in which a proton is converted to a neutron, a positron

and a neutrino ${}^1_1p^+ \rightarrow {}^1_0n + {}^0_1\beta^+ + \nu$. Since the atomic number decreases, the newly formed atom must also eject an electron. The positron is released on a scale of continuous energy up to a certain maximum, as shown in Table 15 and wanders from its site of generation, suffering collision and scattering interactions with other nuclei until its kinetic energy (KE) is low. The distance travelled is known as the positron range (PR), which represents an uncertainty in position which increases with increasing initial positron energy. ${}^{82}\text{Rb}$ has a mean range of 5.9mm in water, compared with 0.6mm for ${}^{18}\text{F}$, and has the largest PR of the commonly used isotopes. The PR introduces an error in image formation, since the location of positron emission is not the same as that of gamma photon production; it can be noted that Rubidium-82 has the largest energy of emission of the isotopes listed, leading to the largest PR, whereas Fluorine has the shortest. When the positron has sufficiently low KE it can combine with an electron, forming positronium, which has a half-life of 10^{-7}s . Positronium suffers annihilation and, in around 99% of cases, forms two 511keV gamma photons emitted at approximately 180° from each other. The exact value of the angle depends on the kinetic energy before annihilation (BAILEY et al.).

PET imaging in the clinical environment consists of injecting compounds labelled with radioisotopes into the body of the patient. These are left for a time to enter into the required metabolic process, known as the uptake period, and then the individual is scanned (DEMIRKAYA; ASYALI; SAHOO, 2008).

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) website¹ shows various radionuclides in common use in PET and SPECT imaging. For each one, a reference is given which details its some specific uses, such Xe-133 gas, which is used for lung scintigraphy. The details about Rb-82 refers to the article STRAUSS et al. (2008) as the reference procedure guide for myocardial perfusion. Although beyond the scope of this thesis, there are details about human dosage and the critical organ that will be affected by that radiopharmaceutical.

¹<<http://www.snmmi.org/ClinicalPractice/doseTool.aspx?ItemNumber=11216&navItemNumber=11218>>

Table 15: Common PET isotopes and their emission characteristics (BAILEY et al., 2005).

Isotope	Half-life (minutes)	Maximum positron energy (MeV)	PR in water (mm) (maximum,mean)
F-18	109.7	0.635	(2.4, 0.6)
C-11	20.4	0.96	(4.1, 1.1)
N-13	9.96	1.19	(5.1, 1.5)
O-15	2.07	1.72	(7.3, 2.5)
Rb-82	1.25	3.35	(14.1, 5.9)

A.1 Instrumentation

The most common method for the detection of gamma photons is the scintillation camera, but also called a gamma camera or anger camera. Other detectors employ gas and semiconductors, and have an important role. Scintillation detectors typically use a material that emits visible light when energy is absorbed from ionizing radiation. The gamma photons strike the crystal, releasing electrons by Compton Scattering or the Photoelectric Effect, that interact with the crystal producing light (POWSNER; POWSNER, 2006). The crystal has a maximum efficiency for gamma photons in the emitted range, and is coupled to an electronic amplifier to analyse the captured signals, such as a photo-multiplier.

Since PET cameras detect paired photon events, the positron decay can be localized without using a collimator, relying solely on the so-called electronic collimator, which uses the principle of coincidence detection. The absence of a collimator greatly improves the sensitivity compared with SPECT systems (GARCIA et al., 2012).

PET image data are a list of events from the detection of pairs of photons which are almost coincident. The coincident lines of response (LORs) are recorded at many angles to create a 3D image using, for example, filtered back-projection. In a time-of-flight (TOF) PET system, differences in arrival times are also measured, allowing better localization of the annihilation event. Even with imperfect timing information, TOF assists reconstruction and reduces noise (KARP, 2006; KARP et al., 2008).

A.2 Image quality

Various factors can affect the quality of the images produced, including the resolution, attenuation, scattering and statistical noise. Spatial resolution limits the ability to distinguish two point sources, and is normally described using Full Width at Half Maximum (FWHM) (BAILEY et al.). The effect of limiting spatial resolution causes a blurring of the borders within the regions of the image. RANGAYYAN (2004) presents an analysis of blurring, defining the point spread function (PSF) as the image obtained when the input is a point or impulse function. The causes of blurring are due to factors such as the thickness of the scintillation crystal. Further details are provided by BAILEY et al.

Attenuation: Attenuation is a phenomenon that reduces the count rate, as events that occur deep inside the tissue are attenuated more than those that occur in surface tissues owing to the increased chance of interaction before detection.

Compton scattering: Compton scattering can cause a photon to be deviated, resulting in a false detection or the loss of a true detection. The effect of the scattered photons is to produce a drop in the resolution and contrast of the image (BAILEY et al., 2005).

Poisson noise: The quality of an image depends on the number of detected photons contained, however *in vivo* images from NM are photon limited to minimise patient radiation exposure. Typical photon density is of the order 10 mm^{-2} compared to about 10^5 mm^{-2} in radiography. Poisson error forms the minimum noise level in low photon count images, being an error of $n^{\frac{1}{2}}$ for measured counts of n (DENDY; HEATON, 2011). Images with lower noise can also be achieved by administering a larger dose of radiation, increasing the exposure time or using cameras with a greater sensitivity.

Partial volume effect: SORET; BACHARACH; BUVAT (2007) describe the Partial Volume Effect (PVE) as an image artefact which makes intensity values in images differ from their ideal value. It is caused by two distinct phenomena. First of all there is a finite spatial resolution inherent in the instrumentation which causes a spillover between regions. Secondly, since radiotracer distribution is sampled on a voxel grid, the contours of the voxels do not match the

contours of tracer distribution so most voxels contain heterogeneous tissues.

HSIEH (2003) shows that the contrast of an image generated by a phantom decreases due to the PVE as slice thickness increases above the thickness of a phantom; the count generated by the slice becomes 'diluted' by the increasing presence of bordering volumes with zero count. A possible way to avoid the PVE is to decrease the pixel size, but in NM images this has the disadvantage of reducing the count in each pixel and so increasing noise.

DAWOOD (2012) argues that in cardiac motion studies, the PVE becomes prominent, resulting from limited resolution of the scanners. The PVE causes blurring in the image because objects smaller than the scanner resolution limit cannot be delimited accurately. An example in cardiac motion which illustrates the problem is to consider imaging of the heart muscle wall during a complete cycle; since its thickness changes during the cycle, there are phases in which the activity is better resolved, when the muscle is thicker, although the total amount of activity remains constant.

A.3 Acquisition

The clinical evolution of the method of gated SPECT (GSPECT) followed from the development of other technical aspects of instrumentation. The term "gated" refers to an acquisition of signals that is synchronised with a physiological signal, in this case the electrocardiogram (ECG). The gating is implemented using the QRS complex of the ECG signal, in which the R wave corresponds to end-diastole. Gated acquisition requires 8, 16 or 32 projection images to be acquired at each projection angle, with each image corresponding to a specific portion of the cardiac cycle, named a frame (ABIDOV et al., 2013).

Acquisition of images is commonly taken and averaged over hundreds of cardiac cycles, since the detections come from the heart in diverse phases of motion during the cardiac cycle, and the statistic produced in each cycle is too low to form an image with acceptably low noise. The ECG signal allows count from different cycles to be placed within a common phase along the cycle and summed to produce an image with adequate statistic.

Increased interest in GSPECT and its development was partly based on its ability to provide clinically useful measurements of left ventricular ejection fraction (LVEF), volumes and wall motion simultaneously with routine myocardial perfusion results. Commercially available software was developed to perform quantification of perfusion and function, including measurements of systolic and diastolic global function, regional wall thickening and motion, and quantification of parameters such as LV mass, geometry, lung-heart ratio and transient ischemic ratio. Examples of available software are Quantitative gated SPECT (QGS) (Cedars-Sinai Medical Center) (GERMANO et al., 1995; GERMANO et al., 2007), Corridor4DM (University of Michigan, Ann Arbor, MI) (FICARO et al., 2007), and Emory Cardiac Toolbox (ECT) (Emory University, Atlanta, GA) (GARCIA et al., 2007) among others. ABIDOV et al. compares features of these software packages.

Gated PET (GPET) is similarly synchronized to the ECG signal producing gated frames over the cardiac cycle, and the above software is also available for this modality.

APPENDIX B – GROUND TRUTH VELOCITY FIELD FOR A ROTATING CYLINDER

This appendix derives an expression for the ground truth (GT) velocity for a rotating cylinder phantom image. Considering a right circular section through the cylinder, as represented in Figure 71, rotating at constant angular velocity, ω . For a point, $P(x_1, y_1)$, at an angle a above the horizontal and radius r from the centre, the velocity vector, $\vec{v}$ has components (v_x, v_y) . Since the magnitude of the velocity is $|\vec{v}| = \omega r$, the velocity components can be written as $(-\omega r \cos(a), \omega r \sin(a))$. As $r \cos(a) = x_1$ and $r \sin(a) = y_1$ the velocity components can be calculated simply from the position vector from the centre to the required point as shown in Equation B.1.

$$\vec{v} = (-\omega y_1, \omega x_1) \quad (\text{B.1})$$

Figure 71: Calculation of ground truth velocity field for a rotating cylinder

APPENDIX C – HOUGH CIRCLE TRANSFORM AND CLUSTER ANALYSIS

Localisation of the LV is performed using cluster analysis, applied to results generated by the Hough Circle Transform (HCT). This appendix provides details about the HCT and provides a demonstration of the cluster analysis using simulated data, with the same format as that returned by the HCT accumulator.

C.1 Hough Circle Transform

The equation of a circle in Cartesian coordinates is given by Equation C.1, where (x, y) is a point on the circumference, (x_0, y_0) is the centre and r is the radius. The method first determines edge pixels, which are transformed to a three-dimensional parameter space (x_0, y_0, r) . Allowing all values of x_0 and y_0 and positive r produces a right circular cone in the parameter space for each edge pixel, as shown in Figure 72(a). Figure 72(b) shows a subset of 5 possible circles produced for an edge pixel, for a given value of radius. If a set of edge pixels in the image are arranged around a circle with parameters x_0, y_0 and r , the resulting loci of parameters for each point passes through the same point (x_0, y_0, r) in parameter space. This means that the set of right circular cones pertaining to these edge pixels intersect at a common point (BALLARD, 1981).

$$(x - x_0)^2 + (y - y_0)^2 = r^2 \tag{C.1}$$

A three dimensional accumulator matrix is created to contain votes from the various edge

Figure 72: Representation of parameter space for the Hough Circle Transform: (a) a single edge pixel is a right cone in the parameter space (x_0, y_0, r) ; (b) a constant value of r has been taken from (a), which creates the dotted red circle, with centre at (x_0, y_0) . All points on the circumference of this circle are possible circle centres which include (x_0, y_0) on their circumference, and five such possible circles (x_1, y_1) to (x_5, y_5) have been representatively shown.

pixels in the image. The cells which gain the largest votes, or vote above some determined threshold, are taken to be positive circle detections.

C.2 Cluster analysis

Table 16 shows the simulated data, made up of 5 circle detection, each showing position of the centre (x, y) and radius.

Table 16: Simulated HCT accumulator data; five circles are shown, with their corresponding centre point coordinates and radii in pixels.

Circle number	x	y	r
1	7.6380	10.7970	3.0000
2	6.4554	10.4986	3.0000
3	6.3607	6.4495	3.0000
4	13.6929	13.5303	3.0000
5	13.8929	13.7303	4.5000

Plots of these circles are shown in Figure 73a, and cluster analysis on the circle centres produces the dendrogram shown in Figure 73b. The dendrogram can be understood by defining

Figure 73: Cluster analysis: (a) Five circle detections; (b) Corresponding dendrogram, with dotted red line showing cut-off distance at 0.75 pixels.

a minimum cut-off distance to join the circle centres together, in this case 1 pixel, and then studying the clusters created. For this example, circles 4 and 5 are grouped together and circles 1, 2, 3 are in separate groups. Next, the standard deviation of circle radius, Equation 4.1, is applied to each cluster. This shows that cluster (4,5) includes potentially concentric circles due to containing circles of varying radii, whereas the others do not. Table 17 shows the resulting groupings for integer pixel cut-off distances from zero to five, showing grouped circles as being inside parentheses. In the case of the cardiac images, the success of the method depends on finding an optimum value of cut-off, where concentric circles are clustered and false detections excluded.

Table 17: Cluster groups, resulting from applying the cluster analysis with various integer cut-off distances between circle centres to Hough circle detection data in Table 16.

Cut-off distance (pixels)	Groups of centres
0	(4),(5),(1),(2),(3)
1	(4, 5),(1),(2),(3)
2	(4, 5),(1, 2),(3)
3	(4, 5),(1, 2),(3)
4	(4, 5),(1, 2, 3)
5	(4, 5, 1, 2, 3)

APPENDIX D – DHHD IMPLEMENTATION

This appendix provides details of the DHHD implementation used in the proposed study. Savings in processing time were achieved by dividing the calculations into those which could be computed only from the finite element mesh, and those which required the input MVF. Figure 74 shows this division graphically for a 16 frame sequence. The arrangement of the following subsections similarly follows this division of processes into MVF independent D.1, summarised by Figure 75a, and dependent D.2, summarised by Figure 75b.

Figure 74: Processing scheme for DHHD, applied to 16 frame image, showing division into motion field dependent and independent calculations.

D.1 Implementation of the DHHD: Motion field independent

Creation of mesh: Finite element techniques were used to find the CF and DF potentials through calculations on a tetrahedral mesh, encompassing the MVF domain. The mesh is geometrically simple compared to many applications, since the MVF domain is a cuboid, composed of cubes of voxel dimensions. MATLAB (v8.1) tetrahedralisation functions were found to be adequate in this case, although gmsh was also tested and found to perform well; a gmsh

Figure 75: Scheme showing operations and data flow for DHHD: (a) calculations independent of the motion field; (b) calculations dependent on motion field, using mesh data calculated beforehand, and resulting in CF and DF potentials

reference manual can be found online (GEUZAINÉ; REMACLE, 2014). The mesh software produces tetrahedron and node tables.

Let the size of a single frame of the gated volume image sequence be size (L, M, N) voxels. The MVF pertaining to this volume is also of size (L, M, N) . In the mesh, each velocity vector corresponds to a node, making a total of $L \cdot M \cdot N$ nodes. The nodes form the vertices of cubic spaces, so there are $(L - 1) \cdot (M - 1) \cdot (N - 1)$ cubic spaces and, with each cubic space divided into 6 tetrahedra, $6 \cdot (L - 1) \cdot (M - 1) \cdot (N - 1)$ tetrahedrons. Figure 76 shows a 2D representation of the mapping from pixel values to MVF and finally to cubic spaces; here a 2×3 grid of pixels (Figure 76a) is converted to a 2×3 grid of MVF vectors using motion detection (Figure 76b), which for the purpose of meshing is a 1×2 grid of square spaces (Figure 76c), each with a MVF vector on the vertices.

Figure 76: Representative figures showing a 2D grid of pixels and resulting motion field spaces: (a) a 2 by 3 grid of pixels, with representative grey scale values; (b) 2 by 3 grid of motion field vectors; (c) resulting 1 by 2 grid of square spaces, each with 4 motion field vectors on its vertices.

A single cube has 8 nodes, one at each vertex, as shown in Figure 77a. Figure 77b shows a single tetrahedron from the cube, marking the centroid or barycentre ($\vec{\xi}_b$) and Figure 77c shows the result of the MATLAB function meshing a 27 node cubic grid; there are $3 \times 3 \times 3$ nodes,

which produces $2 \times 2 \times 2$ cubes, and results in 48 tetrahedra.

Figure 77: Representative figures showing tetrahedral mesh generation: (a) a single cubic element, composed of 8 nodes, with a motion field vector on each vertex, can be divided into 6 tetrahedra (b) a single tetrahedron, showing the barycentre, $\vec{\xi}_b$; (c) Tetrahedralisation of eight cubic elements, each of edge 4×10^{-3} units, composed of 27 nodes and 48 tetrahedra.

Appendix F.1 shows a tetrahedral mesh generated for a single cubic space, consisting of eight nodes on its vertices, with distance of one between the nodes.

Computation of tetrahedral volumes: For a given cube of nodes, such as that shown in Figure 77(a), the volume of a defined tetrahedron can be calculated from three position vectors, $\vec{a}, \vec{b}, \vec{c}$, beginning at a common vertex and extending to other vertices, using Equation D.1. A program was written to calculate the volume of all possible tetrahedra in a single cubic mesh generated by Delaunay tetrahedralisation, and this value was invariably found to be $\frac{1}{6}$ of the cubic space volume. Appendix E investigates this result in more detail.

$$V = \frac{1}{6} \left| \vec{a} \bullet (\vec{b} \times \vec{c}) \right| \quad (\text{D.1})$$

Calculation of gradient of the basis function table:

Values of $\nabla \phi_{ik}$ were calculated for all node-tetrahedron ($i-k$) pairs in the mesh, according to the formula given in TONG et al., and stored in a table. Further details are given in Appendix F.2.

Generation of list of neighbouring tetrahedra and nodes: Equations described in TONG

et al. for calculating CF and DF potentials are evaluated over tetrahedra neighbouring a given node. Lists were precalculated and stored to provide: (i) the set of tetrahedra which border every node i in the mesh and; (ii) the set of neighbouring nodes, j , which constitute the neighbouring tetrahedra of node i . Further details are given in Appendix F.3, including example calculations based on the mesh presented in Appendix F.1.

Generation of list of boundary condition nodes: Boundary condition nodes are those which lie on the exterior surfaces of the MVF domain. A list of these was generated and stored.

Calculation of centroids of tetrahedra: According to TONG et al., the discrete input vector field must be sampled at the centroid of each tetrahedron. The position of the centroid was computed by averaging the coordinates of the 4 tetrahedron vertices for each tetrahedron in the mesh, leaving the sampling to be performed in *motion field dependent* calculations.

Construction of matrices $[S]$ and $[T]$: The sparse matrices $[S]$ and $[T]$ are required as part of the linear system of equations for computing the CF and DF respectively. $[S]$ is of size $(LMN \text{ by } LMN)$ while $[T]$ is of size $(3LMN \text{ by } 3LMN)$, composed of 3×3 submatrices. Element $[S]_{ij}$ is formed by summing the inner products of $\nabla\phi_{ik}$ for the given node i with $\nabla\phi_{jk}$ for neighbouring node j across all triangles k which include i and j . The 3×3 submatrix block $[R]_{ij}$ is computed in a similar way, but using vector products according to the expression derived in Appendix I. Pseudocode and detailed examples for constructing these matrices, used for testing purposes, are detailed in Sections G.1 and H.1. It can be noted that the matrices are diagonally symmetric, offering reductions in processing time for their calculation.

Although not shown in Figure 75a, it is more efficient to apply the necessary boundary conditions to matrices $[D]$ and $[\vec{R}]$ before saving them, otherwise the boundary conditions will need to be applied to the matrices for each frame. This is only possible since the boundary conditions are zero and $(0,0,0)$ for $[D]$ and $[\vec{R}]$ respectively.

Optimisation of DHHD algorithm: The DHHD algorithm, written in MATLAB, was found to run slowly, even on a high performance machine. Therefore techniques were used to decrease running time.

Critical routines were rewritten using vectorisation, or ported to C/MEX and/or parallel processing. Initial attempts to construct the matrix $[S]$ gave a runtime of 8.5 days for a MVF of size $55 \times 55 \times 55$. C/MEX routines were written for the calculation of the matrix elements and parallel processing used where possible, which allowed construction of $[S]$ in approximately 5 minutes.

D.2 Implementation of the DHHD: Motion field dependent

Calculations dependent on the MVF are shown in Figure 75b. The inputs to the routines are the MVF, $\vec{\xi}$ and the results of MVF independent calculations.

Sampling of MVF at centroid position: The MVF was sampled at the centroid position using tricubic interpolation to produce a list of MVF vectors for each tetrahedron, $\vec{\xi}_k$. Appendix F.4 illustrates this procedure using linear interpolation with the single cubic space mesh and sample velocities shown in Appendix F.1.

Construction of vectors $\{b\}$ and $\{c\}$: Elements of the RHS of the two linear systems, $\{b\}$ and $\{c\}$, are computed for given nodes by summing inner and vector products of $\nabla\phi_{i\ k}$ and $\vec{\xi}_k$ respectively, as presented in (TONG et al., 2003). Pseudocode and detailed examples are given in Sections G.2 and H.2

Application of boundary conditions to linear systems: Zero boundary conditions, as suggested in TONG et al., were applied to the two linear systems, defining boundary nodes as those on the exterior surface of the MVF domain. The purpose of this step is to rearrange the system so that only unknown values are in the LHS solution vector and known values in the RHS vector. Further details can be found in Appendix J.

Solution of linear systems: Linear systems were solved using the iterative Generalized Minimum Residuals (GMRES) algorithm. Ten outer iterations of the algorithm were specified, with a tolerance of 10^{-11} .

Application of boundary conditions to solution vectors: Elements of the solution vector

which pertain to boundary condition nodes are replaced with boundary condition values, which are zero for both systems of equations. Further details can be found in Appendix J.

Assembly of potentials into volumes: The solution vectors are shaped into volumes to produce the scalar potential $[D]$ and $[\vec{R}]$, of sizes LMN and $3LMN$ respectively.

APPENDIX E – TETRAHEDRON VOLUME

This appendix explores the observation that meshing software produces 6 tetrahedra of size $\frac{1}{6}$ for each cubic space in the mesh. To form a tetrahedron from a cube, such as that shown in Figure 77a, four nodes from eight are chosen. The analysis can be simplified by always choosing node 1 as the common vertex, since a symmetric result is obtained for any other choice.

A program was run to calculate the tetrahedron volume resulting from each permutation of vertex positions for a cubic grid with unity spacing. Only three possible volumes of the tetrahedron are produced from the permutations; $|T_k| = 0, \frac{1}{6}, \frac{1}{3}$ with frequencies 36, 168 and 6 respectively. Zero volume tetrahedra are produced when the four nodes are in the same plane, but these are not Delaunay tetrahedra, and would not be generated. The tetrahedra that have volume $\frac{1}{3}$ are all congruent, being produced by two nodes on each of two opposite faces, such as nodes (1,3,6,8) in the figure. If a tetrahedron with volume $\frac{1}{3}$ were chosen, there would be 5 tetrahedra in the cube, a situation which never occurs; the software always choose 6 tetrahedra per cube, each with volume $\frac{1}{6}$.

APPENDIX F – DHHD CALCULATIONS ON A MESH FROM A SINGLE CUBIC SPACE

This appendix contains calculations for testing some of the DHHD routines using a simple mesh consisting of a single cubic space with eight nodes, as shown in Figure 78.

F.1 Calculation of node and tetrahedron tables and test values of velocity

The cubic space was meshed into six tetrahedra by the MATLAB (v8.1) Delaunay tetrahedralisation routine. Calculations were performed by hand and compared to those from software.

Table 18a shows the eight node positions, represented visually in Figure 78a. Node positions on the 3D grid, are ordered by column (y), then row (x), then height (z). Table 18b shows the Delaunay tetrahedralisation of the cubic space, with a single tetrahedron represented in Figure 78b. Representative MVF values were created, corresponding to each node in the node table as shown in Table 18c, where velocities in (x, y, z) are (u, v, w) respectively.

Table 18: Example mesh data, resulting from eight motion field vectors, each placed at the vertex of a cube: (a) Node table. Each vector has a corresponding node value and each node has x,y,z coordinates; (b) Tetrahedron table. The resulting six tetrahedra are defined by four node values; (c) Representative velocity vectors $[u,v,w]$ are defined at each of the eight node positions.

(a)				(b)					(c)			
N	x	y	z	tet	V1	V2	V3	V4	N	u	v	w
1	0	0	0	1	5	1	2	3	1	1	11	21
2	0	1	0	2	6	5	2	3	2	3	13	23
3	1	0	0	3	6	7	5	3	3	2	12	22
4	1	1	0	4	6	4	7	3	4	4	14	24
5	0	0	1	5	6	2	4	3	5	6	16	26
6	0	1	1	6	6	8	7	4	6	8	18	28
7	1	0	1						7	7	17	27
8	1	1	1						8	9	19	29

Figure 78: Node numbers and coordinates used for DHHD examples, marked on an 8 node cube, as given by a motion field of size $2 \times 2 \times 2$ voxels: (a) eight nodes comprising a cube; (b) four nodes (5,1,2,3) comprising tetrahedron 1 in Table 18.

F.2 Calculation of tetrahedral volume and gradient of the basis function table

Values of $\nabla \phi_{ik}$, the gradient of the basis function for node i and tetrahedron k , are computed and stored in a table. The magnitude of $\nabla \phi_{ik}$ is calculated using Equation F.1 (TONG et al., 2003), where a_{ik} is the area vector of the face opposite to node i in the tet T_k , pointing towards i . The calculation of $\nabla \phi_{ik}$ for tet 1 in Table 18 is shown below as an example.

$$|\nabla \phi_{ik}| = \frac{|a_{ik}|}{3|T_k|} \quad (\text{F.1})$$

Tet 1 is composed of vertex nodes 5, 1, 2, 3, meaning that $\nabla\phi_{5\ 1}$, $\nabla\phi_{1\ 1}$, $\nabla\phi_{2\ 1}$, $\nabla\phi_{3\ 1}$ must be computed. To calculate $\nabla\phi_{5\ 1}$, the area of the triangle formed by nodes 1,2,3 in the direction of vertex 5 is required. Two vectors forming the triangle are (0,1,0) and (0,0,1), so the area is given by $\frac{1}{2}(1,0,0) \times (0,1,0) = (0,0,0.5)$. The area vector must point in the direction of vertex 5, or the sense of the vector must be reversed. Since (0,0,0.5) is in the direction of vertex 5, it does not need to be reversed. Since $3|T_k| = 0.5$ ($T_k = \frac{1}{6}$), the resulting value for $\nabla\phi_{5\ 1} = (0,0,1)$. Similarly $\nabla\phi_{1\ 1} = (-1,-1,-1)$, $\nabla\phi_{2\ 1} = (0,1,0)$, and $\nabla\phi_{3\ 1} = (1,0,0)$.

The first row of the table used to store values of $\nabla\phi_{i\ k}$ relates to tetrahedron 1 and is composed of four vectors, each with three components, giving a total of 12 columns. These values are shown below. $\nabla\phi_{(i\ k)\ x}$ is the x component of $\nabla\phi_{i\ k}$, etc. It should be noted that the order of nodes i matches the tetrahedron table, Table 18b.

$$\nabla\phi_{(5\ 1)\ x} \nabla\phi_{(5\ 1)\ y} \nabla\phi_{(5\ 1)\ z} \nabla\phi_{(1\ 1)\ x} \nabla\phi_{(1\ 1)\ y} \nabla\phi_{(1\ 1)\ z} \nabla\phi_{(2\ 1)\ x} \nabla\phi_{(2\ 1)\ y} \nabla\phi_{(2\ 1)\ z} \nabla\phi_{(3\ 1)\ x} \nabla\phi_{(3\ 1)\ y} \nabla\phi_{(3\ 1)\ z}$$

Table 19 shows the six rows of table, corresponding to tetrahedra 1 to 6, all of which were calculated by hand and compared to the output of the program.

Table 19: Table showing gradient of the basis function for the six tetrahedra

tet k=1:	0	0	1	-1	-1	-1	0	1	0	1	0	0
tet k=2:	1	1	1	-1	-1	0	-1	0	-1	1	0	0
tet k=3:	0	1	0	1	0	1	-1	-1	0	0	0	-1
tet k=4:	-1	0	0	1	1	0	1	0	1	-1	-1	-1
tet k=5:	0	0	1	-1	0	-1	1	1	0	0	-1	0
tet k=6:	-1	0	0	1	1	1	0	-1	0	0	0	-1

F.3 Determination of neighbouring tetrahedra and nodes

A list of neighbouring tetrahedra for each node of the mesh was determined, and a list of the neighbouring nodes, which are the nodes belonging to the set of neighbouring tetrahedra, was also determined, which is used to calculate the number of non-zero elements in the sparse matrices. For this latter calculation, the i vectors found were sorted in increasing order, and non-unique values removed.

Table 20 shows the neighbouring tetrahedron and node table for the test data shown in Table 18. The manually generated list was used to test the software.

Table 20: Neighbouring tetrahedra and neighbouring nodes for nodes 1 to 8

Reference node	neighbouring tetrahedra	neighbouring nodes
1	1	1,2,3,5
2	1,2,5	1,2,3,4,5,6
3	1,2,3,4,5	1,2,3,4,5,6,7
4	4,5,6	2,3,4,5,6,7,8
5	1,2,3	1,2,3,5,6,7
6	2,3,4,5,6	2,3,4,5,6
7	3,4,6	2,3,4,6,7,8
8	6	4,6,7,8

F.4 Motion field sampling at tetrahedron centroid

The discrete vector field, ξ , can be calculated by sampling at the centroid of each tetrahedra (TONG et al., 2003). The input vector field is defined only at the vertices of the tetrahedra, so the position of the centroid is first determined, then the sampling performed.

According to Table 18, Tetrahedron 1 has node coordinates (0,0,0), (0,1,0), (1,0,0), (0,0,1) and the centroid is at the average of these vertices, (0.25, 0.25, 0.25). Table 21 shows the centroid coordinates for each tetrahedron.

Table 21: Centroids of tetrahedra

tet	x	y	z
1	0.25	0.25	0.25
2	0.25	0.5	0.5
3	0.5	0.25	0.75
4	0.75	0.5	0.5
5	0.5	0.75	0.25
6	0.75	0.75	0.75

Sampling of the velocity field was first performed using linear interpolation to check the software against hand calculations. Final versions used cubic interpolation for improved accuracy. For example, for tetrahedron 3 the velocity field sampled at (0.5, 0.25, 0.75) was found to be (5.75, 15.75, 25.75) by linear interpolation.

APPENDIX G – DHHD: CALCULATING CURL-FREE POTENTIAL

Equation G.1 (TONG et al.) describes the calculation of the scalar curl-free (CF) potential $[D]$ from the input vector field, $\vec{\xi}_k$ evaluated over the tetrahedral grid, where i is the node number, $\mathcal{N}(i)$ are tetrahedra in the neighbourhood of node i , k is the tetrahedron number, $|T_k|$ is the volume of tetrahedron k , and $\nabla\phi_{i\ k}$ is the gradient of the piecewise linear basis function for tetrahedron k and node i .

$$\forall i \quad \sum_{T_k \in \mathcal{N}(i)} \nabla\phi_{i\ k} \bullet (\nabla D)_k |T_k| = \sum_{T_k \in \mathcal{N}(i)} \nabla\phi_{i\ k} \bullet \vec{\xi}_k |T_k| \quad (\text{G.1})$$

This appendix illustrates the construction of a linear system of equations with a simple example using the eight node mesh in Appendix F.1. To simplify the treatment, the LHS and RHS of Equation G.1 will be treated separately.

G.1 Construction of LHS of Equation G.1

The LHS of Equation G.1 can be rewritten in terms of a matrix $[S]$ and vectorised potential $[D]$, as shown in Equation G.2.

$$\forall i \quad \sum_{T_k \in \mathcal{N}(i)} \nabla\phi_{i\ k} \bullet (\nabla D)_k |T_k| = S \vec{D} |T_k| \quad (\text{G.2})$$

The pseudocode, shown in Listing G-1 summarises the construction of matrix $[S]$. In the listing, N_{nodes} is the total number of nodes in the MVF domain, $N_{neighbourNodes}(i)$ is the number

of neighbouring nodes, j , for the node i .

Listing G-1: Pseudocode for construction of matrix $[S]$

```

 $[S] \leq 0$ , with size  $N_{nodes} \times N_{nodes}$ ,
pre-allocate memory for number of non-zero elements in each row  $i$  of sparse matrix
to contain  $N_{neighbourNodes}$ .

Loop for each node  $i$  in motion field domain
  Loop for each neighbouring tetrahedron,  $k$ , in  $\mathcal{N}(i)$ 
    Loop for each node  $j$ 
       $[S_{ij}] \leq [S_{ij}] + \frac{1}{6} \nabla \phi_{ik} \bullet \nabla \phi_{jk}$ 
    End loop
  End loop
End loop

```

The construction of $[S]$ over the simple mesh shown in Tables 18(a) and 18(b) in Appendix F is shown below, and was used for software testing. The expansion is shown only over nodes $i = 1$ to 3.

$[S]$ is symmetric, since if node j neighbours node i , then node i also neighbours j . For large node numbers $[S]$ is sparse since each row i (corresponding to node i) has non-zero elements only for its set of neighbouring nodes.

Node 1 has one neighbouring tetrahedron, $k=1$, composed of nodes 5,1,2,3.

$$\nabla \phi_{1k} \bullet (\nabla D)_k |T_k| = |T_1| \nabla \phi_{11} \bullet (\nabla \phi_{51} D_5 + \nabla \phi_{11} D_1 + \nabla \phi_{21} D_2 + \nabla \phi_{31} D_3) \quad (G.3)$$

Node 2 has neighbouring tetrahedra $k = 1, 2, 5$.

$$\begin{aligned} \nabla \phi_{2k} \bullet (\nabla D)_k |T_k| &= |T_1| \nabla \phi_{21} \bullet (\nabla \phi_{51} D_5 + \nabla \phi_{11} D_1 + \nabla \phi_{21} D_2 + \nabla \phi_{31} D_3) \\ &\quad + |T_2| \nabla \phi_{22} \bullet (\nabla \phi_{62} D_6 + \nabla \phi_{52} D_5 + \nabla \phi_{22} D_2 + \nabla \phi_{32} D_3) \\ &\quad + |T_5| \nabla \phi_{25} \bullet (\nabla \phi_{65} D_6 + \nabla \phi_{25} D_2 + \nabla \phi_{45} D_4 + \nabla \phi_{35} D_3) \end{aligned} \quad (G.4)$$

Node 3 has neighbouring tetrahedra $k = 1, 2, 3, 4, 5$.

$$\begin{aligned}
 \nabla\phi_{3k} \bullet (\nabla D)_k |T_k| &= |T_1| \nabla\phi_{31} \bullet (\nabla\phi_{51}D_5 + \nabla\phi_{11}D_1 + \nabla\phi_{21}D_2 + \nabla\phi_{31}D_3) \\
 &+ |T_2| \nabla\phi_{32} \bullet (\nabla\phi_{62}D_6 + \nabla\phi_{52}D_5 + \nabla\phi_{22}D_2 + \nabla\phi_{32}D_3) \\
 &+ |T_3| \nabla\phi_{33} \bullet (\nabla\phi_{63}D_6 + \nabla\phi_{73}D_7 + \nabla\phi_{53}D_5 + \nabla\phi_{33}D_3) \quad (G.5) \\
 &+ |T_4| \nabla\phi_{34} \bullet (\nabla\phi_{64}D_6 + \nabla\phi_{44}D_4 + \nabla\phi_{74}D_7 + \nabla\phi_{34}D_3) \\
 &+ |T_5| \nabla\phi_{35} \bullet (\nabla\phi_{65}D_6 + \nabla\phi_{25}D_2 + \nabla\phi_{45}D_4 + \nabla\phi_{35}D_3)
 \end{aligned}$$

Group terms for common i and j values, summing across k to create $[S]_{ij}$. So the first row of $[S]$, corresponding to expansion on node $i=1$, is composed of the following non-zero elements (emitting common factor $|T_k| = \frac{1}{6}$):

$$[S]_{11} = \nabla\phi_{11} \bullet \nabla\phi_{11} = (-1, -1, -1) \bullet (-1, -1, -1) = 3$$

$$[S]_{12} = \nabla\phi_{11} \bullet \nabla\phi_{21} = (-1, -1, -1) \bullet (0, 1, 0) = -1$$

$$[S]_{13} = \nabla\phi_{11} \bullet \nabla\phi_{31} = (-1, -1, -1) \bullet (1, 0, 0) = -1$$

$$[S]_{15} = \nabla\phi_{11} \bullet \nabla\phi_{51} = (-1, -1, -1) \bullet (0, 0, 1) = -1$$

The second row of $[S]$ is composed of the following non-zero elements:

$$[S]_{21} = \nabla\phi_{21} \bullet \nabla\phi_{11} = (0, 1, 0) \bullet (-1, -1, -1) = -1$$

$$[S]_{22} = \nabla\phi_{21} \bullet \nabla\phi_{21} + \nabla\phi_{22} \bullet \nabla\phi_{22} + \nabla\phi_{25} \bullet \nabla\phi_{25} = 5$$

$$[S]_{23} = \nabla\phi_{21} \bullet \nabla\phi_{31} + \nabla\phi_{22} \bullet \nabla\phi_{32} + \nabla\phi_{25} \bullet \nabla\phi_{35} = -1$$

$$[S]_{24} = \nabla\phi_{25} \bullet \nabla\phi_{45} = -1$$

$$[S]_{25} = \nabla\phi_{21} \bullet \nabla\phi_{51} + \nabla\phi_{22} \bullet \nabla\phi_{52} = 1$$

$$[S]_{26} = \nabla\phi_{22} \bullet \nabla\phi_{62} + \nabla\phi_{25} \bullet \nabla\phi_{65} = -3$$

The third row of $[S]$ is composed of the following non-zero elements: $[S]_{31} =$

$$\nabla\phi_{31} \bullet \nabla\phi_{11} = (1, 0, 0) \bullet (-1, -1, -1) = -1$$

$$[S]_{32} = \nabla\phi_{31} \bullet \nabla\phi_{21} + \nabla\phi_{32} \bullet \nabla\phi_{22} + \nabla\phi_{35} \bullet \nabla\phi_{25} = -1$$

$$[S]_{33} = \nabla\phi_{31} \bullet \nabla\phi_{31} + \nabla\phi_{32} \bullet \nabla\phi_{32} + \nabla\phi_{33} \bullet \nabla\phi_{33} + \nabla\phi_{34} \bullet \nabla\phi_{34} + \nabla\phi_{35} \bullet \nabla\phi_{35} = 7$$

$$[S]_{34} = \nabla\phi_{34} \bullet \nabla\phi_{44} + \nabla\phi_{35} \bullet \nabla\phi_{45} = -3$$

$$[S]_{35} = \nabla\phi_{31} \bullet \nabla\phi_{51} + \nabla\phi_{32} \bullet \nabla\phi_{52} + \nabla\phi_{33} \bullet \nabla\phi_{53} = -1$$

$$[S]_{36} = \nabla\phi_{32} \bullet \nabla\phi_{62} + \nabla\phi_{33} \bullet \nabla\phi_{63} + \nabla\phi_{34} \bullet \nabla\phi_{64} + \nabla\phi_{35} \bullet \nabla\phi_{65} = 2$$

$$[S]_{37} = \nabla\phi_{33} \bullet \nabla\phi_{73} + \nabla\phi_{34} \bullet \nabla\phi_{74} = -3$$

Putting these components of $[S_{ij}]$ into matrix $[S]$ gives the partial result shown in Equation G.6:

$$[S] = \frac{1}{6} \begin{bmatrix} 3 & -1 & -1 & 0 & -1 & 0 & 0 & 0 \\ -1 & 5 & -1 & -1 & 1 & -3 & 0 & 0 \\ -1 & -1 & 7 & -3 & -1 & 2 & -3 & 0 \\ \vdots & & & \vdots & & & & \vdots \end{bmatrix} \quad (\text{G.6})$$

To measure the sparsity of the matrix, the number of non-zero matrix elements must be found. In the present case, this can be found by summing all neighbouring nodes over all the reference nodes, which is easily performed from the neighbouring node list, illustrated in Subsection F.3. For the small node numbers considered here, there are a total of 64 elements in $[S]$, of which 45 are non-zero, so the sparsity is about 0.7. However, when the size of the voxel space is increased to $24 \times 26 \times 25$, the resulting matrix S is 15600×15600 , with a total of 2.4336×10^8 elements and 2.19306×10^5 non-zero elements, a sparsity of about 0.0009.

G.2 Construction of RHS of Equation G.1

Listing G-2 shows pseudocode for calculation of the RHS of equation G.1.

Listing G-2: Pseudocode for construction of vector $\{b\}$

$\{b\} \leftarrow 0$. $\{b\}$ initialised to have i elements.

Loop **for** each node i in motion field domain

 Loop **for** each neighbouring tetrahedron, k , in $\mathcal{N}(i)$

 Loop **for** each node, j , in tetrahedron, k

$\{b_i\} \leftarrow \{b_i\} + \frac{1}{6} \nabla\phi_{ik} \bullet \xi_k$

```

End loop
End loop
End loop

```

The right hand side of the equation for calculating the curl-free field is shown below for nodes $i = 1$ and 3.

For node 1 there is one neighbouring tetrahedron, $k=1$.

$$\begin{aligned}
 b_1 &= |T_1| \nabla \phi_{1\ 1} \bullet \vec{\xi}_1 \\
 &= |T_1| (-1, -1, -1) \bullet (3, 13, 23) \\
 &= -\frac{39}{6} \\
 &= -6.5
 \end{aligned}$$

Node 3 has 5 neighbouring tetrahedra, $k=1, 2, 3, 4, 5$.

$$\begin{aligned}
 b_3 &= |T_1| \nabla \phi_{3\ 1} \bullet \vec{\xi}_1 + |T_2| \nabla \phi_{3\ 2} \bullet \vec{\xi}_2 + |T_3| \nabla \phi_{3\ 3} \bullet \vec{\xi}_3 + |T_4| \nabla \phi_{3\ 4} \bullet \vec{\xi}_4 + |T_5| \nabla \phi_{3\ 5} \bullet \vec{\xi}_5 \\
 &= \frac{1}{6} \{ (1, 0, 0) \bullet (3, 13, 23) + (1, 0, 0) \bullet (4.75, 14.75, 24.75) \\
 &\quad + (0, 0, -1) \bullet (5.75, 15.75, 25.75) + (-1, -1, -1) \bullet (5.25, 15.25, 25.25) \\
 &\quad + (0, -1, 0) \bullet (4.25, 14.25, 24.25) \} \\
 &= -13
 \end{aligned}$$

APPENDIX H – DHHD: CALCULATING DIVERGENCE-FREE POTENTIAL

Equation H.1 (TONG et al., 2003) describes the calculation of the vector divergence-free potential $[\vec{R}]$ from the input vector field, $\vec{\xi}_k$, evaluated over a tetrahedral grid, where i is the node number, $\mathcal{N}(i)$ are tetrahedra in the neighbourhood of node i , k is the tetrahedron number, $|T_k|$ is the volume of tetrahedron k , and $\nabla\phi_{ik} = \begin{pmatrix} \partial_x\phi_{ik} & \partial_y\phi_{ik} & \partial_z\phi_{ik} \end{pmatrix}$ is the gradient of the piecewise linear basis function for tet k and node i , with $\partial_x\phi_{ik} = \frac{\partial}{\partial x}\phi_{ik}$.

$$\forall i \quad \sum_{T_k \in \mathcal{N}(i)} \nabla\phi_{ik} \times (\nabla \times \vec{W})_k |T_k| = \sum_{T_k \in \mathcal{N}(i)} \nabla\phi_{ik} \times \vec{\xi}_k |T_k| \quad (\text{H.1})$$

This appendix illustrates the construction of a linear system of equations with an example using the eight node mesh in Appendix F.1. To simplify the treatment, the LHS and RHS of Equation H.1 are considered separately.

H.1 Construction of LHS of Equation H.1

The potential, $[\vec{R}]$, can be expressed as a sum of linear basis functions (TONG et al., 2003), as shown in Equation H.2.

$$\nabla \times \left(\sum_i \phi_i \vec{R}_i \right) = \sum_i (\nabla\phi_i \times \vec{R}_i) \quad (\text{H.2})$$

The LHS of Equation H.2 can be written as shown in Equation H.3, where $[T]$ is a matrix

calculated from the mesh, j is a counter over the nodes of each tetrahedron and $\vec{R}$ is a vectorised version of the divergence-free potential, evaluated at each node. TONG et al. does not indicate how to construct the linear system.

$$\forall i \sum_{T_k \in \mathcal{N}(i)} \nabla \phi_{ik} \times \sum_{j=1}^4 (\nabla \phi_j \times \vec{R}_j)_k |T_k| = T \vec{R} \quad (\text{H.3})$$

The double cross product terms $\nabla \phi_{ik} \times \nabla \phi_{jk} \times \vec{R}_j$, can be expressed as a matrix product, $[B_{ik}][C_{jk}]\vec{R}$, where $\vec{R}$ is the vectorised form of the DF vector potential to be calculated. Appendix I derives an expression for $[B_{ik}][C_{jk}]$. Equation H.4 provides the result of this product, $[A_{ij}^k] = [B_{ik}][C_{jk}]$. The double cross product then reduces to the linear system shown in Equation H.5.

$$A_{ij}^k = \begin{pmatrix} -(\partial y(\phi_{ik}) \partial y(\phi_{jk}) & \partial y(\phi_{ik}) \partial x(\phi_{jk}) & \partial z(\phi_{ik}) \partial x(\phi_{jk}) \\ + \partial z(\phi_{ik}) \partial z(\phi_{jk})) & & \\ \partial x(\phi_{ik}) \partial y(\phi_{jk}) & -(\partial x(\phi_{ik}) \partial x(\phi_{jk}) & \partial z(\phi_{ik}) \partial y(\phi_{jk}) \\ + \partial z(\phi_{ik}) \partial z(\phi_{jk})) & & \\ \partial x(\phi_{ik}) \partial z(\phi_{jk}) & \partial y(\phi_{ik}) \partial z(\phi_{jk}) & -(\partial x(\phi_{ik}) \partial x(\phi_{jk}) \\ + \partial y(\phi_{ik}) \partial y(\phi_{jk})) & & \end{pmatrix} \quad (\text{H.4})$$

$$\nabla \phi_{ik} \times \nabla \phi_{jk} \times \vec{R} = A_{ij}^k \begin{pmatrix} r_x \\ r_y \\ r_z \end{pmatrix} \quad (\text{H.5})$$

The pseudocode, shown in Listing H-1 summarises the construction of matrix $[T]$. In the listing, N_{nodes} is the total number of nodes in the MVF domain, $N_{neighbourNodes}(i)$ is the number of neighbouring nodes, j , for the node i . $[T_{ij}]$ is a 3×3 submatrix.

Listing H-1: Pseudocode for construction of matrix $[T]$

$[T] \leq 0$, with size $3N_{nodes} \times 3N_{nodes}$,

pre-allocate memory **for** number of non-zero elements in each row i of sparse matrix to contain $9N_{\text{neighbourNodes}}(i)$.

```

Loop for each node  $i$  in motion field domain
  Loop for each neighbouring tetrahedron,  $k$ , in  $\mathcal{N}(i)$ 
    Loop for each node  $j$ 
       $[T_{ij}] \leftarrow [T_{ij}] + \frac{1}{6}A_{ij}^k$ 
    End loop
  End loop
End loop

```

In the following example, the first six rows of $[T]$ corresponding to $i = 1, 2$ are computed for the mesh shown in Table 18a and 18b.

Node 1 has one neighbouring tetrahedron, $k=1$, composed of nodes 5,1,2,3.

$$\begin{aligned}
 \nabla\phi_{1\ 1} \times (\nabla \times \vec{R})_k |T_k| &= |T_1| \nabla\phi_{1\ 1} \times (\nabla\phi_{5\ 1} \times \vec{R}_5 + \nabla\phi_{1\ 1} \times \vec{R}_1 + \nabla\phi_{2\ 1} \times \vec{R}_2 + \nabla\phi_{3\ 1} \times \vec{R}_3) \\
 &= |T_1| (A_{15}^{k=1} R_5 + A_{11}^{k=1} R_1 + A_{12}^{k=1} R_2 + A_{13}^{k=1} R_3)
 \end{aligned} \tag{H.6}$$

To evaluate $A_{15}^{k=1}$, use $\nabla\phi_{1\ 1} = (-1, -1, -1)$ and $\nabla\phi_{5\ 1} = (0, 0, 1)$ to produce:

$$A_{15}^{k=1} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ -1 & -1 & 0 \end{bmatrix} \tag{H.7}$$

$A_{11}^{k=1}$, uses $\nabla\phi_{1\ 1} = (-1, -1, -1)$ and $\nabla\phi_{1\ 1} = (-1, -1, -1)$ to produce:

$$A_{11}^{k=1} = \begin{bmatrix} -2 & 1 & 1 \\ 1 & -2 & 1 \\ 1 & 1 & -2 \end{bmatrix} \tag{H.8}$$

$A_{12}^{k=1}$, uses $\nabla\phi_{1\ 1} = (-1, -1, -1)$ and $\nabla\phi_{2\ 1} = (0, 1, 0)$ to produce:

$$A_{12}^{k=1} = \begin{bmatrix} 1 & 0 & 0 \\ -1 & 0 & -1 \\ 0 & 0 & 1 \end{bmatrix} \tag{H.9}$$

$A_{13}^{k=1}$, uses $\nabla\phi_{11} = (-1, -1, -1)$ and $\nabla\phi_{21} = (0, 1, 0)$ to produce:

$$A_{13}^{k=1} = \begin{bmatrix} 0 & -1 & -1 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} \quad (\text{H.10})$$

Node 2: has three neighbouring tetrahedra, $k=1,2,5$ which is composed of nodes $\{5,1,2,3\}$, $\{6,5,2,3\}$, $\{6,2,4,3\}$.

$$\begin{aligned} & \nabla\phi_{21} \times (\nabla \times \vec{R})_1 |T_1| + \nabla\phi_{22} \times (\nabla \times \vec{R})_2 |T_2| + \nabla\phi_{25} \times (\nabla \times \vec{R})_5 |T_5| \\ &= |T_1| (A_{25}^{k=1} \vec{R}_5 + A_{21}^{k=1} \times \vec{R}_1 + A_{22}^{k=1} \times \vec{R}_2 + A_{23}^{k=1} \times \vec{R}_3) \\ &+ |T_2| (A_{26}^{k=2} \vec{R}_6 + A_{25}^{k=2} \times \vec{R}_5 + A_{22}^{k=2} \times \vec{R}_2 + A_{23}^{k=2} \times \vec{R}_3) \\ &+ |T_5| (A_{26}^{k=5} \vec{R}_6 + A_{22}^{k=5} \times \vec{R}_2 + A_{24}^{k=5} \times \vec{R}_4 + A_{23}^{k=5} \times \vec{R}_3) \end{aligned} \quad (\text{H.11})$$

In a similar way to node 1, values of A_{ij}^k are shown below, evaluated tetrahedron by tetrahedron on each line.

$$A_{25}^{k=1} = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix}, A_{21}^{k=1} = \begin{bmatrix} -1 & 1 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & -1 \end{bmatrix}, A_{22}^{k=1} = \begin{bmatrix} -1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & -1 \end{bmatrix}, A_{23}^{k=1} = \begin{bmatrix} 0 & 1 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad (\text{H.12})$$

$$A_{26}^{k=2} = \begin{bmatrix} 1 & 0 & -1 \\ -1 & 2 & -1 \\ -1 & 0 & 1 \end{bmatrix}, A_{25}^{k=2} = \begin{bmatrix} 0 & 0 & 1 \\ 1 & -1 & 1 \\ 0 & 0 & -1 \end{bmatrix}, A_{22}^{k=2} = \begin{bmatrix} -1 & 0 & 1 \\ 0 & -2 & 0 \\ 1 & 0 & -1 \end{bmatrix}, A_{23}^{k=2} = \begin{bmatrix} 0 & 0 & -1 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} \quad (\text{H.13})$$

$$A_{26}^{k=5} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ -1 & 0 & 0 \end{bmatrix}, A_{22}^{k=5} = \begin{bmatrix} -1 & 0 & 1 \\ 0 & -2 & 0 \\ 1 & 0 & -1 \end{bmatrix}, A_{24}^{k=5} = \begin{bmatrix} 0 & 0 & -1 \\ -1 & 1 & -1 \\ 0 & 0 & 1 \end{bmatrix}, A_{23}^{k=5} = \begin{bmatrix} 0 & 0 & 0 \\ 1 & 0 & 1 \\ 0 & 0 & 0 \end{bmatrix} \quad (\text{H.14})$$

Having computed the terms for nodes 1 and 2, (3×3) submatrices are summed for pairs (i, j) across tetrahedra, k . For matrices corresponding to node 1, there is only one tetrahedron, so there are no summations to perform. Thus, $\sum_k A_{15} = A_{15}^{k=1}$, $\sum_k A_{11} = A_{11}^{k=1}$, $\sum_k A_{12} = A_{12}^{k=1}$, $\sum_k A_{13} = A_{13}^{k=1}$.

Node 2 has multiple submatrices for node pairs i and j , which are summed.

$$\sum_k A_{21} = A_{21}^{k=1} = \begin{bmatrix} -1 & 1 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & -1 \end{bmatrix} \quad (\text{H.15})$$

$$\sum_k A_{22} = A_{22}^{k=1} + A_{22}^{k=2} + A_{22}^{k=5} = \begin{bmatrix} -3 & 0 & 2 \\ 0 & -4 & 0 \\ 2 & 0 & -1 \end{bmatrix} \quad (\text{H.16})$$

$$\sum_k A_{23} = A_{23}^{k=1} + A_{23}^{k=2} + A_{23}^{k=5} = \begin{bmatrix} 0 & 1 & -1 \\ 1 & 1 & 1 \\ 0 & 0 & 1 \end{bmatrix} \quad (\text{H.17})$$

$$\sum_k A_{24} = A_{24}^{k=5} = \begin{bmatrix} 0 & 0 & -1 \\ -1 & 1 & -1 \\ 0 & 0 & 1 \end{bmatrix} \quad (\text{H.18})$$

$$\sum_k A_{25} = A_{25}^{k=1} + A_{25}^{k=2} = \begin{bmatrix} 0 & 0 & 1 \\ 1 & -1 & 1 \\ 0 & 1 & -1 \end{bmatrix} \quad (\text{H.19})$$

$$\sum_k A_{26} = A_{26}^{k=2} + A_{26}^{k=5} = \begin{bmatrix} 2 & 0 & -1 \\ -1 & 3 & -1 \\ -2 & 0 & 1 \end{bmatrix} \quad (\text{H.20})$$

$[T]$ is constructed using submatrices summed across tetrahedrons, as shown in Equations H.21 and H.22. Here $[A_{ij}] = \sum_k A_{ij}$.

$$T = \begin{bmatrix} [A_{11}] & [A_{12}] & [A_{13}] & [A_{14}] & [A_{15}] & [A_{16}] & [A_{17}] & [A_{18}] \\ [A_{21}] & [A_{22}] & [A_{23}] & [A_{24}] & [A_{25}] & [A_{26}] & [A_{27}] & [A_{28}] \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \end{bmatrix} \quad (\text{H.21})$$

$$T = \frac{1}{6} \begin{bmatrix} -2 & 1 & 1 & 1 & 0 & 0 & 0 & -1 & -1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 2 & 1 & -1 & 0 & -1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -2 & 1 & 1 & 0 & 0 & 1 & 0 & 0 & 1 & 0 & 0 & 0 & -1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -1 & 1 & 0 & -3 & 0 & 2 & 0 & 1 & -1 & 0 & 0 & -1 & 0 & 0 & 1 & 2 & 0 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -4 & 0 & 1 & 1 & 1 & -1 & 1 & -1 & 1 & -1 & 1 & -1 & 3 & -1 & 0 & 0 & 0 & 0 \\ 0 & 1 & -1 & 2 & 0 & -1 & 0 & 0 & 1 & 0 & 0 & 1 & 0 & 1 & -1 & -2 & 0 & 1 & 0 & 0 & 0 & 0 \\ \vdots & & & \vdots & & \vdots & & \vdots & & \vdots & & \vdots & & \vdots & & \vdots & & \vdots & & \vdots & & \vdots \end{bmatrix} \quad (\text{H.22})$$

When vectorised, $[\vec{R}]$ is written according to Equation H.23.

$$\begin{bmatrix} r_{1x} & r_{1y} & r_{1z} & r_{2x} & r_{2y} & r_{2z} & \dots & r_{8x} & r_{8y} & r_{8z} \end{bmatrix}^T \quad (\text{H.23})$$

H.2 Construction of RHS of Equation H.1

Listing H-2 shows pseudocode for calculation of the RHS of equation H.1.

Listing H-2: Pseudocode for construction of vector $\{c\}$

```
{c} <= 0. {c} initialised to have 3i elements.
```

```
Loop for each node i in motion field domain
```

```
    Loop for each neighbouring tetrahedron, k, in  $\mathcal{N}(i)$ 
```

```

Loop for each node, j, in tetrahedron, k
    {ci} <= {ci} +  $\frac{1}{6} \nabla \phi_{ik} \times \xi_k$ 
End loop
End loop
End loop

```

The RHS of Equation H.1 constructs the vector, $\{c\}$ from cross product values calculated on tetrahedra adjacent to a node. Velocity data from Table 18(c) is used to illustrate the calculations.

For node 1, there is one tetrahedron, $k = 1$.

$$\begin{aligned}
 c_1 &= |T_1| \nabla \phi_{11} \times \vec{\xi}_1 = \frac{1}{6} (-1, -1, -1) \times (3, 13, 23) \\
 &= \frac{1}{6} \begin{vmatrix} \vec{i} & \vec{j} & \vec{k} \\ -1 & -1 & -1 \\ 3 & 13 & 23 \end{vmatrix} \\
 &= \frac{1}{6} (-10, -20, -10)
 \end{aligned} \tag{H.24}$$

Node 2 has three neighbouring tetrahedra, $k = 1, 2, 5$.

$$\begin{aligned}
 c_2 &= \frac{1}{6} (\nabla \phi_{21} \times \vec{\xi}_1 + \nabla \phi_{22} \times \vec{\xi}_2 + \nabla \phi_{25} \times \vec{\xi}_5) \\
 &= \frac{1}{6} ((0, 1, 0) \times (3, 13, 23) + (-1, 0, -1) \times (4.75, 14.75, 24.75) \\
 &\quad + (-1, 0, -1) \times (4.25, 14.25, 24.25)) \\
 &= \frac{1}{6} (-10, -20, -10)
 \end{aligned} \tag{H.25}$$

The coefficients of vector $\{c\}$ are stored as shown in Equation H.26, producing the vector $\frac{1}{6}[-10, -20, -10, -10, -20, -10, \dots]$.

$$\begin{bmatrix} c_{1x} & c_{1y} & c_{1z} & c_{2x} & c_{2y} & c_{2z} & \dots & c_{8x} & c_{8y} & c_{8z} \end{bmatrix}^T \tag{H.26}$$

APPENDIX I – EXPRESSING THE VECTOR TRIPLE PRODUCT IN MATRIX FORM

Expansion of the divergence-free potential on the tetrahedral mesh produces terms with a vector triple product, as shown in Equation I.1, where $\nabla\phi_{i\ k}$ and $\nabla\phi_{j\ k}$ are gradients of the basis function for nodes i and j on tetrahedron k and r_j the vector divergence-free potential. This appendix derives an expression which can be used for rewriting Equation I.1 as a matrix product, allowing a linear system to be constructed and values of r_j to be found. The expression is derived for a pair of vectors at a single node of the mesh; the global matrix can then be constructed as shown in TONG et al. (2003).

$$\nabla\phi_{i\ k} \times \nabla\phi_{j\ k} \times \{r_j\} \quad (\text{I.1})$$

First derive an expression for the cross product of two arbitrary vectors in 3D, $\{p\}$ and $\{q\}$, in terms of a matrix $[P]$, as shown in Equation I.2.

$$\begin{aligned} \{p\} \times \{q\} &= \begin{pmatrix} p_2q_3 - p_3q_2 & p_3q_1 - p_1q_3 & p_1q_2 - p_2q_1 \end{pmatrix} \\ &= \begin{pmatrix} 0 & p_3 & -p_2 \\ -p_3 & 0 & p_1 \\ p_2 & -p_1 & 0 \end{pmatrix} \begin{pmatrix} q_1 \\ q_2 \\ q_3 \end{pmatrix} \\ &= [P]\{q\} \end{aligned} \quad (\text{I.2})$$

Next rewrite Equation I.1 for a node pair i and j . Let $\{b\} = \nabla\phi_{i\ k}$ and $\{c\} = \nabla\phi_{j\ k}$, with the divergence-free potential produced only for i and j , $\{r\}$. Then using Equation I.2 the vector triple product can be expressed as shown in Equation I.3

$$\begin{aligned} (\{b\} \times \{c\}) \times \{r\} &= [B]\{c\} \times \{r\} = [B](\{c\} \times \{r\}) \\ &= [B][C]\{r\} \end{aligned} \quad (\text{I.3})$$

Writing $\nabla\phi_{i\ k}$ as $\begin{pmatrix} \partial x\phi_{ik} & \partial y\phi_{ik} & \partial z\phi_{ik} \end{pmatrix}$, where $\partial x\phi_{ik} = \frac{\partial}{\partial x}\phi_{ik}$, etc., and using Equation I.3, Equation I.1 can be expressed as the product of two matrices, $[B_{ik}]$ and $[C_{jk}]$, as shown in Equation I.4. $[B_{ik}]$ and $[C_{jk}]$ are shown in Equations I.5 and I.6.

$$\nabla\phi_{i\ k} \times \nabla\phi_{j\ k} \times \{r\} = [B_{ik}][C_{jk}] \begin{pmatrix} r_x & r_y & r_z \end{pmatrix}^T \quad (\text{I.4})$$

$$[B_{ik}] = \begin{pmatrix} 0 & \partial z\phi_{ik} & -\partial y\phi_{ik} \\ -\partial z\phi_{ik} & 0 & \partial x\phi_{ik} \\ \partial y\phi_{ik} & -\partial x\phi_{ik} & 0 \end{pmatrix} \quad (\text{I.5})$$

$$[C_{jk}] = \begin{pmatrix} 0 & \partial z\phi_{jk} & -\partial y\phi_{jk} \\ -\partial z\phi_{jk} & 0 & \partial x\phi_{jk} \\ \partial y\phi_{jk} & -\partial x\phi_{jk} & 0 \end{pmatrix} \quad (\text{I.6})$$

APPENDIX J – APPLICATION OF BOUNDARY CONDITIONS TO LINEAR SYSTEMS

This appendix describes the application of boundary conditions to the linear systems, necessary for obtaining: (i) the curl-free scalar potential, $\{d\}$; (ii) the divergence-free vector potential, $\{r\}$.

The uniqueness of the DHHD requires the application of proper boundary conditions, and in this case $\nabla\{d\}$ must be normal to the boundary and $\nabla \times \vec{r}$ must be tangential to it (TONG et al. (2003)). Boundary nodes in this situation are the set of nodes on the external surface of the domain.

J.1 Applying boundary conditions to the curl-free linear system

When the linear system is constructed, the scalar CF potential, $\{d\}$, is known for all nodes on the boundary (using conditions given by TONG et al., these values are chosen to be zero), and unknown for all nodes inside the boundary. The opposite is true for $\{b\}$, which is unknown on the boundary and known inside the boundary. Applying boundary condition requires a rearrangement of terms so that the LHS contains all unknown quantities and the RHS all known.

Write the linear system $[S]\{d\} = \{b\}$ as $[S]\{d\} = [I]\{b\}$ in terms of its elements, where $[I]$ is

the identity matrix.

$$\begin{pmatrix} s_{11} & s_{12} & s_{13} & s_{14} & s_{15} & \dots \\ s_{21} & s_{22} & s_{23} & s_{24} & s_{25} & \\ s_{31} & s_{32} & s_{33} & s_{34} & s_{35} & \\ s_{41} & s_{42} & s_{43} & s_{44} & s_{45} & \\ s_{51} & s_{52} & s_{53} & s_{54} & s_{55} & \dots \\ \vdots & & & \vdots & \ddots & \end{pmatrix} \begin{pmatrix} d_1 \\ d_2 \\ d_3 \\ d_4 \\ d_5 \\ \vdots \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & \dots \\ 0 & 1 & 0 & 0 & 0 & \\ 0 & 0 & 1 & 0 & 0 & \\ 0 & 0 & 0 & 1 & 0 & \\ 0 & 0 & 0 & 0 & 1 & \dots \\ \vdots & & \vdots & \ddots & & \end{pmatrix} \begin{pmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \\ b_5 \\ \vdots \end{pmatrix} \quad (\text{J.1})$$

Imagine that nodes 1 and 4 are on the external boundary of the volume (i.e. subject to boundary conditions) and nodes 2,3,5 are not on the boundary (i.e. not subject to boundary conditions). Then d_1, b_2, b_3, d_4, b_5 are knowns and b_1, d_2, d_3, b_4, d_5 are unknowns. The boundary conditions are chosen to be zero.

In order to solve the system, it must be rearranged so that all unknowns are on the LHS and knowns on the RHS. Columns of each matrix and their corresponding vector component can be equated as shown in Equation J.2 and J.3:

$$\begin{pmatrix} s_{11} & s_{21} & s_{31} & s_{41} & s_{51} \end{pmatrix}^t d_1 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \end{pmatrix}^t b_1 \quad (\text{J.2})$$

$$\begin{pmatrix} s_{14} & s_{24} & s_{34} & s_{44} & s_{54} \end{pmatrix}^t d_4 = \begin{pmatrix} 0 & 0 & 0 & 1 & 0 \end{pmatrix}^t b_4 \quad (\text{J.3})$$

Swapping the equations leads to the linear system shown in Equation J.4, where unknowns are on the LHS and knowns on the RHS.

$$\begin{pmatrix} -1 & s_{12} & s_{13} & 0 & s_{15} & \dots \\ 0 & s_{22} & s_{23} & 0 & s_{25} & \\ 0 & s_{32} & s_{33} & 0 & s_{35} & \\ 0 & s_{42} & s_{43} & -1 & s_{45} & \\ 0 & s_{52} & s_{53} & 0 & s_{55} & \\ \vdots & & & & & \end{pmatrix} \begin{pmatrix} b_1 \\ d_2 \\ d_3 \\ b_4 \\ d_5 \\ \vdots \end{pmatrix} = \begin{pmatrix} -s_{11} & 0 & 0 & -s_{14} & 0 \\ -s_{21} & 1 & 0 & -s_{24} & 0 \\ -s_{31} & 0 & 1 & -s_{34} & 0 \\ -s_{41} & 0 & 0 & -s_{44} & 0 \\ -s_{51} & 0 & 0 & -s_{54} & 1 \end{pmatrix} \begin{pmatrix} d_1 \\ b_2 \\ b_3 \\ d_4 \\ b_5 \\ \vdots \end{pmatrix} \quad (\text{J.4})$$

Since boundary condition elements d_1 and d_4 are chosen as zero, the system reduces to:

$$\begin{pmatrix} -1 & s_{12} & s_{13} & 0 & s_{15} & \dots \\ 0 & s_{22} & s_{23} & 0 & s_{25} & \\ 0 & s_{32} & s_{33} & 0 & s_{35} & \\ 0 & s_{42} & s_{43} & -1 & s_{45} & \\ 0 & s_{52} & s_{53} & 0 & s_{55} & \\ \vdots & & & & & \end{pmatrix} \begin{pmatrix} b_1 \\ d_2 \\ d_3 \\ b_4 \\ d_5 \\ \vdots \end{pmatrix} = \begin{pmatrix} 0 \\ b_2 \\ b_3 \\ 0 \\ b_5 \\ \vdots \end{pmatrix} \quad (\text{J.5})$$

The solution of this linear system is a vector of mixed components from $\{d\}$ and $\{b\}$. $\{d\}$ can be obtained by replacing the elements of $\{b\}$ in the solution vector with zeros, b_1 and b_4 in this case.

J.2 Applying boundary conditions to the divergence-free linear system

A similar procedure is used to apply boundary conditions for the DF linear system, but here $[T]\{r\} = \{c\}$ represents a vector system instead of scalars. The matrix $[T]$ is composed of 3×3 submatrices, $[A_{ij}^k]$ and the vectors $\{r\}$ and $\{c\}$ composed of vector elements $\begin{pmatrix} r_1^x & r_1^y & r_1^z & \dots & r_n^x & r_n^y & r_n^z \end{pmatrix}^t$ and $\begin{pmatrix} c_1^x & c_1^y & c_1^z & \dots & c_n^x & c_n^y & c_n^z \end{pmatrix}^t$, which are written as $\begin{pmatrix} \{r_1\} & \{r_2\} & \{r_3\} & \dots & \{r_n\} \end{pmatrix}^t$ and $\begin{pmatrix} \{c_1\} & \{c_2\} & \{c_3\} & \dots & \{c_n\} \end{pmatrix}^t$ to simplify notation, where n is the total number of nodes.

In this case $[I]$ is used to represent a 3×3 identity matrix and $[0]$ is a 3×3 block matrix of zeros and the linear system can be written as shown in J.6.

$$\begin{pmatrix} [A_{11}] & [A_{12}] & [A_{13}] & \dots \\ [A_{21}] & [A_{22}] & [A_{23}] & \\ [A_{31}] & [A_{32}] & [A_{33}] & \\ \vdots & & & \end{pmatrix} \begin{pmatrix} \{r_1\} \\ \{r_2\} \\ \{r_3\} \\ \vdots \end{pmatrix} = \begin{pmatrix} [I] & [0] & [0] & \dots \\ [0] & [I] & [0] & \\ [0] & [0] & [I] & \\ \vdots & & & \end{pmatrix} \begin{pmatrix} \{c_1\} \\ \{c_2\} \\ \{c_3\} \\ \vdots \end{pmatrix} \quad (\text{J.6})$$

Imagine this time that node 2 is a boundary node and that 1 and 3 are free. All boundary nodes have vector potential (0,0,0), which is represented as $\{0\}$ in the following equations. Equation J.6 is rearranged to put unknown on the LHS, creating Equation J.7, which simplifies

to J.8 since $\{r_2\} = \{0\}$.

$$\begin{pmatrix} [A_{11}] & [0] & [A_{13}] & \dots \\ [A_{21}] & [-I] & [A_{23}] & \\ [A_{31}] & [0] & [A_{33}] & \\ \vdots & & & \end{pmatrix} \begin{pmatrix} \{r_1\} \\ \{c_2\} \\ \{r_3\} \\ \vdots \end{pmatrix} = \begin{pmatrix} [I] & -[A_{12}] & [0] & \dots \\ [0] & -[A_{22}] & [0] & \\ [0] & -[A_{32}] & [I] & \\ \vdots & & & \end{pmatrix} \begin{pmatrix} \{c_1\} \\ \{r_2\} \\ \{c_3\} \\ \vdots \end{pmatrix} \quad (\text{J.7})$$

$$\begin{pmatrix} [A_{11}] & [0] & [A_{13}] & \dots \\ [A_{21}] & [-I] & [A_{23}] & \\ [A_{31}] & [0] & [A_{33}] & \\ \vdots & & & \end{pmatrix} \begin{pmatrix} \{r_1\} \\ \{c_2\} \\ \{r_3\} \\ \vdots \end{pmatrix} = \begin{pmatrix} \{c_1\} \\ \{0\} \\ \{c_3\} \\ \vdots \end{pmatrix} \quad (\text{J.8})$$

The solution vector is a mixture of elements in $\{r\}$ and $\{c\}$, and to obtain the DF potential from the solution to the linear system, the calculated values of $\{c\}$ must be replaced with the boundary conditions, in this case the zero vector.

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