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Comparison of nuchal translucency measurements obtained using Volume NT™ and two- and three-dimensional ultrasound

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KEYWORDS: mid-sagittal plane; nuchal translucency; ultrasound; Volume NT™

ABSTRACT

Objective *To evaluate the feasibility of 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.*

Methods *This was a prospective study of 130 singleton pregnancies undergoing NT screening at 11 + 0 to 13 + 6 weeks of gestation. Fetuses with enlarged NT or multiple anomalies and those in the prone position were excluded. Success rate of NT measurement was assessed using Volume NT™, 2D and 3D techniques. In cases in which all three techniques were successful, intra- and interobserver bias and levels of agreement for NT measurements within and between techniques were evaluated using Bland–Altman plots.*

Results *Of 130 cases enrolled into the study, 16 were excluded from analysis due to enlarged NT (n = 3), prone position (n = 2) or missing data (n = 11). Among the 114 cases analyzed, NT measurement was successful by the conventional 2D method in 95.6% (109/114) of cases and by 3D and Volume NT™ measurements in 103 and 93 cases, respectively. Success rate was not significantly different between methods. In 89 cases, NT values were available using all three methods. Among them, mean ± SD 2D-NT was 1.3 ± 0.4 mm, 3D-NT was 1.2 ± 0.4 mm and Volume NT™ was 1.3 ± 0.4 mm. The mean differences of the intra- and interobserver variability of each method were not significantly different from zero for each method.*

Conclusions *Volume NT™, a novel technique for automated NT measurement, is apparently reproducible and comparable with conventional 2D and 3D ultrasound techniques for NT measurement.*

INTRODUCTION

Of the ultrasonographic markers used for trisomy 21 screening, nuchal translucency thickness (NT) is one of those that can be applied earliest in pregnancy[1–3]. For NT measurement to have the best screening result, various criteria, such as acquisition of the correct sagittal plane, appropriate magnification and correct placement of calipers, must be satisfied. Otherwise, NT may be under- or overestimated, resulting in a risk for trisomy 21 that is falsely adjusted from the *a priori* risk[4].

To maximize its reliability, The Fetal Medicine Foundation has provided standards for measurement of NT[5]. Among these standards, delineation of a good fetal sagittal section, appropriate placement of calipers, and a measurement taken at the point where NT is at its maximum are difficult to perform without proper training, and are thus often operator-dependent[6].

The use of nuchal three-dimensional (3D) ultrasound data, allowing manipulation of the volume in order to obtain a proper sagittal plane and measure NT offline, has been considered and proven to have good correlation with two-dimensional (2D) measurements[7–9]. However, obtaining a reliable NT value from stored 3D volume data is still operator-dependent, since the operator's ability to recognize a precise mid-sagittal plane during volume analysis affects the result. Moreover, because this process is performed later, possibly off-site, it is more time consuming compared with obtaining the measurement during the examination[10].

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In light of this a new 3D technology, Volume NT™, was developed, which automatically finds the appropriate mid-sagittal plane and measures the maximum NT distance within seconds. The purpose of our study was to investigate the feasibility of the Volume NT™ function and to compare its NT measurements with those obtained by the conventional 2D method and by manual manipulation of 3D volume data.

SUBJECTS AND METHODS

Study population and NT measurement

The study population consisted of 130 women with singleton pregnancies at 11 + 0 to 13 + 6 weeks of gestation undergoing NT screening between February and September 2010 at Yonsei University Health System. This study was approved by the institutional review board. Multiple pregnancies and fetuses with enlarged NT, in the prone position or with multiple anomalies were considered ineligible.

2D and 3D ultrasound examinations were performed with an Accuvix V20 Prestige (Medison Co, Ltd, Seoul, Korea) ultrasound machine by Operator A (J.Y.K.) and Operator B (H.Y.C.). For the 2D ultrasound NT (2D-NT) measurement, a 2–6-MHz transabdominal transducer was used, while 3D volume acquisition was conducted with a 4–8-MHz volume transducer. Crown–rump length (CRL) was measured according to the standards established by Nicolaides *et al.*[11].

For the 2D-NT measurement, the investigators acquired a mid-sagittal section according to Nicolaides *et al.*[11]. If an appropriate mid-sagittal plane for NT evaluation was not obtained within 15 min, NT measurement using 2D was considered unsuccessful and the patient was asked to return the next day for a retry. If appropriate image acquisition was unsuccessful the next day, the case was excluded from the study. 2D-NT measurements were made by both investigators on the same day, blinded to each other's value. To assess intraobserver variability, each investigator repeated the NT measurement twice, with a minimum 15-min interval between measurements.

Following 2D-NT measurement, one of the operators (J.Y.K.) performed 3D volume acquisition, with harmonic imaging deactivated, as follows. With the fetus facing the transducer, a 2D sagittal plane of the fetus that occupied at least one third of the screen was obtained. The volume box was then adjusted to encompass the fetal head and upper third of the thorax. A 3D sweep was made and the volume data were stored for later use. If the 3D volume acquisition was unsuccessful within 15 min due to unsatisfactory fetal position or excessive fetal movement, the case was considered unsuccessful and excluded from the study.

Both operators obtained a 3D-NT measurement during offline analysis by displaying 3D volumes in the three orthogonal planes in multiplanar mode, and adjusting axes to ensure a correct mid-sagittal plane, blind to the 2D-NT values (Figure 1). There was at least a 2-week time interval between the 2D-NT measurement and the volume manipulation to obtain the 3D-NT measurement. To assess intraobserver variability, each 3D-NT measurement was performed by both investigators twice within a 1-week interval, with the investigator blinded to the first measurement.

The Volume NT™ measurements were made as follows. The same 3D volume data as were used for manual 3D-NT measurement were archived with the NT detector mode in the Volume NT™ program activated. A caliper was placed on the diencephalon region of the fetus and the set key was pressed. This activated the Volume NT™ program, which automatically manipulates the axes based on preset landmarks to correct the initial scanning view and find the most accurate mid-sagittal plane. The mid-sagittal plane was reviewed by both investigators together and if the given plane was inappropriate, the Volume NT™ measurement was considered unsuccessful and excluded from the final comparison. If the given plane was appropriate, a box caliper was placed manually on the

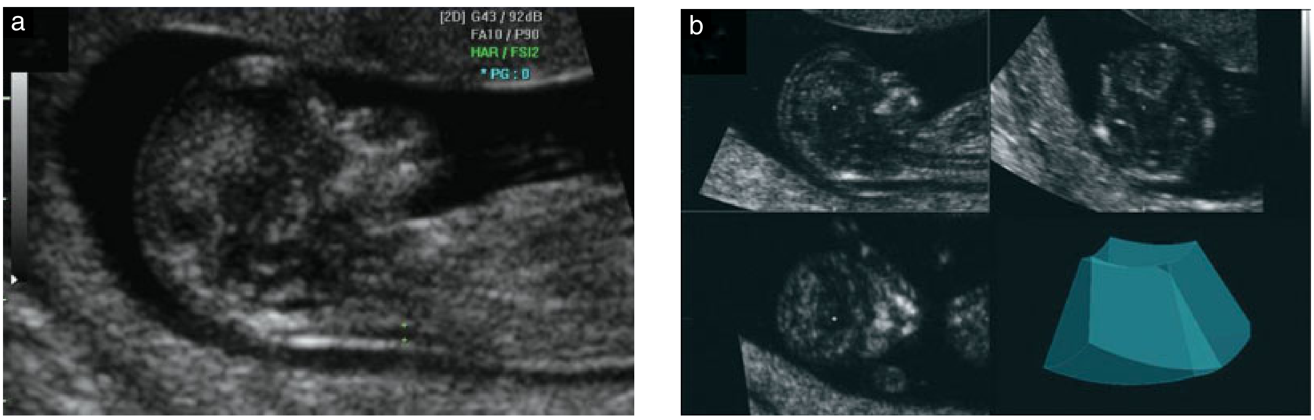

Figure 1 (a) For two-dimensional (2D) sonographic nuchal translucency thickness (NT) measurement, the investigator acquired a mid-sagittal plane according to the standards established by Nicolaides *et al.*[11]. (b) For NT measurement using the three-dimensional (3D) technique, 3D volumes were displayed in the three orthogonal planes that compose the multiplanar mode, and axes were adjusted to obtain the correct mid-sagittal plane.

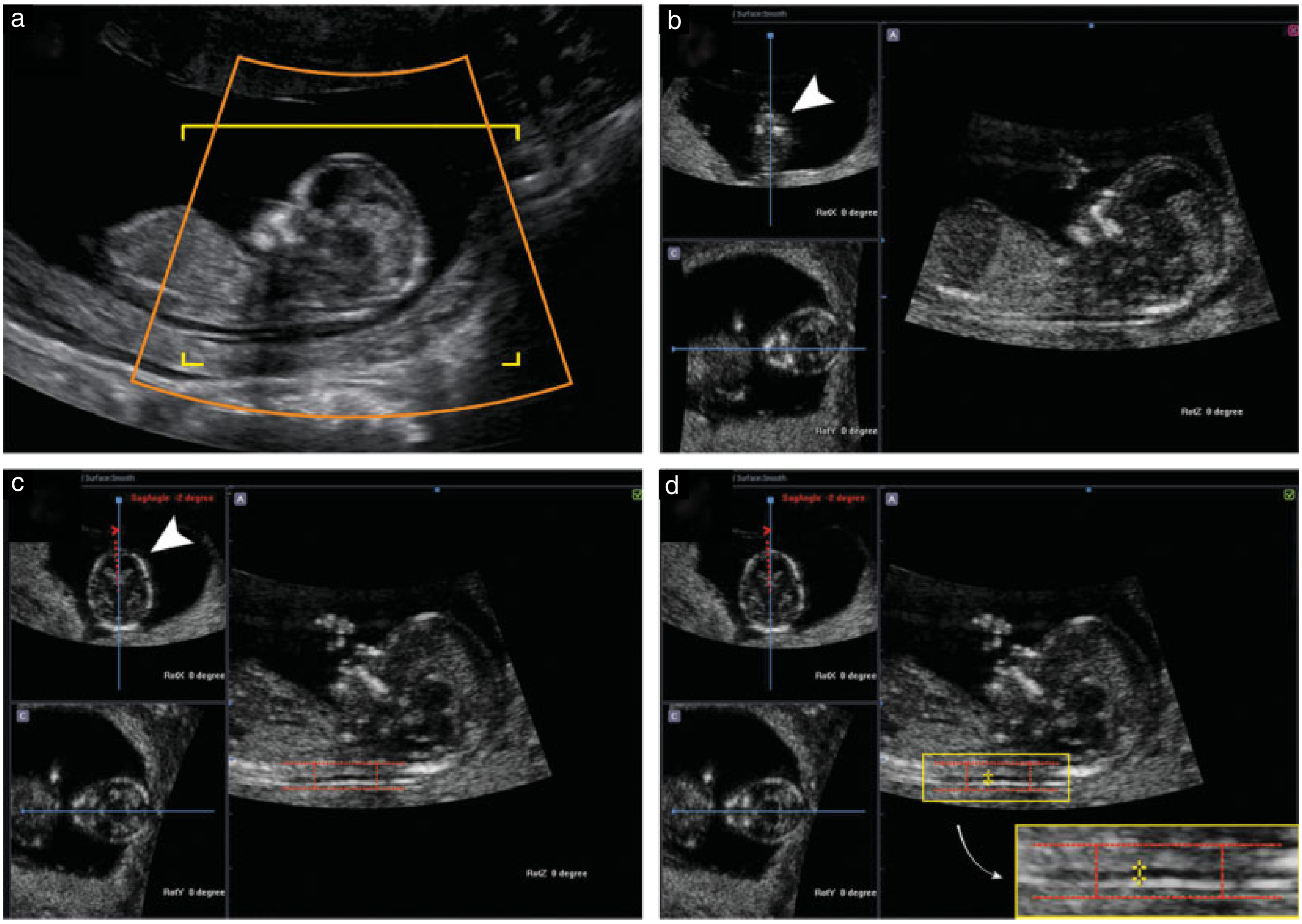

Figure 2 Application of the Volume NT™ technique. The three-dimensional (3D) volume was obtained in nuchal translucency (NT) detector mode (a,b) and the Volume NT™ program automatically adjusted the initial scanning view to obtain the exact mid-sagittal view (c). The NT frame was placed manually on the zone of interest (c) and NT was measured automatically (d).

fetal posterior neck to include the region of interest for NT measurement. The set key was pressed again, initiating automatic measurement of the inner-to-inner distances within the box caliper and display of the maximum value, representing the maximum NT thickness (Figure 2). The Volume NT™ measurement was considered unsuccessful if the caliper placement on the NT was inappropriate. In successful cases, this process was repeated immediately to evaluate the reproducibility.

Statistical analysis

Statistical analysis was conducted using SPSS version 18.0 (SPSS inc., Chicago, IL, USA). The Kolmogorov–Smirnov test was used to confirm normal distribution of the 2D-NT, 3D-NT and Volume NT™ measurements. For analysis of interobserver variability, the mean of each operator's first and second measurements was used. For the inter-method comparison, measurements of a single operator were used. Intra- and interobserver bias and agreement in NT measurements were evaluated by Bland–Altman plot, and the statistical difference was evaluated by Student's *t*-test. The mean differences for 2D-NT vs 3D-NT, 2D-NT vs Volume NT™ and 3D-NT vs Volume NT™ measurements were evaluated by Bland–Altman plot. Eligible cases were categorized according to 2D-NT in 1-mm intervals and CRL in 10-mm intervals for statistical analysis by chi-square test of the success rates of the different measurement methods. Continuous variables are presented as mean ± SD. $P < 0.05$ was considered statistically significant.

RESULTS

Of the 130 cases initially enrolled into this study, 16 were excluded from analysis due to enlarged NT ($n = 3$), prone position ($n = 2$) or missing data ($n = 11$). Of the 114 eligible cases, NT measurement was successful by the conventional 2D ultrasound method in 95.6% (109/114). Of the 114 cases for which 3D volume data were obtained, offline analysis by manual manipulation to obtain a 3D-NT value was successful in 90.4% (103/114). Failure to obtain a 3D-NT value in these 11 fetuses was due to inappropriate fetal position during volume acquisition ($n = 6$), fetal movement during volume acquisition ($n = 2$), unclear demonstration of NT ($n = 2$), and poor image quality due to maternal obesity ($n = 1$). When the eligible 114 cases were reanalyzed using the automated Volume NT™ program, NT measurement was successful in 93 (81.6%) cases.

Intra- and interobserver variability for 2D-NT, 3D-NT and Volume NT™ measurements were assessed for the 89 cases with all three measurements. Among these cases, the mean ± SD maternal age was 32.1 ± 3.4 years, gestational age at NT screening was 12.0 ± 0.9 weeks, CRL was 56.5 ± 9.8 mm and maternal BMI was 20.7 ± 2.3 kg/m^2; none of these values was statistically significantly different from the corresponding values in cases of failure to obtain NT measurements. Mean ± SD 2D-NT was 1.3 ± 0.4 mm, 3D-NT was 1.2 ± 0.4 mm and Volume NT™ was 1.3 ± 0.4 mm. These were not statistically significantly different (Table 1).

Intra- and interobserver variability for 2D-NT and 3D-NT measurements and the reproducibility of Volume NT™ measurement were assessed for the 89 cases with all three measurements; the mean difference did not differ significantly from zero for all comparisons (Table 2 and Figure 3). The intraobserver variability for Operators A and B using each method was comparable, so only the results for Operator A are presented. The mean differences in NT measurements between pairs of methods are shown in Table 3 and Figure 4; there were no significant differences between methods.

The rate of successful measurement of both 3D techniques was then calculated using the 2D technique as a standard, subdivided according to 2D-NT measurement; the overall success rate of 3D-NT measurement was 90.4% and that of Volume NT™ measurement was 81.6%, but the difference was not statistically significant (Table 4). Similarly, CRL was not relevant to the success rate of NT measurement using the Volume NT™ program (Table 5).

Table 1 Study population characteristics with respect to success or failure of nuchal translucency thickness (NT) measurement*

Variable	*Successful NT measurement* (n = 89)	*Failed NT measurement* (n = 25)	P
Maternal age (years)	32.1 ± 3.4	32.4 ± 4.4	0.73
Gestational age (weeks)	12.0 ± 0.9	12.3 ± 0.9	0.19
CRL (mm)	56.5 ± 9.8	60.7 ± 12.1	0.07
BMI (kg/m^2)	20.7 ± 2.3	21.7 ± 4.1	0.24
NT measurement (mm)			
2D ultrasound	1.3 ± 0.4	—	—
3D ultrasound	1.2 ± 0.4	—	—
Volume NT™	1.3 ± 0.4	—	—

Data are given as mean ± SD. *Success refers to successful measurement by all three methods. BMI, body mass index; CRL, crown–rump length.

Table 3 Comparison of nuchal translucency thickness (NT) measurement techniques: two-dimensional ultrasound (2D-US), three-dimensional ultrasound (3D-US) and Volume NT™ ($n = 89$)

NT measurement techniques	*Mean diff ± SD (mm)*	*95% CI of mean diff (mm)*	P
2D-US and 3D-US	0.04 ± 0.46	−0.05 to 0.14	0.35
2D-US and Volume NT™	−0.01 ± 0.47	−0.11 to 0.08	0.72
3D-US and Volume NT™	−0.06 ± 0.35	−0.13 to 0.00	0.08

diff, difference between pairs of measurements.

Table 4 Success rate of nuchal translucency thickness (NT) measurement by three-dimensional ultrasound (3D-US) and Volume NT™ in relation to NT measurement by two-dimensional ultrasound (2D-US)

NT measurement (by 2D-US)	n	*Success rate (n (%))* 3D-US	*Volume NT™*
< 1.0 mm	18	17 (94.5)	17 (94.4)
1.0–1.9 mm	84	76 (90.5)	65 (77.4)
2.0–2.9 mm	12	10 (83.3)	11 (91.7)
Total	114	103 (90.4)	93 (81.6)

$P = 0.45$ (chi-square test).

Table 5 Success rate of nuchal translucency thickness (NT) measurement by two-dimensional ultrasound (2D-US), three-dimensional ultrasound (3D-US) and Volume NT™ in relation to crown–rump length (CRL)

		Success rate (n (%))		
CRL	n	*2D-US*	*3D-US*	*Volume NT™*
40–49 mm	28	27 (96.4)	26 (92.9)	24 (85.7)
50–59 mm	41	40 (97.6)	39 (95.1)	33 (80.5)
60–69 mm	28	27 (96.4)	25 (89.3)	23 (82.1)
70–79 mm	17	15 (88.2)	13 (76.5)	13 (76.5)
Total	114	109 (95.6)	103 (90.4)	93 (81.6)

$P = 0.99$ (chi-square test).

Table 2 Intraobserver and interobserver variability in nuchal translucency thickness (NT) measurement for each technique: two-dimensional ultrasound (2D-US), three-dimensional ultrasound (3D-US) and Volume NT™ ($n = 89$)

	Intraobserver variability			*Interobserver variability*		
NT measurement technique	*Mean diff ± SD (mm)*	*95% CI of mean diff (mm)*	P	*Mean diff ± SD (mm)*	*95% CI of mean diff (mm)*	P
2D-US	−0.02 ± 0.11	−0.04 to 0.00	0.07	0.01 ± 0.25	−0.03 to 0.06	0.59
3D-US	−0.01 ± 0.19	−0.05 to 0.02	0.40	0.07 ± 0.42	−0.01 to 0.16	0.11
Volume NT™	−0.02 ± 0.18	−0.06 to 0.01	0.24	0.06 ± 0.40	−0.02 to 0.14	0.15

diff, difference between pairs of measurements.

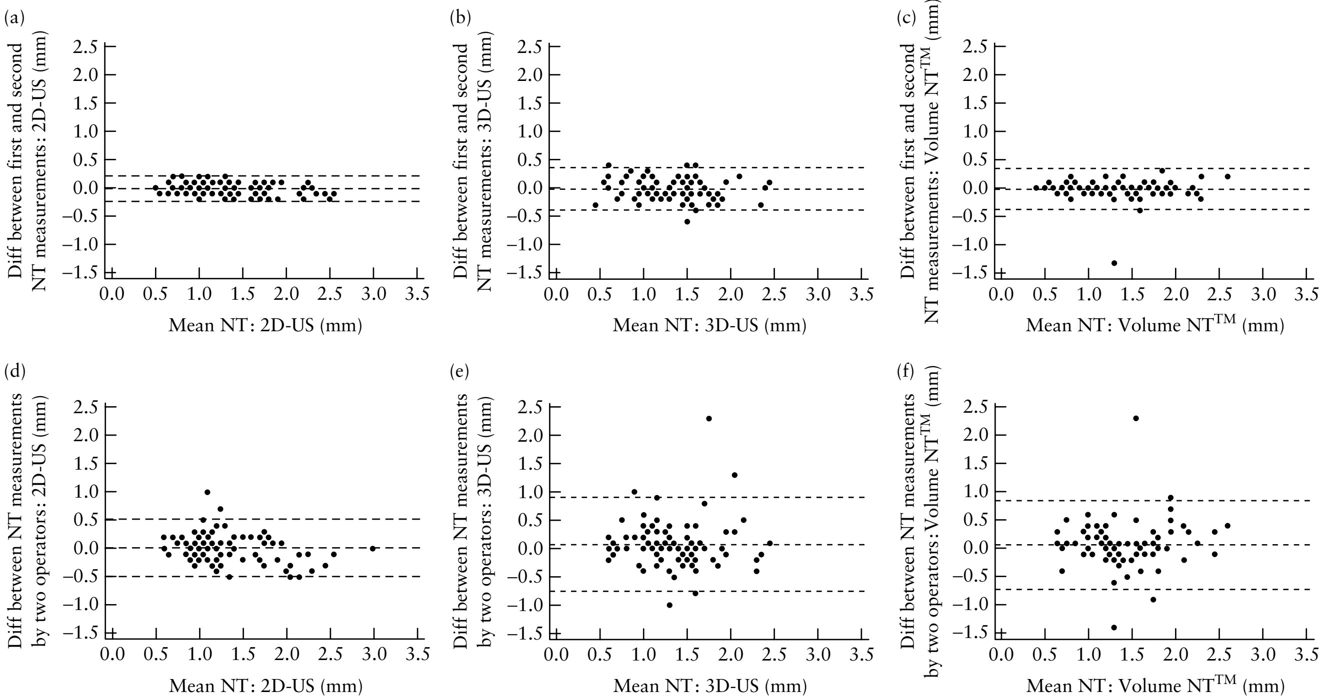

Figure 3 Bland–Altman plots showing intraobserver (a–c) and interobserver (d–f) variability in nuchal translucency thickness (NT) measurement using: (a,d) two-dimensional (2D) ultrasound, (b,e) three-dimensional (3D) ultrasound and (c,f) Volume NT™. Dashed lines represent mean ± 2 SD.

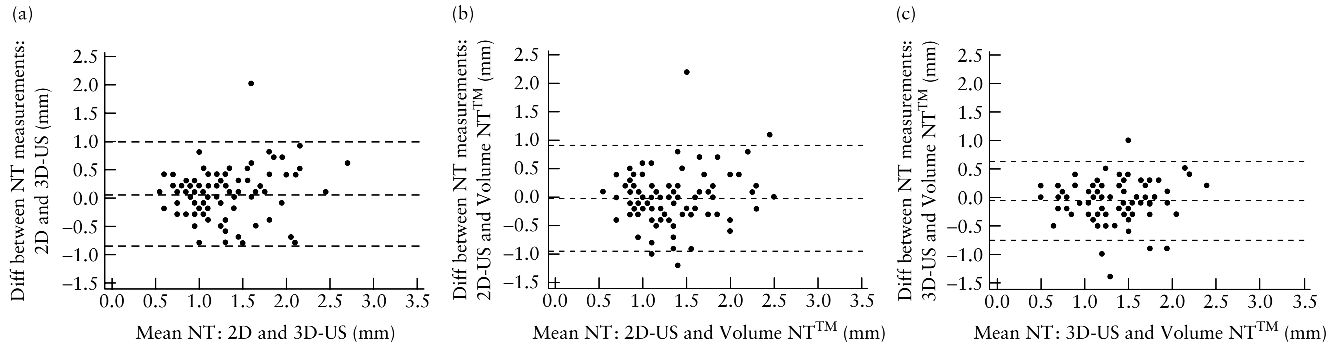

Figure 4 Bland–Altman plots showing variability in nuchal translucency thickness (NT) measurements using: (a) two-dimensional (2D) ultrasound and three-dimensional (3D) ultrasound, (b) 2D ultrasound and Volume NT™ and (c) 3D ultrasound and Volume NT™. Dashed lines represent mean ± 2 SD.

DISCUSSION

Conventional 2D ultrasound is still the gold standard for examining fetal NT[12], though there have been studies investigating the use of 3D volume data of the fetal face to adjust the initial plane in order obtain the correct mid-sagittal plane. Moratalla *et al.*[13] reported the reliability of a semi-automated system for NT measurement, which automatically calculates the largest vertical distance within a box placed over the NT region. However, its applicability is limited if the operator lacks knowledge of the correct mid-sagittal plane.

Recently, the Volume NT™ program was introduced as a way to overcome operator-dependency in the process of obtaining the mid-sagittal plane as well as in selecting the maximum vertical distance. Our study is the first to demonstrate the automated analysis of NT measurement from 3D volume data using Volume NT™ program and to evaluate its reliability and limitations. We found that NT measurement using Volume NT™ was in agreement with NT measurements obtained using conventional 2D and 3D ultrasound techniques.

Since the volume sweep does not need to be performed at the exact mid-sagittal plane, 3D imaging techniques have the advantage of a shorter scanning time in comparison to conventional 2D ultrasound. Application of the Volume NT™ program allows automated mid-sagittal plane adjustment following the 3D volume sweep in as few as 4 s. As for the limitations of NT measurement using manipulation of stored 3D volume data, the procedure requires extra time to manipulate the volume data manually and involves an operator-dependent component.

Some technical shortcomings were also noted while using the Volume NT™ program. Automatic measurement failed in 21/114 (18.4%) cases, of which the program was unable to acquire the correct mid-sagittal plane in 15 and the caliper was mis-placed in six. Further analysis of the cases in which failure was caused by improper plane acquisition shows that this failure was associated with: a large insonation angle deviation of $> 30^\circ$ from the mid-sagittal plane at the time of volume sweep ($n = 6$; angle deviation of 42°, 45°, 49°, 52°, 58° and 60°); fetal movements during volume acquisition ($n = 2$), excessive image blurring due to maternal obesity ($n = 4$); and absence of amniotic fluid in front of the face ($n = 3$) (Figure S1 online). In five of the six cases with incorrect placement of calipers, the automated program misinterpreted the vertical distance between the nuchal skin and the uterine wall because the back of the fetal neck was in close contact with the uterine wall; in the sixth case, significant acoustic shadowing in the NT region caused by the maxilla led to the erroneous caliper placement (Figure S2 online).

In conclusion, the Volume NT™ program is a new technology that offers reliable NT measurement even when performed by less experienced clinicians. However, incorporating this automated system into routine practice as a substitute for the conventional 2D ultrasound method should be preceded by further refinement of the program in order to reduce erroneous NT readings and provide validation in various clinical settings.

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REFERENCES

1. Kagan KO, Etchegaray A, Zhou Y, Wright D, Nicolaides KH. Prospective validation of first-trimester combined screening for trisomy 21. *Ultrasound Obstet Gynecol* 2009; **34**: 14–18.
2. Kagan KO, Wright D, Baker A, Sahota D, Nicolaides KH. Screening for trisomy 21 by maternal age, fetal nuchal translucency thickness, free beta-human chorionic gonadotropin and pregnancy-associated plasma protein-A. *Ultrasound Obstet Gynecol* 2008; **31**: 618–624.
3. Szabó J, Gellén J. Nuchal fluid accumulation in trisomy-21 detected by vaginosonography in first trimester. *Lancet* 1990; **336**: 1133.
4. Abele H, Wagner N, Hoopmann M, Grischke EM, Wallwiener D, Kagan KO. Effect of deviation from the mid-sagittal plane on the measurement of fetal nuchal translucency. *Ultrasound Obstet Gynecol* 2010; **35**: 525–529.
5. Snijders RJ, Noble P, Sebire N, Souka A, Nicolaides KH. UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal-translucency thickness at 10–14 weeks of gestation. Fetal Medicine Foundation First Trimester Screening Group. *Lancet* 1998; **352**: 343–346.
6. Braithwaite JM, Kadir RA, Pepera TA, Morris RW, Thompson PJ, Economides DL. Nuchal translucency measurement: training of potential examiners. *Ultrasound Obstet Gynecol* 1996; **8**: 192–195.
7. Eppel W, Worda C, Frigo P, Lee A. Three- versus two-dimensional ultrasound for nuchal translucency thickness measurements: comparison of feasibility and levels of agreement. *Prenat Diagn* 2001; **21**: 596–601.
8. Kurjak A, Kupesic S, Ivancić-Kosuta M. Three-dimensional transvaginal ultrasound improves measurement of nuchal translucency. *J Perinat Med* 1999; **27**: 97–102.
9. Worda C, Radner G, Lee A, Eppel W. Three-dimensional ultrasound for nuchal translucency thickness measurements: comparison of transabdominal and transvaginal ultrasound. *J Soc Gynecol Investig* 2003; **10**: 361–365.
10. Shaw S, Hsieh TT, Hsu J, Lee C, Cheng P. Measurement of nuchal volume in the first trimester Down screening using three-dimensional ultrasound. *Prenat Diagn* 2009; **29**: 69–73.
11. Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. *BMJ* 1992; **304**: 867–869.
12. Shaw SW, Hsu JJ, Lee CN, Hsiao CH, Chen CP, Hsieh TT, Cheng PJ. First- and second-trimester Down syndrome screening: current strategies and clinical guidelines. *Taiwan J Obstet Gynecol* 2008; **47**: 157–162.
13. Moratalla J, Pintoffl K, Minekawa R, Lachmann R, Wright D, Nicolaides KH. Semi-automated system for measurement of nuchal translucency thickness. *Ultrasound Obstet Gynecol* 2010; **36**: 412–416.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Examples of three cases in which the Volume NT™ program failed to produce an appropriate mid-sagittal plane. Lines in (a), (c) and (e) indicate plane of (b), (d) and (f), respectively. In (a) at time of volume sweep, insonation angle deviated widely from mid-sagittal plane; in (c) the 3D image was not clear due to maternal obesity; in (e) amniotic fluid was lacking around fetal head.

Figure S2 Ultrasound images illustrating reasons for failure to obtain NT measurement using the Volume NT™ program. In (a) the back of the fetal neck was in close contact with the uterine wall, so the Volume NT™ program misinterpreted the vertical distance between the nuchal skin and the uterine wall; attempted measurement indicated by calipers and red line. In (b) the posterior acoustic shadowing (arrow and ellipsoid) in the NT region, caused by the maxilla, did not allow appropriate visualization of the NT region.