

Research Article

Image Classification for Ultrasound Fetal Images with Increased Nuchal Translucency during First Trimester Using SVM Classifier

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Abstract: Increased Nuchal Translucency is an indicator of increased risk for Down syndrome, which is identified by measuring Nuchal Translucency from ultrasound fetal images during 11 to 13⁺⁶ weeks of gestation. Increased NT is associated with chromosomal abnormalities. In this study an efficient classification system based on Discrete Wavelet Transform (DWT) is proposed to detect the normal and abnormal images with NT. Feature extraction is an essential pre-processing step for pattern recognition and machine learning problems. In order to classify the ultrasound image accurately, the texture features must be extracted effectively. In the proposed system, wavelet band signature, energy is used as features to classify the ultrasound image for the detection of Down syndrome using Support Vector Machine (SVM) classifier. The experimental results of pre diagnosed database with Discrete wavelet Transform and SVM classifier give best results for classification of Down Syndrome images with Normal NT and abnormal NT.

Keywords: Chromosomal abnormalities, Discrete Wavelet Transformation (DWT), Down syndrome, Nuchal Translucency (NT), Support Vector Machine (SVM) classifier

INTRODUCTION

Medical imaging technology has revolutionized health care around the world. Extending the human vision, the medical imaging plays a vital role in diagnosis of diseases. Down syndrome or Trisomy 21 is a chromosomal disorders of Babies with an extra chromosome #21 (Kagan *et al.*, 2008) which is caused by an error in cell division that results in an extra 21st chromosome. Chromosomal disorders cause birth defects and mental retardation. Any baby can have chromosome abnormalities, however the chances increases with mother's age (Snijders *et al.*, 1998).

Down syndrome can be detected before the baby is born through a series of prenatal tests. The types of prenatal tests include screening tests and diagnostic tests. Prenatal Screening tests include Ultrasound, First trimester screening is to determine if the baby has an increased risk of Down syndrome. Diagnostic tests determine if the baby has, or will develop after birth, a genetic condition. Prenatal diagnostic tests include Ultrasound, Chorionic Villus sampling and Amniocentesis.

First trimester Screening-To calculate the individual risk it is necessary to take into account the priori risk which depends on maternal age, gestational age, to multiply this by a likelihood ratio, which depends on ultrasound and/or maternal serum

biochemical test to determine the patient specific risk (Kagan *et al.*, 2008). Nuchal Translucency is the sonographic appearance of subcutaneous collection of fluid behind the fetal neck (Nicolaidis *et al.*, 1994, 1992). Studies have shown that in normal fetuses the fluid collection known as NT increases with gestational age until about 13 weeks of gestation and usually disappears after 14 weeks. In the case of an enlarged NT the fluid collection also tends to disappear after this period (Muller *et al.*, 2004).

The NT measurement was first suggested by Nicolaidis *et al.* (1994), which was later confirmed by other researchers. Because of its transient nature NT measurement must be performed between 11 and 13⁺⁶ weeks gestation. The optimal gestational age for the measurement of fetal NT is 11 weeks of gestation to 13 weeks 6 days of gestation (Pandya *et al.*, 1994; Hackshaw *et al.*, 1996; Snijders *et al.*, 1998). The fetal nuchal translucency measurement includes the crown rump length of the fetus. The minimum and maximum fetal crown rump length should be of 45 mm and 84 mm, respectively. Fetal head and upper thorax are included in the image for measurement of NT (Snijders and Nicolaidis, 1996). Increased NT with thickness greater than >2.5 mm between 10 and 14 weeks of gestation is also associated with an increased risk of congenital heart and genetic syndrome (Souka *et al.*, 2001).

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The fetus with increased Nuchal translucency thickness of 3 mm, 4 mm, 5 mm and greater than or equal to 6 mm were approximately associated with the respective 4-fold, 21-fold, 26-fold and 41-fold increases with the maternal age which related to the risk of trisomy 21, 18 and 13 (Pandya *et al.*, 1995a, b, 1994).

The other symptoms of Down Syndrome other than Nuchal translucency includes small head, flat-looking face, presence or absence of the nose and smaller than normal nose, mouth, ears and hands. Their eyes slant upward, with extra folds of skin at the corner of each eye and near the nose. Combined screening of NT and maternal serum markers ((PAPP-A) or beta subunit of human chorionic-gonadotrophin (free β -hCG) provides the better detection rate. Further diagnosis can be done by triplet test and quadruple test. However, skills of the sonographer along with good quality of ultrasound machine can be very effective for accurate detection rate.

LITERATURE REVIEW

Many research papers are been presented with various techniques for the detection of chromosomal abnormalities using NT thickness in the first trimester in singleton pregnancies by manually, semi-automatically and automatically.

Lai *et al.* (2010) proposed multilayer feed forward Neural Network for NT recognition and diagnosis of fetal chromosomal anomalies. NT edge detection is done by Bidirectional Iterations forward propagations method. Largest thickness recorded is the NT measurement in millimeter. Mean and Standard deviations are used to calculate the automatic and manual measurement for maximum NT thickness. The maximum thickness of the subcutaneous translucency between skin and the soft tissue overlying the cervical spine should be measured. Local measurement of intensity, edge strength and continuity were extracted and became the weighted terms for thickness calculation.

Nirmala and Palanisamy (2009) proposed shift analysis and canny operators for Nuchal translucency segmentation. The images were preprocessed and the ROI has been cropped for analysis. NT region has been segmented from the cropped image by applying mean Shift cluster analysis. Blob analysis is used for NT thickness for Detection of Chromosomal Abnormalities during first trimester.

Deng *et al.* (2008) proposes a automatic scheme of NT detection is to estimate fetal NT parameters. Manual measurement of parameters may introduce problems of the variability and reproducibility. Morphologic filtering, which plays a major role for geometry-based enhancement and detection. This scheme firstly establishes the edge map and extracts a preliminary contour by the Gradient Vector Flow

(GVF) snake. The parameters of the NT such as the NT thickness and the NT area are calculated. Overcomes problems of discontinuousness and concavities in the contour extraction and parameters of the fetal NT can be automatically calculated. Hence an automated methodology is used to detect both thickness of NT and area of NT.

Moratalla *et al.* (2010) propose a method to estimate intersonographer and intrasonographer variance components of fetal Nuchal Translucency (NT) thickness measurement using the traditional manual approach and a new semi-automated system. In the semi-automated method the operator places an adjustable box over the relevant area at the back of the fetal neck to measure nuchal translucency thickness. Within the box the automated system draws one line through the center of the nuchal membrane and another line at the edge of the soft tissue overlying the cervical spine. The semi automated method calculates the minimum vertical distance between the two lines at each point along the nuchal membrane and computes the largest of these vertical distances as the nuchal translucency measurement. Semi-automated system reduces substantially the Sonographer variations in the measurement of NT achieved using the traditional manual approach.

Lai *et al.* (2011) propose the reconstruction, visualization and measurement of nuchal translucency using three dimensional approaches for real time computation. Two dimensional ultrasound measurements depend on image position and if any deviation occurs it results in inaccurate measurement. Open-source visualization toolkit VTK was implemented for 3D interactive graphics supports. The methodology entails the virtual slider cutting plane to explicit the internal structure of ultrasound marker. It is concluded that 3D measurements of nuchal translucency provide higher accuracy and consistency of thickness measurement.

Park *et al.* (2013) proposes that the algorithm starts by finding the pose of fetal head using leaner based detectors. NT region is calculated from the statistical relationship between fetal head and the NT region. Its inner and outer edge is approximately determined through Dijkstra's shortest path applied on enhanced image. Finally these two regions are used to define foreground and background seeds for accurate graph cut segmentation. The algorithm detects NT region and provide more accurate results.

Cho *et al.* (2012) proposes a method for the success rate of NT measurement was assessed using Volume NT(TM), 2D and 3D techniques. Volume NT a new technique that automatically archives mid-sagittal plane views and measures the maximum Nuchal Translucency (NT) thickness, by comparing its measurements with those made with conventional two- (2D) and three-dimensional (3D) techniques. For two-

dimensional (2D) sonographic nuchal translucency thickness (NT) measurement, the investigator acquired a mid-sagittal plane according to the standards established by Nicolaides *et al.* (1992). For NT measurement using the three-dimensional (3D) technique, 3D volumes were displayed in the three orthogonal planes that compose the multiplanar mode and axes were adjusted to obtain the correct mid-sagittal plane. It is a novel technique for automated NT measurement.

Nina *et al.* (2013) study was to establish normative data of nuchal translucency distribution in singleton pregnancies, 600 fetuses with known normal outcome were included in this study. The distribution of median values of NT thickness with Crown Rump Length (CRL) in 10 mm intervals and 95th percentile were calculated with linear regression method. This study offers a normative data of fetal NT thickness in normal pregnancy, which can be used as a reference for screening chromosomal abnormalities or other congenital abnormalities in the first trimester.

Spencer *et al.* (2003) aim is to assess whether in screening for trisomy21 by Nuchal Translucency (NT) the delta or the Multiples of the Median (MoM) approach is the most appropriate method for calculating accurate individual Patient-specific risks. Examination reveals that first, if the distribution of NT MoM and \log_{10} (NT MoM) was Gaussian. Second, if the standard deviation of the distributions did not change with gestation. And third, if the median MoM in the affected population was a constant proportion of the median for unaffected pregnancies. All of these features are required to underpin the MoM approach. NT distributions and those of delta-NT were also analyzed. A non-parametric kernel density method was then used to assess the validity of both methods. In the calculation of risk for trisomy 21 by NT the NT MoM approach is inaccurate and inappropriate because the underlying

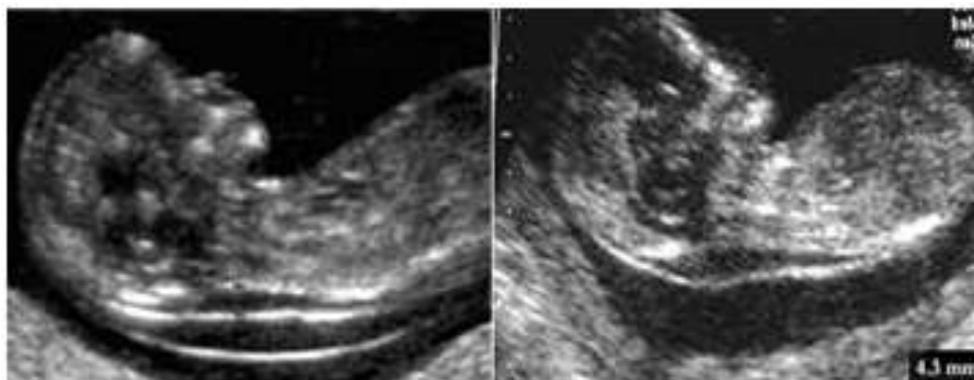
assumptions are not valid. In contrast, the delta-NT approach gives accurate estimates of risk.

Deng *et al.* (2010) propose a hierarchical structural model for the automated detection of the NT region. Three discriminative classifiers are first trained with Gaussian pyramids to represent the NT, head and body of fetuses. Then a spatial model is to denote the spatial constraints among them. Finally the dynamic programming and generalized distance transform are applied for the inference from the model to obtain the optimal solution.

PROPOSED METHODOLOGY

Preprocessing, Feature extraction and classification stage: In the preprocessing stage, Region of Interest (ROI) is extracted by semi-automatically from the fetal ultrasound image which contains the Nuchal translucency region. Despeckle of the image is performed before extracting the features. In the feature extraction stage the ROI images are decomposed by using DWT at predefined decomposition level. The proposed methodology is based on the Support Vector Machine (SVM). SVM is a binary classifier which classifies the extracted features into both normal NT and abnormal NT images. The various process involved in image classification for Nuchal Translucency with the block diagram is shown in Fig. 1.

Fetal images with both normal and abnormal NT is collected from the sonographers through transducer and recorded in the database as image in the jpeg format. The complete data are categorized into both training images and testing images. The two third of images are chosen for the testing. Both the training dataset and testing dataset are given as input and preprocessed with Lee filter to remove the speckle noise. Then Region of Interest (ROI) is extracted and 2D Haar wavelet transformation is applied for the feature extraction and the decomposition of images. The images are decomposed into five levels. The approximate and



(a) Normal NT

(b) Abnormal NT

Fig. 1: Fetal image for Normal NT and abnormal NT

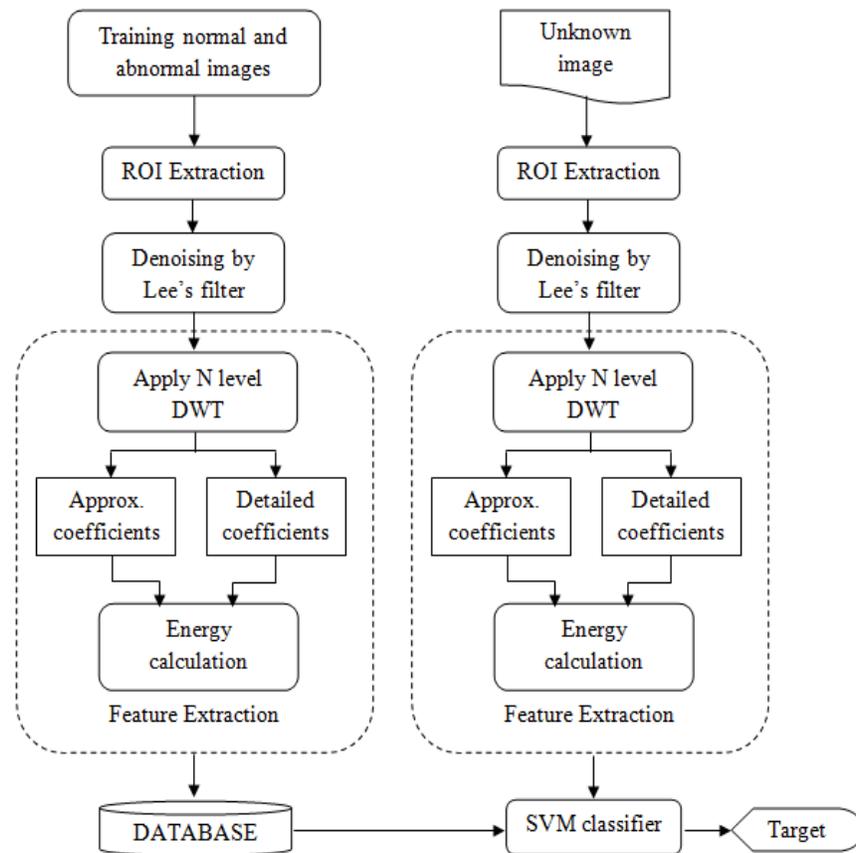


Fig. 2: Architectural diagram for image classification

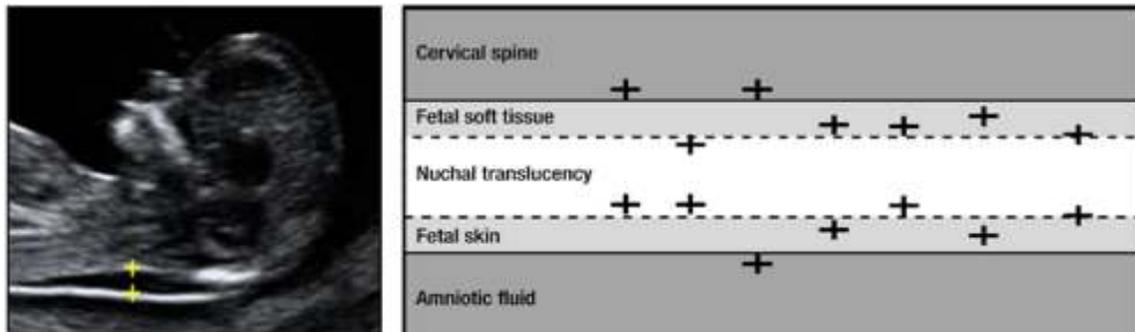


Fig. 3: Position of calipers for NT measurement

detailed coefficients are obtained separately and energy is calculated and stored in database. SVM classifiers are used to classify the image as normal NT or abnormal NT.

Ultrasonography Image Acquisition: Ultrasound fetal images are acquired by the sonographers by using the ultrasound probe, called as transducer. Ultrasonography is a non-invasive method in detecting Down Syndrome in both prenatally and antenatally. Ultrasound images are obtained by sending a pulse of ultrasound echo into tissue using an ultrasound transducer. The transducer

comes in different shapes and produces pulses of sound waves between 3.5 to 7.0 megahertz. The sound reflects and echoes off parts of the tissue, this echo is recorded and displayed as an image to the operator and recorded in the database (Fig. 2).

Nuchal Translucency is the sonographic appearance of subcutaneous collection of fluid behind the fetal neck. NT Thickness is measured with the calipers, which is placed on the inner border of the NT layer. The equipment must have a video loop function which is of good quality and the calipers must be able to provide measurements to one decimal point. A

proper mid-sagittal view of fetal is required for all sonographers for measuring the Nuchal Translucency and Crown Rump length. Protocol to measure the Nuchal translucency are fetus mid-sagittal section should be obtained and measures when fetus is in neutral position and horizontal on the screen. Only the fetal head and upper thorax should be included in the image. More than one measurements are taken during the scan and the maximum is recorded. Figure 3 shows the caliper placement for the correct NT measurement.

Guidelines for NT measurement: Margin of NT edges must be clear, fetus in midsagittal plane, magnifies image, neck must be in neutral position, amnion must be seen as separate from NT line, + Calipers are used to measure NT, caliper must be placed on the inner borders, caliper must be placed perpendicular to the long axis of the fetus and the measurement must be obtained at the widest space of NT (AIUM, 2013).

Preprocessing: The presence of the speckle noise in the ultrasound image reduces the image contrast and resolution thereby reducing the diagnostic value. Hence the image must be free from speckle noise before extracting the features. The standard Adaptive, non linear technique Lee’s Filter is applied to despeckle the image.

Denosing: When the scanner captures images with the transducer it includes extraneous noise to the image. Noise removal is done by smoothing the image. Several de-noising techniques exist for noise removal which includes additive and multiplicative noise. Removal of multiplicative noise is difficult than additive noise. Hence depending on the noise appropriate technique is used. Due to image acquisition of medical image through ultrasound the image is corrupted by noise. Noise must be removed for valuable results Adaptive filtering techniques are proposed for noise reduction. Lee Filter, an adaptive filter is used for noise reduction. Smoothing of images using Lee filter is done when the variance over the area is high near the edges. When the variance is low smoothing will not be performed. Lee filter preserves edges and high texture areas. The formula for Lee filter is:

$$img(i, j) = I_m + N * (C_p - I_m) \tag{1}$$

where, I_m is the mean intensity of the filter window:

$$W = \frac{\sigma^2}{(\sigma^2 + \rho^2)} \tag{2}$$

where, σ^2 is the variance of the pixel values within the filter window and is calculated as:

$$\sigma^2 = \frac{1}{N} \left[\sum_{j=0}^{N-1} (x_j)^2 \right] \tag{3}$$

where,

x_j = Pixel value within filter window at indices j

N = The size of the window

M = The size of the image

y_i = Value of each pixel in the image

$$\rho^2 = \left[\frac{1}{M} \sum_{i=0}^{M-1} (y_i)^2 \right] \tag{4}$$

ROI detection: The function of Region Of Interest (ROI) is very important for image processing in medical application. Particular region of the image is of higher diagnostic importance than others. Measurement of ROI can be both automatic and semi-automatic. In the Image classification of down syndrome images with Nuchal translucency the ROI is extracted semi automatically. The ROI specific area can be marked by a rectangle in the Nuchal translucency area.

FEATURE EXTRACTION

The Discrete Wavelet Transform (DWT), on the other hand, provides sufficient information both for analysis and synthesis of the original signal, with a significant reduction in the computation time and easy to implement. Wavelet performs single-level two-dimensional wavelet decomposition with respect to a particular wavelet or wavelet decomposition filters (Fig. 4 and 5). The input signal is decomposed into two sets of coefficients called approximation coefficient and detail coefficient. The images are decomposed and compute the approximation and detail coefficients matrices such as Horizontal vertical and diagonal. Input signal is filtered and separated into low and high frequency components.

The frequency and time information of a signal at some certain point in the time-frequency plane cannot be known. Though we cannot know what spectral component exists at any given time instant but we can find what spectral components exist at any given interval of time. This is a problem of resolution.

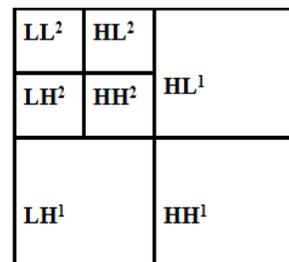


Fig. 4: Pyramid decomposition level 2 using Haar wavelet filter

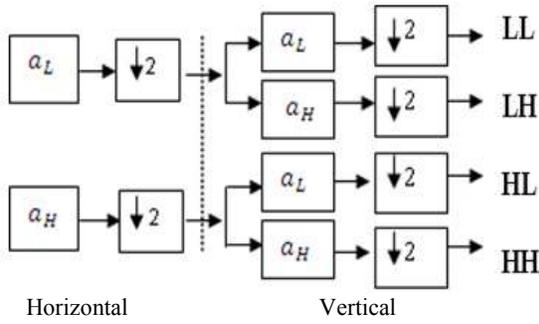


Fig. 5: Filter stage in 2D DWT

The Wavelet functions are given as follows:

$$\psi^H(x, y) = \psi(x)\varphi(y)$$

$$\psi^V(x, y) = \varphi(x)\psi(y)$$

$$\psi^D(x, y) = \psi(x)\psi(y)$$

where, Horizontal (H), Vertical (V), diagonal (D) are the detail coefficient. The low resolution of the image represents as approximation coefficient.

The original signal $x[n]$ is decomposed into $h[n]$ low pass filter and $g[n]$ high pass filter. Both the low pass and high pass filter are not independent and given by:

$$G[L-1-n] = (-1)^n . h[n] \tag{5}$$

Two filtering sub sampling operation can be expressed by:

$$Y_{high}[k] = x[n]g[-n+2k] \tag{6}$$

$$Y_{low}[k] = x[n]h[-n+2k] \tag{7}$$

The signals of 2D ultrasound images are taken as the input.

The image is decomposed into four subimages. Haar wavelet transform is used for decomposition. The frequency information is characterized as four subbands of LL, HH, HL, HH regions. The repeated full decomposition is done in LL regions. Haar wavelet transform. The function is defined as $f(a^L/d^L)$:

$$a^L = (a_1, a_2 \dots a_{N/2})$$

$$d^L = (d_1, d_2 \dots d_{N/2})$$

where,

- L = The decomposition level
- a = The approximation subband
- d = The detail subband:

$$a_m = \frac{f_{2m} + f_{2m-1}}{\sqrt{2}} \text{ for } m = 1, 2, \dots, N/2 \tag{8}$$

$$d_m = \frac{f_{2m} - f_{2m-1}}{\sqrt{2}} \text{ for } m = 1, 2, \dots, N/2 \tag{9}$$

Initially one level of Haar wavelet is applied to each row, then to each column of the image of the previous operation. The resulted image is decomposed into 4 bands LL, HL, LH, HH sub bands. The energy extraction is performed on sub images, which is used to characterize the texture of the image. The energy calculation can be obtained from detailed coefficient and approximate coefficient (Ma and Manjunath, 1995, 1996). The mean of the magnitude of the subimage coefficients is used as its energy. The mean and standard deviation of the magnitude of the sub image coefficients also can be calculated as texture feature If the sub image is $x(m, n)$, with $1 \leq m \leq M$ and $1 \leq n \leq N$, its energy is represented as:

$$e = \frac{1}{MN} \sum_{i=1}^M \sum_{j=1}^N |x(i, j)| \tag{10}$$

Classification: Classification involves two phases of training phase and testing phase used to determine the abnormal and normal NT of ultrasound images. The extracted features are classified with SVM classifier.

Linear SVM classifier: Support Vector Machines are supervised learning models with related learning algorithms which is used for classification and data analysis. Support Vector Machine was proposed by Vapnik. Optimum linear separating hyperplane is used to separate two sets of data. The hyperplane on both the sides separates the two margin and maximizes the distance (Bazzani and Bevilacqua, 2000). The margin which is the maximum margin that separates the hyperplane is $\frac{2}{\|w\|}$.

Given training data $\{x_i, y_i\}$ for $i = 1 \dots n$, $y_i \in \{-1, 1\}$, $x_i \in R^d$ where y_i is either -1 or 1 indicating to which the point belongs. The decision boundary should classify all points correctly. The training data are linearly separable there exists two hyperplane which separates the two classes. The two hyperplane maximizes the distance which separates the margin between two classes (Fig. 6). The linear function takes the form:

$$f(x) = w.x + b \tag{11}$$

The function $f(x)$ yields:

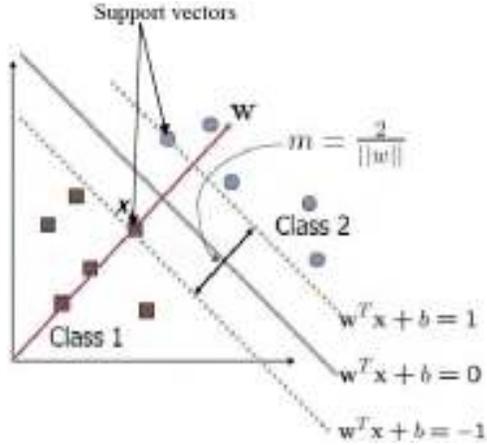


Fig. 6: SVM classification with a hyperplane that maximize the separating margin between the two classes

$$f(x_i) \geq 0 \text{ for } y_i = +1 \text{ and}$$

$$f(x_i) < 0 \text{ for } y_i = -1$$

where, w is the weight vector normal to the hyperplane. Hyperplane cause largest separation between the decision function values for the borderline. For the given training set there exist many hyperplanes that separate the two classes. SVM classifier is based on the hyperplane that maximizes the separating margin between the two classes for the linearly separable case, the support vector algorithm simply looks for the separating hyperplane with largest margin. This can be formulated as follows:

$$w^T .x_i + b \geq +1 \text{ for } y_i = +1 \tag{12}$$

$$w^T .x_i + b \leq -1 \text{ for } y_i = -1 \tag{13}$$

where, $i = 1, 2, 3 \dots l$

These constraints can be combined and written more compactly as:

$$y_i(w.x_i + b) \leq 1 \quad i = 1, 2, \dots l \tag{14}$$

Training data may not be completely separable by a hyperplane. In this case, slack variables are introduced to relax the separability constraints in (4) as follows:

$$y_i(w.x_i + b) \geq 1 - \xi_i \geq 0 \quad \xi_i \geq 0 \tag{15}$$

where, $i = 1, 2, \dots l$.

Accordingly the cost function in (2) can be modified as follows:

$$j(w, \xi) = \frac{1}{2} \|w\|^2 + C \sum_{i=1}^l \xi_i \tag{16}$$

where, C is a user specified positive, regularization parameter, the variable ξ_i is a vector that contains all slack variables.

EXPERIMENTAL RESULTS AND DISCUSSION

Classification accuracy is measured by using confusion matrix which includes the Sensitivity, specificity and accuracy. It is commonly used statistical measures to illustrate the effectiveness of the classification test and especially, used to compute the consistency of the test. Sensitivity evaluates the classification correctly at detecting abnormal NT. Specificity measures how the proportion of babies with normal Nuchal Translucency measurement can be correctly ruled out. The association between both the sensitivity and specificity measures is defined by the graphical representation of the Receiver Operating Characteristics (ROC) curve and this helps to make a decision to find the optimal model to determine the best threshold for the image classification. Accuracy can be concluded with the aid of the sensitivity and specificity measures. In order to compute the values, we to need calculate the values for true positive, true negative, false positive and false negative. The confusion matrix is defined as True Positive (TP), False Positive (FP), False Negative (FN) and True Negative (TN). The sensitivity and specificity are calculated by the following:

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$

$$\text{Specificity} = \frac{TN}{TN + FP}$$

$$\text{Accuracy} = \left[\frac{TP + TN}{TP + TN + FP + FN} \right]$$

The Confusion Matrix for NT image classification are categorized as the normal and abnormal NT fetal

Table 1: Confusion matrix for NT image classification

		Predicted	
		Positive	Negative
Actual	Positive	30 (TP)	10 (FP)
	Negative	2 (FN)	29 (TN)

Table 2: Result analysis of NT image classification

DWT		SVM Classifier-Classification rate		
Decomposition				
level		Normal NT	Abnormal NT	Average
1		75	64.10	69.55
2		75	66.67	70.83
3		87.5	66.67	77.08
4		84.37	66.67	75.52
5		93.75	74.35	84.05

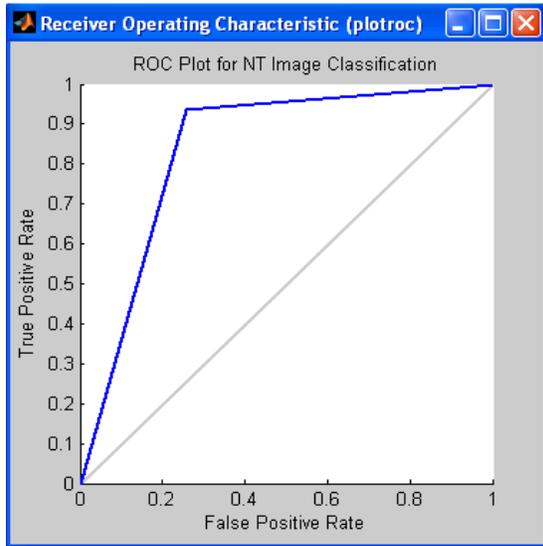


Fig. 7: ROC curve for image classification

images (Table 1). The TP shows the correctly classified normal NT images and TN shows the correctly classified abnormal images. The FP and TN shows abnormal images incorrectly classified as normal and normal NT images incorrectly classified as abnormal. Experimentations are conducted based on evaluation parameters Sensitivity and Specificity with 93.8 and 74.4%, respectively (Fig. 7 and Table 2).

CONCLUSION

The proposed methodology helps the physician to classify both normal and abnormal images accurately. The speckle noise is removed efficiently from ultrasound fetal images by using Lee filter before ROI extraction, which retains the features of the image. After despeckling of noise, feature extraction is done by discrete wavelet transformation by calculating the energy band. The down syndrome images are classified using SVM classifier for abnormal NT and normal NT images. This method of classification produces high detection rate for down syndrome images in singleton pregnancies. Experimentations are conducted based on evaluation parameters Sensitivity and Specificity with 93.8 and 74.4%, respectively. The experimental results showed that the proposed method achieved significant results with 84% of accuracy in NT image classification.

REFERENCES

AIUM (American Institute of Ultrasound in Medicine), 2013. Practice guideline for the performance of obstetric ultrasound examinations. *J. Ultras. Med.*, 32: 1083-1101.

Bazzani, S. and A.D. Bevilacqua, 2000. Automatic detection of clustered micro calcifications in digital mammograms using an SVM classifier. *Proceeding of the European Symposium on Artificial Neural Networks (ESANN'2000)*. Bruges, Belgium, pp: 195-200.

Cho, H.Y., J.Y. Kwon, Y.H. Kim, K.H. Lee, J. Kim, S.Y. Kim and Y.W. Park, 2012. Comparison of nuchal translucency measurements obtained using Volume NT(TM) and two- and three-dimensional ultrasound. *Ultrasound Obst. Gyn.*, 39(2): 175-80.

Deng, Y., Y. Wang and P. Chen, 2008. Estimating fetal nuchal translucency parameters from its ultrasound image. *Proceeding of the International Conference on Bioinformatics and Biomedical Engineering (ICBBE, 2008)*, pp: 2643-2646.

Deng, Y., Y. Wang and P. Chen, 2010. Automated detection of fetal nuchal translucency based on hierarchical structural model. *Proceeding of the IEEE 23rd International Symposium on Computer-Based Medical Systems (CBMS, 2010)*, pp: 78-84.

Hackshaw, A.K., N.J. Wald and J.E. Haddow, 1996. Down's syndrome screening with nuchal translucency. *Lancet*, 348: 1740.

Kagan, K.O., D. Wright, C. Valencia, N. Maiz and K.H. Nicolaides, 2008. Screening for trisomies 21, 18 and 13 by maternal age, fetal nuchal translucency, fetal heart rate, free beta-hCG and pregnancy-associated plasma protein-A. *Hum. Reprod.*, 23(9): 1968-1975.

Lai, K.W., A. Adeela and S. Eko, 2010. Computerized automatic nasal bone detection based on ultrasound fetal images using cross correlation techniques. *WSEAS T. Inform. Sci. Appl.*, 7(8): 1068-1077.

Lai, K.W., Y.C. Hum and S. Eko, 2011. Computerized nuchal translucency three dimensional reconstruction, visualization and measurement for trisomy 21 prenatal early assessment. *Int. J. Phys. Sci.*, 6(19): 4640-4648.

Ma, W.Y. and B.S. Manjunath, 1995. A comparison of wavelet transform features for texture image annotation. *IEEE Image Proc.*, 2(23-26): 256-259.

Ma, W.Y. and B.S. Manjunath, 1996. Texture features and learning similarity. *Proceeding of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition (CVPR'96)*, pp: 425-430.

Moratalla, J., K. Pintoffl, R. Minekawa, R. Lachmann, D. Wright and K.H. Nicolaides, 2010. Semi-automated system for measurement of nuchal translucency thickness. *Ultrasound Obst. Gyn.*, 36: 412-416.

Muller, M.A., E. Pajkr, O.P. Bleker, G.J. Bonsel and C.M. Bilardo, 2004. Disappearance of enlarged nuchal translucency before 14 weeks gestation relationship with chromosomal abnormalities and pregnancy outcome. *Ultrasound Obst. Gyn.*, 24(2): 169-174.

- Nicolaides, K.H., G. Azar, D. Byrne and C. Mansur, 1992. Fetal nuchal translucency: ultra-sound screening for chromosomal defects in first trimester of pregnancy. *BMJ*, 304: 867-869.
- Nicolaides, K.H., M.L. Brizot and R.J.M. Snijders, 1994. Fetal nuchal translucency: Ultrasound screening for fetal trisomy in the first trimester of pregnancy. *Brit. J. Obstet. Gynaec.*, 101: 782-786.
- Nina, M., K. Ashwini, Mouli, V.C. Mouli Rayapureddi, M. Ajit and Krishnapriya, 2013. Variaton of nuchal translucency with increasing crown rump length and gestational age in normal singleton pregnancies. *IOSR J. Dent. Med. Sci.*, 6(3): 16-19.
- Nirmala, S. and V. Palanisamy, 2009. Measurement of nuchal translucency thickness for detection of chromosomal abnormalities using first trimester ultrasound fetal images. *Int. J. Comput. Sci. Inf. Secur.*, 6(3): 101-106.
- Pandya, P.P., M.L. Brizot, P. Kuhn, R.J.M. Snijders and K.H. Nicolaides, 1994. First trimester fetal NT thickness and risk for trisomies. *Obstet. Gynecol.*, 84: 420-423.
- Pandya, P.P., A. Kondylis, L. Hilbert, R.J. Snijders and K.H. Nicolaides, 1995a. Chromosomal defects and outcome in 1015 fetuses with increased nuchal translucency. *Ultrasound Obst. Gyn.*, 5(1): 15-19.
- Pandya, P.P., R.J.M. Snijders, S.P. Johnson, M. De Lourdes Brizot and K.H. Nicolaides, 1995b. Screening for fetal trisomies by maternal age and fetal nuchal translucency thickness at 10-14 weeks of gestation. *Brit. J. Obstet. Gynaec.*, 102: 957-962.
- Park, J.H., M. Sofka, S.M. Lee, D.Y. Kim and S.K. Zhou, 2013. Automatic nuchal translucency measurement from ultrasonography. *Proceeding of International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI, 2013)*.
- Snijders, R.J.M. and K.H. Nicolaides, 1996. Sequential Screening. In: Nicolaides, K.H. (Ed.), *Ultrasound Markers for Fetal Chromosomal Defects*. Parthenon, Carnforth, UK, pp: 109-113.
- Snijders, R.J.M., P. Noble, N. Sebire, A. Souka and K.H. Nicolaides, 1998. UK multicentre project on the assessment of risk of trisomy 21 by maternal age and fetal nuchal-translucency thickness at 10-14 weeks of gestation. *Lancet*, 351: 343-346.
- Souka, A.P., E. Krampfl, S. Bakalis, V. Heath and K.H. Nicolaides, 2001. Outcome of pregnancy in chromosomally normal fetuses with increased nuchal translucency in the first trimester. *Ultrasound Obst. Gyn.*, 18(1): 9-17.
- Spencer, K., R. Bindra, A.B. Nix, V. Heath and K.H. Nicolaides, 2003. Delta-NT or NT MoM: Which is the most appropriate method for calculating accurate patient-specific risks for trisomy 21 in the first trimester. *Ultrasound Obst. Gyn.*, 22: 142-148.