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Semi-automated system for measurement of nuchal translucency thickness

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KEYWORDS: automated measurement; first-trimester screening; nuchal translucency; trisomy 21; ultrasound

ABSTRACT

Objective *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.*

Methods *A semi-automated method was developed for measurement of the NT. In this method, the operator places an adjustable box over the relevant area at the back of the fetal neck. The system draws a line through the center of the nuchal membrane and another line at the edge of the soft tissue overlying the cervical spine. The system then identifies the largest vertical distance between the two lines. The images of 12 fetuses at 11–13 weeks of gestation satisfying the guidelines of The Fetal Medicine Foundation for measurement of NT were selected. They were exported in DICOM format from the ultrasound system, and four versions of each image were stored under different names. The resulting 48 images were presented in random order for electronic assessment. A total of 20 sonographers measured the NT in each set of 48 pictures, twice using the semi-automated system and twice using the manual system, according to a randomized block design. Within- and between-operator variance components were estimated. Relative biases were assessed by comparing the means from the two methods.*

Results *The estimated between-operator SD using the semi-automated method was 0.0149 mm compared with 0.109 mm for the manual method. The respective within-operator SD values were 0.05 mm and 0.126 mm. The intraclass correlation coefficients for different sonographers measuring the same images were 0.98 and 0.85 for the semi-automated method and the manual method, respectively.*

Conclusion *The measurement of fetal NT is more reliable when a semi-automatic approach is used rather than the traditional manual method. Copyright © 2010 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Fetal nuchal translucency (NT) thickness is the most effective marker of trisomy 21 and all other major chromosomal defects. Increased NT is also associated with many fetal defects, genetic syndromes and an adverse pregnancy outcome[1,2].

The use of NT in the assessment of accurate patient-specific risks for chromosomal and other abnormalities necessitates adherence to a standard measurement technique in order to achieve uniformity of results among different operators. A good sagittal section of the fetus should be obtained and the NT should be measured with the fetus in the neutral position. The maximum thickness of the subcutaneous translucency between the skin and the soft tissue overlying the cervical spine should be measured. The calipers should be placed on the lines that define the NT thickness; however, in magnifying the image (either pre- or postfreeze zoom), the nuchal membrane on one side and the edge of the soft tissue overlying the cervical spine on the other side become thicker and consequently the translucent area between them becomes smaller. In order to avoid this underestimation during measurement of the NT, the operator should aim to place the calipers at the point of maximum echogenicity, which lies in the center of the nuchal membrane rather than at its inner border.

There are two elements in the assessment of NT that can introduce operator bias and either underestimation

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or overestimation of the measurement and consequent increase in the variability of measurements. First, the selection of the exact place behind the fetal neck containing the maximum vertical distance between the nuchal membrane and the edge of the soft tissue overlying the cervical spine, because the two lines are not usually parallel; and, second, the selection of the exact position within the thickness on the two lines for accurate placement of the calipers. In order to avoid these problems a semi-automated method of measuring NT thickness has been developed.

The aim of this study was to compare the variability in the measurements of NT using the traditional manual approach and the new semi-automated system.

METHODS

Transabdominal ultrasound examination (RAB 4-8L probe, Voluson 730 Expert; GE Healthcare Technologies, Milwaukee, WI, USA) was performed in singleton pregnancies at 11 + 0 to 13 + 6 weeks of gestation as part of routine first-trimester screening for chromosomal defects. Images of 12 fetuses satisfying the guidelines of The Fetal Medicine Foundation (www.fetalmedicine.com) for measurement of NT were selected for the study, which was approved by King's College Hospital Research Ethics Committee.

We selected images with a NT between 1.5 and 3.0 mm, with over-representation of measurements between 2.3 and 2.7 mm, because small changes in measurements within this range have large effects on the estimation of risk for trisomy 21. Each of these 12 images was reproduced four times, thus giving a total of 48 images that were randomly ordered and numbered from 1 to 48.

Twenty sonographers who had obtained The Fetal Medicine Foundation Certificate of Competence in the 11–13 week scan were then instructed to measure the NT offline in each set of 48 images twice using the semi-automated system and twice using the manual system and to enter their data into a computer system.

In the semi-automated method the operator places an adjustable box over the relevant area at the back of the fetal neck (Figure 1). The box should include a large segment of the fetal NT, which has clearly visible proximal and distal edges and contains the area with the maximum NT. The automated system first interrogates the whole length of the nuchal membrane within the box and draws a line through the center of the nuchal membrane. Second, the system draws a line at the edge of the soft tissue overlying the cervical spine. For the detection of both lines, the brightness information inside the box, as well as the gradient information derived from an edge-detection algorithm, is used. This processing minimizes the influence of gain on the position of the two lines. Third, the system calculates the maximum vertical distance between the two lines. To do this, each point on one line is virtually connected to all possible points on the other line. From all lines that diverge from a single point on the first line, the minimum distance is remembered by the system. The final result is the longest of all the minimum distances (Figure 2).

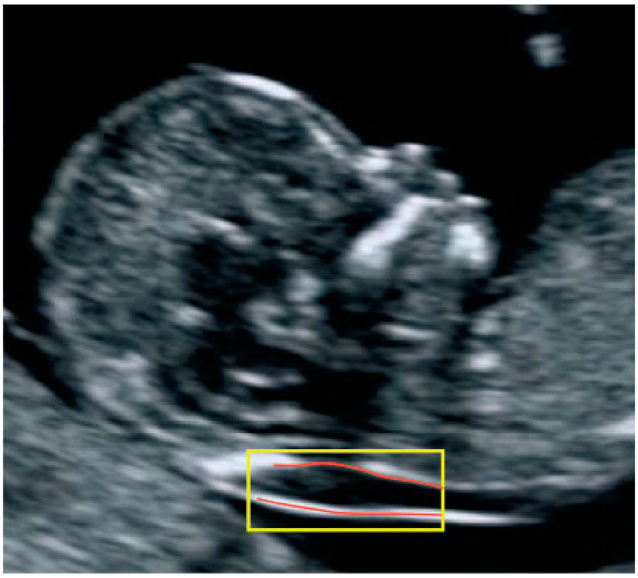

Figure 1 Mid-sagittal section of the fetal head and upper thorax. In the semi-automated method the operator places an adjustable box (yellow outline) over the relevant area at the back of the fetal neck to measure nuchal translucency thickness. Within the box the automated system draws one line through the center of the nuchal membrane and another line at the edge of the soft tissue overlying the cervical spine.

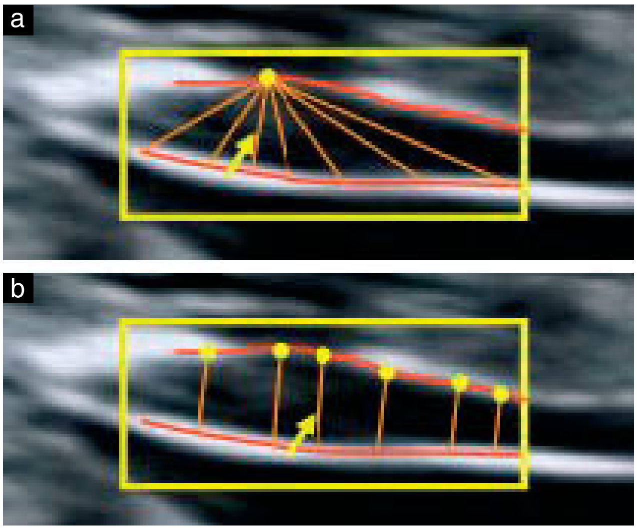

Figure 2 In the semi-automated method the system calculates the minimum vertical distance between the two lines at each point along the nuchal membrane (a) and computes the largest of these vertical distances as the nuchal translucency measurement (b).

Statistical analysis

The study was designed with the aim of estimating within- and between-sonographer components of variance. A sample of 20 operators enables estimation of the between-sonographer variance, and taking eight replicate measurements for each sonographer for each method enables estimation of the within-sonographer variance[3].

Between- and within-operator variance components were estimated using Bayesian methods implemented using WinBUGS[4]. The results are presented in terms of within- and between-operator SD values. The calculation of intraclass correlation coefficients for the two methods was problematic because of the small number of images selected. The approach taken was to estimate the true variance of NT in screening populations from a large prospective dataset of over 37000 pregnancies using the manual method[5]. Fetal NT values in excess of 4 mm were excluded to remove the influence of extremely large NT measurements that inflate the variance of NT. Bland–Altman plots were used to assess the bias of the semi-automatic method relative to the manual method.

RESULTS

Sonographer effects on the measurement of fetal NT using the manual and semi-automated methods are shown in Figure 3 as means (95% CI) for repeated measurements of the same 12 images. In the manual method there were very clear differences between sonographers in the measurement of NT, whereas in the semi-automated method there was very little evidence of any substantive sonographer differences. The within-sonographer variation, as measured by deviations from the sonographer mean for each image, is shown in Figure 4.

The estimated between-operators SD with 95% confidence intervals for the manual method of measuring fetal NT was 0.109 (0.0782–0.152) mm. Assuming a Gaussian distribution, this would mean that 95% of operator effects lie within ± 0.2 mm of the true measurement. For the semi-automated method, the between-operators SD was reduced by a factor of seven to 0.0149 (0.0105–0.0209) mm. The within-operator SD was also reduced with the automated method, from 0.126 (0.121–0.129) to 0.050 (0.0484–0.0516) mm.

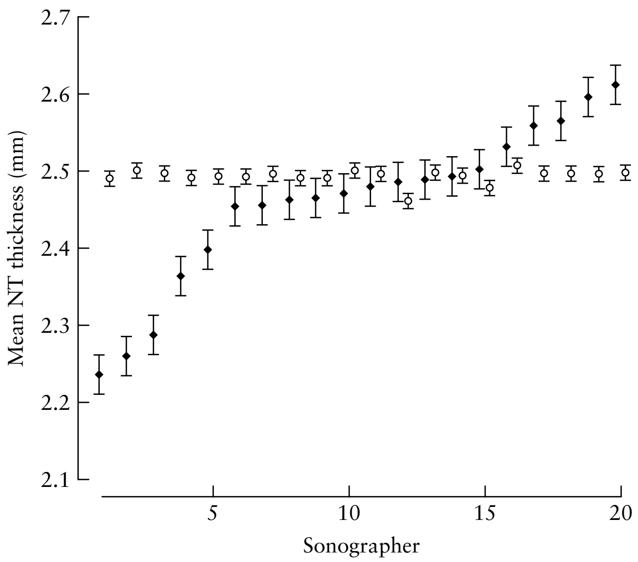

Figure 3 Between-sonographer variation. Measurements of fetal nuchal translucency (NT) thickness made by 20 sonographers using the manual method (◆) and the semi-automated system (○) are shown as mean (95% CI). The sonographers were numbered according to the mean measurement obtained using the manual method.

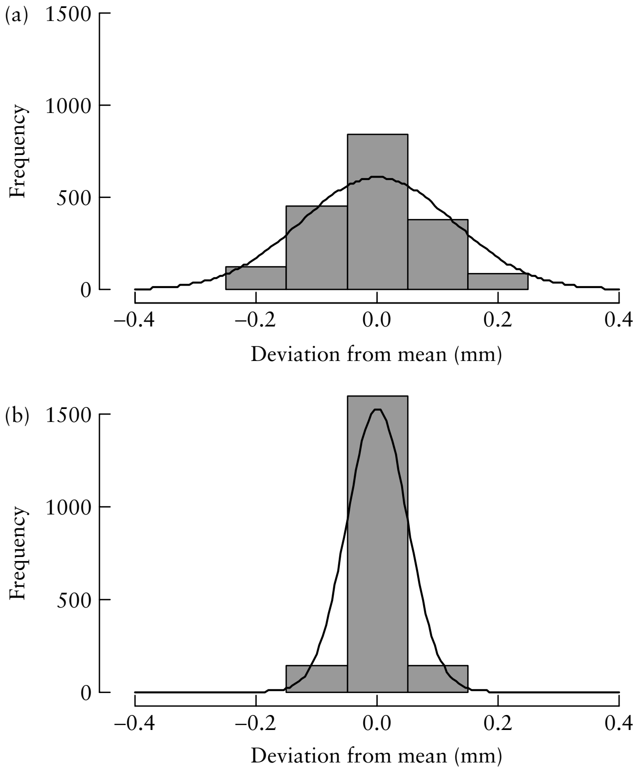

Figure 4 Within-sonographer variation for the manual (a) and semi-automated (b) methods of measuring fetal nuchal translucency thickness. Deviations from image means for each operator were pooled over the 20 operators and 12 images. The smooth curves are the fitted Gaussian distributions for the within-sonographer SD.

The estimated population SD from the manual method was obtained from data reported previously[5]. After exclusion of measurements in excess of 4 mm, this was 0.425, which is close to the median absolute deviation estimate of SD of 0.445 for the same dataset with no exclusions. The true variance of NT, after the removal of within- and between-components of variance, is given by $0.153 = 0.425^2 - 0.109^2 - 0.126^2$. This leads to intraclass correlation coefficients of 0.98 and 0.85 for the semi-automated and manual methods, respectively.

The estimated SD of differences between repeated measurements of the same NT by different operators using the manual method was $\sqrt{2(0.109^2 + 0.126^2)} = 0.24$ mm, compared with $\sqrt{2(0.0149^2 + 0.050^2)} = 0.05$ mm for the semi-automated method.

The relative bias between the semi-automated and manual methods is shown in Figure 5. In the 12 images examined, the semi-automated measurements tended to be slightly higher, by about 0.04 mm.

DISCUSSION

The findings of this study suggest that the semi-automated method has the potential to remove most of the variation

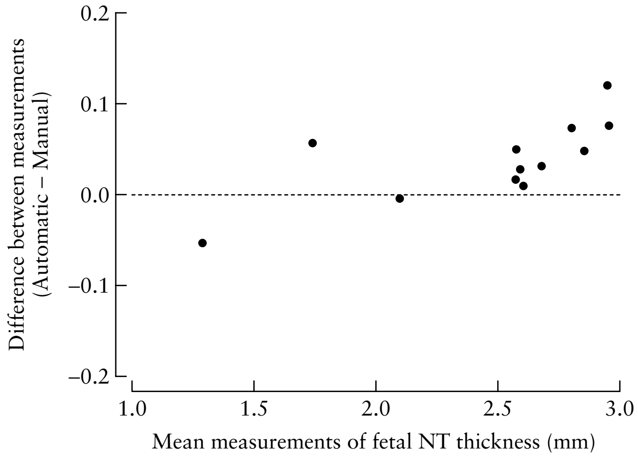

Figure 5 Bland–Altman plot of mean measurements of fetal nuchal translucency (NT) thickness for the 12 images.

between sonographers in the measurement of NT from a given image and to reduce substantially the variation in within-sonographer measurements.

The estimated SD of differences between repeated measurements of the same NT made by different operators using the manual method was 0.24 mm, compared with 0.05 mm for the semi-automatic method. The somewhat smaller SD for the manual method in this study, compared with those reported in previous studies examining the repeatability of NT measurements (SD values of 0.29[6] and 0.35[7]) may be a consequence of the increased magnification of images in the present study compared with those used in the early 1990s. We have previously reported that a large part of the variation in measurements of NT is due to placement of the calipers rather than generation of the image[6] and it is likely that with a bigger image the accuracy of placing the calipers is improved. However, a disadvantage of magnifying the image is that the measurement of fetal NT becomes smaller because the nuchal membrane and the edge of the soft tissue overlying the cervical spine become thicker. A study of 120 pregnancies demonstrated that with increases in image magnification from 60 to 100% and 60 to 200% there was a decrease in mean (SD) fetal NT from 1.52 (0.57) mm to 1.35 (0.53) mm and from 1.52 (0.57) mm to 1.18 (SD 0.48) mm, respectively[8]. Another, similar, study of 561 pregnancies demonstrated that with increasing image magnification from 60 to 100% and 60 to 200% there was a decrease in mean fetal NT from 2.01 (0.48) mm to 1.67 (0.39) mm and from 2.01 (0.48) mm to 1.55 (0.42) mm, respectively[9].

Another factor that results in thickening of the lines that define fetal NT, and therefore underestimates the measurement, is pre- and postprocessing imaging by the application of harmonics and speckle reduction imaging (SRI), respectively, which are being used with increasing frequency in ultrasound scanning. In order to avoid the problem of underestimation in fetal NT measurements it was recommended that these pre- or postprocessing imaging modalities should be avoided (thus reducing the potential gain conveyed by these imaging modalities) in order to minimize the thickness of the nuchal membrane and the soft tissue overlying the cervical spine (www.fetalmedicine.com). However, this recommendation introduces a gain-dependent subjectivity to the measurement of NT, in addition to the two other elements of potential subjectivity, namely, selection of the maximum vertical distance between the nuchal membrane and the edge of the soft tissue overlying the cervical spine, and accurate placement of the calipers on the two lines. The semi-automated method of measuring NT thickness can avoid all three elements of potential subjectivity and this was reflected in the finding of significant reduction in the scatter of results for each image.

Automated systems of ultrasound-based measurements have been incorporated into routine practice in other fields of medicine, such as measurement of carotid intima–media thickness, because of superior repeatability of measurements compared with manual techniques[10–12]. Semi-automatic methods have also been reported for measurement of fetal NT, but these have not been incorporated in the software of ultrasound machines[13,14]. These methods are based on tracing the inner border of the nuchal membrane and consequently they do not avoid the problem of underestimation of fetal NT associated with increased magnification of the image[13,14]. In our method the automated system draws a line through the center of the nuchal membrane, which is independent of the settings of the ultrasound machine and of the magnification of the image.

The semi-automated system reduces substantially the within- and between-sonographer variation in the measurement of NT achieved using the traditional manual approach. However, the semi-automated system does not avoid the need for appropriate training of sonographers to, first, obtain the correct mid-sagittal section of the fetus in the neutral position and, second, select the box that includes a large segment of the fetal NT with clearly visible proximal and distal edges and containing the area with the maximum NT, but excluding structures that may lead to an incorrect measurement, such as the amniotic membrane, umbilical cord or intracerebral translucency. The lines drawn automatically by the system are displayed in the ultrasound image and the sonographer should inspect these lines to confirm that they have been drawn through the appropriate structures before accepting the displayed measurement of fetal NT.

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