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碩士論文

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Characterization of Benign and Malignant Solid Breast Masses Using Vascular Morphology in 3D Power Doppler Ultrasound Images

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摘要

根據中華民國癌症醫學會的統計，乳癌在台灣婦女的癌症發生率已及死亡率中已經躍居第一，乳癌已經是對婦女健康威脅最重大的疾病之一。乳癌並非不可治癒的，相對地它是屬於比較容易早期發現的癌症，越早期發現乳癌，便能越早提供治療以降低乳癌的死亡率。而在腫瘤的發展過程中，血管新生(angiogenesis)扮演著非常重要的角色。血管新生是近年來研究癌症重要的主題之一，由於腫瘤的擴大常伴隨著腫瘤週遭許多新生的血管擷取人體內的養分提供給腫瘤，以壯大腫瘤本身，所以觀察血管新生的發展以及利用抑制劑去抑止腫瘤血管擴張也成為熱門的主題，而觀察腫瘤週遭的血管變化以及發展情形更可以提供進一步的腫瘤病理判斷。

三維都卜勒超音波影像，相較於以往的彩色超音波與能量超音波，它有著較好的雜訊與斑點處理能力。此外，三維都卜勒超音波也能偵測出細小的血流訊號與血流的方向性。對於檢查乳房腫瘤而言，三維都卜勒超音波除了能發現腫瘤的形狀，也能偵測血流的強度與方向，以及腫瘤血管週遭的變化跟形態。本研究從一系列良性和惡性乳房腫瘤診療過程中的彩色超音影像，將其中的彩色訊號(代表血流訊號)擷取出來，將血管訊號建立出一個三維的模型之後，再從中取出形態學上的血管特徵，利用這些擷取出來的血管特徵進行進一步的追蹤訓練以及分類器的判斷跟比較，找出何種特徵對於良性和惡性的腫瘤有較大的影響，並利用這些特徵去判斷影像中的腫瘤是良性或惡性。

關鍵字：乳房腫瘤，三維超音波，形態學特徵，血管特性，血管新生

ABSTRACT

Angiogenesis is a popular issue and indicator in the assessment of tumor's growth and metastasis. Three-dimensional (3-D) power Doppler ultrasound images could characterize benign and malignant breast masses. Therefore, this study extracts the features vascularization from 3-D ultrasound images and selects seven morphological features to diagnose benign and malignant breast tumors by using support vector machine (SVM). These features are trained by the Az value under the receiver operating characteristic (ROC) curve to distinguish the more important features from others. The simulations evaluate 30 benign and 30 malignant breast tumor cases by using the morphological features. The classification performance of the proposed method in term of A*z* value for the ROC curve of the features derived from 3-D power Doppler is 0.8423. The result shows that the vascular morphology in 3-D power Doppler ultrasound images could be used to diagnose benign and malignant breast tumors.

Keywords: Angiogenesis, 3-D power Doppler, vascularization, breast tumor, morphological feature,

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CHAPTER1

INTRODUCTION

Breast cancer is one of the most serious cancers for women. According to report of the American Cancer Society (ACS), breast cancer has become the highest cancer disease for female cancers in 2009. Early diagnosis and treatment is the most effective way of reducing mortality caused by breast cancer [1;2]. For early detection of breast cancer, mammography and sonography are the most popular methods used screening modalities in the past years [3-5]. In recent years, using ultrasound images to diagnose breast tumors have become more wide and popular. More and more vascular information could be analyzed from ultrasound examination which is more convenient and safe than other tools for diagnosing breast with patients.

Three dimensional (3-D) power Doppler ultrasound images are one of the most popular ultrasound images to diagnose diseases. Huang *et al.* [6] assessed the vascularization of tumor through 3-D power Doppler ultrasound and proposed a decision model for the classification of benign and malignant breast tumors. Chen *et al.* [7] proposed a computer-aided diagnosis (CAD) algorithm, which is effective and reliable to distinguish between benign and malignant lesions tumors. Then, there is a new CAD system based on 3-D thinning algorithm and neural network for quantifying 3-D power Doppler ultrasound images [8]. Thus, using vascular morphology in

ultrasound images to characterize benign and malignant breast masses is a famous issue in these years.

Angiogenesis has been confirmed with the growth of tumor and the nutrient of blood vessel [9;10]. Angiogenesis is the physiological process involving the growth of new blood vessels from preexisting vessels. Metastasis of the tumors also has a close relationship with angiogenesis. But the vascularization of tumor is usually irregular and complex, medical diagnosis would not immediately determine malignant or benign solid breast masses. The original 3-D power Doppler ultrasound images contains noisy and speckles. 3-D vascular model also have so much the noise of blood vessel that physicians are difficult to diagnose breast cancer from vascular images which were not preprocessed. As a result, the vascularization of tumor which surround and developed from tumor can provide as a morphological feature to diagnose breast tumor. Vascular length, curve, branch, direction and division will provide as a morphological feature for diagnosis.

The 3-D power Doppler ultrasound images also provide the information of directional flow to observe blood vessels' model and feature extractions from the vascularization of tumor. This research performed a sequence of 3-D mathematical and morphological operations to extract the morphological features of vascularization. Afterward, thirteen morphological features were trained from support vector machine

(SVM) to identify what the useful feature is. All features were also trained by the Az value under the receiver operating characteristic (ROC) curve. Finally, we use sixty breast cancers to diagnose benign or malignant breast cancer by using seven morphological features. Figure 1 is the flow chart of this study.

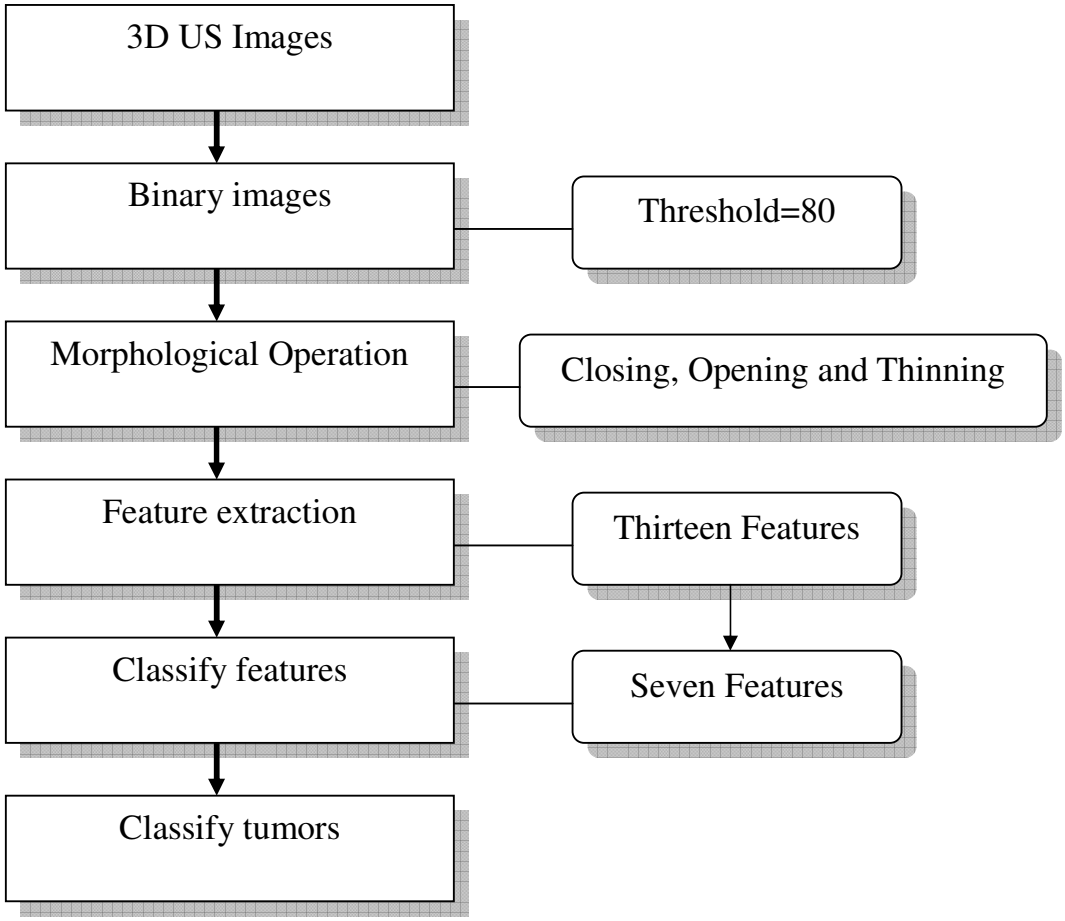

Fig. 1. The flow chart of this study

CHAPTER2

MATERIALS AND METHOD

2.1 DATA ACQUISITION

During the period of January to June 2009, there were thirty benign and thirty malignant breast tumors in sixty patients were collected. In this study sonographic examinations were done by using 3-D power Doppler ultrasound with the high-definition flow (HDF) function (Voluson 730, GE Medical Systems, Zipf, Austria). A linear-array broadband probe with frequency of 6-12 MHz, a scan width of 37.5mm, and a sweep angle of 5◦ to 29◦ to obtain 3-D volume scanning was used. Physician kept a fixed sweep angle of 20◦ and power Doppler settings of mid frequency, 0.9 kHz pulse repetition frequency, -0.6 gain, and 'low 1' wall motion filter in all cases All obtained images were stored on the hard disk and transferred to a personal computer using a DICOM (Digital Imaging and Communication in Medicine) connection for image analysis . Each 3-D power Doppler images contained 155 to 199 2D image, the width and the high of each image were 199 and 140 to 200 pixels, respectively.

2.2 VASCULAR EXTRACTION

Before we extracted the vascular features, the 3-D power Doppler ultrasound

images needed to use image preprocessing. Figure 2 is the original 3-D power Doppler ultrasound image. Ultrasound image usually contains a large number of noisy and speckles. Hence, original ultrasound image needed to process previously for extracting the vascularization of tumor.

Fig. 2. An original 3-D power Doppler ultrasound image

To preprocess the 3-D power Doppler ultrasound images, which were converted into the binary images by applying a predefined threshold T_{voxel} which is based on the vessels intensity (the average value of the red, blue and green color channel). This study tested many different values of T_{voxel} (10-120), and proposed the threshold set to eighty because this range of T_{voxel} retained most of the information of blood flow and caused least multiple vessels wide skeletons (MVWS) regions. The MVWS region was defined as a surface region which can't be thinned correctly since the shape of the

input 3-D object is complex. Figure 3 shows the example vascular image about MVWS problem. From Figure 3, it could be find many skeletons region in blood vessels. In this paper, T_{voxel} was manually selected to be eighty by experience. If T_{voxel} selected lower than eighty, 3-D power Doppler ultrasound images could be lost too much the information of image and many morphological features. In other words, we could not get correct information and feature to analyze. If T_{voxel} selected higher than eighty, 3-D power Doppler ultrasound images could contains a large number of noise and speckles. These noise and speckles would affect image preprocessing and the result of diagnosis. Figure 4 is an example image for doing binary operation.

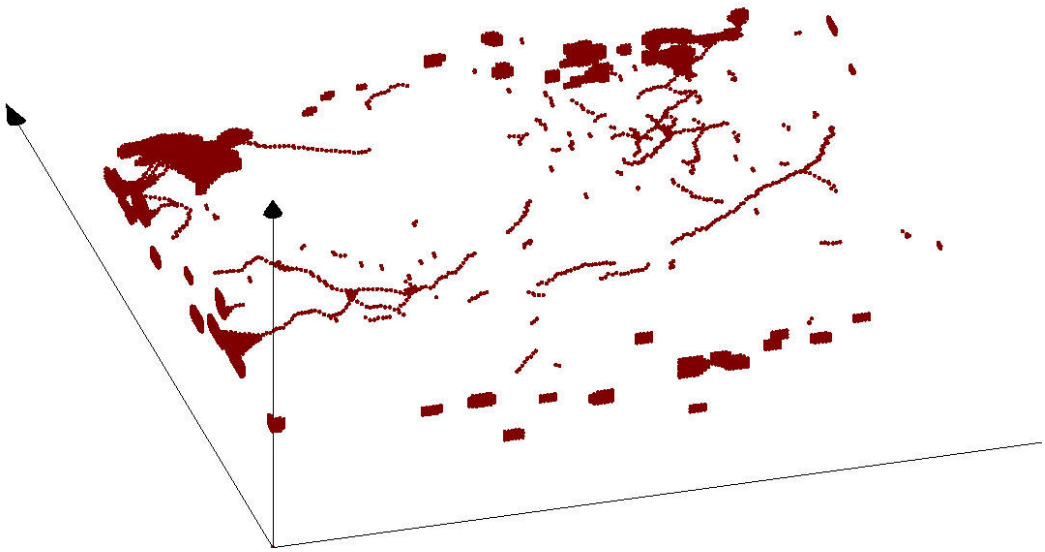

Fig. 3. The result after 3-D thinning and there are some boundary multiple voxels wide skeletons regions and internal multiple voxels wide skeletons

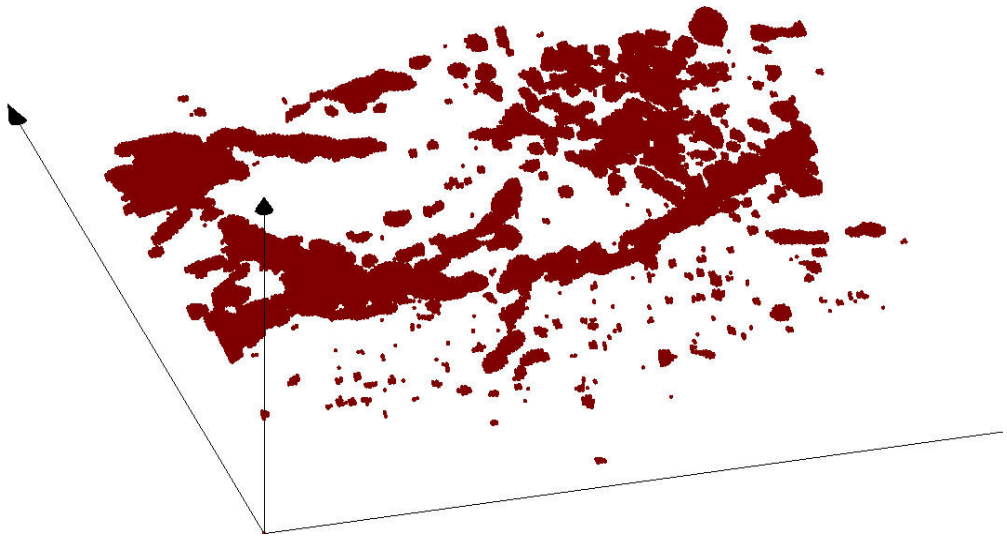

Fig. 4. An example for doing binary operation of images

Next, this study used the morphological operations (closing and opening) to reduce noise and speckles. The noise and speckles were unfavorable for extracting vascular centerlines. Therefore, this study performed a sequence of 3-D mathematical morphological operation [11-13] to reduce noise and speckles before extracting vascular centerlines. The process of erosion and dilation was must be an important step [14] because the thinning methods attempted to obtain a centerline by iteratively removing points. The removing points fit at least one of a sequence of structure elements from the boundary of images.

In this research, constructing the centerline of blood vessels in the 3-D object would help finding skeletons of blood vessels. 3-D thinning operators [15;16] attempt to produce a centerline by iteratively removing simple points from the boundary of an

object. The thinning operator set out from the object's boundary and continues inward until no more simple points can be removed. Thinning operator would help to set the complete construct of blood vessels. After the images removed the speckle and used thinning operator, this study could extract morphological features from the image after preprocessing. Figure 5 is the result image after 3-D thinning. Figure 6 shows the reconstruction result of the direction of blood flow. In this paper, the color of the vessels was signed to red or blue in the vascular centerlines when the color of the corresponding points was red or blue in the original 3-D image, respectively. When the vessels of the vascular centerline didn't exist in the original image (were generated by the noise reduction step, e.g. the noise which interrupted the originally connected blood flow points) were signed to green.

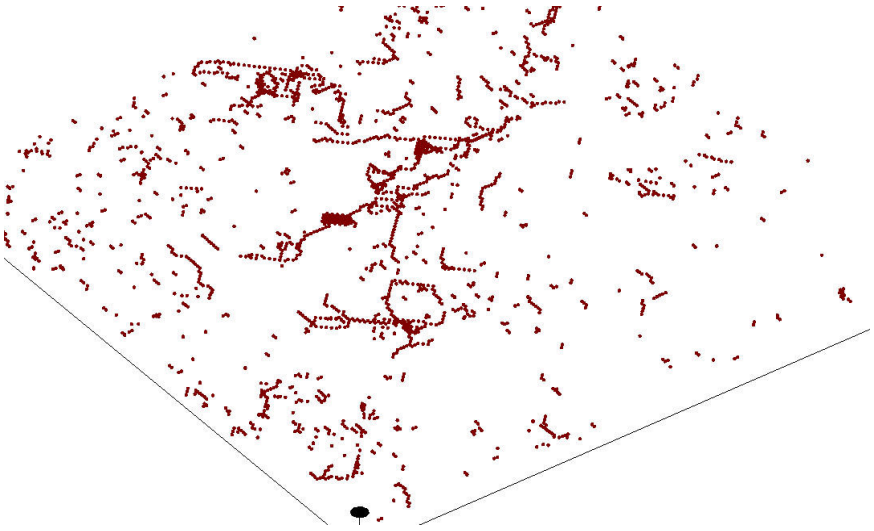

Fig. 5. The result image after 3-D thinning

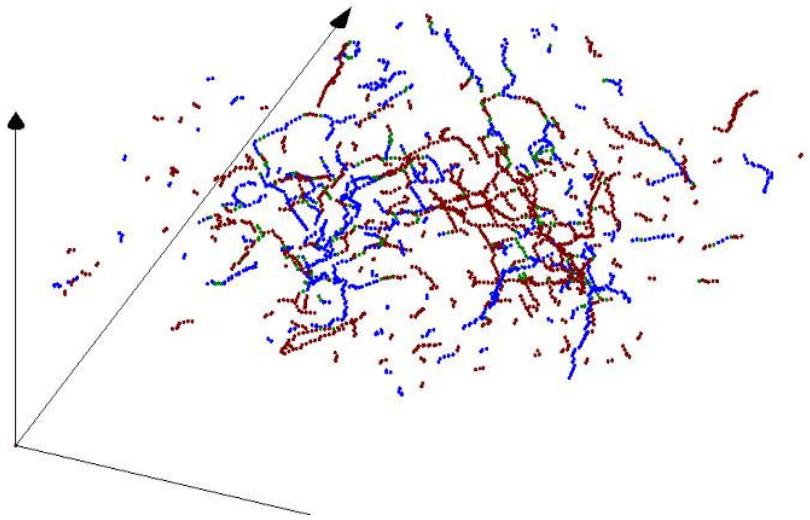

Fig. 6. The reconstruction result of the direction of blood flow

2.3 VASCULAR FEATURE EXTRACTION

To diagnose breast tumors, we selected thirteen morphological features from 3-D power Doppler ultrasound images. In order to extract the morphological features of vascularization correctly, this paper stored the original 3-D power Doppler ultrasound images, the preprocessed 3-D images, vascular centerlines and volume of interest (VOI) into four 3-D matrices, respectively. The four matrices are *Pm, Im, Cm, Vm*.

Pm is defined as original 3-D power Doppler ultrasound images matrix. *Im* is defined as preprocessed image matrix. *Cm* is defined as vascular centerline matrix after thinning. *Vm* is defined as VOI matrix stored the range of the VOI generated from the original 3-D power Doppler ultrasound images. We would count all of

vascular pixels and coordinates and recorded in these four matrices. Thirteen features were described and calculated the value by these matrices.

We selected features are VI, NT, LV, NB, NN, BN, PDM, ADM, NC, MR, FI, NTD and RB. The following will descriptive these thirteen features.

- VI is the ratio between the color vessels and the total number of vessels in the 3-D power Doppler ultrasound imaging.
- NT is the number of vascular centerlines in *Cm*, a connecting region in *Cm* was regarded as a vascular centerline. When one or more points of a centerline locate were inside of the VOI, this centerline was belong to the inside VOI, and so did for boundary VOI.
- LV is the sum of the length of vascular centerlines in *Cm*. In *Cm*, a connection between two points meant that one point was in the connectivity of the other point, and the length of this connection between the two points was the Euclidean distance multiplied by the vessels scale.
- NB is the number of branching point of vascular centerlines in *Cm*. A point had three or more points in the connectivity of this point were regarded as a branching point.
- NN is the average number of neighbor points of all points of vascular centerlines in *Cm*.

- BN is the average number of neighbor points of the branching points in *Cm*.
- PDM is the weighted average of all vascular centerlines in *Cm*. The DM of a curve was denoted as a ratio between the actual path length and the linear distance between the two endpoints of this curve. Before calculating the PDM of one examination, the local PDM value of each vascular centerline in *Cm* was calculated respectively. The local PDM of a vascular centerline was the weighted average of all DM values, which were calculated every two endpoints of this centerline (the weighted value was the actual path length between every two endpoints).
- ADM is the average of all vascular centerlines in *Cm*. Before calculating the ADM of one examination, the local ADM value of each vascular centerline in *Cm* was calculated respectively. The local ADM of a vascular centerline was the average of all DM values, which were calculated every two endpoints of this centerline.
- NC is the number of cycles of vascular centerlines in *Cm*.
- MR is the average of the radius of vascular centerlines in *Cm*. To calculate the MR, this study applied an iterative loop morphological erosion to erode *Im* until no point can be removed. When a point in *Im* was tending to disappear during the iterative loop erosion and there was a point with the

same coordinate in *Cm*, then the radius of this point was the execution times of erosion.

- FI is the average of the intensity of the points with the value greater than T_{voxel} in the 3-D power Doppler ultrasound imaging.
- NTD is the ratio between the blue points and total points with the intensity greater than T_{voxel} in the 3-D power Doppler ultrasound imaging.
- RB is the ratio between the number of branch points and the sum of the length of vascular centerlines.

These morphological features all would be utilized as the input vectors for the SVM classifier to test their effect with classify the breast tumors.

2.4 CLASSIFICATION

Before we used these morphological features to diagnose solid breast masses, firstly this study used SVM to analyze and classify the Az value of feature. SVM is a machine learning system developed by statistical learning theories used to classify data points in to two classes [17;18].

The SVM classify the correct classification by means of the optimal separating hyperplane with the maximal margin, which is written as

$$wx + b = 0, \tag{1}$$

then try to maximize the distance between two parallel hyperplanes that separates the data points on each side. The two input vectors must be defined

$$y_l = wx_l + b \geq 1, \tag{2}$$

$$y_l = wx_l + b \leq -1, \tag{3}$$

By (2) and (3), these can be rewritten as

$$y_l(wx_1 + b) \geq 1. \tag{4}$$

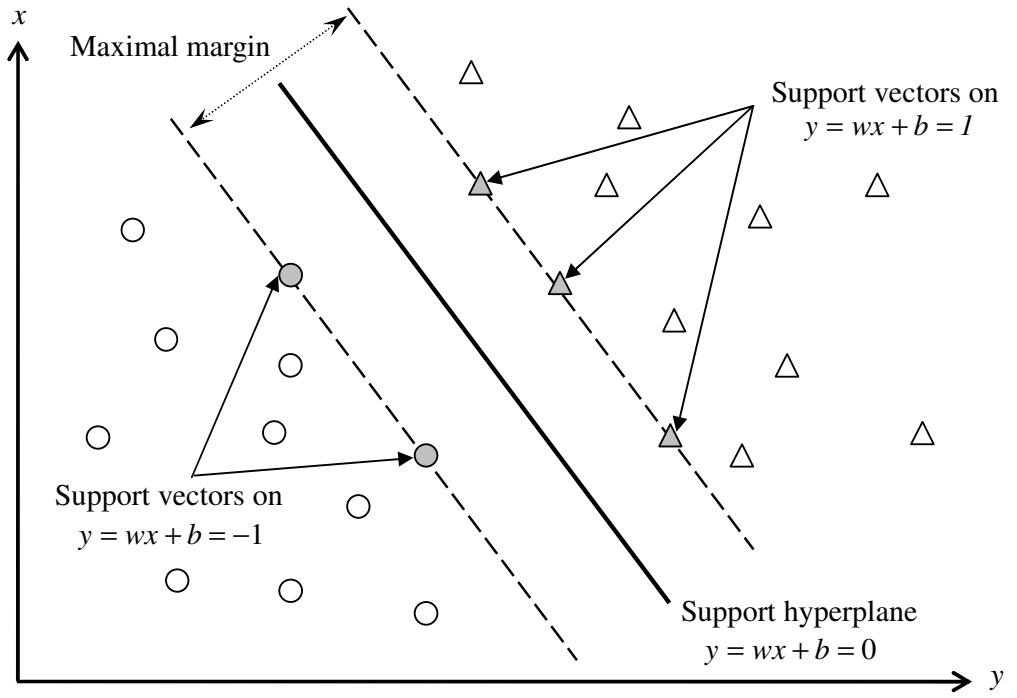

Fig. 7. An optimal separating hyperplane with the largest margin, and the points outside of the margin border denote the support vectors

Figure 7 shows an optimal separating hyperplane with the largest margin, and the points outside of the margin border denote the support vectors. The classification solution is given by the decision function

$$f(x) = sign\left(\sum_{i=1}^{n} \alpha_i \, y_i k(s_i, x) + b\right), \tag{5}$$

where α_i is the positive Lagrange multiplier, s_i are the support vectors (n in total), and $k(s_i, x)$ is the function for convolution of the kernel of the decision function. The support vector is the same class with $y = 1$ when $f(x) \geq 0$ and $y = -1$ when $f(x) < 0$. The radial kernels performs best in our experimental comparison, hence is chosen in the proposed diagnosis system. The radial kernels is defined as

$$k(x, y) = \exp\left(-\gamma(x - y)^2\right), \tag{6}$$

where $\gamma \in R$ is a non-zero parameter.

As mentioned above, we used thirteen morphological features to classify sixty breast tumors as benign or malignant by using SVM to training feature's data and calculated the Az value under the ROC curve. The Az value under the ROC curve is an index of the quantitative measure of the overall performance of a diagnosis. All of features were independently as an input vector for SVM to observe the effect. Table.1 is the Az value with thirteen morphological features.

Table 1. The Az value with thirteen morphological features

Features	Az value
VI	0.6381
NT	0.6922
LV	0.7145
NB	0.6234
NN	0.7438
BN	0.712
PDM	0.6254
ADM	0.6036
NC	0.747
MR	0.7502
FI	0.6572
NTD	0.7595
RB	0.7679

CHAPTER3

EXPERIENCE RESULTS

Sixty patient cases (including thirty benign breast tumors and thirty malignant breast tumors) through support vector machine (SVM) would be classified benign tumors and malignant tumors. Seven morphological features used as the input vector for the SVM classifier and receiver operating characteristic (ROC) curves to classify sixty solid breast masses. Table 1 shows the Az value with thirteen morphological features. The Az values by using the features VI, NT, NB, PDM, ADM and FI were lower than 0.7. This study abandoned these six features and selected the other seven features to be inputs of the SVM classifier. Table 2 lists the accuracy recognition of different gamma and the classify results. Table 3 shows the classification of breast tumors by SVM system.

Table 2. Recognition accuracy

Kernel	Gamma	FP	FN
radial	0.001	6	9
radial	0.003	6	11
radial	0.025	5	7
radial	0.03	4	6
radial	0.035	4	8
radial	0.04	5	8
radial	0.05	5	10

Table 3. Classification by proposed SVM with gamma = 0.03

	Benign	Malignant
SVM Output	TN 26 FP 4	FN 6 TP 24

TN = true-negative; FN = false-negative;
FP = false-positive; TP = true-positive.

According to Table 2 and Table 3, Classification of false-negative (FN) and false-positive (FP) is the best which gamma is 0.03. This research test many gamma value and the gamma value 0.03 was the best gamma value. Another value' FP and FN were not better than 0.03. Table 4 shows the seven morphological feature's Az value. Table 5 shows the description of seven morphological features.

Table 4. Seven feature's Az value

NC	MR	LV	NN	BN	RB	NTD
0.747	0.7502	0.7145	0.7438	0.712	0.7679	0.7595

Table 5. Seven feature's Description

Features	Description
NC	The number of cycles of vascular centerlines
MR	The average of the radius of vascular centerlines
LV	The sum of the length of vascular centerlines
NN	The average number of neighbor points of all points of vascular centerlines
BN	The average number of neighbor points of the branching points
RB	The ratio between the number of branch points and The sum of the length of vascular centerlines
NTD	The ratio between the blue points and total points with the intensity greater than T*voxel* in the 3D power Doppler ultrasound imaging

Table 4 shows these seven morphological features of vascularization and their Az value. It illustrated that the vascularization of tumor has more bifurcation and more turning point be a malignant tumor with high probability than benign. The vascular length and cycle which are more long and curved also has high probability to be a malignant tumor than benign. The volume of tumor is a favorable target to decide breast cancer. From now on seven features could be selected to put in ROC analysis.

The most common means of measuring diagnostic accuracy for reconstructed images are based on ROC analysis. Another measure is the Az value, which was calculated by ROC curves.

Once all of seven feature's Az values were calculated and picked out, these seven Az values put in SVM and calculated the final Az value. The final Az value is 0.8423, so ROC curve is based on 0.8423 to construct. Figure 8 shows the ROC curve form seven features. In Fig. 8, we compared 3 test results of different features. Seven features' Az value are higher than 0.7, this data set is the best result for this study. Ten features included the features which Az value are higher than 0.63, the ROC result is 0.8074. Thirteen features' test result is 0.7923. It illustrates seven features which Az value are higher than 0.7 is the best data set in this study. We test all set of features in SVM classifier. Thus, seven morphological features which Az value is 0.8423. Before calculating, this study already tests another morphological feature. But those Az value were not higher than 0.7. So we selected seven of the best Az value to calculate. Finally, use these seven morphological features of vascularization to classify tumor.

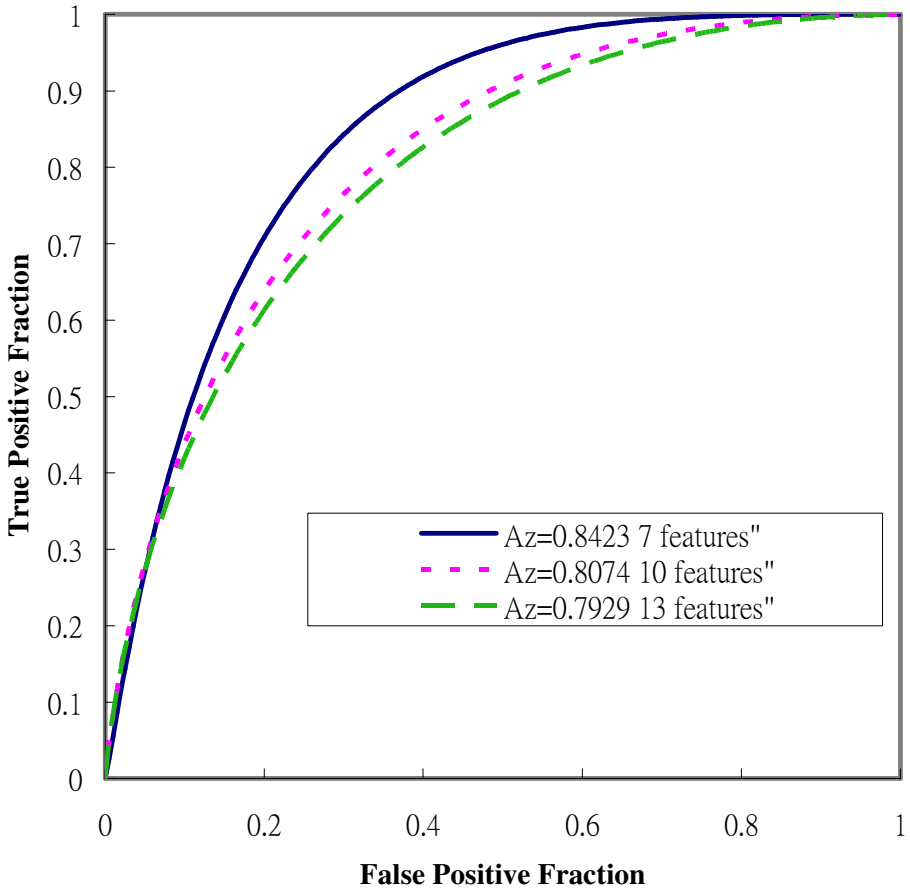

Fig. 8. ROC curve of the proposed method

CHAPTER4

CONCLUSION

This research proposed sequence of 3-D morphological operations to extract the morphological features of vascularization and used seven features which were selected into SVM to classify breast tumor. T_{voxel} was a threshold to process image, and the threshold was manually selected to be eighty by experience. The multiple vessels wide skeletons problem happened in T_{voxel} which is lower than eighty. This paper would illustrate multiple vessels wide skeletons (MVWS) problems and an example with some boundary multiple vessels wide skeletons regions around the boundary and internal multiple vessels wide skeletons regions in the central of the 3-D images. T_{voxel} was set to eighty because this threshold T_{voxel} retained most of the information of blood flow and caused least multiple vessels wide skeletons regions.

Afterward we using morphological operation and thinning algorithm extracted the vascular features. Thirteen morphological features classified sixty breast tumors as benign or malignant by using SVM to training feature's data and calculate the area Az under ROC curve. All of morphological features would be abandoned which Az value is lower than 0.7. Selecting seven morphological features include NC, MR, LV, NN, BN, RB, NTD were used in SVM to identify breast tumors. The area Az under the ROC curve is an index of the quantitative measure of the overall performance of a

diagnosis. Therefore, these features were independently calculated in SVM to observe the effect. The Az value from ROC curve analysis of the proposed method is 0.8423.

It can illustrate that the vascularizaiton of tumor and architecture can affect malignant and benign solid breast masses. According to this research, morphological feature of vascularization indeed use to diagnose patient. The morphological feature of vascularization is based on angiogenesis to extract the model of blood vessels and architecture. The length of blood vessels, curvature, complexity and all volume of blood vessels could affect characterization of benign and malignant solid breast. In the future work, we would apply the more effective 3-D thinning algorithm and more morphological features to test and diagnose breast tumors.

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