

Nasal-bone length in euploid fetuses at 16–24 weeks' gestation by three-dimensional ultrasound

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ABSTRACT

Objective To establish a normal range of nasal-bone length at 16–24 weeks' gestation by the use of three-dimensional (3D) ultrasound and to investigate the effect of deviations from the exact mid-sagittal plane on the measurement of nasal-bone length.

Methods We acquired 3D volumes of the fetal profile from 135 normal fetuses at 16–24 weeks' gestation. The multiplanar mode was used to obtain the exact mid-sagittal plane and to produce parasagittal and oblique views of the fetal face. Nasal-bone length was measured in each plane and the sonographic landmarks of each profile view were examined.

Results Nasal-bone length increased with gestational age from a mean of 4.1 mm at 16 weeks to 7.1 mm at 24 weeks. There was a tendency to underestimate nasal-bone length when the measurements were taken in parasagittal planes and to overestimate the measurements when they were taken in oblique views, compared to the exact mid-sagittal plane. The mean difference in nasal-bone length from the one in the mid-sagittal plane was 0.42 and 0.63 mm for parasagittal measurements at 1 and 2 mm, respectively, from the midline, –0.08 and –0.51 mm for oblique measurements at 10° and 20° rotation along the z-axis and –0.69 mm for rotation of 20° along the z-axis and 10° along the y-axis. The vomeral bone was the only sonographic landmark defining the exact mid-sagittal plane of the face that was not visible in the parasagittal and oblique planes.

Conclusions Parasagittal and oblique scanning planes may produce different degrees of under- or over-estimation of nasal-bone length compared to measurements systematically taken in the exact mid-sagittal plane.

Inclusion of the vomeral bone in the definition of the exact mid-sagittal plane of the face could improve the reproducibility of measurements of nasal-bone length. Copyright © 2010 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

A common phenotypic feature of individuals with trisomy 21 is a small nose, as originally described by Langdon Down in 1866¹. Prenatal ultrasonographic studies have reported that at 11 to 13 + 6 weeks' gestation the nasal bone is absent, due to delayed ossification, in 1–3% of euploid fetuses and in about 65% of fetuses with trisomy 21^{2,3}. In second-trimester fetuses with trisomy 21 the nasal bone is absent in about 30% of cases and short in a further 30%⁴. The definition of short nasal bone varies in different studies primarily because of variations in the reported normal ranges, which were essentially derived from two-dimensional (2D) ultrasound examinations (Figure 1)^{5–11}. For example, the reported 5th percentile at 20 weeks varied between 4.4¹⁰ and 6.0 mm⁵. One possible explanation for the differences in measurements of the nasal bone observed in previous studies is that 2D ultrasound does not provide the ability to confirm that the nose is consistently measured in the exact mid-sagittal plane of the face. In addition, there are actually two nasal bones, which may not have identical lengths.

The aims of this study were firstly, to establish a normal range of nasal-bone length at 16–24 weeks' gestation by the use of the multiplanar mode of three-dimensional (3D) ultrasound to ensure that the measurement is taken in the exact mid-sagittal plane and secondly, to investigate the

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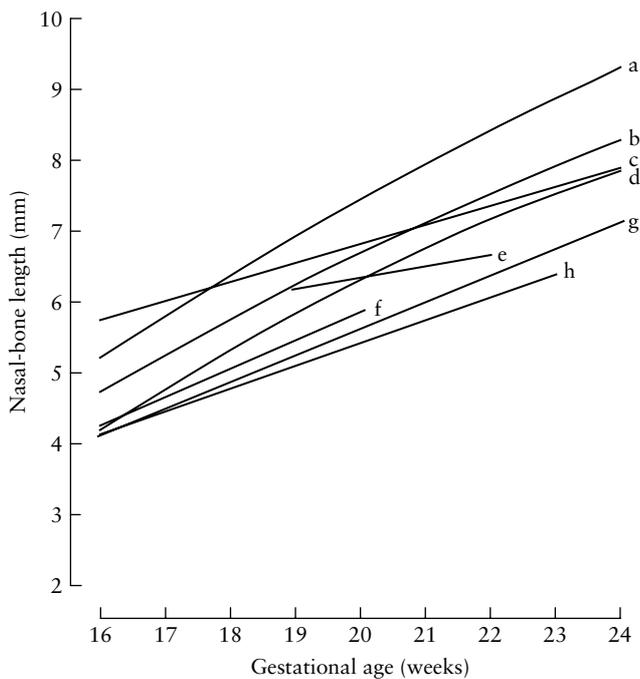


Figure 1 Relationship between mean nasal-bone length and gestational age at 16–24 weeks' gestation in previous two-dimensional ultrasound studies (a⁵, b⁶, c⁷, d⁸, e⁹, f¹⁰, h¹¹) and in this study (g).

effect of deviations from the exact mid-sagittal plane on the measurement of nasal-bone length.

METHODS

We measured the nasal-bone length using stored 3D volumes of the fetal face, which had been acquired from singleton pregnancies with appropriately growing fetuses and no sonographic evidence of fetal abnormality. These patients were attending our fetal medicine centers for routine ultrasound examination at 16–24 weeks' gestation, and for this study we prospectively selected 15 consecutive cases per gestational week (for a total of 135 cases). In each case transabdominal ultrasound (RAB 4-8L probe, Voluson 730 Expert, GE Medical Systems, Milwaukee, WI, USA) was carried out by sonographers with extensive experience in 3D ultrasound. A 3D volume of the fetal head had been acquired in the mid-sagittal plane of the face with an angle between the transducer and the long axis of the nose close to 45°⁴. Care was taken to avoid the presence of limbs or umbilical cord between the ultrasound source and the fetal face in order to ensure correct insonation of both nasal bones.

The 3D volumes were examined off-line using the multiplanar mode to verify the exact mid-sagittal plane and to make minor corrections from the original acquisition plane when necessary. The exact mid-sagittal plane was defined by the presence of the nose, upper and lower lips, the maxilla (primary palate) and the chin anteriorly, and by the presence of the secondary palate with the overlying vomeral bone posteriorly (Figure 2)¹². In the multiplanar view three images were displayed:

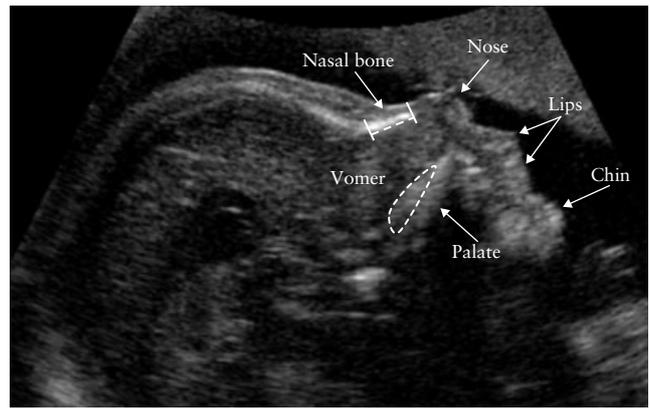


Figure 2 Ultrasound image of a fetus at 20 weeks' gestation showing the exact mid-sagittal plane of the face with its sonographic landmarks and measurement of nasal-bone length.

firstly, the mid-sagittal plane, secondly, a transverse plane depicting the nasal bridge at the level of the two eye sockets and thirdly, a coronal view (Figure 3). In the transverse plane tomographic ultrasound imaging (TUI) was then used to produce three parallel lines at a distance of 1 mm from each other and this resulted in the display of three profile views: the exact mid-sagittal plane with a parasagittal plane on the left and a parasagittal plane on the right. On-screen calipers were then used to measure the length of the nasal bone in each of the three profiles. Subsequently, the distance between the lines was set from 1 to 2 mm and nasal-bone length was measured in the two parasagittal profiles (Figure 4).

In 30 cases, including five cases at each of 16, 18, 20, 21, 22 and 24 weeks, the transverse plane of the head was rotated away from the exact mid-sagittal plane of the face around a point placed below the nasal bridge, at the level of the two eye sockets, by (a) 10° along the *z*-axis, (b) 20° along the *z*-axis, (c) a combination of 20° rotation along the *z*-axis and 10° along the *y*-axis. For each rotational step an oblique view of the profile was displayed and nasal-bone length was measured (Figure 5). In this group, for each parasagittal and oblique view obtained we looked for the presence or absence of all the sonographic landmarks used for identification of the mid-sagittal plane.

All nasal-bone measurements in the exact mid-sagittal plane were made independently by two sonographers. In addition, one of the sonographers measured 93 randomly selected cases on two occasions.

Statistical analysis

Regression analysis was used to determine the significance of the association between nasal-bone length and gestational age and maternal racial origin. The Kolmogorov–Smirnov test was used to confirm normality of distribution of nasal-bone measurements. To compare nasal-bone length measured in parasagittal and oblique views with measurements taken in the exact mid-sagittal plane of the face, the differences between nasal-bone length from each of the different planes and that from the



Figure 3 Ultrasound images from a fetus at 20 weeks' gestation showing the sagittal (a) and corresponding transverse (b) and coronal (c) planes of the fetal head at the level of the two eye sockets in the exact mid-sagittal plane.

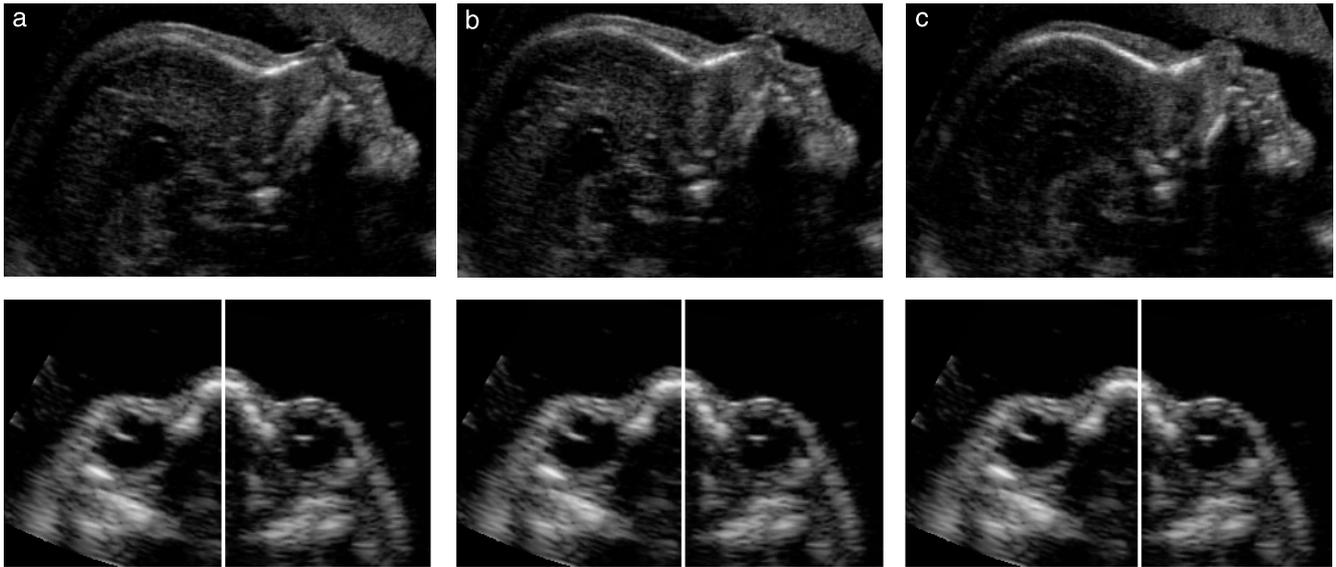


Figure 4 Ultrasound images obtained with the use of tomographic ultrasound imaging showing sagittal and corresponding transverse planes of the fetal head at the level of the two eye sockets in the exact mid-sagittal plane (a), and in parasagittal planes at a distance of 1 mm (b) and 2 mm (c) from the midline.

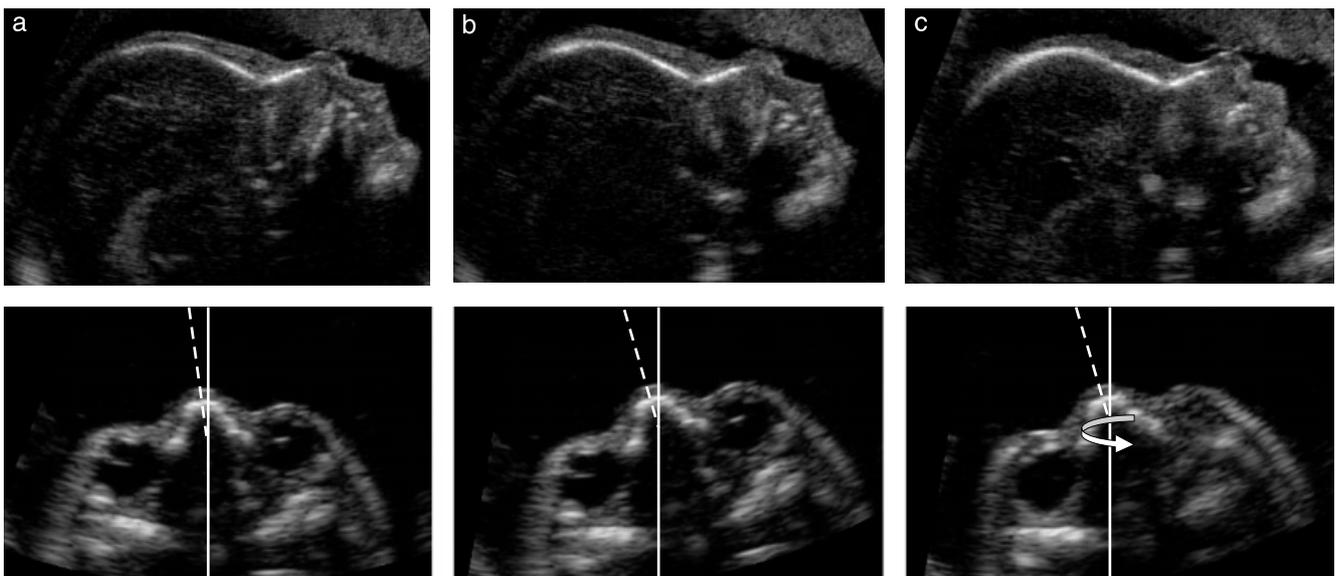


Figure 5 Ultrasound images showing sagittal and corresponding transverse planes of the fetal head after rotation away from the exact mid-sagittal plane around a point placed below the nasal bridge, at the level of the two eye sockets, by 10° along the z-axis (a), 20° along the z-axis (b) and a combination of 20° rotation along the z-axis and 10° along the y-axis (c).

mid-sagittal plane were plotted against the mean between two paired measurements. The mean difference and 95% limits of agreement (LOA) with their 95% CIs were calculated. The *t*-test was used to evaluate the differences between means of nasal-bone length measured in left and right parasagittal planes. Bland–Altman analysis was used to compare the measurement agreement and bias for a single examiner and between two examiners¹³. The data were analyzed using the statistical software SPSS 12.0 (SPSS, Chicago, IL, USA) and Excel for Windows 2003 (Microsoft Corp., Redmond, WA, USA).

RESULTS

The median maternal age was 32 (range, 17–45) years and the median gestational age when the measurements were made was 20.5 (range, 16–24) weeks. Maternal racial origin was Caucasian in 94 (69.6%), African in 27 (20.0%), South Asian in five (3.7%), East Asian in five (3.7%) and Mixed in four (3.0%) cases.

Regression analysis demonstrated that nasal-bone length increased significantly with gestation and that there was no significant contribution from maternal racial origin ($P = 0.233$). The median nasal-bone length was 4.1 mm at 16 weeks and it increased linearly with gestation to 7.1 mm at 24 weeks (nasal-bone length = $-1.820 + (0.372 \times \text{gestational age in weeks})$; $r = 0.850$, $P < 0.01$, $SD = 0.586$; Figure 6).

There was no significant difference between left and right parasagittal measurements at 1 mm from the mid-sagittal plane (mean difference = 0.020 (LOA (95% CI), $-0.457 (-0.527 \text{ to } -0.387)$) to 0.497 (0.427 to 0.567)), $P = 0.341$) and between left and right measurements at 2 mm from the mid-sagittal plane (mean difference = 0.009 (LOA (95% CI), $-0.417 (-0.480 \text{ to } -0.355)$) to 0.435 (0.373 to 0.498)), $P = 0.691$). Therefore, the average of the left and right measurements at a given distance from the midline was used for subsequent analysis.

The mean difference, 95% CIs and the SD of the difference for measurements undertaken in parasagittal and oblique planes compared to nasal-bone length measured in the mid-sagittal plane are shown in Table 1. There was a tendency to underestimate nasal-bone length when the measurements were undertaken in parasagittal planes compared to the exact mid-sagittal plane. In the

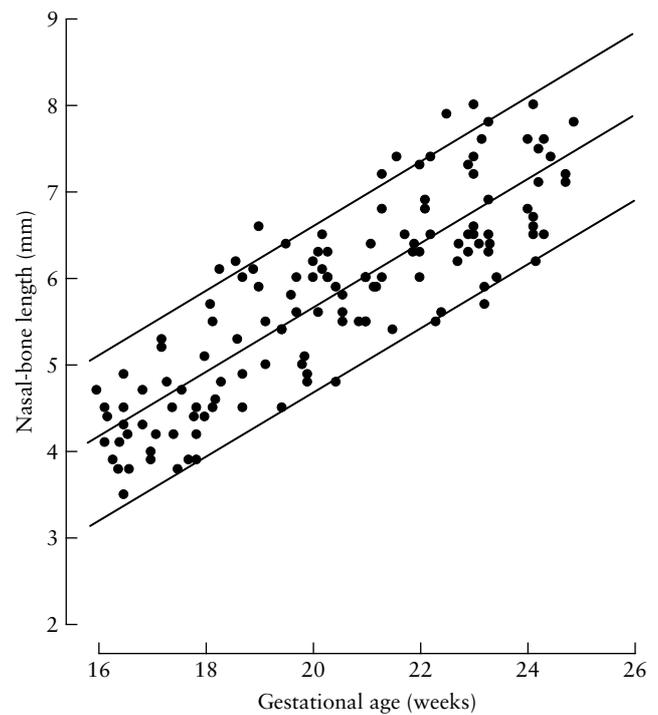


Figure 6 Measurements of nasal-bone length in 135 normal fetuses at 16–24 weeks' gestation, showing the expected mean, 5th and 95th percentiles.

subgroup of 30 cases in which oblique views of the profile were obtained there was a progressive overestimation of nasal-bone length for each step of deviation from the midline compared to measurements performed in the mid-sagittal plane. The variation in the difference between two measurements increased with the distance and degree of deviation from the midline, with consequent widening of the 95% CIs and reduced reproducibility of the measurements.

The fetal nose, lips, maxilla and chin were visible in all parasagittal and oblique views. Similarly, the echogenic frontal process of the maxilla was not visible in any case in either the mid-sagittal plane or in the parasagittal views at 1 or 2 mm from the midline or with rotation at 10° or more. The secondary palate was visible in all parasagittal views and in all cases in which the head was rotated by 10° away from the mid-sagittal plane. If the rotation was 20° or more the secondary palate was visualized in 25 of 30 (83.3%) cases. The vomeral bone was visible in all 30

Table 1 Mean difference, 95% limits of agreement (LOA) with their 95% CIs and SD of the difference for nasal-bone length measured in parasagittal and oblique planes compared to measurements performed in the exact mid-sagittal plane

Scanning plane	Mean difference (LOA (95% CI))	SD
Parasagittal		
1 mm from the midline	0.418 (–0.173 (–0.260 to –0.086) to 1.008 (0.921 to 1.095))	0.301
2 mm from the midline	0.627 (–0.158 (–0.274 to –0.043) to 1.413 (1.298 to 1.529))	0.401
Oblique (rotation from the midline)		
10° along the z-axis	–0.077 (–0.530 (–0.597 to –0.464) to 0.377 (0.310 to 0.444))	0.231
20° along the z-axis	–0.507 (–1.242 (–1.350 to –1.133) to 0.228 (0.120 to 0.337))	0.375
20° along the z-axis and 10° along the y-axis	–0.693 (–1.658 (–1.800 to –1.516) to 0.271 (0.129 to 0.413))	0.492

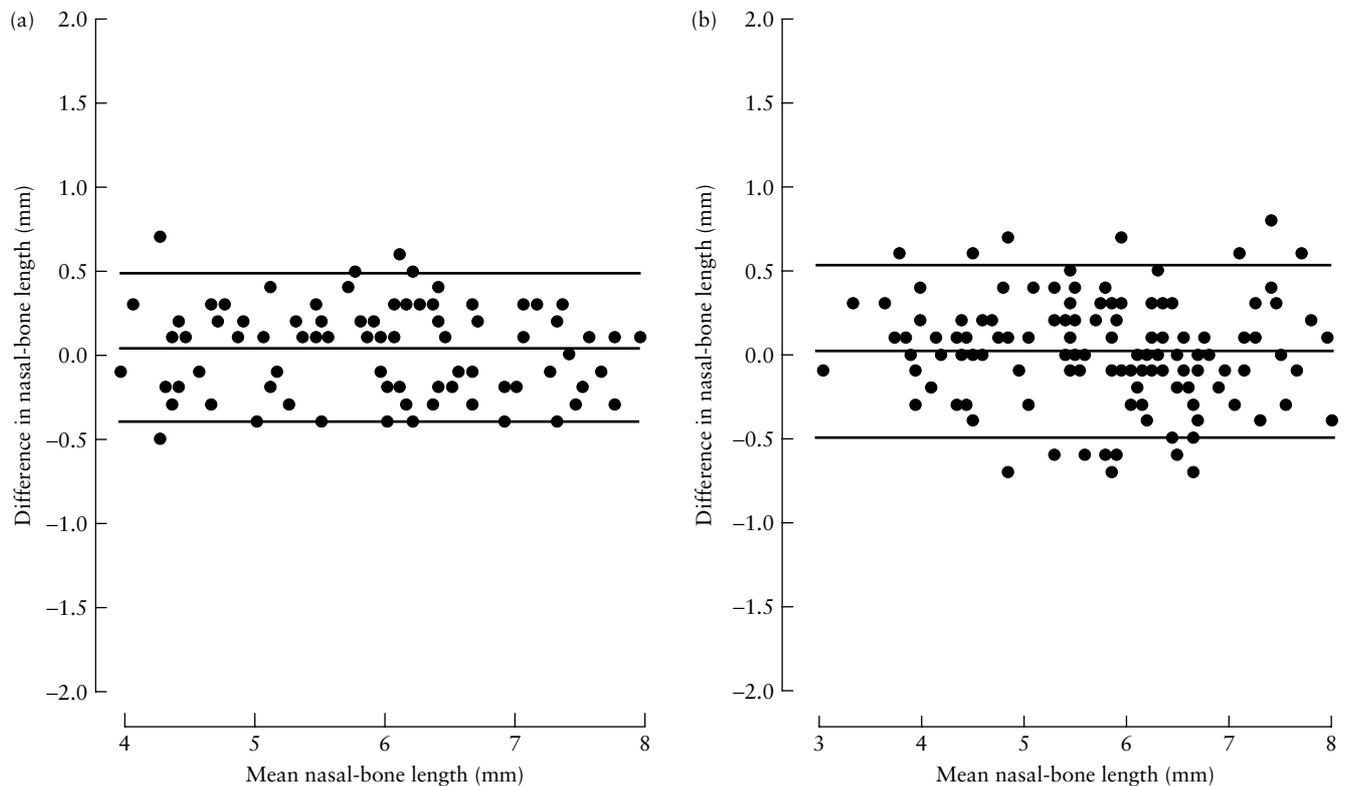


Figure 7 Mean difference and 95% limits of agreement between paired measurements of nasal-bone length in the exact mid-sagittal plane by the same sonographer (a) and between paired measurements by two different observers (b).

cases in the mid-sagittal plane, in 29 (96.7%) cases with parasagittal views at a distance of 1 mm from the midline, in 27 (90.0%) cases in which the head was rotated by 10° away from the mid-sagittal plane, but in none of the cases with parasagittal views at a distance of 2 mm or oblique views with a rotation of the head of 20° or more away from the mid-sagittal plane.

The mean difference and the 95% LOA between paired measurements of nasal-bone length in the exact mid-sagittal plane by the same observer were 0.035 (-0.470 to 0.541) mm and the respective values in paired measurements by two different observers were 0.016 (-0.589 to 0.620) mm (Figure 7).

DISCUSSION

This study provides normal reference values for nasal-bone length at 16–24 weeks' gestation using the multiplanar mode of 3D ultrasound to ensure that the measurements are taken in the exact mid-sagittal plane of the fetal face. In addition, our results show that parasagittal and oblique scanning planes may produce different degrees of under- or overestimation of nasal-bone length compared to measurements systematically taken in the exact mid-sagittal plane.

In first-trimester fetuses the mid-sagittal plane of the face is defined by the presence of the echogenic tip of the nose and the rectangular shape of the palate¹⁴. This view is routinely used for the measurement of nuchal

translucency thickness and assessment of the nasal bone at 11–13 weeks' gestation. Minor deviations away from this plane cause non-visibility of the tip of the nose and visualization of the frontal process of the maxilla as an echogenic structure between the nasal bone above and the anterior part of the maxilla below. In the second trimester, non-visibility of the frontal process of the maxilla is not useful for ensuring that the plane of scanning is mid-sagittal because the maxillary bone is wider, and its frontal processes are more lateral, than those of first-trimester fetuses. Similarly, the sonographic landmarks commonly used to examine the fetal profile and to measure nasal-bone length, including the nose, upper and lower lips, the maxilla and the chin, are also visible in parasagittal and oblique sections of the profile.

We observed that, when parasagittal and oblique sections were obtained, the only significant change in the appearance of the fetal profile was related to visualization of the vomeral bone, which courses diagonally along the midline and on top of the secondary palate from the maxilla anteriorly towards the sphenoid bone posteriorly¹⁵. The vomer is visible in the vast majority of cases even with minor deviations from the midline, such as parasagittal sections at a distance of 1 mm and rotation of the head by 10° away from the mid-sagittal plane. In such cases the differences in measurement of the nasal bone are very small. However, with greater deviations from the mid-sagittal plane the vomeral bone is not visible, and this is associated with significant under- and overestimation of nasal-bone length. In addition,

measurements taken in these views were less reproducible than those taken in the exact mid-sagittal plane, and in 95% of cases the difference between two measurements was within 1.7 mm. For example, in a fetus at 20 weeks nasal-bone length could vary between 4.3 mm, which is below the 2.5th percentile and therefore classified as hypoplastic, and a normal measurement of 6 mm, with different implications for the management of pregnancy and counseling of the parents.

In a previous study Benoit and Chaoui¹⁶ used 3D ultrasound to examine the nasal bones of 18 euploid fetuses and 20 fetuses with trisomy 21 at 17–33 weeks' gestation. The authors reported a difference in length between the left and right nasal bones ranging between 0.4 and 1 mm. In this study we found that nasal-bone length decreased with increasing distance from the midline equally on each side and that in 95% of cases the values obtained for left and right parasagittal length were within 0.5 mm of each other.

As far as the second trimester of pregnancy is concerned, nasal-bone absence or hypoplasia is one of the most important markers for trisomy 21⁴, together with measurement of nuchal fold¹⁷ and prenatal thickness¹⁸. However, a prerequisite for the incorporation of nasal-bone length into screening policies is good reproducibility of the measurements. Our results suggest that inclusion of the vomeral bone in the definition of the exact mid-sagittal plane of the face could reduce the variation between measurements within acceptable limits. In this study we used the multiplanar mode of 3D ultrasound to ensure accurate measurement of nasal-bone length in the exact mid-sagittal plane. However, the vomeral bone that defines this plane can easily be identified by 2D ultrasonography.

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