INDIANA UNIVERSITY SOUTH BEND

COLLEGE OF LIBERAL ARTS AND SCIENCES

Master of Science in Applied Mathematics and Computer Science

THESIS PROPOSAL ROUTE SHEET

DEPARTMENT: **Computer Science**______________________________________

PROPOSAL TITLE: **Evaluation of Morphology Descriptors in CT Images of the___ Aorta as Indicators of the Presence of Plaque______________**

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ABSTRACT

This document proposes a study designed to compare the ability of five descriptors characterizing the morphology and elasticity of the descending aorta in CT images in an attempt to identify CT slices which contain potential areas of plaque. It is hypothesized that regions of plaque will distort the normal lumen, with corresponding changes in the CT image. This image distortion would allow us to infer the presence of plaque by identifying deviations in the smoothness, symmetry, or circularity of the lumen border or by measurements that allow for an estimate the elastic properties of the arterial wall. The method will include manually locating the descending aorta from a CT dataset, segmenting the lumen in each candidate slice, and computing descriptors from the resulting images. The descriptors to be computed are the lumen circularity, lumen centroid displacement, and fractal dimension of the lumen border, as well as the percentage expansion in lumen area and the dispersion of the lumen centroid during the cardiac cycle. An assessment of the ability of each descriptor to identify the image slices containing potential plaque will be included.

1. INTRODUCTION

Heart disease remains the leading cause of death in the United States, accounting for approximately 26.6% of the 2,450,000 deaths in 2005. In addition, cerebrovascular diseases or stroke comprised an additional 5.9% [1]. Coronary artery disease is an underlying factor in the majority of cardiovascular disease cases [2]. The health of the vascular system is reflected in the condition of the aorta. Specifically, studies have established that atherosclerosis of the thoracic aorta is an indicator for generalized atherosclerosis, that is, coronary, carotid, and peripheral arterial disease [3].

The severity of atherosclerosis is often characterized by the amount and structure of observed plaque. A plaque is generally defined as a protrusion of the intimal surface of the vessel at least 2 mm thick which is different in appearance from the intimal surface. Plaques less than 4mm are considered small while those greater than or equal to 4 mm are classified as large or severe [4] [5]. An ulceration is a discrete indentation of the luminal surface of the plaque with base width and maximum depth of at least 2 mm each [5]. In addition, approximately 90% of patients with cardiovascular disease exhibit vascular calcification which can diminish wall elasticity [6].

Computed tomography (CT) has become a mainstay in non-invasive imaging for vascular anatomy and pathology and is a common method for diagnosing aortic disease [7]. It allows for rapid imaging and can minimize motion artifacts [2]. The administration of contrast agent allows visualization of plaque-related lumen displacement [6]. A sample image is shown in Figure 1.

Specifically, since soft plaque is substantially transparent to x-ray, this study will use images of the aorta obtained in CT studies in the presence of a contrast agent. In areas displaced by plaque, the resulting lumen border is expected to be less circular, less symmetric, or more irregular. In addition, plaque deposits may cause changes in the elastic properties of the aortic wall that may be detectable by comparing the lumen border in images obtained throughout the cardiac cycle.

2. LITERATURE REVIEW

The first task to be accomplished in this project involves the manual location of a volume of interest containing the descending aorta from a CT dataset. Kurkure, Avila-Montes, and Kakadiaris [8] developed a method to locate and segment the thoracic aorta in non-contrast CT images to replace the manual annotation of calcified plaques. Their method used a series of 2D slices from the CT data based on the assumption that the aorta runs approximately vertically in this section of the abdomen. After preprocessing, a Hough circle transform was applied on regions of interest for the ascending and descending aorta and an optimal combination of the Hough circles was found by using a cost function which minimized the change in horizontal position between circles in adjacent slices, the change in radius between circles in adjacent slices, and the Hough value of points in Hough space. An additional cost function was able to further refine gaps and smooth out the horizontal boundary. This method compared favorably when evaluating the results against the aortic boundaries manually annotated by an expert. Consistent with the Kurkure method, this proposal will take advantage of the vertical orientation of the descending aorta and process the subset of image slices in which the 2D cross-section of the aorta is approximately circular. Both the circularity descriptor and the measurement of the displacement of the centroid from the artery center are based on this assumption.

The next step of the evaluation is to segment the lumen to estimate the border between lumen and tissue. Renard and Yang [9] developed a technique for segmenting both the lumen and the arterial wall in contrast-enhanced CT images of the coronary arteries by determining a centerline and classifying the tissues within a cylinder that they centered on that line. They separated the tissues into lumen, wall, and surrounding myocardium and noted that the lumen intensity was the brightest among the three classes. The difference in the cross-sectional areas of the lumen and the wall regions was then used to estimate plaque regions. While this proposal will also use the brightness of the contrast-enhanced lumen to distinguish it from the surrounding tissues; it will concentrate on characteristics of the lumen border outline to indicate potential plaque areas.

Once this lumen boundary has been estimated, its characteristics can be described. Nguyen, and Rangayyan [10] found that the fractal dimension was a good shape feature to quantify the complexity and irregularity of an object's boundary. The technique was successfully applied to contours that were hand drawn by an expert on over 100 mammogram masses and a clear separation of benign and malignant masses was found, with the smoother contours of the benign masses generating a lower fractal dimension. The box-counting method that they used to calculate fractal dimension will be used to estimate the complexity and irregularity of the lumen border.

In addition to static descriptors to identify image slices containing potential areas of plaque, the project will explore information about the elastic properties of the aortic wall from time series images. These images are recorded at increments within the R-R interval, the duration of the cardiac cycle. The hypothesis is that the presence of plaque might be associated with stiffness or asymmetry in the expansion of the aortic cross-sectional area during the cardiac cycle. Stefanadis et al [11] verified that aortic elastic properties represent a substantial independent risk factor in predicting coronary events in patients with coronary artery disease. They considered distensibility, calculated from the percentage change in cross-sectional area between diastole and systole, in evaluating elastic properties. Galante et al [12] segmented the aorta from multi-detector CT images and estimated shape and size features using a temporal resolution of ten frames per cardiac cycle. They were able to verify a decrease in elasticity and strain in vessels containing aneurysms and their measurements compared well with current methods which require doctors to perform manual measurements of aortic diameters at specific anatomical sites. This proposal will consider the percentage expansion of the lumen as an indicator of distensibility and the dispersion of the centroid value as a measure of asymmetry.

Although this project relies on contrast-enhanced CT images, which require intravenous injection of contrast agent and exposure to x-rays, the techniques developed in this analysis may later be applied to phase-contract MRI images of the aorta which do not require intravenous contrast and do not expose the patient to ionizing radiation.

3. PROPOSED SOLUTION

The focus of this study is a comparison of the ability of descriptors to characterize images of the aorta to identify those with potential areas of plaque. The project method will include:

- Manual selection of a region of interest containing the descending aorta from a complete CT scan.

- Segmentation of the lumen border outline by:
    - Initial highlighting of lumen candidate pixels using a pulse coupled neural network.
    - Tracing the outer border of the identified area.
- Calculation of descriptors based on border outline of a single image including:
    - Circularity based on perimeter and area of lumen.
    - Difference between the best estimate of the center of the artery and the centroid of the lumen.
    - Fractal dimension of the border outline.
- Incorporation of time series information for image slices recorded at intervals during the cardiac cycle including:
    - Dispersion of the centroid value as a measure of asymmetry in aortic expansion.
    - Distensibility based on the percentage expansion of the area of the lumen.
- Comparison of the ability of each descriptor to identify the set of image slices containing potential plaque areas that have been validated by a medical expert.

3.1 Segmentation

The descending section of the aorta can be roughly selected from the complete CT scan dataset as a volume of interest to facilitate and minimize the amount of processing required. As in the Kurkure study [8], the analysis will take advantage of the vertical orientation of the descending aorta and process the series of 2D image slices in which the cross-section of the aorta is approximately circular. Figure 1 is an example of one full CT slice with a region of interest including the descending aorta identified. Figure 2 shows a sample of slices from the selected regions of interest.

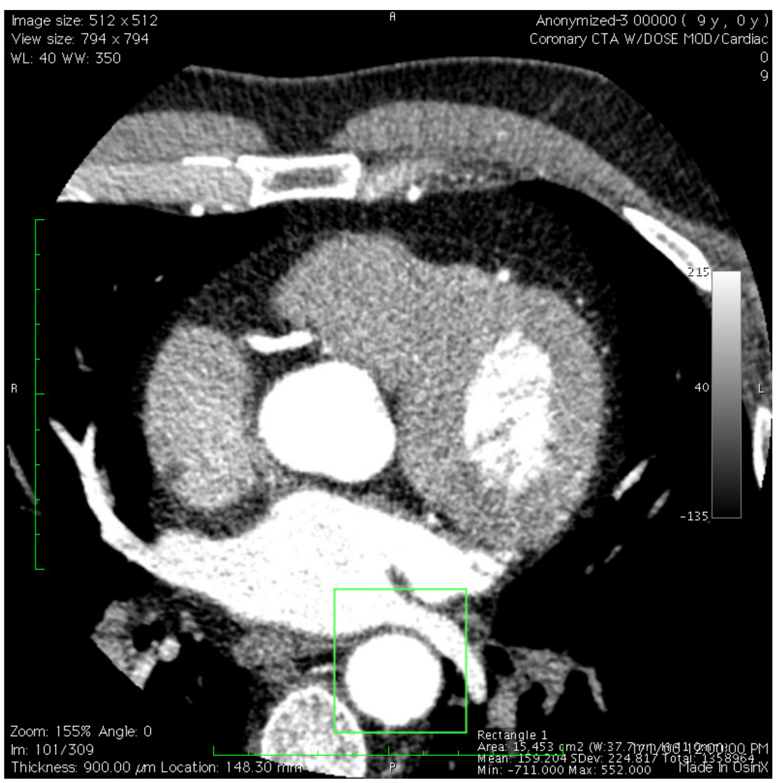

Figure 1: Full CT scan with a manually selected region of interest.

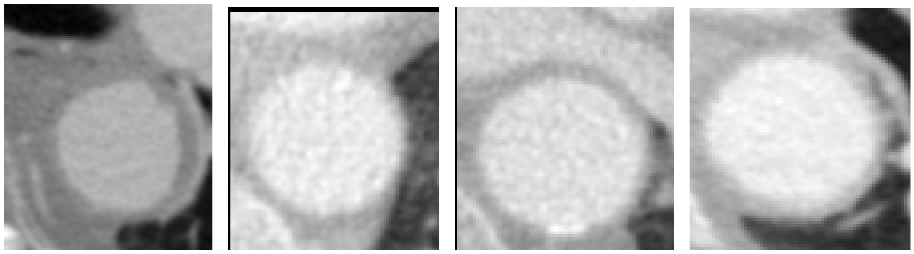

Figure 2: Sample of selected input images.

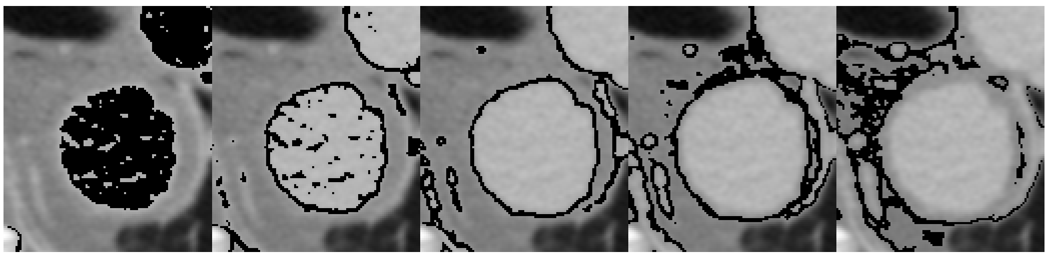

Figure 3: Binary output from the PCNN superimposed in black on the leftmost image from Figure 2.

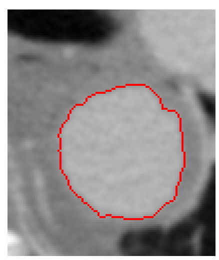

Figure 4: Estimated location of the lumen border.

To help identify the lumen, a pulse-coupled neural network (PCNN) will be applied to each selected image [13]. This produces a series of binary images associated with visually interesting features and boundaries. A preliminary assessment using a PCNN to preprocess the slices was performed resulting in the series of images in Figure 3. Figure 4 shows the estimated location of the lumen border based on the PCNN output. This image outline has been validated by a cardiologist. The following sections will describe the descriptors of this outline in more detail.

3.2 Single Image Descriptors

The first descriptor calculates the perimeter and the area enclosed by the outline to form an estimate of the circularity of the lumen. The perimeter will be estimated by the length of the outer contour of this connected region *R*, treated as an 8-neighborhood. The measurement weights vertical and horizontal segments by 1 and diagonal segments by $\sqrt{2}$. Since this method of calculation generally overestimates the real perimeter, the value is corrected by a factor of 0.95 which is found to work satisfactorily even for relatively small regions [14]. The area estimation used will be a simple count of the image pixels that comprise the region *R*. Circularity can be approximated from the perimeter and the area as a measure of compactness or roundness which is invariant to translation, rotation, or scale factors:

$$\text{Circularity}(R) = 4\pi \cdot \text{Area}(R) \,/\, \text{Perimeter}^2(R)$$

The circularity will be 1 for a perfectly round region and a value in the range [0, 1) for all other shapes [14].

For a second descriptor, a Hough circle transform will be used to calculate the best circle fit to the image outline obtained by the PCNN. The Hough circle transform has been found to be robust even under conditions which occlude parts of the boundary. This is in contrast to the centroid which can be moved away from its central position by defects or boundary occlusions [15]. The descriptor to be considered is the distance between the centroid of the lumen and the center of the Hough circle expressed as a percentage of the radius.

A third descriptor that will be applied to a single image is the fractal dimension as described by Nguyen and Rangayyan [10] to quantify the complexity of the lumen boundary. The fractal dimension will be calculated by using the box-counting method and estimating the slope of the best-fitting line for the graph of the log of the number of boxes containing lumen border pixels to the log of the magnification index for each box-partitioning stage.

3.3 Time Series Descriptors

As in the studies by Galante et al and by Stefanadis et al [11] [12], the alternate method will be an estimation of elastic properties of the aorta using images obtained throughout the cardiac cycle. The dispersion of the centroid values will be calculated as a measure of asymmetry in aortic expansion. In addition, the percentage change in the area of the lumen at systole and diastole will be estimated to calculate a measure of distensibility. The series in the study contain slices acquired at different times expressed as a fraction of the R-R interval in the cardiac cycle.

3.4 Assessment

The five descriptors to be compared are the circularity of the lumen outline, the distance between the centroid of the lumen and the center of the Hough Transform circle, the fractal dimension of the lumen outline, the dispersion of the centroid values, and the percentage change in the area of the lumen. They will be evaluated on their ability to identify slices which contain potential areas of plaque. In the absence of an available, non-invasive, "gold standard", and consistent with other studies [8] [9] [12], the slice classification will be assessed against the observation of a domain expert.

These results will be reported as a series of Receiver Operating Characteristic (ROC) curves to characterize their respective sensitivity and specificity. The area under the ROC curve will be estimated to assess the accuracy of each descriptor [16].

4. AVAILABLE RESOURCES

4.1 Data

The project scope will incorporate approximately 200 slices from four CT studies, validated by a domain expert as those likely to be atherosclerotic as well as those without visually detectable plaque indications. The images used will be stored in the DICOM format; the standard for producing, storing, and displaying medical images.

4.1 Software

A variety of open source software packages supplemented by custom programming will be used to facilitate processing the CT datasets, including the following:

- Osirix: an image processing software package which is compliant with the DICOM standard. It was designed for the visualization of multidimensional images and contains 2D, 3D, and 4D viewers. It can read and display DICOM format files as well as the DICOM meta-data contained in the file headers. In addition, it can write a DICOM file from a 2D/3D reconstruction which will allow manual inspection and selection of a volume of interest from the full CT scan dataset [17].
- The Insight Toolkit (ITK): modules for performing registration and segmentation of medical images. It also provides the ability to read and write a DICOM format file, and it contains numerous filtering, geometric transformation, and statistical functions. It is primarily a C++ package but many of the functions have been wrapped for alternative programming languages such as Python [18].
- Other available tools: Python, NumPy to process multidimensional arrays, SciPy for scientific applications, and the Visualization Toolkit (VTK) for 2D and 3D visualization[19].
- Custom software developed for PCNN pre-processing [20] [21].

4.1 Hardware

The Apple computers in the Informatics Lab have been made accessible for use in this project. The Osirix and ITK software packages described above have been installed. In addition, the Enthought Python Distribution (EPD), a convenience distribution of Python available for Mac OS X, has been installed to include the additional Python tools required [19]. Additional processing will be accomplished on similarly-configured personal computers.

5. SUMMARY

This study will compare morphological features from CT cross-sectional images of the aorta. Using an estimated outline of the lumen border, several static image descriptors will be calculated and compared. The border will also be used as a basis to compare the elastic properties of the aorta as the border outline varies in time during the cardiac cycle. The project will compare how well these descriptors are able to identify slices exhibiting evidence of plaque as determined by a medical expert.

BIBLIOGRAPHY

[1] Hsiang-Ching Kung, Ph.D.; Donna L. Hoyert, Ph.D.; Jiaquan Xu, M.D.; and Sherry L. Murphy, B.S.; "Division of Vital Statistics, Deaths: Final Data for 2005", U.S. Department of Health and Human Services, National Center for Health Statistics, Centers for Disease Control, National Vital Statistics System, Volume 56, Number 10, April 24,2008.

[2] Gil Kimel, MD, MSc; Gordon Andrews, MD; Bruce Forster, MD; Dean Malpas, "Multidetector Computed Tomography of the Coronary Arteries—Pictorial Essay"

[3] Ariel Cohen "Atherosclerosis of the Thoracic Aorta: Further Characterization for Higher Risk of Vascular Events", J. Am. Coll. Cardiol. 2008;52;862-864 doi:10.1016/j.jacc.2008.04.063 http://content.onlinejacc.org/cgi/content/full/52/10/862, accessed September 2008.

[4] Itzhak Kronzon, MD; Paul A. Tunick, MD, "Aortic Atherosclerotic Disease and Stroke", American Heart Association, Inc., Circulation. 2006;114:63-75 http://circ.ahajournals.org/cgi/content/full/114/1/63, accessed October 2008.

[5] Marco R. Di Tullio, Shunichi Homma, Zhezhen Jin, and Ralph L. Sacco, "Aortic Atherosclerosis, Hypercoagulability, and Stroke: The APRIS (Aortic Plaque and Risk of Ischemic Stroke) Study", J Am Coll Cardiol.2008; 52: 855-861 http://content.onlinejacc.org/cgi/content/full/52/10/855, accessed September 2008.

[6] Catherine L. Higgins, Seth A. Marvel, Joel D. Morrisett, "Quantification of Calcification in Atherosclerotic Lesions", Arteriosclerosis, Thrombosis, and Vascular Biology. 2005;25:1567, American Heart Association, Inc.
http://atvb.ahajournals.org/cgi/content/full/25/8/1567, accessed January 2009.

[7] Tongfu Yu, MDa, Xiaomei Zhu, MDa, Lijun Tang, MDa, Dehang Wang, MDa, Nael Saad, MB, BCh, "Review of CT Angiography of Aorta", Radiologic Clinics of North America.

[8] Kurkure, U.; Avila-Montes, O.C.; Kakadiaris, I.A., "Automated segmentation of thoracic aorta in non-contrast CT images", 5th IEEE International Symposium on Biomedical Imaging: From Nano to Macro, May 2008, Paris, Page(s):29 – 32.

[9] Renard, F. and Yang, Y., "Coronary Artery Extraction and Analysis for Detection of Soft Plaques in MDCT Images", 2008 5th IEEE International Symposium on Biomedical Imaging: From Nano to Macro, Paris, France, May 14-17, 2008 http://www-video.eecs.berkeley.edu/Proceedings/ICIP2008/pdfs/0002248.pdf, accessed January 2009.

[10] T.M. Nguyen; R.M. Rangayyan, "Shape Analysis of Breast Masses in Mammograms via the Fractal Dimension", 27th Annual International Conference of the Engineering in Medicine and Biology Society 2005, Shanghai, January 2006, Page(s):3210 – 3213.

[11] C. Stefanadis, J. Dernellis, E. Tsiamis, C. Stratos, L. Diamantopoulos, A. Michaelides and P. Toutouzas, "Aortic stiffness as a risk factor for recurrent acute coronary events in patients with ischaemic heart disease", *European Heart Journal* (2000) 21, 390–396.

[12] V Galante1, C Corsi, F Veronesi1, V Russo, R Fattori, C Lamberti, "Dynamic Characterization of Aorta Morphology and Function in Presence of an Aneurysm", Computers in Cardiology 2007;34:765−768, http://www.cinc.org/Proceedings/2007/pdf/0765.pdf, accessed October 2008.

[13] Thomas Lindblad and Jason M. Kinser, *ImageProcessing using Pulse-Coupled Neural Networks*, Springer Verlag, 1998.

[14] Burger, W. and Burge, M., *Digital Image Processing*, Springer, New York, 2008, pp.223-224.

[15] Davies, E.R., *Machine Vision*, Morgan Kaufmann, San Francisco, California, 2005, pp.214-217, 287.

[16] Tape, Thomas G, MD, "Interpreting Diagnostic Tests", University of Nebraska Medical Center, http://gim.unmc.edu/dxtests/Default.htm, accessed January 2009.

[17] "OsiriX Imaging Software - About OsiriX", http://www.osirix-viewer.com/AboutOsiriX.html, accessed October 2008.

[18] "NLM Insight Segmentation and Registration Toolkit (ITK)", http://www.itk.org/index.htm, accessed October 2008.

[19] "Enthought Scientific Computing Solutions - Products", http://www.enthought.com/products/epd.php, accessed October 2008.

[20] J. Wolfer, S.H. Lee, J. Sandelski, R. Summerscales, J.S. Soble, and J. Robergé, "Endocardial Border Detection in Contrast Enhanced Echocardiographic Cineloops using a Pulse Coupled Neural Network", *IEEE Computers in Cardiology,* September, 1999.

[21] Charles Guse, Susan L. Gordon, A. Blake Robertson, and James Wolfer, "Exploring the Pulse Coupled Neural Network for Mammogram Preprocessing: an Preliminary Assessment", Proceedings of the Safety, Health, and Environment World Congress, July, 2008 p21-25.