



**UNIVERSITI PUTRA MALAYSIA**

***COMPUTER-ASSISTED DIAGNOSIS SYSTEM FOR ANGIOGENESIS  
DETECTION AND CLASSIFICATION IN COMPUTED TOMOGRAPHY  
LASER MAMMOGRAPHY***

**AFSANEH JALALIAN**

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LASER MAMMOGRAPHY**

By

**AFSANEH JALALIAN**

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia,  
in Fulfillment of the Requirements for the Degree of Doctor of Philosophy**

**June 2017**

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## DEDICATION

*This thesis dedicated to my beloved husband, Babak Karasfi, to my dear and lovely daughter Parmida, to my little sweet son Bardia, to my dear mother Tooba Soltanieh and my lovely father Hossein Jalalian, and compassionate sisters Elham and Ameneh jalalian that I owe them all of success in my life*



Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the Degree of Doctor of Philosophy

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DETECTION AND CLASSIFICATION IN COMPUTED TOMOGRAPHY  
LASER MAMMOGRAPHY**

By

**AFSANEH JALALIAN**

**June 2017**

**Chairman : Syamsiah bt. Mashohor, PhD**  
**Faculty : Engineering**

Computed Tomography Laser Mammography (CTLM) is a full tomographic system to explore neo-angiogenesis in the breast by generating a volumetric image. Angiogenesis is a new forming of blood vessels which supply the tumour and seen in different shapes such as free standing, polypoid, ring shaped, dumb-bell shaped, diverticular, and spindle shaped. The manual detection of angiogenesis and differentiation of the shapes is a challenging procedure for physician and a CAD system is expected to help radiologists as a second reader.

In this research, a CAD on CTLM images is proposed to detect and classify the angiogenesis. The proposed CAD systems contain four main steps which are segmentation, objects dissociation, feature extraction, and classification. In segmentation stage, three automatic segmentation techniques are implemented to extract and reconstruct the volume of interests (VOIs) on CTLM images. The ground truth is extracted from window-level technique on the original CTLM images.

As the pre-processing before feature extraction step, the VOIs have been dissociated to sub-VOIs. The two region properties features include centroid and extrema which have been utilised to prepare the dissociation model of VOIs. According to the characteristics of abnormalities in CTLM image that critically depends on shape and intensity, various shape and texture properties are extracted in the feature extraction level. Three different compactness features are extracted from dissociated objects (sub-VOIs). The Harlick's features are extracted based on 3D Grey Level Co-occurrence (GLCM) matrix. Hence, different combination of shape features and Harlick's features have been used for the training procedure.

In the image classification, support vector machine (SVM) and multilayer perceptron neural network (MLPNN) have been used to classify the abnormality in CTLM images. CTLM data set in this work includes 180 patients which are diagnosed by two expert radiologists that considered 132 cases as benign and 48 cases as malignant. In order to overcome the imbalanced dataset, various techniques such as soft margin, kernel function transformation, and oversampling method have been applied to enhance the performance of the proposed classifiers.

The Jaccard and Dice coefficients in addition to the volumetric overlap error are employed to quantify the accuracy of segmentation methods. According to the outcomes, the 3D Fuzzy C-Means clustering presents reasonable results compared to other methods.

The K-fold cross-validation with  $k=10$  is used in the training and test of the proposed classifier. The experimental results show that SVM with radial basis function (SVM-RBF) on oversampled data by Adaptive Synthetic Sampling (ADASYN) method achieved the highest performance in terms of accuracy, sensitivity, and specificity which are 98.6%, 97.78% and 99.43%, respectively.

The results of angiogenesis diagnosis by SVM-RBF on oversampled data by ADASYN completely matched with the reports of two expert radiologists in localisation and shapes of angiogenesis. The proposed CTLM-CAD recognise the diverticular shape, polypoid, spindle shaped and free standing shape of angiogenesis.

Abstrk tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Doktor Falsafah

**SISTEM DIAGNOSIS BERBANTU KOMPUTER UNTUK  
PENGESANAN DAN KLASIFIKASI ANGIOGENESIS DALAM  
TOMOGRAFI LASER MAMMOGRAFI**

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Computed Tomography Laser Mammography (CTLM) adalah sistem tomografik penuh untuk meneroka neo-angiogenesis pada payudara dengan menjana imej berisipadu. Angiogenesis adalah pembentukan saluran darah baru yang membekalkan tumor dan ia boleh dilihat dalam pelbagai bentuk seperti berdiri bebas, polypoid, cincin berbentuk, bisu-loceng berbentuk, diverticular, dan gelendong berbentuk. Pengesanan manual angiogenesis dan pembezaan bentuk adalah prosedur mencabar bagi pakar perubatan dan sistem diagnosis berbantu computer (CAD) dijangka untuk membantu ahli radiologi sebagai pembaca kedua.

Dalam kajian ini, CAD mengenai imej CTLM dicadangkan untuk mengesan dan mengklasifikasikan angiogenesis. Sistem CAD yang dicadangkan mengandungi empat langkah utama iaitu segmentasi, objek pemisahan, pengekstrakan ciri, dan klasifikasi. Dalam peringkat segmentasi, tiga teknik segmentasi automatik dilaksanakan untuk mengekstrak dan membina semula jumlah minat (VOI) pada imej CTLM. Kebenaran tanah diekstrak dari teknik tetingkap pada imej CTLM asal.

Sebagai pra-pemprosesan sebelum langkah pengekstrakan ciri, VOIs telah dipisahkan kepada sub-VOIs. Ciri-ciri hartanah dua wilayah termasuk centroid dan extrema yang telah digunakan untuk menyediakan model pemisahan VOI. Menurut ciri-ciri kelainan dalam imej CTLM yang secara kritikal bergantung pada bentuk dan keamatan, pelbagai bentuk dan sifat tekstur diekstrak dalam tahap pengekstrakan ciri. Tiga ciri padat yang berbeza diekstrak dari objek yang dipisahkan (sub-VOI). Ciri-ciri Harlick diekstrak berdasarkan matriks 3D Grey Level Co-occurrence (GLCM). Oleh itu, gabungan ciri-ciri bentuk yang berbeza dan ciri-ciri Harlick telah digunakan untuk prosedur latihan.

Dalam klasifikasi imej, mesin vektor sokongan (SVM) dan rangkaian neural perceptron multilayer (MLPNN) telah digunakan untuk mengklasifikasikan kelainan pada imej CTLM. Data CTLM yang ditetapkan dalam kerja ini termasuk 180 pesakit yang didiagnosis oleh dua ahli radiologi ahli yang menganggap 132 kes sebagai benigna dan 48 kes sebagai malignan. Untuk mengatasi dataset yang tidak seimbang, pelbagai teknik seperti margin lembut, transformasi fungsi kernel, dan kaedah oversampling telah digunakan untuk meningkatkan prestasi pengelasan yang dicadangkan.

Pekali Jaccard dan Dice di samping ralat pertindihan isipadu digunakan untuk mengukur ketepatan kaedah segmentasi. Berdasarkan hasil, 3D Fuzzy C-Means kelompok menghasilkan keputusan yang memuaskan berbanding dengan kaedah lain. *K-fold* pengesahan silang dengan  $k = 10$  digunakan dalam latihan dan ujian pengelasan yang dicadangkan. Keputusan eksperimen menunjukkan bahawa SVM dengan fungsi asas jejarian (SVM-RBF) data terlebih sampel oleh kaedah sintetik persampelan bolehubah (ADASYN) mencapai prestasi tertinggi dari segi ketepatan, kepekaan, dan kekhususan yang 98.6%, 97.78% dan 99.43%, masing-masing.

Hasil diagnosis oleh SVM-RBF data terlebih sampel oleh ADASYN dipadankan sepenuhnya dengan laporan dua pakar radiologi dalam penempatan dan bentuk angiogenesis. Kaedah CTLM-CAD yang dicadangkan berjaya mengenalpasti angiogenesis bentuk diverticular, polypoid, gelendong berbentuk dan berdiri bebas.



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**Afsaneh Jalalian**



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- the research conducted and the writing of this thesis was under our supervision;
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## LIST OF ABBREVIATIONS

ABC	Array Box Constraint
ABUS	Automated Breast Ultrasound
ADASYN	Adaptive Synthetic Sampling
ANN	Artificial Neural Network
AUROC	Area under Receiver Operating Characteristic Curve
BDT	Boosted Decision Tree
BPNN	Back Propagation Neural Network
BUS	Breast Ultrasound
C	Compactness
CADe	Computer Aided Detection
CADx	Computer Aided Diagnosis
CADs	Computer Aided Detection /Diagnosis Systems
C-CONT	Compactness-Contrast
C-COR	Compactness-Correlation
C-ENR	Compactness-Energy
C-ENT	Compactness-Entropy
CDOM	Centroid-Based Object Dissociated Model
CE	Classification Entropy
C-GLCM 3D	Compactness-Grey Level Co-occurrence 3D
C-INT	Compactness-Inertia
C-IVAR	Compactness-Inverse Variance
C-HOMO	Compactness-Homogeneity
C-MPROB	Compactness-Max Probability

CNN	Combined Neural Network
CQ	Colour Quantization
C-SMEAN	Compactness-Sum mean
CTLM	Computed Tomography Laser Mammography
C-VAR	Compactness-Variance
DEOWNN	Differential Evaluation Optimized Wavelet Neural Network
DNA	Deoxyribonucleic Acid
DTF	Decision Tree Forest
EDOM	Extrema-Based Object Dissociated Model
FCM	Fuzzy C-means Clustering
FN	False Negative
FNAB	Fine Needle Aspiration Biopsy
FNB	Fine Needle Biopsy
FP	False Positive
FPR	False Positive Rate
FSVM	Fuzzy Support Vector Machine
FTB	Front to Back Projection
GABOR	GABOR Feature
GLCM	Grey Level Co-occurrence Matrix
GONN	Genetically Optimized Neural Network
GT	Ground Truth
IDS	Imaging Diagnostic System
KNN	K-Nearest Neighbour
LDA	Linear Discriminant Analysis

LM	Levenberg-Marquardt
LPSVM	Linear Programming Support Vector Machine
LSVM	Lagrangian Support Vector Machine
LS-SVM	Least Squares Support Vector Machine
LTEM	Law Texture Energy Measure
MIP	Maximum Intensity Projection
MLP	Multilayer Perceptron
MLPNN	Multilayer Perceptron Neural Network
MRI	Magnetic Resonance Imaging
NBC	Nave Bayes Classifier
NIR	Near-Infrared
NPV	Negative Predictive Value
NSVM	Newton Lagrangian SVM
OSS	One Side Selection
PC	Partition Coefficient
PET	Positron Emission Tomography
PNN	Probabilistic Neural Network
PPV	Positive Predictive Value
PSOWNN	Particle Swarm Optimized Wavelet Neural Network
RBF	Radial Basis Function
RDM	Radial Distance Measure
RNN	Recurrent Neural Network
ROC	Receiver Operating Characteristic
S	Separation Index

SBC	Scalar Box Constraint
SC	Partition Index
SDT	Single Decision Tree
SGLD	Spatial Grey level Dependence
SMOTE	Synthetic Minority Oversampling Technique
SONN	Swarm Optimized Neural Network
SVM	Support Vector Machine
SVM-ABC	Support Vector Machine-Array Box Constraint
SVM-L-ABC	SVM-Linear-Array Box Constraint
SVM-L-ADASYN	SVM- Adaptive Synthetic Sampling
SVM-L-SBC	SVM-Linear-Scalar Box Constraint
SVM-RBF-ADASYN	SVM- Radial Basis Function - Adaptive Synthetic Sampling
SVM-RBF-SBC	SVM- Radial Basis Function -Scalar Box Constraint
SVM-SBC	Support Vector Machine-Scalar Box Constraint
SSVM	Smooth Support Vector Machine
St-SVM	Standard Support Vector Machine
TN	True Negative
TP	True Positive
TPR	True Positive Rate
US	Ultrasound
VOE	Volumetric Overlap Error
VOI	Volume of Interest
WNN	Wavelet Neural Network

## CHAPTER 1

### INTRODUCTION

#### 1.1 Introduction

Breast cancer is the most prevalent cancer that affects women all over the world. Early detection and diagnosis of breast cancer play a significant role to reduce the mortality rate as well as to increase the prognosis of patients. Mammography is the golden standard for breast imaging. Breast screening with mammography involves passing radiation (x-ray) through the breast. Evidence indicates the growth of risk of breast cancer with exposure to multiple mammographies, especially in women with genetic predisposition due to impaired DNA (Deoxyribonucleic Acid) repair mechanisms (Helbich et al. 2012). The results show the sensitivity in women with fatty breast is roughly 88% but drastically decreased in women with dense breast which is 62% (Carney et al. 2003). On top of that, the risk of developing breast cancer in dense breasts is 4 to 6 times higher than in non-dense breasts (Boyd et al. 2007).

In recent years, several studies have been conducted to find alternative methods to adjunct mammography in order to enhance sensitivity and specificity. Ultrasound is a valuable tool that acts as an adjunct to mammograms due to its characteristics, namely availability, non-invasive, and costs-effective. Ultrasound has potential benefits to supplement mammographic screening of women with dense breast tissue. Magnetic resonance imaging (MRI) is another alternative that is suggested for screening women who have a high risk of developing breast cancer, or it can be used to investigate suspicious areas found by the mammogram to help measure the size mass.

Computed Tomography Laser Mammography (CTLM) is an optical imaging technique which is presented for breast screening presented by imaging diagnostic system company (IDSI)(IDSI 2016) , particularly in women under the age of 40 and who have dense breasts. CTLM is a non-invasive and cost-effective modality that uses Near-Infrared light propagation through the tissue to assess its optical properties. Different tissue components have unique scattering and absorption characteristics for each wavelength. In new forming tumours, the blood flow increases and the CTLM then looks for high haemoglobin concentration (angiogenesis) in the breast to detect neovascularisation, which may be hidden in mammography images, especially in dense breast (Flöry et al. 2010, Eid, Hegab, and Schindler 2006, Poellinger et al. 2008a). Malignant lesions will be detected based on their higher optical attenuation compared to the surrounding tissue, which is mainly related to the increase in light absorption by their higher haemoglobin content (Zhu et al. 2005).

Some issues have increased the miss diagnosis of radiologists in visual manner assessment such as technical reasons which are related to imaging quality and human error due to the structural complexity in appearance. Computer-Aided



Detection/Diagnosis (CAD) systems have been developed for automatic detection and classification of the suspicious area on different modality. CAD systems help the radiologist in the interpretation of medical images to detect and differentiate between benign and malignant lesions. CAD systems are used as a double reader for accuracy enhancement and final decision which is made by the physician. In recent years, several computerised diagnosis approaches have been developed on different modalities for breast cancer detection/diagnosis such as the mammography (Xi et al. 2016, Abbas, Fondo'n, and Celebi 2015), Ultrasound (US) (Abdelwahed, Eltoukhy, and Wahed 2015, Jinsamol, Shiji, and Thomas 2015, Rizzi and D'Aloia 2014), Magnetic Resonance Imaging (MRI) (Song et al. 2015, Meyer-Baese et al. 2015) and thermography (Calderon-Contreras et al. 2015) .

Some automated frameworks have been proposed for angiogenesis detection in chick embryo chorioallantoic membrane (Alacam et al. , Shi et al. 2014, Doukas et al. 2006) and fluorescence angiogram image (Zhao et al. 2015). The proposed methods conducted on 2D image and have considered the branch structure of vessels to detect angiogenesis areas. While CTLM image is a 3D imaging modality which angiogenesis detection rely on the characteristics of shape volumes and intensity of vascularity pattern. The existing angiogenesis detection framework unable to adopt for angiogenesis detection in CTLM image. Based on literature review, a similar study has not been conducted as a computer assisted system to detect and classify the angiogenesis area in CTLM images.

## **1.2 Problem Statement**

CTLM is an optical imaging modality that uses Near-Infrared (NIR) laser light propagation to investigate the optical characteristics of the breast tissue, and is expected to play a significant role in breast cancer detection (Herranz and Ruibal 2012). During the CTLM screening, the NIR light in 808 nm penetrates through the breast. CTLM acts on the principle that different tissue components have different absorption and scattering coefficient (Poellinger et al. 2008a). In the screening procedure, both the absorption and scattering light by tissue are recorded. After the screening is completed, the images are reconstructed and displayed in three plane, namely Sagittal, Axial, and Coronal as well as a 3D view of the whole breast. CTLM is sensitive to high haemoglobin concentration that is associated with cancer growth. Malignant lesions are detected based on their higher optical attenuation compared to their surrounding tissues and visualised brighter in the vascular areas (Floery et al. 2005, Qi and Ye 2013).

The radiologist need a lot of practice to be familiar with regular appearance in CTLM image and ability to discriminating between normal blood vessels and angiogenesis. A variety of benign lesions also demonstrated increased vessels which may be considered as malignant lesion (Qi and Ye 2013). Analysis of CTLM image is based on the absorption pattern of haemoglobin in vessels. Bright areas indicate the aggressiveness of cancer while angiogenesis can appear in any shade of green. The detection of angiogenesis in CTLM images does not only rely on the brightness but also the various

abnormality shapes and volumes (Qi and Ye 2013, Poellinger et al. 2008b). The radiologist needs to explore in a 2D plane to find any bright green areas that show distortion or deviation and investigates the irregular shape of angiogenesis in 3D view (Qi and Ye 2013).

The fact that diagnosis in CTLM images for a radiologist is time-consuming and complicated due to variety of angiogenesis shapes (Poellinger et al. 2008b). The essence of machine learning algorithms can be apply to find out the significant characteristics of angiogenesis which is a sign of tumour growth.

The purpose of this study is to design a computer assisted framework for angiogenesis detection and classification normal vessels and angiogenic areas in CTLM image. The proposed system would act to help radiologist in order to reduce miss diagnosis as well as to discriminate between normal vessels and angiogenesis within the breast.

### **1.3 Objectives of the Study**

The overall hypothesis that motivate this work is that computer-assisted systems for breast cancer detection on different modalities can enhance the performance of radiologists to classify suspicious lesions. The aim of this work is to design an automated system for angiogenesis detection and classify the suspicious lesions into normal vascularity and angiogenesis. The presented CTLM-CAD system can improve the accuracy of expert and non-expert readers to discriminate angiogenesis. We propose the following specific objectives:

- 1) To achieve a reliable segmentation technique to extract the vascularity structure from the background of CTLM image.
- 2) To design a dissociated model for dividing the extracted vascularity volume into small objects in order to exploit the specific characteristics of normal vascularity and angiogenesis.
- 3) To extract and select the best combinations of 3D shape and 3D GLCM texture features from dissociated objects according to the characteristics of the normal appearance and angiogenesis in CTLM.
- 4) To obtain the best solution for imbalanced data phenomena on the training data set and compare the outcome of supervised classification techniques to discriminating the normal vascularity and angiogenesis.

### **1.4 Scope and Motivation of Research**

In this study, the CTLM breast images of women have been acquired from clinical screening in Breast Wellness centre, Malaysia and two datasets from Medoc centre in Budapest, Hungary and TATA Hospital in Mumbai, India. The data collection in Malaysia has been conducted between April 2014 and September 2015. A total of 180 patients has been examined with CTLM and ultrasound for patients under the age of 40, while CTLM, ultrasound, and mammography were conducted for those above the

age of 40. The patients have been examined for breast ultrasound and mammography in the Golden Horses Health Sanctuary (GHHS) Malaysia.

The contribution of this research is in two respects. From the medical viewpoint, this CAD system would be effective by significantly enhancing radiologists' overall performance to detect and diagnosis of angiogenesis through sensitivity and specificity. From the technical view point, the first contribution is to create a dissociation model and identify the best combination features to classify angiogenesis and normal vascularity. Solving the imbalance data phenomena and tuning of supervised classifiers for angiogenesis diagnosis is the other aspect of technical contributions. The results of our system are matched to the report of expert radiologists with a correlation of mammography and ultrasound images.

## **1.5 Organization of the Thesis**

In Chapter 1, a brief review related to background of research, problem statement, objectives of research, and scope of research is presented. In Chapter 2, a general literature review related to the medical aspects of CTLM modality for breast cancer detection will be introduced. This section is then followed by the introduction on different modalities for breast cancer detection and review on CAD systems on these modalities. The cornerstones of the CAD system are investigated in the rest of this section. In Chapter 3, the details of the proposed methodology are explained. The 3D segmentation and reconstruction techniques are described in this section to extract volume of interests (VOIs) for further analysis. The overview of dissociation model to split VOIs and the extracted features are also described in details. The classification techniques and resolving methods in the imbalanced dataset are presented in this chapter. In the next section of this chapter, the experimental design and evaluation approaches to assess the proposed CAD system are presented. In Chapter 4, the experimental results and discussion to discover the most optimal 3D segmentation technique in CTLM images are presented. The impact of combination features in different proposed classification methods are investigated in his section. Finally, the performance of SVM and MLP classification methods are evaluated. The conclusion is provided together with the limitations of CTLM CAD system and future works are offered in Chapter 5.

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