Poul M. F. Nielsen · Martyn P. Nash ·
Xinshan Li · Karol Miller ·
Adam Wittek *Editors*

Computational Biomechanics for Medicine

Towards Translation and Better Patient Outcomes

Springer

Computational Biomechanics for Medicine

Poul M. F. Nielsen · Martyn P. Nash · Xinshan Li ·
Karol Miller · Adam Wittek
Editors

Computational Biomechanics for Medicine

Towards Translation and Better Patient Outcomes

Springer

Editors
Poul M. F. Nielsen
Auckland Bioengineering Institute
University of Auckland
Auckland, New Zealand

Xinshan Li
Department of Mechanical Engineering
University of Sheffield
Sheffield, UK

Adam Wittek
Intelligent Systems for Medicine
Laboratory
The University of Western Australia
Perth, WA, Australia

Martyn P. Nash
Auckland Bioengineering Institute
University of Auckland
Auckland, New Zealand

Karol Miller
Intelligent Systems for Medicine
Laboratory
The University of Western Australia
Perth, WA, Australia

ISBN 978-3-031-09326-5 ISBN 978-3-031-09327-2 (eBook)
https://doi.org/10.1007/978-3-031-09327-2

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Computational biomechanics exploits our knowledge of physics and physiological and biological processes, to enable quantitative predictions of outcomes resulting from the complex interactions that occur in living systems. Biomechanical models increasingly provide valuable tools to improve the diagnosis, treatment, and monitoring of many diseases, as well as enhancing our understanding of how healthy bodies function.

The first volume in the Computational Biomechanics for Medicine book series was published in 2010. Since then, the book has become an annual forum for specialists in computational sciences to describe their latest results and discuss the application of their techniques to computer-integrated medicine. The twelfth volume in the Computational Biomechanics for Medicine book series comprises fifteen of the latest developments in continuum biomechanics and patient-specific computations, by researchers from New Zealand, Australia, Serbia, Denmark, France, the United Kingdom, Argentina, and the United States of America. Topics covered in this book include:

- Tissue biomechanics;
- Patient-specific modelling;
- Vessel fluid mechanics;
- Biomedical instrumentation;
- Medical image analysis.

The Computational Biomechanics for Medicine book series provides the community with the most up-to-date source of information for both researchers and practitioners.

Auckland, New Zealand — Poul M. F. Nielsen
Auckland, New Zealand — Martyn P. Nash
Perth, Australia — Karol Miller
Perth, Australia — Adam Wittek
Sheffield, UK — Xinshan Li

The original version of this chapter has been revised. "All authors contributed equally to the manuscript" has been incorporated in Chapter https://doi.org/10.1007/978-3-031-09327-2_4

Contents

Solid Mechanics

Towards Accurate Measurement of Abdominal Aortic Aneurysm Wall Thickness from CT and MRI

Andy T. Huynh and Karol Miller

Abstract Abdominal Aortic Aneurysm (AAA) is the focal dilation or widening of the infrarenal artery. It is a vascular disease commonly found in older adults with prevalence increasing steadily with age. The disease is often discovered by unrelated medical examinations and screenings due to its asymptomatic nature. People unaware of their condition may only find out after the catastrophic event of a ruptured AAA, where most patients will not survive if left untreated. The current clinical rupture risk indicator for AAA repair is a AAA diameter exceeding 5.5 cm. There are many limitations with the clinical rupture risk indicator due to its derivation coming from population statistics and not patient-specific circumstances. Computation of AAA wall stress using three-dimensional (3D) reconstructions of patient CT scans have often been used by researchers as a potential patient-specific rupture risk indicator. A property that has a great influence on the stress distribution and magnitude is the aortic wall thickness. Unfortunately, there are no validated, non-invasive methods for measuring aortic wall thickness of patients with AAA. Researchers have utilised either CT or MRI as input into their custom wall detection algorithms, however, there has not yet been a study which utilises both. Therefore, this study aims to develop a non-invasive, and patient-specific method of detecting aortic wall thickness utilising both CT and MRI scans.

Keywords Abdominal aortic aneurysm · Aortic wall thickness · Measurement · Patient-specific · Computed tomography · Magnetic resonance imaging

A. T. Huynh (✉) · K. Miller
Intelligent Systems for Medicine Laboratory, The University of Western Australia, Perth, WA, Australia
e-mail: andy.huynh@research.uwa.edu.au

K. Miller
e-mail: karol.miller@uwa.edu.au

K. Miller
Harvard Medical School, Boston, MA, USA

P. M. F. Nielsen et al. (eds.), *Computational Biomechanics for Medicine*,
https://doi.org/10.1007/978-3-031-09327-2_1

1 Introduction

Abdominal Aortic Aneurysm (AAA) is the focal dilation or widening of the infrarenal artery and is most commonly fusiform in shape [1]. It is a vascular disease commonly found in older adults with prevalence increasing steadily with age [2]. Although the prevalence and incidence of AAA has declined globally, there have been rising AAA rates in many regional areas around the world, including the Oceanic region [2]. In Australia, approximately 7% of elderly men aged 65 years and above suffer from AAA—equating to about 114,000 Australian men [3]. This highlights the need for improved disease surveillance and prevention.

Due to the asymptomatic nature of the disease, it is often discovered by unrelated medical examinations and screening [1]. People unaware of their condition may only find out after the catastrophic event of a ruptured AAA. The majority of patients with a ruptured AAA will not survive if left untreated, having an overall mortality rate of approximately 80–90% [4]. Unfortunately, even with immediate surgery by experienced vascular surgeons, the mortality remains high between 41 and 55% [5]. As such, it is crucial for doctors to identify the location on the AAA vessel at highest risk of rupturing prior to the catastrophic event.

There are many limitations to the current clinical rupture risk indicator due to its derivation coming from population statistics and not patient-specific circumstances. Clinical rupture risk indicator for elective repair only factors the AAA diameter size (>5.5 cm for men and >5 cm for women), growth rate (>1 cm/year) and some patient symptoms [1]. This is insufficient as there are many other patient-specific factors such as age, smoking, atherosclerosis, hypertension, ethnicity, and family history [1]. Further evidence indicates that 60% of AAAs that were recommended for elective repair often remained stable [6] and 20% of small AAA have ruptured [7]. Research is currently being undertaken to visualise and understand patient-specific biomechanics of AAA. This novel approach aims to develop a non-invasive and patient-specific biomechanical rupture risk assessment for AAA.

Computation of AAA wall stress using three-dimensional (3D) reconstructions of patient CT scans have often been used by researchers as a potential rupture risk indicator [8–10]. Although it was recently discovered that neither stress magnitude nor stress distribution alone had any noticeable relationship with AAA symptoms [11], wall stress calculations still holds great practical importance in research. Wall thickness is a property that has a great influence on the stress distribution and magnitude [8, 12]. Unfortunately, there are no validated, non-invasive methods for measuring aortic wall thickness [13]. Additionally, the poor soft tissue contrast of CT scans alone limit the visibility and measurement of the aortic wall, resulting in a majority of AAA rupture risk studies assuming a uniform wall thickness [14]. BioPARR is a software system used for estimating the rupture potential index (RPI) for AAA [14]. The software only requires the segmentation of the AAA and wall thickness specification as manual user inputs with all other steps being automated. Unfortunately, the wall thickness specification is applied either by assuming uniform wall thickness or manually measuring wall thickness at sparse locations and using them to generate

the walls through interpolation and smoothing [14]. As such, substantial research efforts are needed to investigate patient-specific aortic wall thickness measurement techniques for reliable estimates of AAA wall stress.

Researchers have utilised either CT or MRI as input into their custom wall detection algorithms, however, there has yet been a study which utilises both. Semi-automatic wall detection from CT has been developed based on common image analysis techniques using image intensity and contours [13, 15]. Similarly, MRI has also been studied to detect wall contours based on image gradient measurements [16].

In our method, both CT and MRI are used to detect aortic wall thickness with the assistance of common image processing techniques. Utilising both modalities, advantages such as cross-checking measurements and having improved visibility of the aortic walls can be achieved. Exact methods to achieve this have not been clearly outlined in existing literature. This study therefore aims to develop a non-invasive, and patient-specific method of detecting aortic wall thickness utilising both CT and MRI scans.

2 Methods

The aortic walls were detected from patient CT and MRI data using image processing techniques included in the MATLAB software. Our method involves registering the CT and MRI scans of the patients using open-source software 3D Slicer [17] to align the datasets. This is followed by importing the data into an in-house MATLAB script to detect the aortic walls using Canny edges. Canny edges use adaptive thresholding with hysteresis to detect edges based on the intensity gradients of the image [18]. The edges produced from the CT and MRI slices are overlaid to give an improved structural visibility of the wall thickness for measurement. This process simplifies the analysis of the images by reducing the amount of data to be processed while preserving useful structural information [18].

2.1 Patient Data

A pilot cohort of four patient CT and MRI scans were used in this study. Patient data were acquired randomly from the MRI in AAA to predict Rupture or Surgery (MA^3RS) study [19]. The patients were under surveillance for AAA with maximum diameter greater than 4 cm [14]. The scans were previously used by Joldes et al. and is described in their BioPARR paper [14].

2.2 Registration of Patient CT and MRI Scans

Image registration is the process of aligning two or more images and has many applications in the medical field. The patient's MRI and CT data sets were registered using open-source software 3D Slicer. The automatic registration of inter-modality images is difficult since different image modalities reveal and represent different information about the organ [14]. To overcome this difficulty, a label map registration algorithm outlined in the BioPARR paper was followed in this study [14]. A disadvantage of using this registration method is that it cannot account for local deformations [14]. A summary of the steps is shown below [14].

Manual segmentation of the AAA was applied to both the CT and MRI scans using the 'Editor' module within the 3D Slicer software. Labels of the segmented AAA were produced for each modality and are used to acquire the registration transformation.

The general registration and resampling algorithm (BRAINSFit and BRAINSResample) were used to register the CT and MRI images. This involved using the resulting transformation acquired from the label map registration to register the MRI and CT images and bring them to the same coordinate system. The deformed MRI and CT images (Fig. 1) will be used for further image processing to detect the aortic walls.

2.3 Detection of Aortic Wall from CT and MRI

The aortic wall detection algorithm was developed using MATLAB and the Image Processing Toolbox included. The Image Processing Toolbox allows users to use a variety of different algorithms for image processing, visualisation, and analysis.

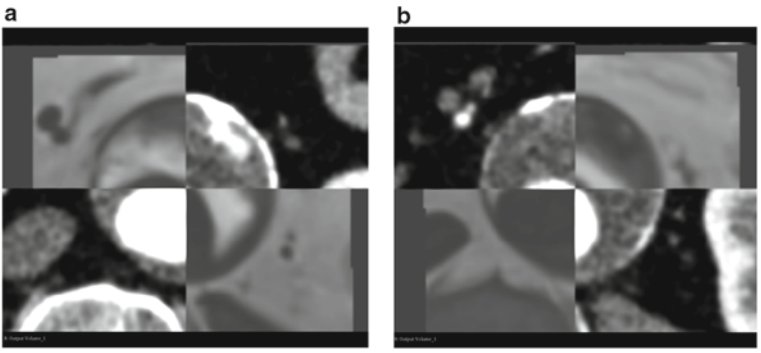

Fig. 1 The registration of the CT and MRI dataset using 3D slicer **a** checkerboard with MRI top-left **b** checkerboard with CT top-left

The CT and deformed (registered) MRI scans were read into the MATLAB script. The files were in '.nrrd' format and required adjustment to the coordinate system in order to visualise and save the images. Users can specify the number of sample of slices to analyse from the patient's CT/MRI volume and scale of the image size that the wall detection algorithm will be applied. In this experiment, a sample size of 50 image slices and scale factor of 4 was used. The size of the sample will be subject to the time available to the user (depending on the clinical workflow) and the computational hardware available. The scale factor will depend on the quality/resolution of the scans. Further parameters are specified by the user for semi-automatic segmentation of the aortic walls based on the contrast and quality of the image being assessed. This includes in-built MATLAB functions such as low-light image enhancement and edge detection using the Canny method. The algorithm first enhances the visibility of the aortic walls using low-light image enhancement techniques and then produces edges using Canny edge detection. Figure 2 shows the aortic walls from the CT and MRI.

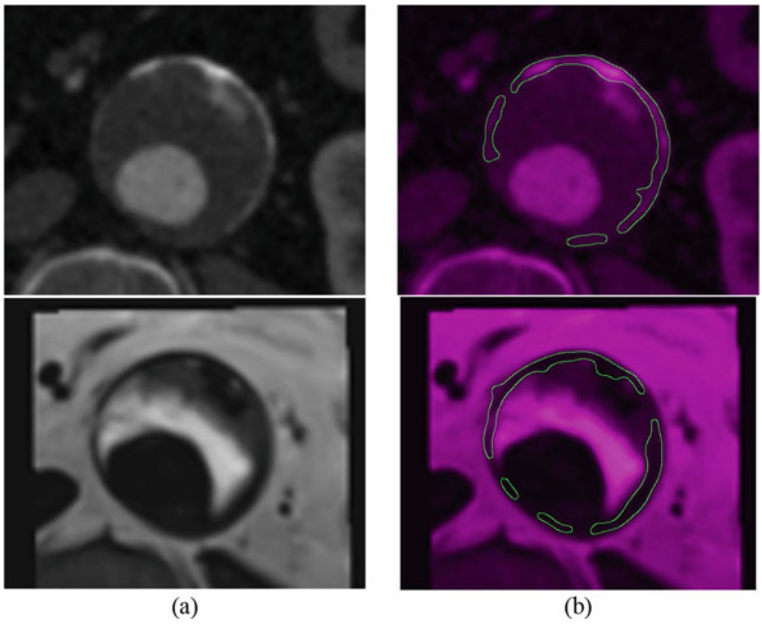

Fig. 2 Detection of aortic walls, Top = CT and Bottom = MRI **a** original image **b** aortic wall detection using our algorithm

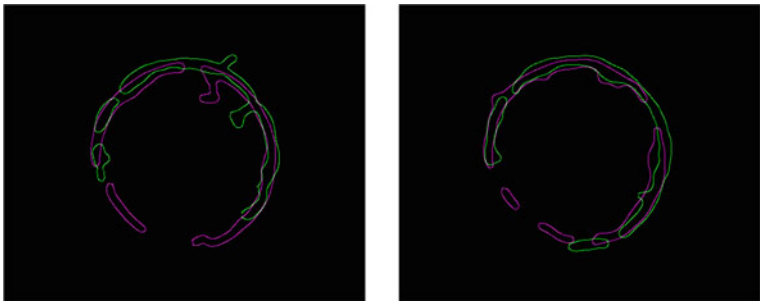

Fig. 3 Samples of overlaying wall edges detected from CT and MRI. Green = CT and magenta = MRI

2.4 Overlaying Wall Edges of CT and MRI

By overlaying the edges detected from the CT and MRI scans, an improved visualisation of the aortic walls can be produced. From Fig. 3, a sample of aortic wall edges detected using our algorithm is displayed. The images include both edges detected from CT (in green) and MRI (in magenta).

2.5 Measurement of Aortic Wall Thickness

Measurement of the aortic wall thickness was done manually using open-source software, ImageJ. The software allows for users to define the spatial scale so measurements can be presented in millimetres. A total of 50 axial slices were analysed for each patient in which 10 of the best quality edges produced by our algorithm were selected for measurement. For each slice, four approximately equidistant aortic wall measurements were taken by measuring the shortest distance between the outer wall and inner wall. This totals to 80 measurements per patient. Additionally, only measurements where both the CT and MRI edges are aligned at either the inner or outer wall were taken as this has a higher chance for the edges to represent the aortic wall. It is also used as a reference point to compare measurements from the CT edges and MRI edges. Alignment of edges is represented as white, edges from CT is represented as green and edges from MRI is represented as magenta (Fig. 4). It should be noted that this method may overestimate the wall thickness measurements due to the slices not being perpendicular to the aortic axis.

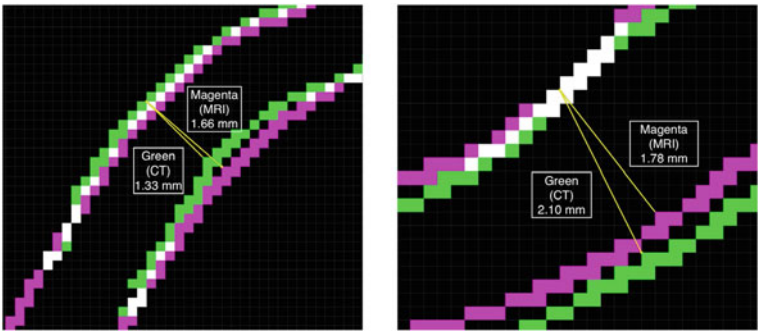

Fig. 4 Example measurement of aortic wall thickness for CT (green) and MRI (magenta) pair

Table 1 Summary of overall aortic wall thickness measurements for each patient

Patient	Modality	Mean (mm)	SD (mm)	Minimum (mm)	Maximum (mm)
1	CT MRI	2.05 1.88	0.28 0.29	1.44 1.54	2.58 2.97
2	CT MRI	1.97 2.05	0.36 0.31	1.56 1.56	3.25 2.81
3	CT MRI	1.97 1.77	0.29 0.16	1.34 1.47	2.54 2.10
4	CT MRI	1.92 1.75	0.25 0.13	1.42 1.44	2.59 2.03

3 Results

3.1 Summary of Results

For each patient, pairs of CT and MRI aortic wall thickness were measured, totalling to 80 measurements per patient (40 for CT and 40 for MRI). The summary of results of aortic wall thickness measurements from CT and MRI for each patient are summarised below (Table 1).

3.2 Statistical Analysis

The mean ± standard error of the aortic wall measurements from edges created by CT and MRI are displayed below (Fig. 5). For each patient, a sample size of 10 slices was used. Each slice was used to manually measure 4 pairs (CT and MRI)

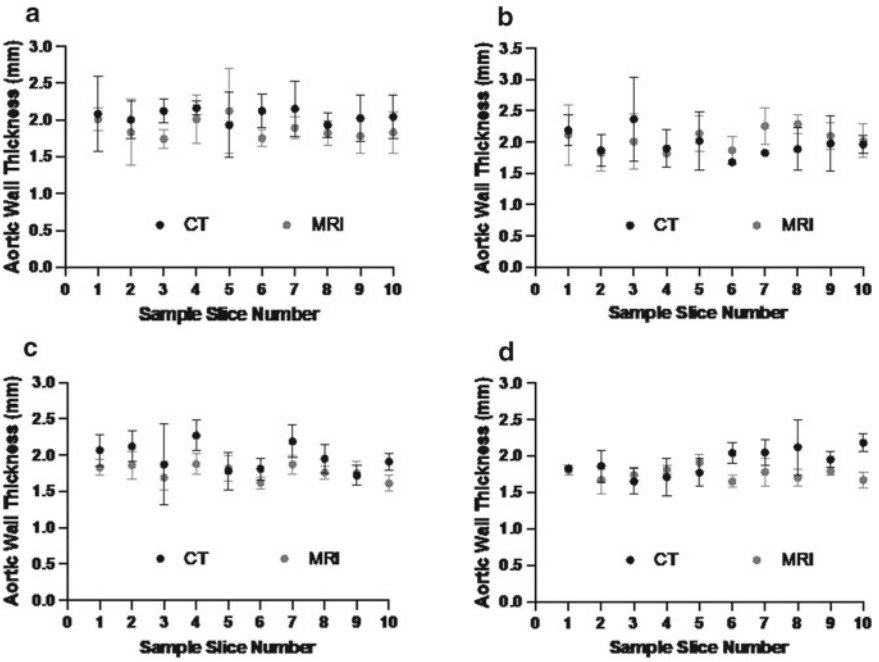

Fig. 5 Plots showing mean ± standard error of aortic wall measurement from CT and MRI for each sample slice **a** Patient 1 **b** Patient 2 **c** Patient 3 **d** Patient 4

of approximately equidistant aortic wall thickness. The results show thickness variability depending on the location of the aneurysm in both axial and coronal/sagittal planes.

Bland–Altman plots were used to assess the agreement between the aortic wall thickness measurements from edges created using CT and edges created using MRI. This graphical assessment uses an approach based on quantifying the variation of the differences between measurements by two different methods on the same subject [20]. We use this method of analysis to see if measuring wall thickness from edges created from CT and MRI are comparable and if they can be used interchangeably. This is important as one of the main advantages of using our method for wall thickness measurements is the increased visibility of the surrounding wall over methods which uses only one or the other modality.

The plots display the difference between the measurements by the CT and MRI for each subject against their average (Fig. 6). For patient 1, the plot shows a positive bias of 0.18 mm ± 0.3 mm, suggesting that on average the CT measures 0.18 mm more than the MRI measures. Additionally, the 95% limits of agreement (LOA) ranged from −0.41 mm (mean +1.96 SD) to 0.76 mm (mean −1.96 SD). Patient 2 shows a negative bias of −0.08 mm ± 0.38 mm with 95% LOA ranging from − 0.82 mm to 0.67 mm. Patient 3 shows a positive bias of 0.20 mm ± 0.26 mm with

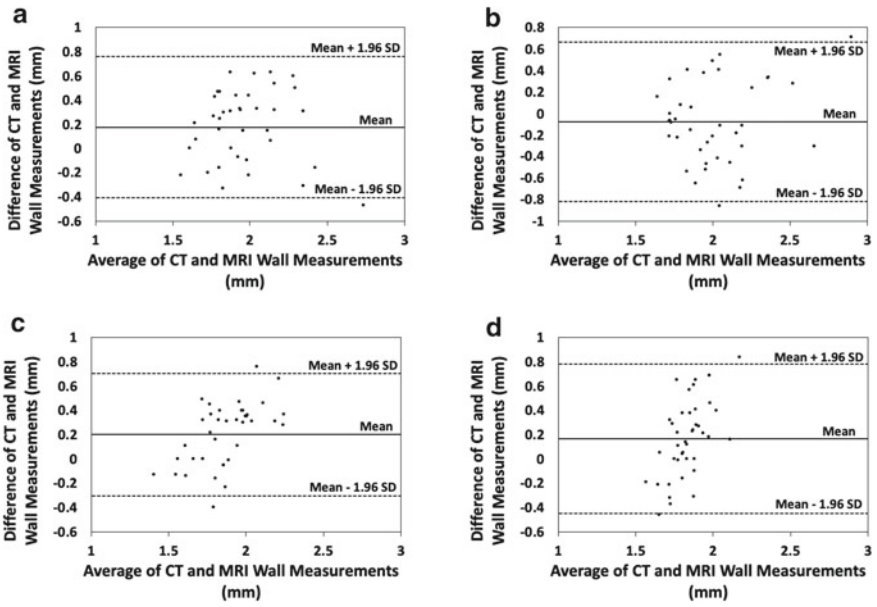

Fig. 6 Bland–Altman plots of the difference between the paired aortic wall thickness measurements from CT and MRI **a** Patient 1 **b** Patient 2 **c** Patient 3 **d** Patient 4. The difference between CT and MRI-based measurement can be as much as 0.6 mm, approximately a pixel size (0.625 mm) in the original images. This shows that it is difficult to obtain accuracies better than the pixel size of the original image

95% LOA ranging from −0.30 mm and 0.70 mm. Lastly, patient 4 shows a positive bias of 0.17 mm ± 0.31 mm and 95% LOA of −0.45 mm to 0.78 mm.

4 Discussion and Conclusions

In this study, we present a patient specific and non-invasive method to measure the aortic wall thickness by overlaying patient CT and MRI data. This was achieved using an in-house script incorporating image processing techniques included in the MATLAB software. Most researchers have used either CT or MRI for measuring wall thickness, however, the lack of information from using one or the other may be compensated by overlaying both modalities.

The need for modelling non-uniform wall thickness in abdominal aortic aneurysm biomechanics has been a problem for many researchers. The comparison between assuming uniform wall thickness and variable wall thickness for tension and stress field computation was presented by Joldes et al. [8]. The paper suggested that incorporating wall thickness measurements is necessary for a reliable estimation of AAA stress field.

Using our method, local measurements of the aortic wall thickness can be achieved. By overlaying CT and MRI, an improved 'completeness' of the aortic wall is produced allowing researchers to conduct more local wall thickness measurements to reliably describe their AAA geometric model. Our results show that aortic wall thickness varies along both axial and coronal/sagittal planes (Fig. 5). This gives the possibility for researchers to develop geometric biomechanical models with varying local thickness. Unlike raw CT or MRI, Canny edges allows users to measure the wall thickness based on the pixel edges reflecting the outer and inner wall boundaries. This avoids the random error associated with measuring wall thickness using raw CT or MRI where users are required to distinguish between the unclear boundaries of the inner and outer wall.

Currently, using both CT and MRI to measure aortic wall thickness may not be common practice, as it is an expensive process to acquire both modalities. However, it should be noted that the processes used to detect the aortic walls from these images are both computationally and financially feasible. If the quality of the CT is sufficient for the user to detect the walls, then an additional MRI may not be necessary, lowering the cost of the process. There are studies which use either CT or MRI to detect and measure aortic wall thickness but use interpolation algorithms [15] or mean distance [21]. With the expense of requiring both modalities, the method presented here allows users to locally measure wall thickness without any interpolation algorithms to estimate the wall boundaries.

A limitation in our study is that the measurement results are not compared to ground truth as it is not available. Bland–Altman plots were used to assess the agreement of using aortic wall thickness measurements using edges created between CT and MRI. The plots show that the bias (or mean difference) was close to the ideal zero value across all four patients, ranging between −0.08 to 0.20 mm. Additionally, plots across all patients only have 1–2 values lying outside the 95% LOA. It is also observed that depending on the modality, measurement of wall thickness may vary by as much as 1 pixel size of the original image.

Another limitation is the uncertainty of measurements due to several factors. Image resizing was incorporated in the script as the original CT and MRI resolution quality was too low for the algorithm to detect and produce Canny edges. The nearest neighbour interpolation was used to resample the pixels and scale the image by a factor of 4. This may introduce noise and jagged boundaries [22] which can affect accuracy of measurements as aortic walls are rounded in shape. Registration of CT and MRI was also a necessary step to produce overlayed edges. Accuracy of registration methods determines the reliability of the aortic wall thickness measurements. Since the method of registration has not yet been validated for our application, the registration error may have significant effects on our results.

We believe the next step to progress this novel technique of patient specific, non-invasive detection of local aortic wall thickness is to introduce a larger cohort of patient data and validating our method using ground truth wall thickness measurements. Additionally, the method could be simplified by automating the significant step of manually measuring the aortic wall thickness, improving both the repeatability and accuracy of this approach.