Indian Journal of Science and Technology, *Vol 9(21), DOI: 10.17485/ijst/2016/v9i21/95174, June 2016*
ISSN (Print) : 0974-6846
ISSN (Online) : 0974-5645

Early Detection of Down Syndrome Marker by Measuring Fetal Nuchal Translucency Thickness from Ultrasound Images during First Trimester

R. Sonia[1]* and V. Shanthi[2]

[1]Sathyabama University, Chennai - 600119, Tamil Nadu, India; sonia.j25@gmail.com
[2]St Joseph's College of Engineering, Chennai - 600119, Tamil Nadu, India; drvshanthi@yahoo.co.in

Abstract

Objectives: Nuchal Translucency (NT) thickness measurement is a Down syndrome marker for chromosomal abnormalities which is detected by non-invasive test during first trimester. **Methods**: In this paper, a computerized method to measure NT thickness is proposed. It consists of region of interest extraction, NT segmentation using morphological operation with Otsu thresholding. The NT thickness is measured from the segmented area. The performance is analyzed on 80 ultrasound fetal images. **Findings**: Proposed approach for NT measurement is implemented in MATLAB software. Experimental results show that NT thickness for normal foetus is 1.99±.62 mm and abnormal foetus is 4.10±.90 mm during first trimester of pregnancy from 11 to 13^{+6} weeks of gestation. The proposed algorithm efficiently computes NT measurement and produces consistent result during first trimester in singleton pregnancies. **Applications/Improvements**: Proposed semi-automated technique helps the medical sonographer for accurate NT thickness measurement to detect Down syndrome marker during first trimester ultrasound scan.

Keywords: Down Syndrome, Morphological Operation, Nuchal Translucency, Trimester, Thresholding

1. Introduction

Down syndrome or Trisomy 21 is the chromosomal abnormalities caused by extra copies of chromosome 21, which cause birth defects[1]. Down syndrome chances increases with increased maternal age of mother 35 and above. Fetal NT along with maternal age is the significant method to measure trisomy 21[2]. Detection of chromosomal abnormalities is done through prenatal diagnostic and screening tests. Trisomy 21 is detected through ultrasound scan imaging which is a diagnostic test. Nuchal translucency is the accumulation of enlarged fluid at the back of fetal neck. NT measurement depends on the CRL which is between 45mm and 84mm from head to toe[3]. Measurement of NT thickness is done during 11 to 13^{+6} weeks of gestation, as it would disappear during second trimester[4]. Criteria to measure the risk for chromosomal abnormalities includes maternal age and gestational period which is priori risk and multiply by set of factors (or) likelihood ratio's. Patient's specific risk is manipulated by the likelihood ratio with priori risk, along with increased Crown rump length NT also increases with higher likelihood ratio and new risk[4]. NT measurement can be performed through trans-abdominal and transviginal in midsagittal view[5]. A study was performed on 693 chromosomally normal pregnancies. Fetal images for NT thickness is 3.5mm during the first trimester at increased risk with chromosomal abnormalities[6]. Figure 1 (a) and (b) shows the abnormal and normal NT thickness images respectively.

Accumulation of fluid behind the fetal neck appears only in first trimester and disappears after 14 weeks of gestation. Protocols for NT measurement includes

- Measured by trans abdominal ultrasound.
- Fetal CRL must be between 45 and 84 cm.
- Fetal upper thorax image in midsaggital view is required.

*Author for correspondence

- The value of fetal neck when hyper extended and flexed are increased .6mm and decreased .4mm respectively.
- Measurements are recorded by placing the caliper above and below.
- More than one measurement is taken by the sonographer for better results.

Fetus with subcutaneous collection of fluid behind the neck is measured by correct placement of caliper. NT thickness is measured by placing the caliper on the border lines of the fluid when the fetus is in midsagittal view. Figure 2 (a) and (b) shows the Correct and incorrect alignment of caliper respectively.

Fetus with increased Nuchal translucency thickness from 3mm to 6mm or above is associated with 4-fold to 41 fold with respect to maternal age. Further accurate diagnosis is done by triple and quadruple test. However the quality depends on the ultrasound machine and sonographer. Trisomy 21 screening is performed by measuring NT and biochemical markers. Biochemical markers are PAPP-A, pregnancy associated plasma protein-A and free beta-hCG, the beta subunit of human gonadotropin. This combined screening results in 82-87% of better chromosomal abnormal detection rate[7].

Various techniques have been proposed for detecting Down syndrome marker by measuring NT thickness measurement during first trimester. NT measurement was proposed by Nicolaides. Due to its transient nature the NT measurement is performed between 11 and 13^{+6} weeks. Multilayer feed forward neural network is proposed for NT measurement by measuring largest thickness in mm for detecting Down syndrome marker[8]. Automatic and manual detection is done with mean and standard deviation. NT segmentation technique shift analysis and canny operators are used for NT thickness measurement using blob analysis[9]. Segmentation is performed on cropped image using mean shift and cluster analysis. Automatic detection of NT is implemented by using Hierarchical structural model[10]. Gaussian pyramids train the classifiers. To end with dynamic programming, distance transform is applied to acquire ideal solution. Semi-automated system[11] is proposed by placing a box on the NT region and lines are drawn inside the box and the largest line between the distances shows NT thickness measurement. Measure estimates intersonographer and intrasonographer in traditional manual approach. Hence both semi automated and traditional manual approach are performed.

(a) (b)

Figure 1. **(a)** Abnormal NT. **(b)** Normal NT.

(a) (b)

Figure 2. **(a)** Correct alignment of caliper. **(b)** Incorrect alignment of caliper.

NT thickness measurement between the fetal head and NT region which is determined approximately through Dijikstras shortest path and applied on edge enhanced image and these regions are used for graph cut segmentation[12]. Two dimensional and three dimensional approaches are proposed for NT measurement, where the 2D does not provide correct measurement and if any deviations occur, open source toolkit is implemented for 3D measurement which provides consistent measurement[13]. NT volume measurement is proposed by using 2D and 3D techniques. The volumes are displayed in mid sagittal view and 3D orthogonal planes which constitute multiplanar mode[14]. NT thickness measurement with respect to Crown rump length using linear regression method is proposed for measurement[15]. A study was performed on 600 fetuses with normal Nuchal translucency in normal pregnancy.

2. Methods and materials

Nuchal Translucency thickness is measured to detect Down syndrome marker from ultrasound fetal images. NT measurement depends on the CRL. During the measurement of CRL the baby position should not be too flexed and extended. CRL must be between 45 and 84 cm in standard position. The following sections explain the Region of Interest (ROI) selection, NT segmentation, and Morphological Operation, thresholding and thickness measurement. The ultrasound foetus image is given as input and the second step is to select the region of interest. The ROI selected is the fluid filled NT area.

Next NT segmentation is done by applying Mathematical morphology, Otsu thresholding and logical operation. After the NT segmentation the segmented NT area appears as white pixels from NT thickness measurement. The proposed approach for NT thickness measurement is shown in Figure 3.

2.1 Pre-Processing and ROI

Pre-processing of NT normal and abnormal images are done using the Lee filter[16]. From the preprocessed image ROI is selected to measure the particular region of image. ROI is manually extracted by placing a rectangular box on the NT area of ultrasound fetal image. NT region has to be separated from amniotic fluid which is irrelevant fluid. The Figure 4(a) and 4(b) shows the ROI extraction and caliper placement.

2.2 NT Segmentation

2.2.1 Morphological Technique

Morphological operations deal with form and structure of ultrasound images. They remove the imperfection in images, which are introduced during segmentation. Morphological operations are performed on structuring element. Our proposed system gives new processed image when the structuring element is moved across every pixel in the original image. Erosion and Dilation modify geometric features of image. The morphological technique starts with erosion followed by dilation and they are performed using the following equation

$$A\Theta B = \left\{ i, j \,|\, B_{i,j} \subseteq A \right\} \tag{1}$$

$$A \oplus B = \{ i, j \,|\, B_{i,j} \cap A \neq \phi \} \tag{2}$$

Where A represents the binary or gray scale image and B denotes the structuring element and (i, j) indicates the current pixel element. Structuring element is a binary image of any size or mask having 0's and 1's, which defines an arbitrary neighbourhood structure for morphological process. Structuring element B is positioned with its origin at $g(x, y)$ and new pixel value is determined using the rule $g(x, y) = 1$ if S fit erosion of the image or $g(x, y) = 0$. Erosion can split apart joined objects and can also strip away extrusions, whereas the Dilation can repair breaks and intrusions. It is determined using the rule $g(x, y) = 1$ if S hits the image or $g(x, y) = 0$otherwise. Figure 5 shows the Structuring element used in morphological with 0, 30, 60 and 90 degree.

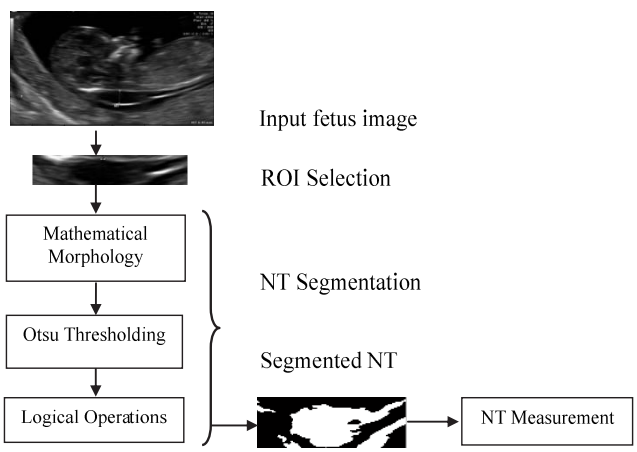

Figure 3. Proposed NT measurement approach.

Figure 4. **(a)** ROI selection for normal NT. **(b)** ROI selection for abnormal NT.

2.2.2 Otsu Thresholding

Thresholding is applied to separate NT and Otsu is the most significant method which is applied for NT segmentation from background image

- Algorithm to select threshold-
- Select the global threshold T.
- Image is to be divided into two classes c_1 and $c_2$with a threshold T at level k such that c_1 denotes pixels with levels
- $[1, k]$ and $c_2$denotes pixels with levels $[k+1, L]$
- Compute the average of pixels for two classes.
- Otsu Method

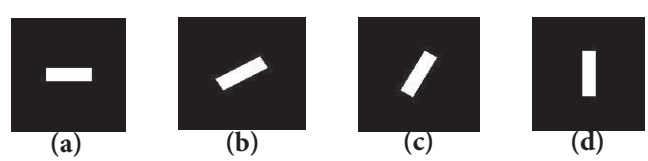

Figure 5. **(a)** 0 degree. **(b)** 30 degree. **(c)** 60 degree. **(d)** 30 degree.

The image is taken a *mxn* with intensity L from 1 to L. The given image is represented in gray scale image. The pixels in image are denoted by n_i at level I and total number of pixels are denoted by N. The probability distribution is given by

$$p_i = \frac{n_i}{N},\ p_i \geq 0,\ \sum_{i=1}^{L} p_i = 1 \tag{3}$$

That is, the number of pixels with intensity levels [1...L] where i[th] intensity level is given $\sum_{i=1}^{L} p_i = 1$ value i divided by the total number of pixels. The probabilities of class occurrence (the odds that a randomly chosen pixel will be of a particular class) and the class mean levels are as follows:

$$\omega_0 = \Pr(c_0) = \sum_{i=1}^{k} p_i = \omega(k) \tag{4}$$

$$\omega_1 = \Pr(c_1) = \sum_{i=k+1}^{L} p_i = 1 - \omega(k) \quad and \tag{5}$$

$$\mu_0 = \sum_{i=1}^{k} i \Pr(i \mid c_0) = \sum_{i=1}^{k} \frac{ip_i}{\omega_0} = \frac{\mu(k)}{\omega(k)} \tag{6}$$

$$\mu_1 = \sum_{i=k+1}^{L} i \Pr(i \mid c_1) = \sum_{i=k+1}^{L} \frac{ip_i}{\omega_1} = \frac{\mu T - \mu(k)}{1 - \omega(k)} \tag{7}$$

Where

$$\mu_T = \mu(L) = \sum_{i=1}^{L} ip_i \tag{8}$$

is the cumulative mean level of the original image

The class variances are given by

$$\sigma_0^2 = \sum_{i=1}^{k} (i - \mu_0)^2 \Pr(i \mid c_0) = \sum_{i=1}^{k} (i - \mu_0)^2\, p_i / \omega_0 \tag{9}$$

$$\sigma_1^2 = \sum_{i=k+1}^{L} (i - \mu_1)^2 \Pr(i \mid c_1) = \sum_{i=k+1}^{L} (i - \mu_1)^2\, p_i / \omega_1 \tag{10}$$

which require the calculation of second-order cumulative moments. The proposed measure of optimality uses the following discriminant condition measures or measures of class separability:

$$\lambda = \sigma_B^2 / \sigma_W^2;\ k = \sigma_T^2 / \sigma_W^2;\ \eta = \sigma_B^2 / \sigma_T^2 \tag{11}$$

Where

$$\sigma_W^2 = \omega_0 \sigma_0^2 + \omega_1 \sigma_1^2 \tag{12}$$

$$\sigma_B^2 = \omega_0 (\mu_0 - \mu_T)^2 + \omega_1 (\mu_1 - \mu_T)^2 \tag{13}$$

$$\sigma_T^2 = \sum_{i=1}^{L} (i - \mu_T)^2 p_i \tag{14}$$

are the within, the between, and the total variance of levels. The σ_T^2 is constant over the whole image, the expense of its calculation can be disregarded. Since σ_W^2 requires first and second order statistics, but σ_B^2 requires only first-order statistics, η is the simplest criterion to calculate.

If σ_B^2 is larger find k to maximize η

- Compute the normalize Histogram Pi.
- Compute $\omega_0 = \Pr(c_0) = \sum_{i=1}^{k} p_i = \omega(k)$.
- Compute $\mu_T = \mu(L) = \sum_{i=1}^{L} ip_i$.
- Compute $\sigma_B^2 = \omega_0 (\mu_0 - \mu_T)^2 + \omega_1 (\mu_1 - \mu_T)^2$.
- Obtain Otsu threshold $k^* \leftarrow \max_{1 \leq k < L} \sigma_B^2(k)$.
- Compute $\eta(k^*) = \sigma_B^2(k^*) / \sigma_T^2$.

The optimal threshold k^* that maximizes, or equivalently maximizes the between-class variance σ_B^2 is selected by sequential search using the following derivations of the previous formulae:

$$\eta(k) = \sigma_B^2(k) / \sigma_T^2 \tag{15}$$

$$\sigma_B^2(k) = \frac{\left[\mu T \omega(K) - \mu(k)\right]^2}{\omega(k)[1 - \omega(k)]} \tag{16}$$

As σ_T^2 is constant, the solution can be given as:

$$k^* \leftarrow \max_{1 \leq k < L} \sigma_B^2(k) \tag{17}$$

This solution provides a crisp threshold value which gives the best distinction between foreground and background pixels according to statistical analysis[15].

2.2.3 NT Measurement

NT is the measurement after performing logical AND operation on the binary output image. The output obtained is processed with Otsu thresholding and logical AND operation is applied on binary image. The pixel values in the background image are 0 and foreground NT region are 1. It is calculated by taking the white pixels area

wise and maximum number of white pixels column wise. It is taken as the maximum height for NT measurement and corresponding average and standard deviations are obtained.

3. Results and Discussions

The work focuses on NT thickness measurement for both normal and abnormal images for first trimester and second trimester. The performance of the proposed approach is assessed for 80 images which include 50 Normal and 30 abnormal images. The stages of Structure element are performed for 0 degree, 30 degree, 60 degree and 90 degree for both normal and abnormal fetus. For dilation and erosion structure element of line shape is used with various angles. The Table 1 shows the measurement of normal fetus with NT thickness and abnormal fetus with enlarged fluid thickness at the back of the neck. For abnormal fetus, only few images with NT measurement above 4 mm are considered.

Table 1 shows the measurement during first trimester of pregnancy from 11 to 13^{+6} weeks of gestation. For normal and abnormal fetal image of NT images with various measurements were considered. Erosion is applied and the image is eroded with 0 degree, 30 degree, 60 degree and 90 degree. Similarly dilation is applied and the image is dilated at each stage for 0 degree, 30 degree, 60 degree and 90 degree.

Table 1. NT Thickness and area measurement for normal and abnormal fetus

NT Thickness (Normal fetus)	NT Area (Normal fetus)	NT Thickness (Abnormal fetus)	NT Area (Abnormal fetus)
2.03	26.97	4.93	133.4
1.74	41.76	4.35	186.47
1.45	26.68	2.32	81.2
1.16	37.12	4.35	152.25
1.74	61.77	4.35	127.6
3.19	70.76	4.35	77.72
2.32	29.87	-	-
2.32	7.83	-	-
Avg 1.99375	37.845	4.108333	126.44
SD 0.628466	20.28046	0.906298	41.80871

4. Conclusion

The proposed work measures the NT thickness very efficiently from ultrasound fetal images during first trimester of gestation week. Morphological operation and Otsu thresholding segments the Nuchal translucency area exactly. The NT thickness measurement is performed during 13^{+6} weeks of gestation. Segmented NT area appears to be white pixels in both area and height wise. Average and standard deviation calculated for height of NT thickness for normal and abnormal fetus is 1.99±0.62 mm and 4.10±.90 mm respectively. Similarly Average and Standard Deviation for area of NT measurement is also measured for both normal and abnormal fetus with 37.84±20.28 mm and 126.44±41.80 mm respectively. Hence the proposed approach measures the ROI of NT more accurately in singleton pregnancies. Along with the abnormality of NT screening, maternal serum markers can be performed for further detection rate.

5. References

1. Kagan KO, Wright D, Valencia C, Maiz N, Nicolaides KH. Screening for trisomy's 21, 18 and 13 by maternal age, fetal nuchal translucency, fetal heart rate, free beta-hCG and pregnancy-associated plasma protein-A. Human Reproduction. 2008 Sep; 23(9):1968–75.
2. Snijders RJM, Noble P, Sebire N, Souka A, Nicolaides KH. 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. 1998 Aug; 352(9125):336–7.
3. Muller MA, Pajkrt E, Bleker OP, Bonsel GJ, Bilardo CM. Disappearance of enlarged nuchal translucency before14 weeks gestation relationship with chromosomal abnormalities and pregnancy outcome. Ultrasound in Obsteterics Gynecology. 2004 Aug; 24(2):169–74.
4. Snijders RJM, Nicolaides KH. Sequential screening. In: Nicolaides KH, editor. Ultrasound markers for fetal chromosomal defects. Carnforth, UK: Parthenon Publishing; 1996. p. 109–13.
5. Elahifar MA, Hasanzadeh M, Dahmardeh H, Elahifar A. The relationship between thickness of nuchal translucency and down syndrome in the first trimester of pregnancy. Zahedan Journal of Research in Medical Sciences. 2012 Jun; 14(4):26–8.
6. Souka AP, Krampl E, Bakalis S, Heath V, Nicolaides KH. Outcome of pregnancy in chromosomally normal fetuses with increased nuchal translucency in the first trimester , Ultrasound Obsteterics & Gynecology, 2001 Jul , 18(1), pp. 9–17.

7. Casals E, Aibar C, Martinez J M, Borrell A, Soler A, Ojuel J, Ballesta A M, Fortuny A. First-trimester biochemical markers for Down syndrome , Prenatal Diagnosis, 1999 Jan, 19(1), pp. 8–11.
8. Wee L K, Min T Y, Arooj A, Supriyanto E. Nuchal translucency marker detection based on artificial neural network and measurement via bidirectional iteration forward propagation. WSEAS Transactions on Information Science and Applications. 2010 Aug; 7(8):1025–36.
9. Nirmala S, Palanisamy V. Measurement of nuchal translucency thickness for detection of chromosomal abnormalities using first trimester ultrasound fetal images. International Journal of Computer Science and Information Security (IJCSIS). 2009 Dec; 6(3):101–6.
10. Deng Y, Wang Y, Chen P. Automated detection of fetal nuchal translucency based on hierarchical structural model. IEEE International Symposium on Computer-Based Medical Systems (CBMS); Perth, WA. 2010 Oct. p. 78–84.
11. Moratalla J, Pintoffl K, Minekawa R, Lachmann R, Wright D, Nicolaides KH. Semi-automated system for measurement of nuchal translucency thickness. Ultrasound in Obsteterics and Gynecology. 2010 Oct; 36(4):412–6.
12. Park JH, Sofka M, Lee SM, Kim DY, Zhou SK. Automatic nuchal translucency measurement from ultrasonography. Medical Image Computing and Computer-Assisted Intervention-MICCAI. Springer-Verlag: Berlin Heidelberg; 2013; 16(Pt 3):243–50.
13. Wee LK, Chai HY, Supriyanto E. Computerized nuchal translucency three dimensional reconstruction, visualization and measurement for trisomy 21 prenatal early assessment. International Journal of the Physical Sciences. 2011 Sep; 6(19):4640–8.
14. Cho HY, Kwon JY, Kim YH, Lee KH, Kim J, Kim SY, Park YW. Comparison of nuchal translucency measurements obtained using Volume NT(TM) and two- and three-dimensional ultrasound. Ultrasound in Obsteterics Gynecology. 2012 Feb; 39(2):175–80.
15. Mahale N, Kumar A, Rayapureddi VCM, Mahale A, Krishnapriya. Variation of nuchal translucency with increasing crown rump length and gestational age in normal singleton pregnancies. IOSR Journal of Dental and Medical Sciences. 2013 May-Jun; 6(3):16–9.
16. Anitha U, Malarkkan S. A novel approach for despeckling of sonar image. Indian Journal of Science and Technology. 2015 May; 8(S9):252–9.