AN IMPROVED GA-MILSVM CLASSIFICATION APPROACH FOR DIAGNOSIS OF BREAST LESIONS FROM STAIN IMAGES

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ABSTRACT

Cancer cells spread to more distant parts of the body through the lymphatic system or bloodstream. Not all tumors are cancerous. Benign tumors do not grow uncontrollably, do not invade neighboring tissues, and do not spread throughout the body. Intraductal Carcinoma is a noninvasive condition in which abnormal cells are found in the lining of a breast duct. The abnormal cells have not spread outside the duct to other tissues in the breast. In some cases, Intraductal Carcinoma may become invasive cancer and spread to other tissues, although it is not known at this time how to predict which lesions will become invasive. Intraductal cancer is the most common type of breast cancer in women. Memory Intraductal includes 3-types of cancer: Usual Ductal Hyperplasia (UDH), Atypical Ductal Hyperplasia (ADH), and Ductal Carcinoma in Situ (DCIS). So the system of detecting the breast microscopic tissue of UDH, ADH, DCIS is proposed. The current standard of care is to perform percutaneous needle biopsies for diagnosis of palpable and image-detected breast abnormalities. UDH is considered benign and patients diagnosed UDH undergo routine follow-up, whereas ADH and DCIS are considered actionable and patients diagnosed with these two subtypes get additional surgical procedures. The system classify the tissue based on the quantitative feature derived from the images. The statistical features are obtained. The approach makes use of preprocessing, Cell region segmentation, Individual cell segmentation, Feature extraction technique and MILSVM classifier for the detection of cancer and optimized using Genetic Algorithm An overall accuracy of 87.9% precision is obtained using GA and 4.5% recall are achieved on the entire test data. The test accuracy of 82.6% precision and 3.5% recall are obtained using MILSVM. When compared with MILSVM, GA has a great potential in improving diagnostic accuracy and reproducibility.

KEYWORDS: Intraductal Carcinoma, Percutaneous, Cell Segmentation **,** Feature Extraction**,** SVM Classifier**,** Genetic Algorithm

I. INTRODUCTION

Medical imaging is one of the fastest growing areas within medicine at present, both in the clinical setting in hospitals. Medical imaging is the technique and process used to create images of the human body for clinical purposes or medical science. Medical imaging is often perceived to designate the set of techniques that noninvasively produce images of the internal aspect of the body. Medical imaging can be seen as the solution of mathematical inverse problems. This means that cause is inferred from effect. This is very important to help improve the diagnosis, prevention and treatment of the diseases. Medical imaging is a part of biological imaging and incorporates radiology, nuclear medicine, investigative radiological sciences, endoscopy, thermography, medical photography and microscopy.

1.1. Background

The continuum of intraductal breast lesions, which encompasses the usual ductal hyperplasia (UDH), atypical ductal hyperplasia (ADH), and ductal carcinoma in situ (DCIS), are a group of cytologically

and architecturally diverse proliferations, typically originating from the terminal duct-lobular unit and confined to the mammary duct lobular system. These lesions are highly significant as they are associated with an increased risk of subsequent development of invasive breast carcinoma, albeit in greatly differing magnitudes. Clinical follow-up studies indicate that UDH, ADH, and DCIS are associated with 1.5, 4–5, and 8–10 times of increased risk respectively, compared to the reference population for invasive carcinoma.

Patients diagnosed UDH are advised to undergo routine follow-up, while those with ADH and DCIS are operated by excisional biopsy followed by possible other surgical and therapeutic procedures. The pathology diagnoses are typically made according to a set of criteria defined by the World Health Organization (WHO), using formalin fixed paraffin embedded tissue specimens, which are stained with a mixture of hematoxylin/eosin (H&E), no single criterion is absolute[4]. Thus, subjective assessment and weighing the relative importance of each criterion are performed to categorize the lesions. The proposed system applies segmentation and feature extraction techniques for detection of cancer.

1.2. Breast Lesions

A lesion is an area which is an abnormality or alteration in the tissue's integrity. Lesions can occur in any area of the body consisting of soft tissue, commonly found on the skin. There are numerous types of lesions with different naming classifications. When this lesion develops in the breast tissues, they are referred to as breast lesions. Breast lesions usually come in the form of lumps or swellings in or around the breast area, and they are frequently felt during a self breast examination or when examined by a physician. Some breast lesions, however, may be present but not felt. These are called non-palpable lesions, and they are mostly detected during a screening mammogram test, which is more like an x-ray of the breast.

The normal breasts have various types of tissues with different consistencies. One type of tissue found in the breasts is the glandular tissue, which is nodular and firm to the touch. Breasts also have fats that are generally soft to the touch. It is normal for the breast tissues to undergo changes such as lumpiness or tenderness, especially during the menstrual cycle. Most of these breast changes normally occur in response to hormonal changes going on in the body.

Breast Lesions[6] (malignant breast neoplasm) is cancer originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk. Cancers originating from ducts are known as ductal carcinomas; those originating from lobules are known as lobular carcinomas. Breast cancer is a disease of humans and while the overwhelming majority of cases in humans are women. Size, stage, rate of growth, and other characteristics of the tumour determine the kinds of treatment. Treatment may include surgery, drugs, radiation and/or immunotherapy. Surgical removal of the tumour provides the single largest benefit, with surgery alone being capable of producing a cure in many cases.

The following sub divisions have Related Works, Proposed Schema, Experimental Results and Conclusion

II. RELATED WORKS

J. Rozai et al. [4] focuses on "borderline lesions" of the breast. ADH is the most popular and classical borderline breast lesion. It is defined as the atypical intraductal epithelial proliferation, which mimics low-grade ductal carcinoma in situ (DCIS), and they are mostly small. The significance of ADH is its relative risk for developing invasive carcinomas on both breasts. Some breast carcinomas with peripheral ADH associations are found. In those cases, the area of peripheral ADH are recommended to be removed together with carcinoma, as they may be connected to the main lesion through the duct profiles.

P. L. Fitzgibbons et al. [2] states that tumor size as a prognostic variable in cases of invasive carcinoma is robust. It is used to measure the various clinical estimates and mammograms. Tumor size is directly related to an increasing probability of regional metastasis, increasing average number of auxiliary lymph nodes and probability of recurrence and death. The favorable prognosis of non palpable invasive carcinoma is relative to palpable ones. Precise assessment of tumor size is

necessary to properly stratify patients, particularly since screening mammography has resulted in a steadily increasing proportion

A.P.Dempster, N. M. Laird, et al. [1] proposed a general approach to iterative computation of maximum-likelihood estimates when the observations can be viewed as incomplete data. Since each iteration of the algorithm consist of an expectation step followed by a maximization step, it is called as EM algorithm. The EM algorithm is remarkable process because of its simplicity and generality of the associated theory.

L. Vincent and P. Soille, et al.[5] states that Watersheds are one of the classics in the field of topography, a gray-level image is considered a topographic relief where the gray level of a pixel is interpreted as its elevation. The water flows along a topographic relief following a certain descending path to eventually reach a catchment basin. Blobs in the image can be separated using this concept by identifying the limits of adjacent catchment basins and then separating them. The lines separating catchment basins are called watersheds.

D. Page and W. Dupont, et al[6] states that breast imaging have made a positive impact on breast cancer screening and detection. The growing use of image-detected biopsies has led to increased diagnosis of ductal carcinoma in situ and high-risk proliferative breast lesions. This progress, has created a challenge for pathologists. In lieu of the fact that these entities are difficult to diagnose even in tissue sections taken from surgically excised lesions, pathologist are now expected to diagnose them in small and often fragmented tissue/cellular samples obtained from image-guided biopsies. Some proliferative lesions are associated with an increased risk of finding neighboring malignant.

M. M. Dundar, S. Badve, V. Raykar,et al[9]Pathology diagnoses are made according to a set of criteria defined by the World Health Organization(WHO). While these criteria are generally easy to identify for most lesions, there are borderline cases where it becomes difficult to determine with absolute certainty whether a lesion is malignant or benign. Often times this difficulty is in one or more of the criteria being somewhat ambiguous, thus leading to a diversity of opinionsamong pathologists. Diagnoses are typically made using formalin fixed paraffin embedded tissue specimens, which are counterstained with hematoxylin or a mixture of hematoxylin/eosin (H&E). Morphological characterization of the cells within the tissue specimen being examined, helps the pathologist decide whether the lesion is cancerous or not.

III. PROPOSED SCHEME

The proposed system applies preprocessing, Cell region segmentation, Individual cell segmentation, Feature extraction technique for the detection of cancer. The first step of preprocessing involves the min-max normalization preprocessing. Three different lesion subtypes are used: Clustering algorithm is used to identify region of cells in the H&E stained breast microscopic tissue. This was followed by a watershed-based algorithm which identifies individual cells. The segmented cells are used to derive size, shape and intensity based feature characterizing each ROI. Segmentation is done using cell region segmentation and individual cell segmentation. Feature extraction is implemented using ROI and MILSVM classifier is used. Figure 1 represents overall process of automatic detection of breast lesions.

3.1. Preprocessing

Preprocessing can be applied easily. It improves the effectiveness and performance. Min-max normalization is used for preprocessing. Min-Max normalization is the process of taking data measured in its engineering units and transforming it to a value between 0.0 and 1.0. The lowest (min) value is set to 0.0 and the highest (max) value is set to 1.0. It provides an easy way to compare values that are measured using different scales or different units of measure.

3.2. Segmentation

The purpose of image segmentation is to partition an image into meaningful regions with respect to a particular application .It is based on measurements taken from the image and might be greylevel, colour, texture, depth or motion. It is to partition a image into multiple segments. The goal of segmentation is to simplify and/or change the representation of an image into something that is more meaningful and easier to analyze. Image segmentation is typically used to locate objects and

boundaries (lines, curves, etc.) in images. Cell region segmentation and Individual cell segmentation are used to segment the input breast lesion.

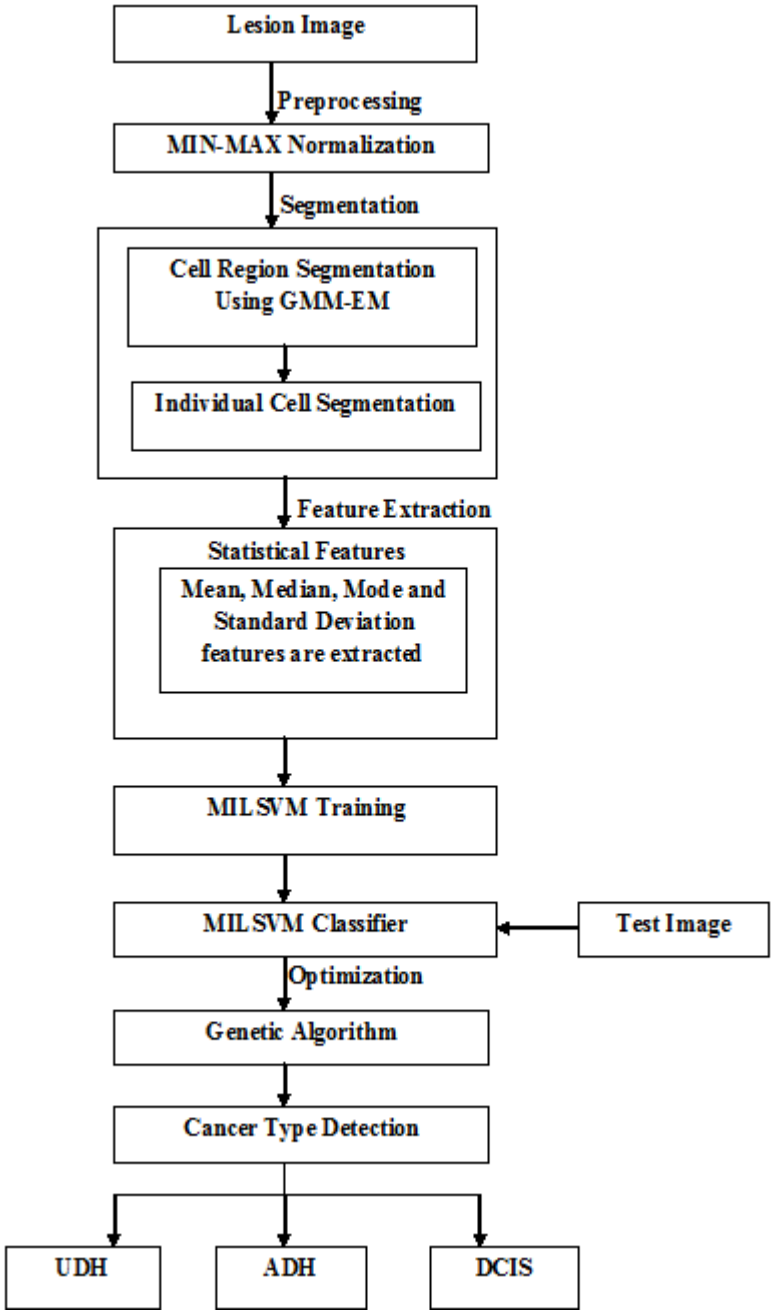

Figure 1. Overall process of the system

3.2.1. Cell Region Segmentation

Cell segmentation would be the first step toward automated analysis of histopathological slides. This is implemented in two steps. In the first step, cell regions are segmented by clustering the pixel data and in the second step segmented cell regions are further processed by a watershed-based segmentation algorithm to identify individual cells. The cell region segmentation performs the following steps:

1) ROI images are converted into RGB color space then to L a*b*.

2) La*b* color space also separates the luminance and the chrominance information such that: L channel corresponds to illumination and a*and b* channels correspond to color-opponent dimensions.

The equation to convert RGB to La*b* color space are as follows:

L=(116*var_Y)-16;a=500*(var_X-var_Y); b=200*(var_Y- var_Z)

Segmentation performs maximum likelihood estimation of gaussian mixture model by using expectation algorithm [1]

EM Algorithm

Expectation step (E-step): Calculate the expected value of the log likelihood function, with respect to the conditional distribution of given under the current estimate of the parameter:

$$Q(\theta|\theta^{(t)})=E_{Z|X,\theta^{(t)}}[\log(\theta;X,Z)]$$

Maximization step (M-step): The parameter that maximizes this quantity:

$$\theta^{(t+1)}=\arg\max_{\theta} Q(\theta|\theta^{(t)})$$

The expectation maximization (EM)[1] algorithm is implemented using the a*, b* channels to estimate the parameters of the GMM model. The resulting mixture distribution is used to classify pixels into four categories. Those classified into the cellular component are further clustered in the L channel by dynamic thresholding [7] to eliminate blue–purple pixels with relatively less luminance.

3.2.2. Individual Cell Segmentation

Segmentation maps of cell regions obtained are converted to gray level images before they are used in this stage. Since most segmented regions contain multiple overlapping cells with cells only vaguely defined due to the presence of holes inside them, connected components in these images do not necessarily represent individual cells. These images are first preprocessed using hole filling and cleaning steps suggested in[8]. Overlapped cells result in blobs in the segmentation map. To separate these blobs properly so as to identify individual cells, we used a watershed algorithm [5] based on immersion simulations.
The watersheds algorithm performs the following steps:

1) RGB image obtained are converted to gray-level images.
2) A gray-level image is considered a topographic relief where the gray level of a pixel is interpreted.
3) The water flows along a topographic relief following a certain descending path to eventually reach a catchment basin.

3.3. Feature Extraction

Feature extraction and selection methods are to obtain the most relevant information from the original data and represent that information in a lower dimensionality space. When the cost of the acquisition and manipulation of all the measurements is high we must make a selection of features. The goal is to select, among all the available features, those that will perform better. Example: Features that should be used for classifying a student as a good or bad one. The available features for student classification are :marks, height, sex, weight, IQ. Feature selection would choose marks and IQ and would discard height, weight and sex. The feature extraction performs the following steps:

1) The perimeter, the ratio of major to minor axis, and the mean of the gray-level intensity are computed.
2) For each connected component identified in an ROI.
3) Statistical features involving the mean, standard deviation, median, and mode are computed to obtain features at the ROI level.
4) Thus, each ROI is characterized by a total of 12 features (3 × 4).

3.4. Classifier Training

The goal of classification is to use an object's characteristics to identify which class (or group) it belongs to. A linear classifier achieves this by making a classification decision based on the value of a linear combination of the characteristics**.** Each slide contains multiple ROIs and a positive (actionable) diagnosis is confirmed when *at least one of the ROIs* in the slide is identified as positive. For a negative diagnosis (UDH), the pathologist has to rule out the possibility of *each and every ROI* being actionable. The objective here is to develop a classifier to optimize classification accuracy at the slide level. Traditional supervised training techniques which are trained to optimize classifier performance at the instance level yield suboptimal performance in this problem.*MILSVM Classifier:* Multiple Instance Learning (MIL) is to classify bags of instances[9]. During training, the learner is given a set of positive and negative training bags. Example: results of repeated medical test generate sick/healthy bag (bag = person). A bag is a collection of feature vectors called instances. During testing, a new test bag is classified to be either positive or negative. A bag is positive if it contains at least one positive instance and negative if it contains only negative instances.MIL is a learning problem with incomplete data where the class labels of the instances are latent variables. In the learning process many methods also label the instances of the training bags. So to avoid the MIL problem SVM is used. MILSVM method is used for both labeled and unlabeled data It uses a unlabeled mapping to transform the original training data into a higher dimension. With the new dimension, it searches for the linear optimal separating hyperplane .With an appropriate nonlinear mapping to a sufficiently high dimension, data from two classes can always be separated by a hyperplane MIL.SVM finds this hyperplane using support vectors ("essential" training tuples) and margins (defined by the support vectors).

MILSVM Steps:

1) By using the stastistical features like mean, median, mode and standard deviation.
2) The system is trained using these statistical features.
3) The features are trained and tested by using the SVM classified
4) After testing the classified image is obtained.
5) Lesion is detected.

3.5. Optimization (Genetic Algorithm)

Genetic Algorithm (GA) is a search heuristic that mimics the process of natural evolution. This heuristic is routinely used to generate useful solutions to optimization and search problems. Genetic algorithms belong to the larger class of evolutionary algorithms (EA), which generate solutions to optimization problems using techniques inspired by natural evolution, such as inheritance, mutation, selection and crossover. In a genetic algorithm, a population of strings (called chromosomes or the genotype of the genome), which encode candidate solutions (called individuals, creatures, or phenotypes) to an optimization problem, evolves toward better solutions. Traditionally, solutions are represented in binary as strings of 0s and 1s, but other encodings are also possible. The evolution usually starts from a population of randomly generated individuals and happens in generations. In each generation, the fitness of every individual in the population is evaluated, multiple individuals are stochastically selected from the current population (based on their fitness), and modified (recombined and possibly randomly mutated) to form a new population. The new population is then used in the next iteration of the algorithm. Commonly, the algorithm terminates when either a maximum number of generations has been produced, or a satisfactory fitness level has been reached for the population. If the algorithm has terminated due to a maximum number of generations, a satisfactory solution may or may not have been reached.

3.5.1. Advantages (Genetic Algorithm)

1) It can solve every optimisation problem which can be described with the chromosome encoding.
2) It solves problems with multiple solutions.
3) The genetic algorithm execution technique is not dependent on the error surface, we can solve multi-dimensional, non-differential, non-continuous, and even non-parametrical problems.

4) Structural genetic algorithm gives us the possibility to solve the solution structure and solution parameter problems at the same time by means of genetic algorithm.
5) Genetic algorithm is a method which is very easy to understand and it practically does not demand the knowledge of mathematics.
6) Genetic algorithms are easily transferred to existing simulations and models.

3.5.2. Optimization (Genetic Algorithm) Steps

1) Choose the initial population of individuals
2) Evaluate the fitness of each individual in that population
3) Repeat on this generation until termination (time limit, sufficient fitness achieved, etc.)
4) Select the best-fit individuals for reproduction
5) Breed new individuals through crossover and mutation operations to give birth to offspring
6) Evaluate the individual fitness of new individuals
7) Replace least-fit population with new individuals

IV. EXPERIMENTAL RESULT

Fig. 2 shows the stain image of breast lesion. Lesions can be seen in the stain image. Breast Lesions is cancer originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk. Cancers originating from ducts are known as ductal carcinomas. Fig. 3 shows the preprocessed image using the min-max normalization method. In MIN-MAX normalization the values lies between -1 and 0. It avoids the numerical problems.

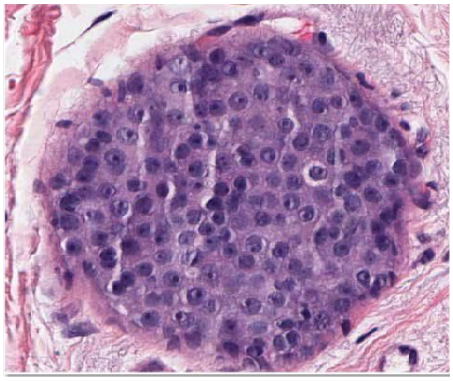

Figure 2. Stain Image

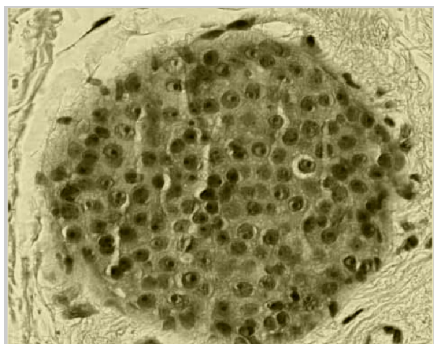

Figure 3. Min-Max Preprocessed Image

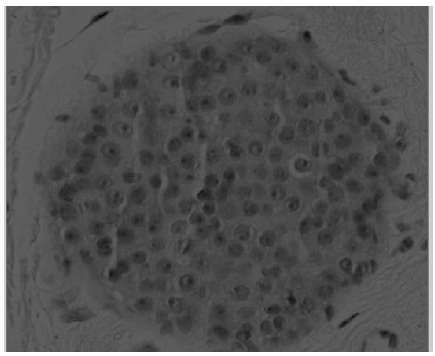

Figure 4. L-Channel Image

Figure 5. A-Channel Image

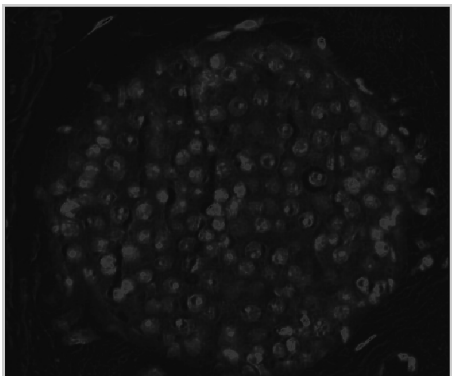

Figure 6. B-Channel Image

Fig. 4,5,6 shows the La*b* image. The RGB image of breast lesion is converted to L a*b* images and from that L, a, b-channels are extracted.

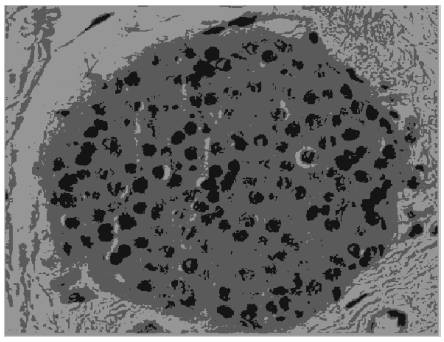

Figure 7. L-Segmented Cell Regions

Figure 8. A-Segmented Cell Regions

The results were over segmented by both methods; by using cell region segmentation and individual cell segmentation segmented cells were detected. Fig.7,8,9 shows the segmented cell regions of L a*b* image.

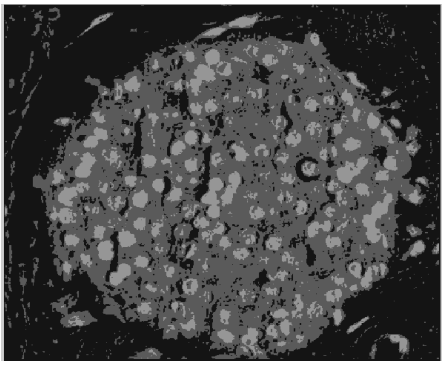

Figure 9. B-Segmented Cell Regions

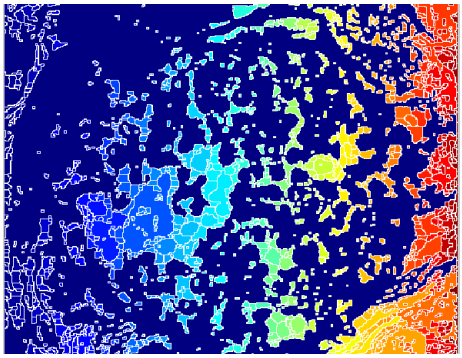

Figure 10. Individual Segmented Cells

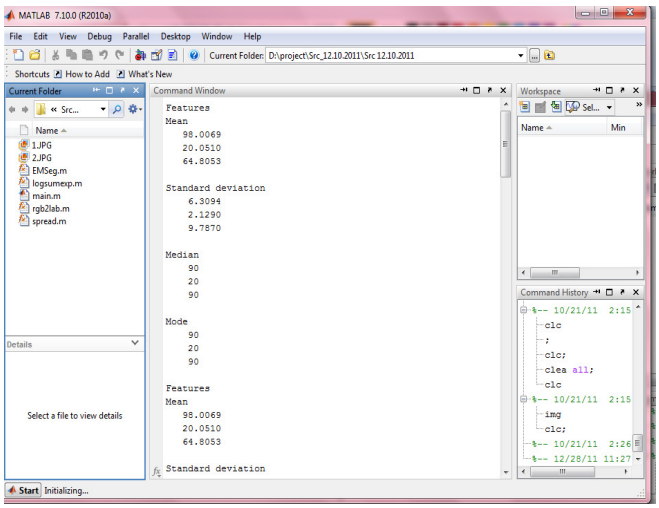

Figure 11. Statistical Features

Fig 10 shows the segmented cells which are detected using individual cell segmentation. Fig 11 shows the statistical features which are being extracted .Fig 12,13 shows the MILSVM training and the tested images. By using the statistical features training is being completed and while testing it detects the lesion whether it is UDH or ADH lesion by using MILSVM classifier.

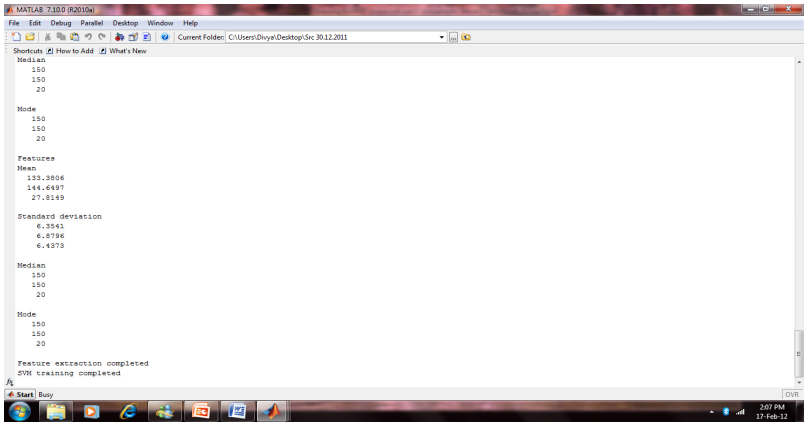

Figure.12 MILSVM training

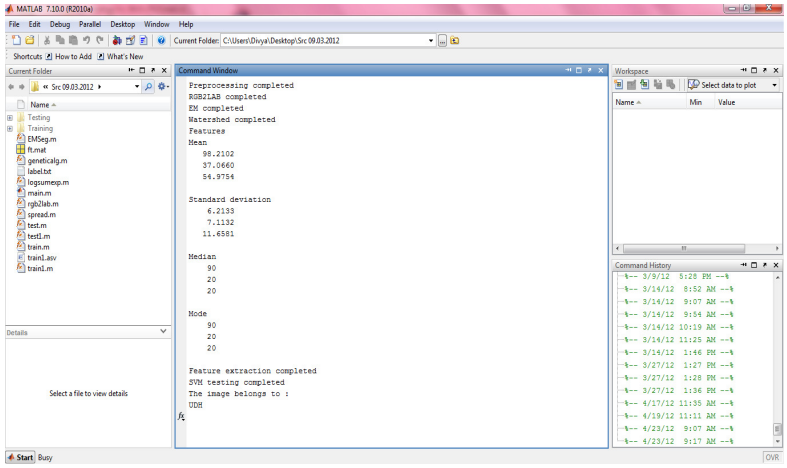

Figure.13 MILSVM tested image

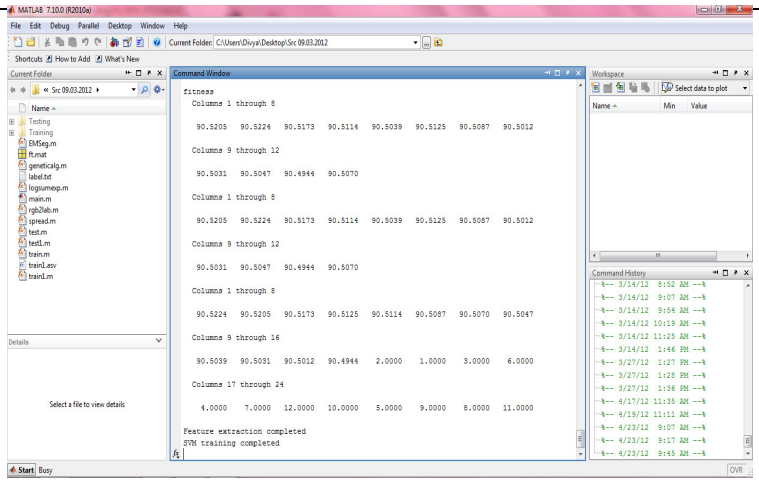

Figure.14 Trained values using GA for classification

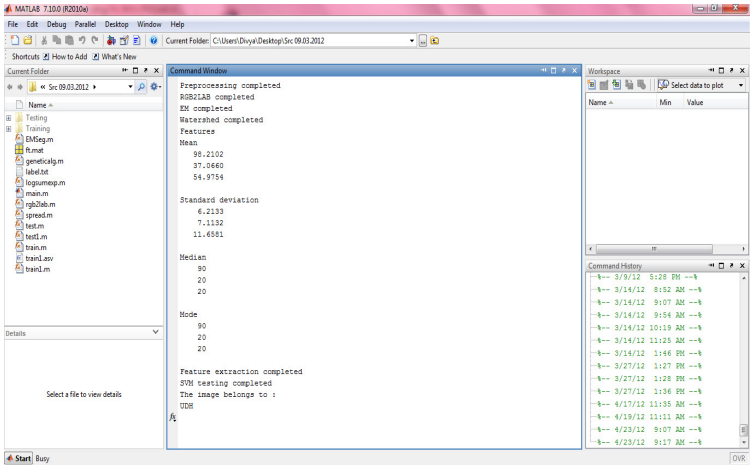

Figure.15 Announcing the type of cancer using GA

Table 1. Accuracy based on Precision

Model	MILSVM	GA
DCH	61	64
ADH	82	85
DCIS	22	24

Table 2. Accuracy based on Recall

Model	MILSVM	GA
DCH	28	35
ADH	40	43
DCIS	12	15

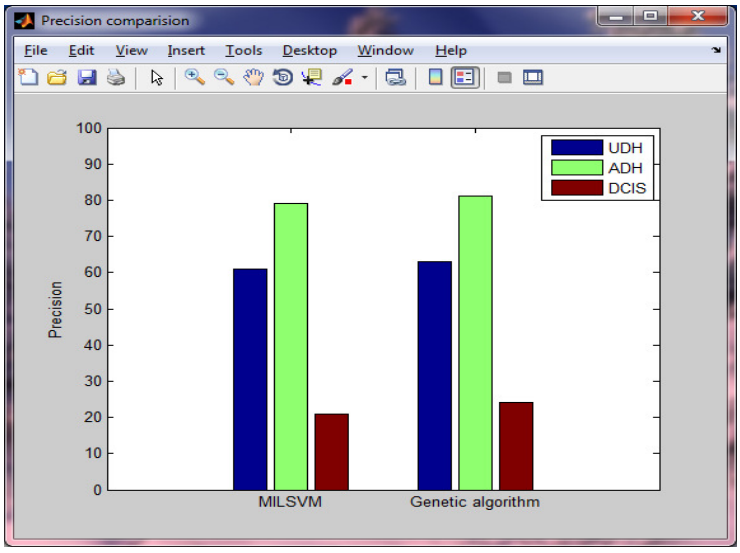

Figure 16 . Accuracy of MILSVM and GA based on precision

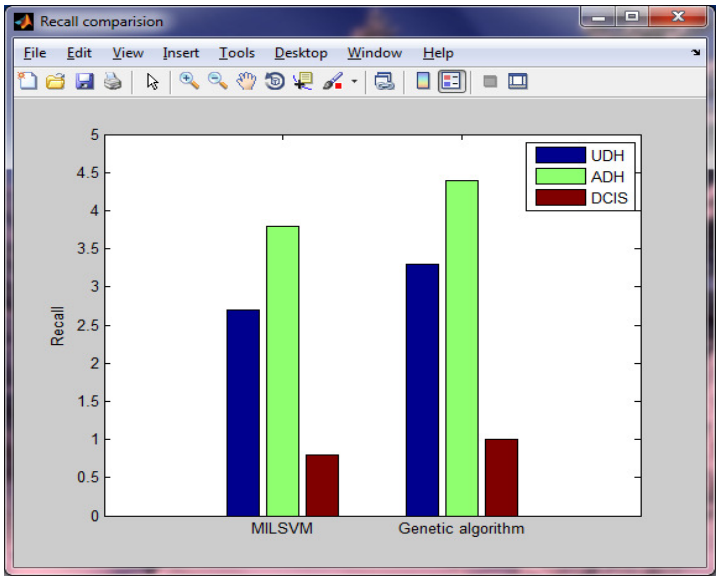

Figure 17. Accuracy of MILSVM and GA based on recall

Table 1and 2 represents the accuracy of the model based on precision and recall. All feature extracted cells obtained from different image segmentation models are ranked as shown in Fig. 16 and 17.
An overall accuracy of 87.9% precision is obtained using GA and 4.5% recall are achieved on the entire test data. The test accuracy of 82.6% precision and 3.5% recall are obtained using MILSVM. When compared with MILSVM, GA has a great potential in improving diagnostic accuracy and reproducibility.

V. CONCLUSION

The proposed cell region segmentation, individual cell segmentation and feature extraction is used to identify the breast lesions. EM algorithm is used for cell segmentation. In this approach step of initialization is necessary to prevent settling down on a bad local maximum. Then the EM algorithm gets an opportunity to explore the parameter space and it may converge to a better maximum. Generally, the clustering-based initialization method provides a better final result for the EM algorithm than random initialization does, and it also contributes to the convergence speed. This will involve developing intermediate models to map image features onto descriptors pathologists use for classification. This new approach can help as an automated medical image analysis tool to validate

our hypothesis in an accurate and specific manner. The MILSVM classifier detects the type of breast lesions. The MILSVM could closely detecting the type of breast lesions and optimized using Genetic Algorithm.

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