THE REPUBLIC OF TURKEY
BAHCESEHIR UNIVERSITY

3D VESSEL SEGMENTATION AND ANALYSIS IN CORONARY CT ANGIOGRAPHY IMAGES

Master's Thesis

İLKAY ÖKSÜZ

ISTANBUL, 2013

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Signature

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This is to certify that we have read this thesis and we find it fully adequate in scope, quality and content, as a thesis for the degree of Master of Science.

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İlkay Öksüz

ABSTRACT

3D VESSEL SEGMENTATION AND ANALYSIS IN CORONARY CT ANGIOGRAPHY IMAGES

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Electrical and Electronics Engineering Program

Thesis Supervisor: Assist. Prof. Dr. Devrim Ünay

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Vessel Segmentation is a popular topic in biomedical engineering since the morphological and statistical properties of vessels play an important role in detection of cardiovascular diseases and can be used for understanding stenosis and pressure changes in the related vessels. There is a vast amount of coronary Computer Tomography images waiting to be analyzed thanks to the high interest in this topic and the advancements in imaging technology. But manual analysis of these images is a difficult and time-consuming task. Therefore, automated tools are required. Such tools should automatically detect coronary arteries and lung vessels, segment them properly, and measure their statistical properties like stenoses and aneurysm of a vessel.

For accurate segmentation of coronary arteries and lung vessels, in this thesis a novel method using Region Growing over Frangi Vesselness Values is proposed, and its results are compared with three other state-of-the-art methods; Region Growing, Frangi Vesselness, and Connected Component Anaysis on Frangi Vesselness Values.

Accuracy of the methods are validated both visually and quantitatively over synthetic and real images. Results show that, applying Region Growing on Frangi Vesselness Values leads to more accurate segmentation as compared to the other methods. Also, on the segmented coronary arteries a plane fitting is applied to detect and quantify the stenoses on vessels.

Keywords: Medical Image Segmentation, Coronary Arteries, 3-D CTA, Stenosis Detection, Lung Vessels, Frangi Vesselness,Region Growing , Vessel Segmentation

ÖZET

KORONER BT ANJİYOGRAFİ GÖRÜNTÜLERİNDE DAMAR BÜLÜTLEMESİ VE GÖRÜNTÜ ANALİZİ

İlkay Öksüz

Elektrik - Elektronik Mühendisliği Programı

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Damar Bölütlemesi Biyomedikal Mühendisliği'nin popüler konularından birisidir. Bunun nedeni damarların morfolojik ve istatiksel özelliklerinin kardiyovasküler hastalıkların tespiti ve daralma noktalarındaki basınç değişimlerinin anlaşılmasında önemli rol oynamasıdır.. Bu konuya olan yoğun ilgiye ve görüntüleme teknolojilerindeki ilerlemelere bağlı olarak önemli miktarda koroner bigisayarlı tomografi görüntüsü birikmiştir ve bunların hepsi analiz edilmeyi beklemektedir. Ancak bu resimlerin elle işlenmesi hem zor hem de vakit alan bir işlemdir. Bu nedenle otomatik araçlara gerek duyulmaktadır. Bu araçlar koroner arterleri ve akciğer damarlarını tespit etmeli, uygun bir şekilde bölütlemeli ve daralma, anevrizma gibi istatiksel özelliklerini ölçmelidir.

Koroner arterlerin ve akciğer damarlarının doğru bir şekilde bölütlenebilmesi için Frangi damarlık değerleri üzerine bölge büyütme kullanan bir metodun kullanılması önerilmiştir. Bu tezde bu metodun sonuçları literatürde bilinen diğer yöntemlerden; Bölge Büyütme, Frangi Damarlık ve Frangi Damarlık Değerleri üzerine bağlanırlık metodlarıyla karşılaştırılmıştır.

Segmentasyon sonuçları hem görsel hem de sayısal olarak sentetik ve gerçek görüntüler üzerinde doğrulanmıştır. Bu sonuçlara göre Frangi Damarlık Değerleri üzerine uygulanan Bölge Büyütme metodu, diğer metodlara göre daha doğru sonuçlar vermektedir. Ayrıca bu yöntem sonucu bulunan damarlara düzlem oturtma yöntemi uygulanarak daralma miktarı belirlenmesi üzerine çalışılmıştır.

Anahtar Kelimeler: Medikal Görüntü İşleme, Koroner Arterler,3B BTA,Daralma Tespiti,Akciğer Damarları, Frangi Damarlık, Bölge Büyütme, Damar Bölütlemesi
.

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ABBREVIATIONS

LCX	:	Left Circumflex
LAD	:	Left Anterior Descending
RCA	:	Right Coronary Artery
2D	:	Two Dimensional
3D	:	Three Dimensional
CTA	:	Computer Tomography Angiography
MRI	:	Magnetic Resonance Imaging
DSA	:	Digital Substraction Angiography
SI	:	Similarity
OVM	:	Overlap Measure
WHO	:	World Health Association
HU	:	Hounsfield Unit
PPV	:	Positive Predictive Value
RMS	:	Root Mean Square

SYMBOLS

Hessian Matrix	: H
Image Intensity values at a point	: I
Dissimilarity Measrue	: R_B
Largest cross section are of elipsoid	: R_A
Constant values in Frangi Vesselness	: α, β, c,
Skewness	: S
Eigenvalues of Hessian matrix	:λ_1,λ_2, λ_3
Vesselness measure	: V
Normal nectır	: n
Threshold	: T
Cartesian coordinates of a centerline point	: x_c,y_c,z_c
Median of diameters	: m
Diameter at a centerline poinr	:f_i

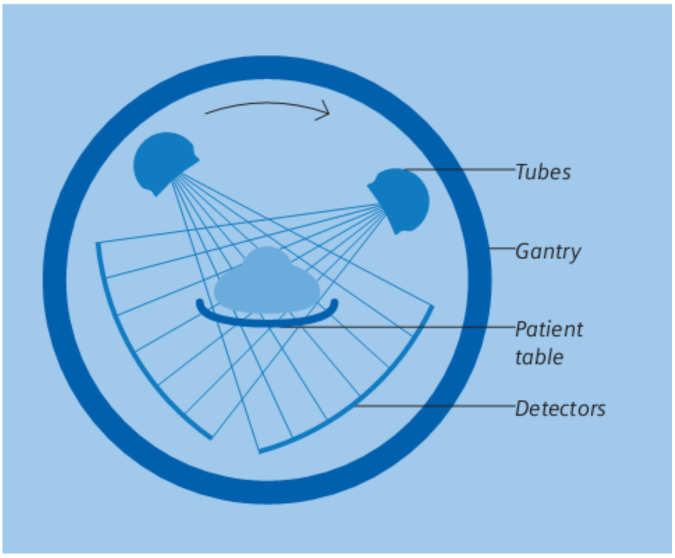
1. INTRODUCTION

The invention of computed tomography is considered to be the greatest innovation in the field of radiology since the discovery of X-rays. This cross-sectional imaging technique provided diagnostic radiology with better insight into the anatomy of the body, thereby increasing the chances of recovery. In 1979, G.N. Hounsfield and A.M. Cormack were awarded the Nobel Prize in medicine for the invention of CT.

Today, CT is one of the most important methods of radiological diagnosis. It delivers non-superimposed, cross-sectional images of the body, which can show smaller contrast differences than conventional X-ray images. This allows for better visualization of specific differently structured soft-tissue regions, which could otherwise not be visualized satisfactorily. Since the introduction of spiral CT in the nineties, computed tomography has seen a constant succession of innovations (Budoff and Shinbane 2010).

A cross-sectional image is produced by scanning a transverse slice of the body from different angular positions while the tube and detector rotate 360° around the patient with the table being stationary (Figure1.1). The image is reconstructed from the resulting projection data. If the patient moves during acquisition, the data obtained from different angular positions are no longer consistent. Thus the image is degraded by motion artifacts and may be of limited diagnostic value. The tomographic technique is suitable only to a limited extent for the diagnosis of anatomical regions with automatism functions such as the heart or the lung (Fitzpatrick and Milan 2009).

Figure 1.1: CT Image acquisition

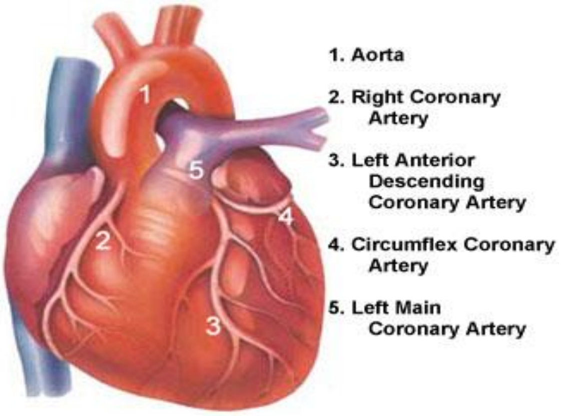


(Fitzpatrick and Milan 2009)

Segmentation of vascular structures, an indispensible part of biomedical imaging applications, is an important step towards diagnosis of and planning the surgical approach, for vascular disorders. Modern 3D angiography produces increasingly large and detailed images that have to be analyzed and interpreted by medical experts. Accordingly, the need for automated or semi-automated segmentation methods for processing medical images has become more indispensible than ever to reduce the burden on the experts.

Coronary arteries are the first arteries coming out of the aorta on ostias and supplies much needed nutrient and oxygen to the heart muscle (myocardium). The coronary arteries are separated into two main arteries: right coronary artery and left main coronary artery. Furthermore, the latter has two major branches Left Circumflex (LCX) and Left Anterior Descending (LAD). This specialization appears differently in different patients in their morphology, in the placement of different bifurcations, stenosis and plaques. Therefore, automated and accurate segmentation of coronary arteries in CT Images is much needed (Hariqbal et.al 2010).

Figure 1.2: Image of heart and coronary arteries



(Hariqbal et.al 2010)

This thesis is organized as follows. In Section 2, literature survey will be given with a summary table and explanations of some studies from this table will be presented. In this part, studies will be compared based on the main parts of vessel segementation; modality, pre-processing, segmentation method, automation, results type and evaluation.

In Section 3, methods used in this thesis will be explained. Image acquisition, preprocessing steps will be briefly given at the beginning of this part. Then, methods applied for the segmentation of coronary arteries and lung vessels in this thesis, region growing, Vesselness filter by Frangi (1998),connected component labeling and proposed method by Oksuz et.al (2013) will be explained in detail.

In Section 4, segmentation results obtained via methods explained in Section 3 will be presented for different datasets separately. In Section 5, comparison of these results and comments on the overall status of the thesis in the light of these results will be discussed.

2. LITERATURE SURVEY

Accurate segmentation of the coronary arteries is a crucial task due to the significance of abnormalities on these vessels. Stenosis and calcification of coronary arteries are life threatening issues for humans. Coronary artery segmentation algorithms are critical components of related computer aided diagnosis systems. Early works on coronary artery image analysis focused on DSA (Digital Substraction Angiography) and X-Ray coronary angiogram (fluoroscopy) images, but did not provide any evaluation.

Extraction of coronary arteries from DSA images is discussed in Stansfield (1986), where a rule-based expert system, ANGY, is proposed to segment coronary vessels. The ANGY system consisted of a preprocessing stage containing low-level image processing routines, and a rule-based expert system with low-and high-level reasoning. Knowledge-based systems exploit *a priori* knowledge of the anatomical structure. These systems employ some low-level image processing algorithms, such as thresholding, thinning, and linking, while guiding the segmentation process via high-level knowledge. Artificial intelligence based algorithms perform well in terms of accuracy, but the computational complexity is much larger than other approaches. Sarwal and Dhawan (1994) introduced a coronary artery centerline extraction algorithm using DSA images, where they attack the problem from the computer vision aspect by aligning the images using epipolar geometry, and reconstructing the coronary arteries in three dimensions (without any user interaction).

Segmentation of coronary arteries using fluoroscopic images has been a popular research topic as well. Eiho and Qian (1997) proposed a semi-automatic method based on morphological operations to detect the coronary artery tree in cine-angiograms. First a top-hat operator is applied to enhance vessel contours and afterwards morphological erosion followed by half-thresholding operations are used to remove false detections. Then starting from a user-given point on the result, the system extracts the whole coronary artery tree by average gray level based neighborhood processing, and the extracted tree is skeletonized via thinning. Finally, the edges of the arteries are detected by applying watershed transformation on the binary image obtained from a dilation operation on the binary skeleton. Haris et al. (1997) realizes automatic extraction of coronary arteries on fluoroscopic images using watersheds. The algorithm combines recursive sequential tracking, morphological tools of homotopy modification, and watersheds. The authors state that their solution is inadequate in extracting the complete coronary tree. Sun et al. (2009) combined morphological opening and closing algorithms with watersheds to achieve segmentation of coronary arteries, but did not carry out evaluation of their results via golden data (expert segmentations). Recently, Kang et al. (2010) implemented a transition-region extraction method for extracting coronary arteries. Although this semi-automatic method is tested on fifty angiograms, the evaluation approach used is not clarified in the paper. The semi-automatic method proposed by Lara et al. (2009) combines 2D region growing algorithm with a 2D hessian matrix based vesselness measurement to segment the coronary arteries. The results are evaluated for five different datasets, and the average accuracy –in terms of intersecting portions between the artery center lines and the resultant segmented arteries - is measured as 88.9%.

Recently, CTA (Computer Tomography Angiography) has become the modality-of-interest in the field of coronary artery segmentation , because it is a non-invasive diagnostic method (contrary to DSA) and it offers detection and visualization of calcification with better spatial resolution (contrary to fluoroscopy and MR). A graph-cuts based semi-automatic segmentation solution is implemented by Li et al. (2009) to extract the coronary arteries. The input image for graph cuts is prepared by otsu thresholding and a clustering algorithm. Raman and Then (2008) presented a hybrid method that sequentially applies the fast marching algorithm and level sets. Then the centerlines of the coronary arteries are detected by a minimum cost path approach. Main disadvantage of this system is the interactive control needed during the process. Another work making use of minimum cost path approach is introduced by Benmansour and Cohen (2009). Their anisotropic filter based algorithm requires user interaction, and therefore is slow, but it is robust to bifurcations and provides the radius information of the coronary arteries. Chen et al.’s (2010) solution finds the centerlines of the vessels by making use of geometric moments, and calculates the vessel radius with the help of snakes. The method is tested on eight datasets and achieved about 95 percent overlap with expert annotations. Lesage et al. (2008) presented a semi-automatic method based on a tracking framework, where a geometric model is iteratively updated by adding new sphere centers that lie on the surface of the preceding sphere using Monte-Carlo estimation, and achieved an accuracy of 94.5% in nineteen cases. One of the most recent works focusing on coronary artery segmentation is published by Wang et al. (2012), where a 2D level set algorithm with the addition of local and global intensity information is used. The method is fully automatic and robust to artifacts such as kissing (touching) vessels. The results are tested on eighteen CTA datasets from various sources and approximately 94% true positive rate is achieved.

Independent of modality, automatic coronary vessel segmentation is still a challenging task, and robust segmentation algorithms are indispensable in today's world. Moreover, detection and quantification of stenosis in coronary arteries is the next challenging task for researchers. There are challenges and workshops organized internationally to contribute to the advancement of this problem. As an example, MICCAI 2009 hosted a coronary artery centerline extraction workshop, and in MICCAI 2012 a challenge on detection and quantification of stenosis in coronary arteries was organized.

Segmentation of the lung vessels is another challenging problem (that has similarities with coronary artery segmentation). According to WHO (2011) the number of deaths related to lung cancer in 2008 was around 1.4 million people [1]. In order to prevent these deaths early diagnosis of the disease is crucial. Even though there are many methods related to nodule segmentation (Armato et.al 2001) (Rettico et al. 2008), there are limited number of methods proposed for automatic segmentation of the lung vessel tree. These methods mainly focus on region growing (Schmitt et al. 2002) and level set techniques (Queck and Kirbas 2001), whilerecent methods make use of the Hessian matrix based approaches (Descoteaux et al. 2008).

Table 2.1: Summary of Literature Survey

Study	Modality	Segmentation Method	Preprocessing	Automated	Result type	**Datasets+Evaluation**
Stansfield, 1986	DSA	Edge and strip detection	Yes	Yes	Centerlines	**None**
Sarwal and Darwan, 1994	DSA	Epipolar geometry	No	Yes	Centerlines+reconstruction	**None**
Eiho and Qian, 1997	Coronary X-ray	erosion+dilation,Morphological Top-Hat	Yes	No	Centerlines and whole tree	**None**
Haris et al., 1997	Fluoroscopy	Watershed	No	Yes	Centerlines and whole tree	**None**
Sun et al., 2009	Fluoroscopy	Morphological opening+watershed	Yes	Yes	Centerlines	**None**
Kang et al., 2010	Fluoroscopy	transition region extraction	Yes	No	Whole tree	**50 Angiograms** **No Evaluation**
Lara et al., 2009	Fluoroscopy	Region growing+hessian matrix	Yes	No	Whole tree	**5LCA+5RCA** **88.79% intersection accuracy**
Li et al., 2009	CTA	Graph cuts,region average shift	Yes	No	Whole tree	**16 CTA datasets** **No Evaluation**

Raman and Then, 2008	CTA	Fast Marching+ Level Set	Yes	No	Whole tree	**None**
Benmansour and Cohen, 2009	CTA	Anisotropic filtering	Yes	No	Whole tree+Radii	**2 CTA datasets** **No Evaluation**
Chen et al., 2010	CTA	Geometric moments based tracking+snakes	Yes	No	Whole tree+Radii	**8 CTA datasets** **%94.7 Overlap**
Lessage et al., 2008	CTA	Bayesian tracking	Yes	Yes	Whole tree+Radii	**19 CTA datasets** **SI=94.8%**
Wang and Liatsis 2012	CTA	2D Level Sets,global and local intensity info. İn energy calculation,pdf+cdf	Yes	Yes	Whole tree	**Synthetic image + 8 CTA** **%95 OM on synthetic** **%78 OM on CTA**

DSA:Digital Substraction Angiography; CTA: Computed Tomography Angiography; SI:Similarity Index SI= $\frac{2TP}{2TP+FN+FP}$; OM: Overlap Measure

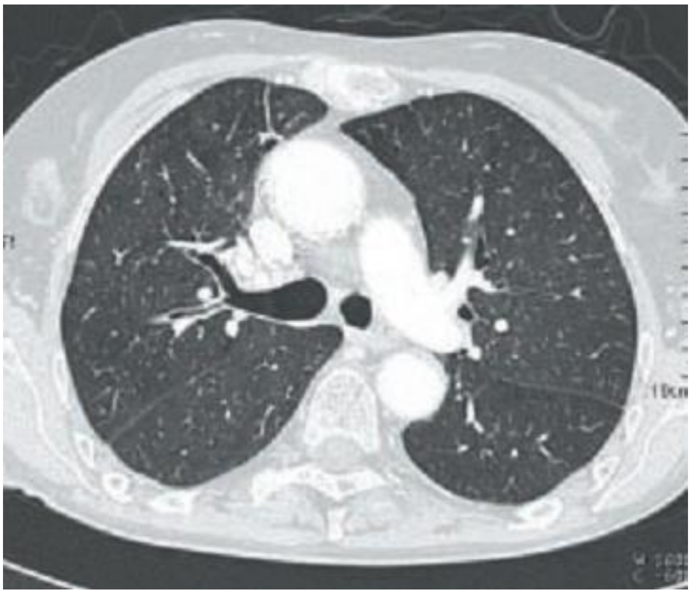
3. METHODS

In this section Image acquisition followed by the approaches used in this study (Region Growing, Frangi Vesselness, Connected Component Analysis, the Proposed Method, and Plane Fitting and Stenosis Detection) will be explained respectively.

3.1 IMAGE ACQUISITION

The images used in this study are acquired from multiple resources. Coronary CT Images are taken from the PACS system of Maltepe University Medical School. Each 512 X 512 and 16 bit intensity z-stack contains 100-200 layers and the distance between these layers is 1 mm. For stenoses detection purposes the Rotterdam Coronary Artery Challenge Framework by Kirisli et.al (2013) is used. The images from that database consist of a set from 3 different centers with different pixel spacing and slice thicknesses. For the lung vessel tree analysis, ISBI 2012 VESSEL12 Challenge Training data is processed and evaluated. This database contains images Each 512 X 512 and 16 bit intensity z-stack contains 150-250 layers and the distance between these layers varies between 0.5-1 mm.

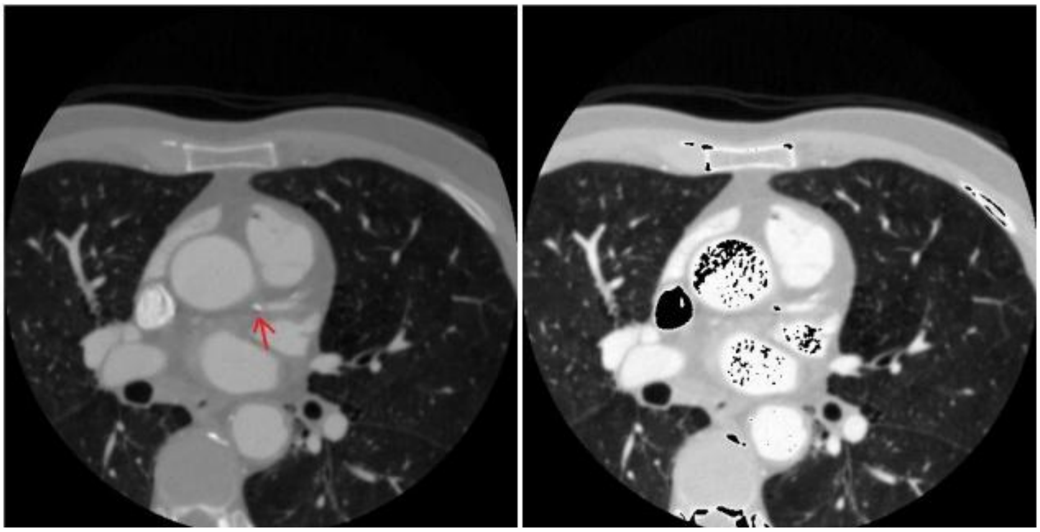
Figure 3.1: An image from the database showing a slice of the CT Image



3.2 PREPROCESSING

The acquired images further include the pulmonary vessels from the lung region observed as high intensity regions, which need to be excluded from the analysis. To this end, a threshold of -400 HU (Hounsfield Unit) is used to extract the lung region from images.The extracted region is used as a mask with the help of morphological dilation. The voxels with intensities higher than 500 HU is also removed due tothe fact that they belong to a calcified region. The calcifications are not part of a vessel lumen and they could lead to false segmentations.

Figure 3.2: Result of Preprocessing; on left: original image with calcification, on right: preprocessed image with calcification region removed



3.3 REGION GROWING

The algorithm requires seeds for the foreground and the background to be provided.. Seeds are used to compute the initial mean gray level for each region. The region growing criteria is thedifference of a gray level of a candidate pixel and the mean grey level intensity of the region. At each step of the algorithm a candidate with the smallest intensity is added to the region and all the neighboring pixels that are not yet assigned to any region are added to the candidate list. Seeded region growing algorithm is proposed by Adams and Bischof (1994).

3.4 FRANGI VESSELNESS FILTER

In this work the Hessian matrix based method proposed by Frangi (1998) for extracting tubular structures from an image is used to determine the vesselness of any voxel in the data. It uses the cylindrical structure of the vessels and segments them by employing a line enhancement filter.

The Hessian matrix consists of the second order gradients of an input image, I. The orientation of the eigenvalue of the matrix is the basis for the vesselness filter

$$H = \begin{bmatrix} \partial^2 I/\partial x^2 & \partial^2 I/\partial x \partial y & \partial^2 I/\partial x \partial z \\ \partial^2 I/\partial x \partial y & \partial^2 I/\partial y^2 & \partial^2 I/\partial y \partial z \\ \partial^2 I/\partial x \partial z & \partial^2 I/\partial z \partial y & \partial^2 I/\partial z^2 \end{bmatrix} \qquad (3.1)$$

Where I refers to the image and ∂ the gradient operator, respectively gradients of the three dimensional image. The calculation of Hessian matrix is repeated at each voxel location with different scales.

Using these values a vesselness value can be calculated (3.5).

$$R_A = \frac{|\lambda_1|}{|\lambda_2|}$$

(3.2)

$$R_B = \frac{\lambda_1}{\sqrt{\lceil \lambda_2 \lambda_3 \rceil}}$$

(3.3)

$$S = \|H\|_F = \sqrt{\sum_{i<3} {\lambda_i}^2}$$

(3.4)

$$V = \begin{cases} 0, & \lambda_2 > 0 \; or \; \lambda_3 > 0 \\ (1 - e^{\frac{{R_A}^2}{2\alpha^2}})\, e^{-\frac{R_B}{2\beta^2}} \left(1 - e^{\frac{s^2}{2c^2}}\right), & otherwise \end{cases}$$

(3.5)

where 'V' is the normalized vesselness value for each voxel on the data; α, ß and c represent the weights, and the values of R_A , R_B and S are calculated from different eigenvalues of the Hessian matrix.Figure 3.3 shows eigenvectors corresponding to the eigenvalues. The scale is empirically set to 2 following the experiments on the training dataset. The Figure 3.4 shows the final f-values comparison of different scale selections. There is a trade off between the increasing f-measure performance of greater scale and the computational cost. Scale 2 is selected as the optimum point for the variety of scales.

Figure 3.3 Eigenvectos in Frangi Vesselness Filter

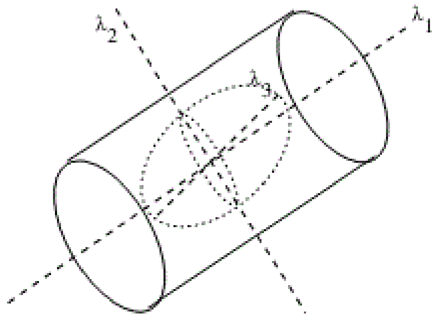
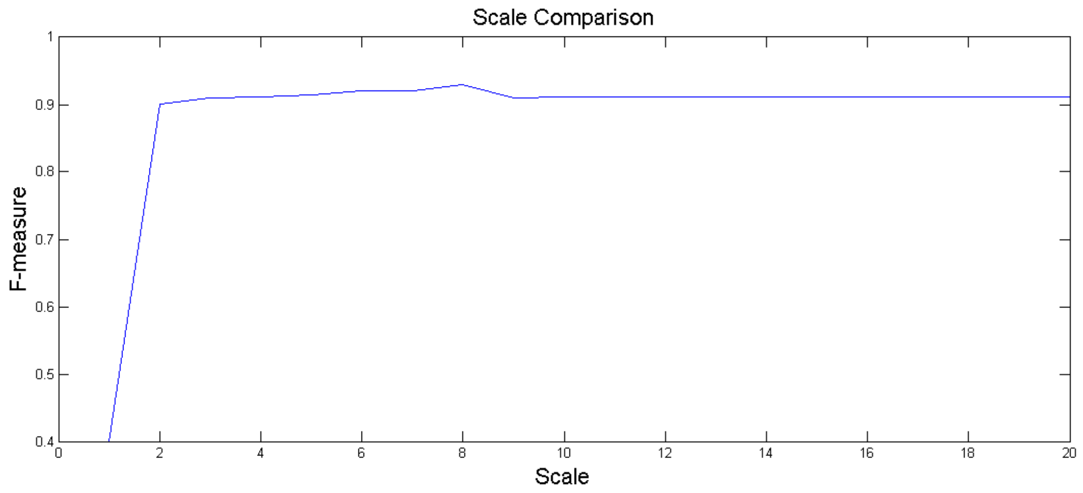


Figure 3.4 F-measure comparison with different scales



3.5 CONNECTED COMPONENT LABELING

On Frangi vesselness probabilities a threholding is applied and then the biggest twocomponents will refer to the coronary arteries. Connected components labeling scans an image and groups its pixels into components based on pixel connectivity, *i.e.* all pixels in a connected component share similar pixel intensity values and are in some way connected with each other. Once all groups have been determined, each pixel is labeled with a gray level according to the component it was assigned to (Gonzalez and Woods, 1992).

Connected component labelling works by scanning an image, pixel-by-pixel in order to identify connected pixel regions, *i.e.* regions of adjacent pixels which share the same set of intensity values *V*.

Connected component labelling works on binary or gray level images and different measures of connectivity are possible. However, for CT images we assume binary input images and *8-connectivity*. The connected components labelling operator scans the image by moving along a row until it comes to a point *p* (where *p* denotes the pixel to be labelled at any stage in the scanning process) for which $K=\{1\}$. When this is true, it examines the four neighbours of *p* which have already been encountered in the scan (*i.e.* the neighbours (i) to the left of *p*, (ii) above it, and (iii and iv) the two upper diagonal terms). Based on this information, the labelling of *p* occurs as follows:

i. If all four neighbors are 0, assign a new label to *p*, else
ii. if only one neighbor has $K=\{1\}$, assign its label to *p*, else
iii. if more than one of the neighbors have $K=\{1\}$, assign one of the labels to *p* and make a note of the equivalences.

After completing the scan, the equivalent label pairs are sorted into equivalence classes and a unique label is assigned to each class. As a final step, a second scan is made through the image, during which each label is replaced by the label assigned to its equivalence classes (Ballard and Brown, 1982).

Using the connected component approach on binary Frangi vesselness results would give us the desired coronary arteries region.

3.6 PROPOSED METHOD

In order to segment the points belonging to the coronary arteries, a 3D region growing operation with adaptive thresholding is used on the vesselness maps of the data; and to initialize the region growing algorithm, multiple seed points from both right and left coronary arteries are employed. The resulting point cloud is then fed into the subsequent stenosis detection algorithm.

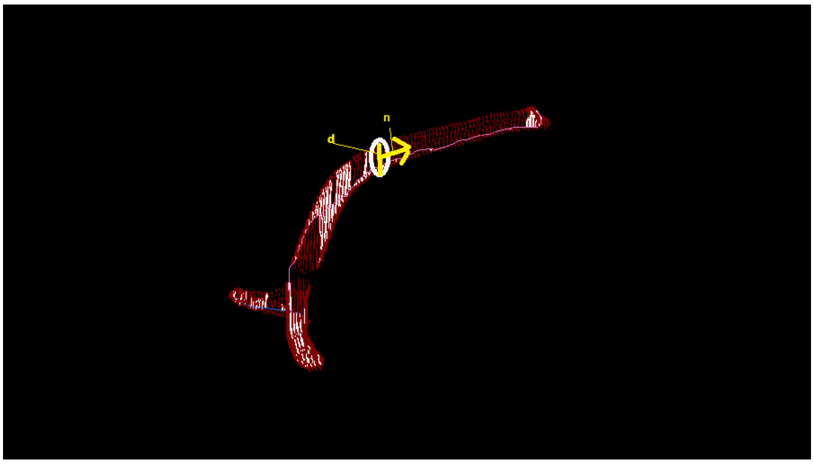
3.7 PLANE FITTING AND STENOSIS DETECTION

Plane fitting is performed for every centerline point, where the corresponding vessel diameter is determined. As a plane can be described with a point and a normal to the plane, we employ the detected centerline point and the dominant eigenvector of the Hessian matrix at that location as the normal vector. Based on the familiar plane equation defined in a three-dimensional space, where (n_x, n_y, n_z) refers to the normal vector, T is an empirically set 2-voxel threshold (T=s) while (x_c, y_c, z_c) and (x, y, z) define the Cartesian coordinates of the centerline location and that of another arbitrary point from the lumen data, respectively. Accordingly, luminal data points that satisfy the above equation are said to belong to the plane-of-interest and, thus, are used to compute the diameter at the corresponding centerline location. Here the diameter is defined as twice the average Euclidean distance between the lumen points (satisfying the above equation) and the corresponding centerline location

$$n_x(x - x_c) + n_y(y - y_c) + n_z(z - z_c) \leq T$$

(3.6)

Figure 3.5. Illustration of diameter (d) calculation via plane fitting using the normal vector (n) at a centerline point



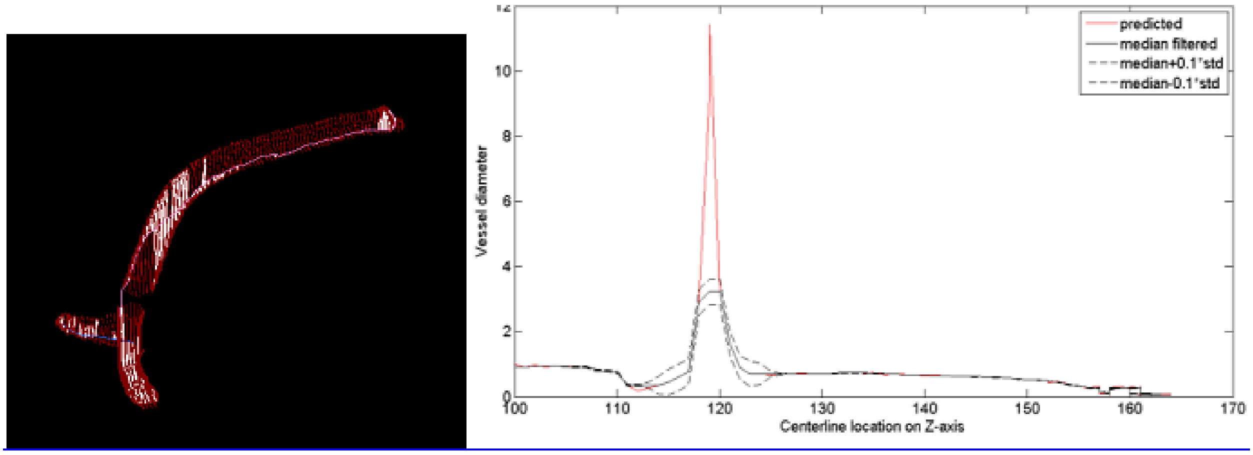
In order to quantify local diameter variations along an artery, which can be a sign of stenosis, we make use of the arterial diameter profiles. We apply 1D running window (size 7) based median (m) and standard deviation (σ) filtering to the profile data (Fig. 5), and then quantify stenosis at each centerline location as

$$\text{stenosis} = \begin{cases} \dfrac{\arg\min\{f_i - (m_i + 0.1\sigma_i), f_i - (m_i - 0.1\sigma_i)\}}{f_i} & , if\ positive \\ 0 & , otherwise \end{cases}$$

(3.7)

where f_i is the diameter value at the centerline location investigated for every centerline point and certain decrease in diameter are marked as possible stenoses points for the vessel. The percentage between the smallest diameter and adjacent diameter to stenosis gives the CTA Grade. QCA grade is proportional with the length of the stenosis.

Figure 3.6. Stenosis detection: Segmented vessel (left); Corresponding diameter profile and its filtering results (right).



4. RESULTS

In order to validate the results of coronary arteries and lung vessel tree segmentation and coronary artery stenosis section and quantification methods, we have used 5 different CT images with manually segmented coronary arteries by the experts from Maltepe Univesirty Medical School.

Evaluation of segmentation accuracy is realized by the F-measure, defined as a measure of a test's accuracy. It considers both the precision and the recall of the test to compute the score Equation (4.1) is used for the calculation of F-measure. In this equation recall measures the proportion of actual positives which are correctly identified as such. Precision measures the proportion of negatives which are correctly identified as such of segmentation result obtained using an automated segmentation method. The F measure score can be interpreted as a weighted average of the precision and recall, where a F measure score reaches its best value at 1 and worst score at 0.

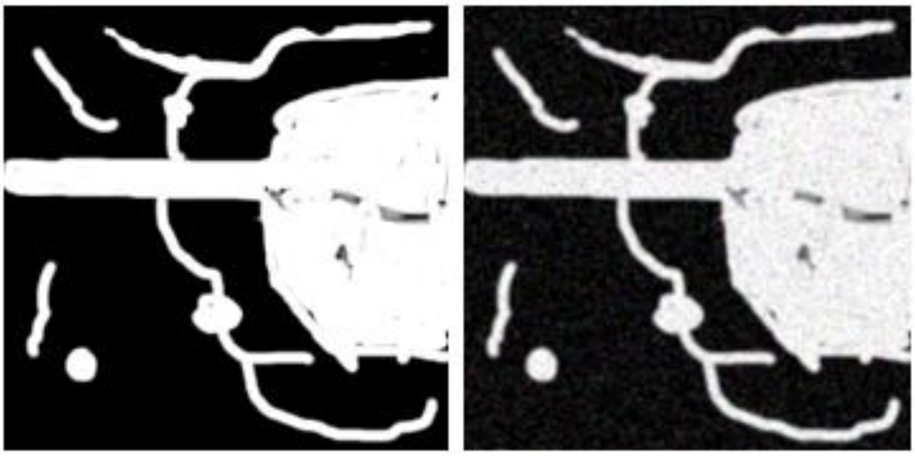
$$F\_measure = \frac{\text{2xPrecisionxRecall}}{\text{Precision} + \text{Recall}} \tag{4.1}$$

In the following sections we first explain the synthetic dataset that we built to test the performance of our algorithm. Then, the results of each algorithm will be presented separately using both F-measure and visual analyses that contain four different images. After that, we will show the whole 3D Coronary Artery Segmentation results and their 2D representations for each method.

4.1 RESULTS OF SYNTHETIC DATA

In order to segment multiple vessel segmentation algorithms, a 2D Synthetic Data is created, considering the anatomical and pathological variations in coronary arteries (Figure 4.1). To that purpose, aneurysms, bifurcations and stenoses with varying sizes are added to the left and right coronary arteries. Moreover, random noise and Gaussian blurring in the range of 0-to-20 per cent is added to the synthetic image. With the help of these variations a more realistic coronary artery dataset is created (Figure 4.1).

Figure 4.1: Examples from Sytnhetic Dataset, left: Noisefree data, right: Noise added data

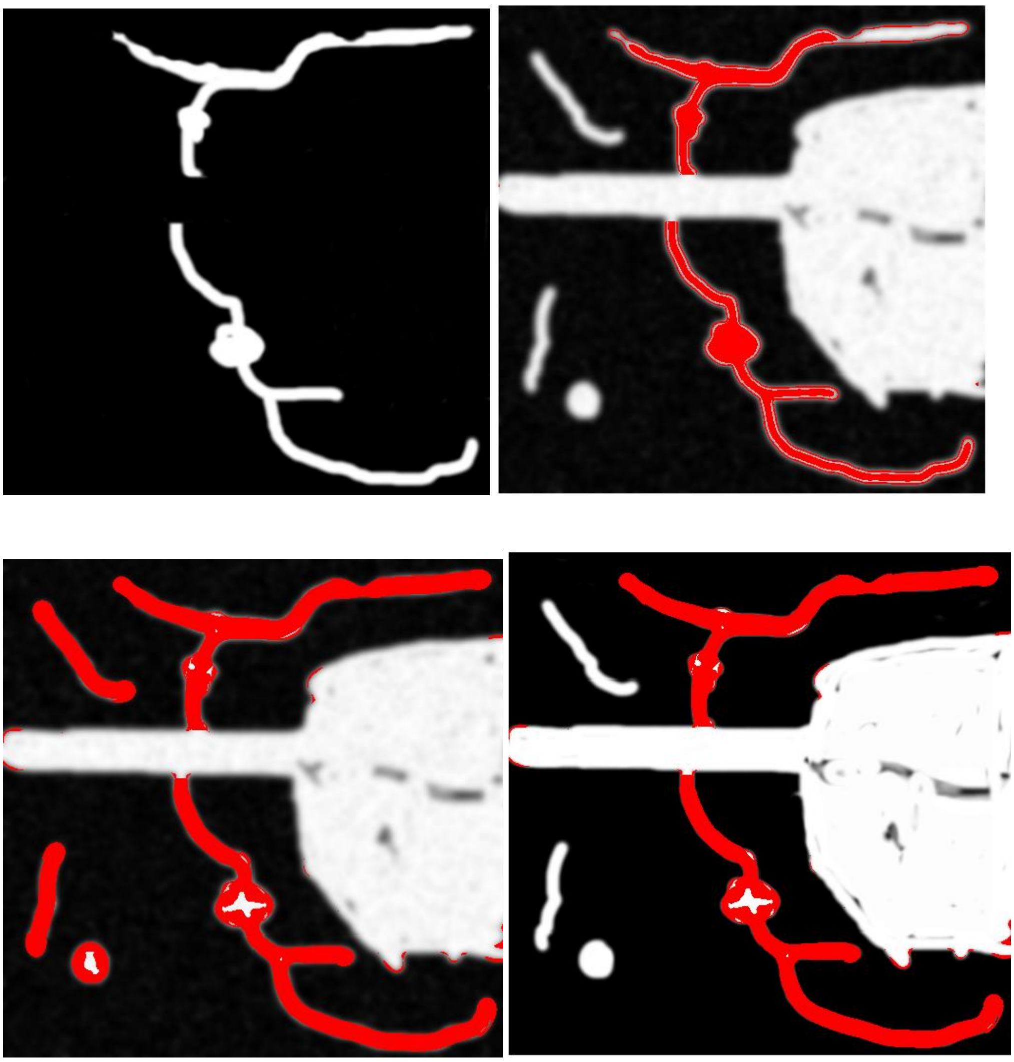


The synthetic dataset is tested with four different methods and evaluated based on specificity, sensitivity and F-measure. Table 4.1 compares the F-measure results and figure compares the specificity-sensitivity graphs of the algorithms. The true positive points for the algorithms are selected as the right and left coronary arteries. Ostia and left ventricle regions are not added to the evaluation, since they can be removed automatically with post-processing.

The proposed method is compared with region growing, Frangi vesselness, and connected component labeling over Frangi vesselness approaches. For each approach multiple threshold values are tried and the optimal threshold values are used. Table 4.1 shows that proposed method clearly outperforms its counterparts quantitatively. As the figure shows Frangi vesselness method has low sensitivity and region growing has low performance on stenosis locations due to the lack of vesselness information at those regions. The proposed method, however, solves that problem with the help of the high vesselness values on the stenosis region. The connected component labeling has the setback of under segmenting aneurysm regions, where many false negative points can be seen. Therefore, this method has lower sensitivity values.

Finally, for statistical significance analysis paired T-test is applied on the segmentation results (Table 4.2). Our analysis revealed that the results of the proposed method are significantly different (*p*-value <0.04) than those of both region growing, Frangi vesselness, and connected component analysis over Frangi vesselness approaches.

Figure 4.2: Results of synthetic coronary artery segmentation top left:synthetic coronary arteries, top right: region growing result, middle left: Frangi vesselness result, middle right: Frangi connectivity result, bottom left: proposed method result, bottom right: Zoom in comparison of connectivity and the proposed method



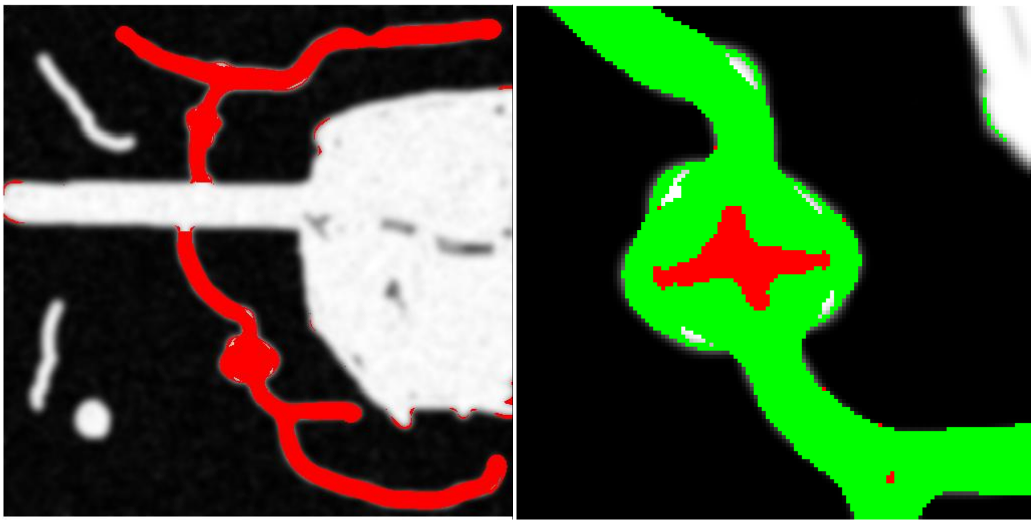


Table 4.1: F measure based comparison of the methods, B: Gaussian blur N:Random Noise

G (%)	B (%)	Frangi	Region Growing	Frangi Connectivity	**Proposed Method**
0	0	0.741	0.321	0.870	**0.928**
5	10	0.068	0.734	0.866	**0.895**
10		0.736	0.214	0.867	**0.902**
15		0.046	0.740	0.603	**0.891**
20		0.016	0.742	0.600	**0.876**
10	5	0.746	0.228	0.877	**0.927**
	10	0.736	0.214	0.867	**0.902**
	15	0.724	0.191	0.843	**0.886**
	20	0.712	0.102	0.818	**0.831**

Figure 4.3: Sensitiviy-specificity comparison of different methods with varying thresholds

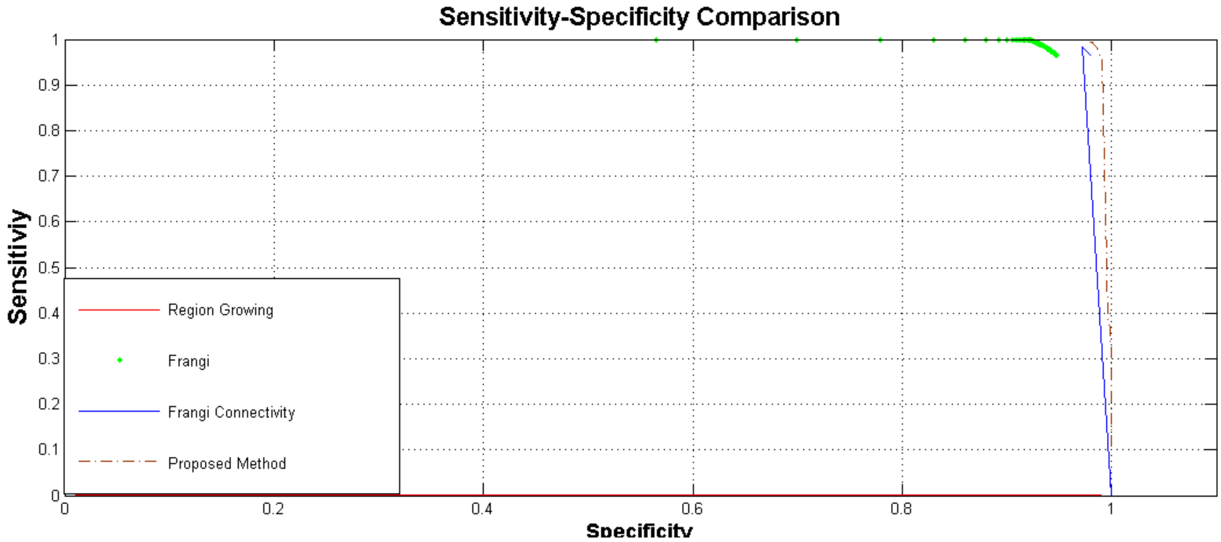


Table 4.2: P-values comparison

P Values	Frangi	Region Growing	Frangi Connectivity
Proposed Method	0.0089	0.0005	0.0348

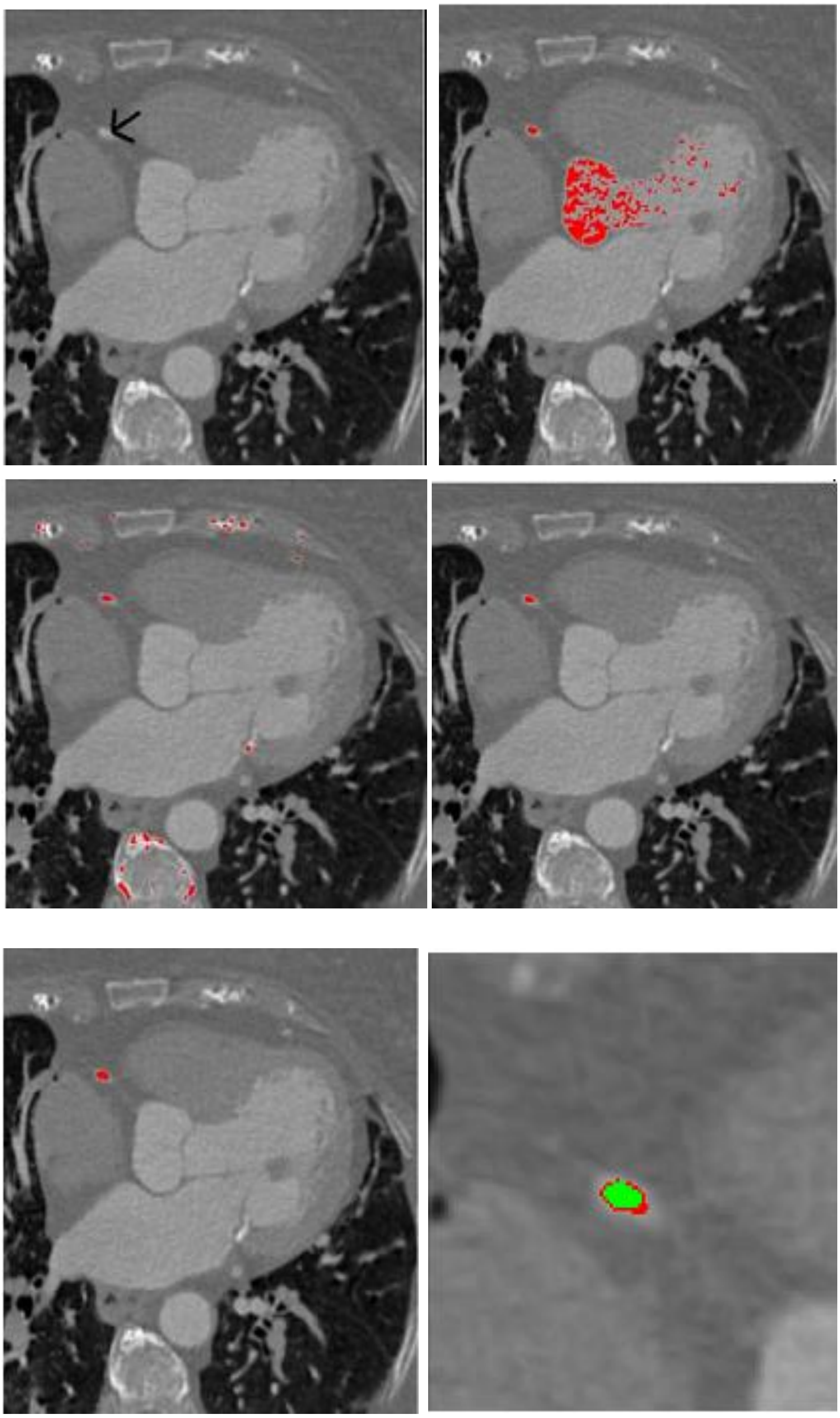
4.2 RESULTS OF OF 3D CORONARY ARTERIES DATA

The methods are evaluated on 3D CT data which is annotated by an expert in Maltepe Medical School. The dataset consists of 5 different subjects. Figure 4.3 shows the 2D slices overlapped with the segmentation. The first image shows the right coronary artery on that slice. The visual results clearly show that many of the false positives of the Frangi vesselness results are eliminated with the help of the proposed algorithm. Region growing on the original data creates many false positives at the aorta and left ventricle regions. The 3D connected component analysis over Frangi vesselness values gives better results than the other two methods. However, the zoomed in images in Figure 4.4 clearly show that the method has more false negatives than the proposed method

Table 4.3: F-Measure based comparison of 3D Coronary Artery Data

	Frangi	Region Growing	Frangi Conncectivity	**Proposed Method**
Subject 1	0.341	0.412	0.652	**0.858**
Subject 2	0.312	0.734	0.866	**0.895**
Subject 3	0.456	0.521	0.867	**0.931**
Subject 4	0.567	0.679	0.853	**0.903**
Subject 5	0.216	0.723	0.832	**0.955**

Figure 4.4: Results of coronary artery segmentation top left: right coronar artery region, top right: region growing result, middle left: Frangi vesselness result, middle right: Frangi connectivity result, bottom left: proposed method result, bottom right: Zoom in comparison of connectivity and the proposed method



4.3 RESULTS OF STENOSIS DETECTION AND QUANTIFICATION

The algorithm is tested on the Rotterdam Coronary Artery Stenoses Detection and Quantification challenge training file, which consists of 18 different datasets. The execution time of an average dataset on 2.4 GHz processor is approximately ten minutes with the algorithm. The results for training dataset can be seen on Table.1.

Our method promises a novel solution for coronary artery stenoses detection and quantification. The method should be optimized in terms of minimizing user interaction and execution time. Also, as adjacent stenoses in the training data are lumped in a single stenosis and classified as one, modification of the present algorithm is warranted towards dividing a segment into its multiple stenoses and treating each as a separate entity.

Table 4.4 Training Dataset Results

	QCA Sens. %	**QCA P.P.V. %**	**CTA Sens %**	**CTA P.P.V. %**	**QCA Avg. diff. %**	**QCA R.M.S diff. %**	**CTA Kappa** K
Detection	0.29	0.56	0.08	0.14			
Quantification					29.8	37.4	-0.06

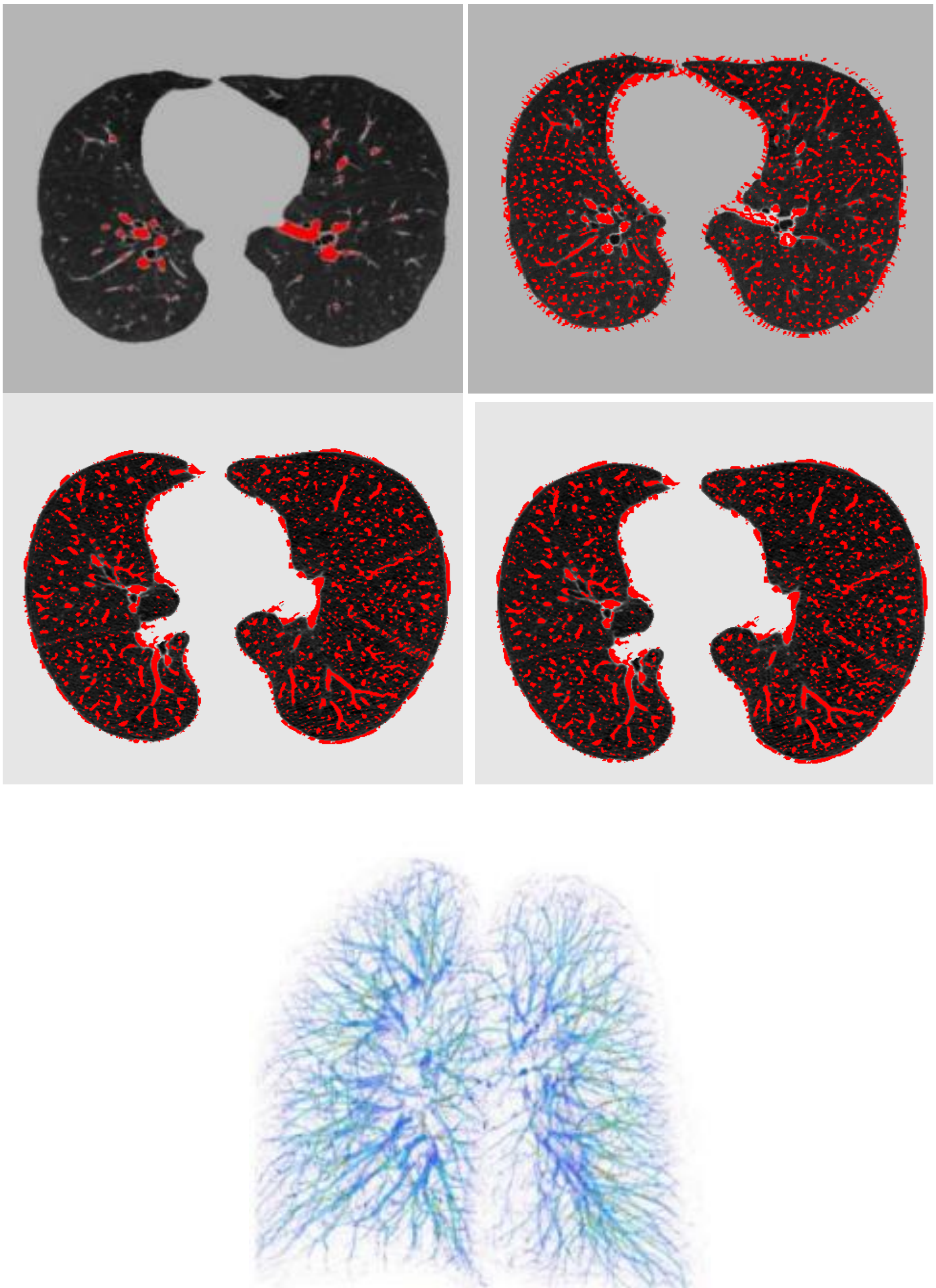
4.4 RESULTS OF LUNG VESSELS

The same methods are applied on lung vessel tree segmentation problem. For this purpose ISBI2012 VESSEL12 Challenge Training Dataset is used. The dataset consists of three different subjects. The results are summed up in the table below. It can be clearly seen that the proposed method outperforms the other methods in the literature.

Table 4.5 F measure results on the Lung Vessel Tree Dataset

	Region Growing	Frangi	Frangi Connectivity	**Proposed Method**
Subject 1	0.458	0.895	0.876	**0.912**
Subject 2	0.563	0.873	0.892	**0.932**
Subject 3	0.623	0.819	0.829	**0.862**

Figure 4.5: Results of lung vessel tree segmentation top left: region growing result, top right: Frangi vesselness result, middle right: Frangi connectivity result, middle left: proposed method result, bottom : 3D visualization of proposed method



5. DISCUSSIONS AND RESULTS

5.1 RESULTS

Vessel segmentation in CT images is one of the most important research areas of biomedical engineering since the morphological and statistical properties, such as number, length and volume of the vessels, can play a role in learning process or can be used for understanding the reasons and effects of cardiovascular diseases and lung cancer (Queck and Kirbas, 2002). But manual analysis of coronary arteries and lung vessels is hard and time-consuming since there is a vast amount of data thanks to the advances in the imaging technology. Therefore, these analyses should be done by using automated tools, which should detect coronary arteries and lung vessels, segment them properly and make a post-analysis for calculating the statistical properties of the vessels and monitoring the abnormalities.

In this thesis we worked on segmentation of the coronary arteries and the lung vessel tree. Our main aim is to create an automated tool that will analyze and track abnormalities of vessels, where the accuracy of such analyses is directly connected to the accuracy of segmentation. Therefore, automated segmentation results must be close as close as possible to the manual segmentations of the experts.

We propose to use Region Growing over Frangi Vesselness Values method (Oksuz et al., 2013) for the segmentation of coronary arteries and lung vessels. In this method, the image is first masked by a Hounsfield unit based mask to work on the desired vessels. Afterwards a two scale Frangi filter is used on the whole data. The twp scale is selected optimizing the results that have been made use of in terms of the f-measures results obtained. Finally a region growing operation is applied over the probabilistic vesselness values.

Accuracy of the proposed method is compared on coronary synthetic and real CT Angiography images with three other state-of-the-art methods: (1) Region Growing (2) Frangi Vesselness (1998), and (3) Connected Component Labeling on Frangi Vesselness Values.

Among the four segmentation methods used Region Growing resulted in the lowest accuracy, since it is not able to overreach the stenoses regions and causes a lot of false positives in blood-filled areas. Frangi Vesselness outperforms region growing in terms of true positive predictive value. However, many false positives are created by this method. A connected component analysis on Frangi vesselness values established an F-measure of up to 0.85 (Table 4.1). Nevertheless in some cases this method has many false negatives and shows a low positive predictive value. On the other hand, the proposed method provides an F-measure as high as 0.95.

5.2 FUTURE WORKS

In the present work, accuracy of the region growing on Frangi vesselness approach needs two seed points for both coronary arteries and two lungs. To this end, prior to segmentation supervalvular sinus region could be found automatically with minimal error. In order to make this segmentation method fully automated, a solution that finds the ostias automatically needs to be improved from that point.

Current results for coronary arteries segmentation are evaluated in a relatively small database. We plan to test our algorithm on a larger database to stabilize our algorithm. Furthermore, we also think to test this vessel segmentation approach on different vessels of human body such as, carotid artery and liver vessels.

From this thesis, two papers have been published:

i. Oksuz, I, Unay, D, Kadipasaoglu, K “Region Growing on Frangi Vesselness Values in 3-D CTA Data” Proc. SIU, Girne – Northern Cyprus, 2013

ii. Oksuz, I, Unay, D, Kadipasaoglu, K, “Segmentation of lung vessel tree in 3-D CTA data”, Proc. MASFOR, Istanbul - Turkey, 2012.

We also contributed in other publications (see the published papers of the curriculum vitae). Moreover, we are planning to submit another publication summarizing the results of this work to an IEEE Journal in the near future.

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- Rudyanto R. et.al.(including **Oksuz, I** and Unay, D.) "Comparing algorithms for automated vessel segmentation in computed tomography scans of the lung: The VESSEL12 study" (in preparation)

- **Oksuz, I**, Unay, D, Kadipasaoglu, K "Region Growing on Frangi Vesselness Values in 3-D CTA Data" Proc. SIU, Girne – Northern Cyprus, 2013

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