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Papageorghiou A. T
University of Oxford

Sarris I
University of Oxford

oannou C I
University of Oxford

Todros T
University of Turin

Carvalho M
Aga Khan University

See next page for additional authors

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Authors
Papageorghiou A. T, Sarris I, oannou C I, Todros T, Carvalho M, Pilu G, and Salomon L. J

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AT Papageorghiou,[a] I Sarris,[a] C Ioannou,[a] T Todros,[b] M Carvalho,[c] G Pilu,[d] LJ Salomon,[e] for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st)

[a] Nuffield Department of Obstetrics & Gynaecology and Oxford Maternal & Perinatal Health Institute, Green Templeton College, University of Oxford, Oxford, UK [b] Department of Obstetrics & Gynecology, University of Turin, Sant'Anna Hospital, Turin, Italy [c] Faculty of Health Sciences, Aga Khan University, Nairobi, Kenya [d] Department of Obstetrics & Gynecology, University of Bologna, Bologna, Italy [e] Université Paris V—René Descartes, Maternité Hôpital Necker-Enfants Malades, AP-HP, Paris, France
Correspondence: Dr AT Papageorghiou, Nuffield Department of Obstetrics & Gynaecology, University of Oxford, Women's Centre, Level 3, John Radcliffe Hospital, Headington, Oxford OX3 9DU, UK. Email aris.papageorghiou@obs-gyn.ox.ac.uk

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A unified protocol is essential to ensure that fetal ultrasound measurements taken in multicentre research studies are accurate and reproducible. This paper describes the methodology used to take two-dimensional, ultrasound measurements in the longitudinal, fetal growth component of the INTERGROWTH-21st Project. These standardised methods should minimise the systematic errors associated with pooling data from different study sites. They represent a model for carrying out similar research studies in the future.

Keywords Fetal biometry, fetal growth, INTERGROWTH-21st, standards, ultrasound.

Introduction

The International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) is a large-scale, population-based, multicentre project involving health institutions from eight geographically diverse countries, which aims to assess fetal, newborn and preterm growth under optimal conditions, in a manner similar to that adopted by the World Health Organization (WHO) Multicentre Growth Reference Study (MGRS).[1] The INTERGROWTH-21st Project has three major components, which were designed to create: (1) longitudinally derived, prescriptive, international, fetal growth standards using both clinical and ultrasound measures; (2) preterm, postnatal growth standards for those infants born at $\geq 26^{+0}$ but $<37^{+0}$ weeks of gestation in the longitudinal cohort; and (3) birthweight-for-gestational-age standards derived from all newborns delivering at the study sites over an approximately 12 month period.[2]

To ensure that ultrasound measurements in the longitudinal component of the INTERGROWTH-21st Project—the Fetal Growth Longitudinal Study (FGLS)—are accurate and reproducible, it was essential that participating centres adopted uniform methods because it is well recognised that there are differences in practice between countries and ultrasonographers. For example, different protocols exist describing how to take fetal measurements, including where to place callipers, and ultrasound equipment may not be calibrated correctly.[3]

To achieve uniformity in FGLS, we used identical ultrasound equipment in all the study sites; developed standardised methodology to take fetal measurements, and employed locally accredited ultrasonographers who underwent standardisation training and monitoring. This paper describes the methodology used to take fetal measurements in FGLS.

Overview of the ultrasound procedures

The following ultrasound procedures are performed: (1) crown–rump length (CRL) measurement to confirm the

gestational age at 9^{+0} to 13^{+6} weeks of gestation; (2) serial measurement of biparietal diameter (BPD), occipito-frontal diameter (OFD), head circumference (HC), transverse abdominal diameter (TAD), anterior-posterior abdominal diameter (APAD), abdominal circumference (AC) and femur length (FL) to describe fetal growth; (3) serial assessment and measurement of amniotic fluid volume; and (4) documentation of placental localisation and fetal presentation. The INTERGROWTH-21st Steering Committee agreed the study methodology and definitions, which were derived from published studies and consensus documents.[3–9] The fetal measurements were selected because they form part of standard clinical care and they have been evaluated in a number of large randomised controlled trials.[10]

The ultrasound schedule

All mothers have a transabdominal ultrasound scan at 9^{+0} to 13^{+6} weeks from the first day of the last menstrual period to: (1) confirm the presence of a viable, singleton, intrauterine pregnancy and (2) use the CRL measurement to confirm the gestational age based on the last menstrual period.[11,12] Details of the methodology for CRL measurement are presented elsewhere.[13] Following this initial dating scan, participants in FGLS have up to six fetal growth scans at intervals of 5 ± 1 weeks from 14^{+0} weeks of gestation onwards until delivery, but not beyond 42^{+0} weeks of gestation.

All scans from 14^{+0} weeks of gestation onwards are performed using the same commercially available ultrasound machine (Philips HD-9, Philips Ultrasound, Bothell, WA, USA) with curvilinear abdominal transducers (C5-2, C6-3, V7-3). The decision to use this machine was based on several factors including the cost; feasibility of future use in developing countries; acceptance by doctors and women; manufacturer's ability to provide technical support and willingness to make the software changes needed to allow blinding of measurements (i.e. values do not appear on screen, so as to avoid potential bias associated with 'expected' values); advice of experts in the field, and technical recommendations from the Royal College of Radiologists.[14]

We conducted site visits to a number of manufacturers and explored a range of equipment from portable machines to very sophisticated equipment with market prices ranging from US$40,000 to US$150,000. We even considered using second-hand equipment that could be adapted to our needs. We identified three major technical requirements: image clarity, resolution and the ability to differentiate tissue structures (see full list of requirements in Supporting Information, Appendix S1). It was decided to use new equipment because there is some evidence that the narrow ultrasound beam width in more modern machines is associated with lateral measurements that are more representative of true length.[15] Candidate machines were then tested against these criteria bearing in mind the need to ensure that the machine eventually chosen should be affordable in the future in developing countries.

2-dimensional ultrasound measurements

Using three separate images, three blinded measurements are taken of each fetal biometric variable: BPD, OFD, APAD, TAD, FL, HC and AC, with the woman in the lateral recumbent position. In addition, the Amniotic Fluid Index, to assess amniotic fluid volume, and the fetal presentation and placental position are documented. All images are stored on the machine's hard drive.

The three head measurements (BPD, OFD, and HC using the ellipse facility) are all taken in the same view (Figure 1). To achieve this, a cross-sectional view of the fetal head at the level of the thalami is taken as close as possible to the horizontal (angle of insonation as close as possible to 90°). The head should be oval in shape, symmetrical, centrally positioned and filling at least 30% of the monitor. The midline echo (representing the falx cerebri) should be broken anteriorly, at one-third of its length, by the cavum septi pellucidi. The thalami should be located symmetrically on either side of the midline. For the BPD measurement, the intersection of the callipers should be placed on the outer border of the parietal bones ('outer to outer') at the widest part of the skull. For the OFD measurement, the intersection of the callipers should be placed on the outer border of the occipital and frontal bones ('outer to outer') at the longest part of the skull. At this point, the image (with the callipers visible) is saved. Following this, the callipers are removed and, on the same still view, the HC is measured using the ellipse facility. The line of the ellipse should be placed on the outer border of the skull. The measurements of BPD, OFD and HC are repeated twice more on two, newly acquired views. The HC is also calculated from the BPD and OFD measurements using the formula $HC = \pi(BPD + OFD)/2$.

The three measurements of the abdomen (APAD, TAD and AC using the ellipse facility) are all taken in the same view (Figure 2). To achieve this, a cross-sectional view of the fetal abdomen is taken as close as possible to circular, with the umbilical vein in the anterior third of the abdomen (at the level of the portal sinus), with the stomach bubble visible. The abdomen should fill at least 30% of the monitor. The spine should preferably be positioned at either 3 or 9 o'clock to avoid internal shadowing. The kidneys and bladder should not be visible. The ultrasonographer should avoid applying too much pressure with the transducer, which can distort the circular shape of the fetal abdomen. For the measurements, the intersection of the callipers is placed on the outer borders of the body outline
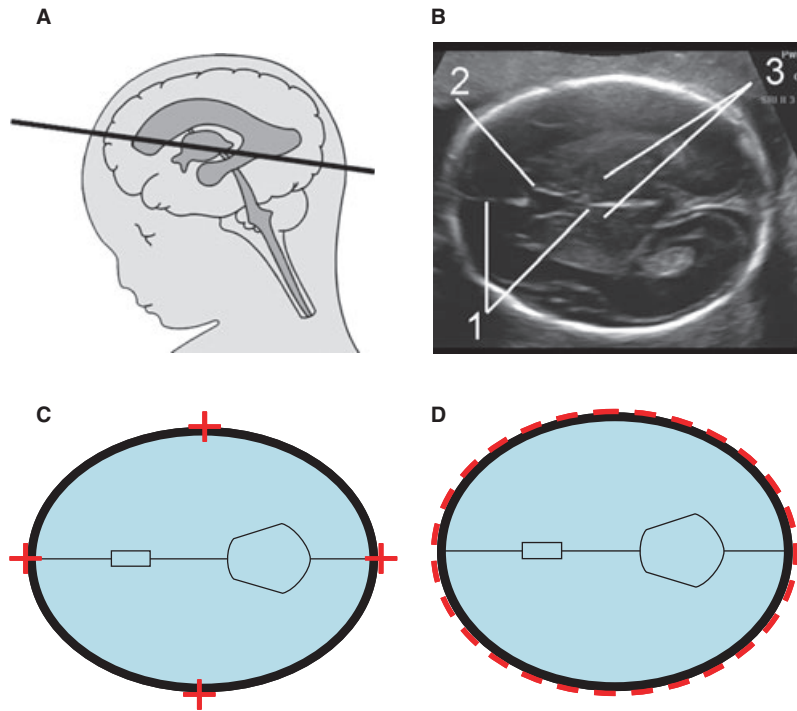
Figure 1. The level of the cross-section through the fetal head for correct measurement (A). The image (B) is well magnified, the head is horizontal, oval in shape and symmetrical. The landmarks are seen with a centrally positioned and continuous midline falx cerebri (1), the midline echo is broken anteriorly at one-third of its length by the cavum septi pellucidi (2) and the thalami are located symmetrically (3). Callipers are placed so that their intersection is on the outer border of the bones (C). When using the ellipse facility this should run along the outer border of the skull (D).
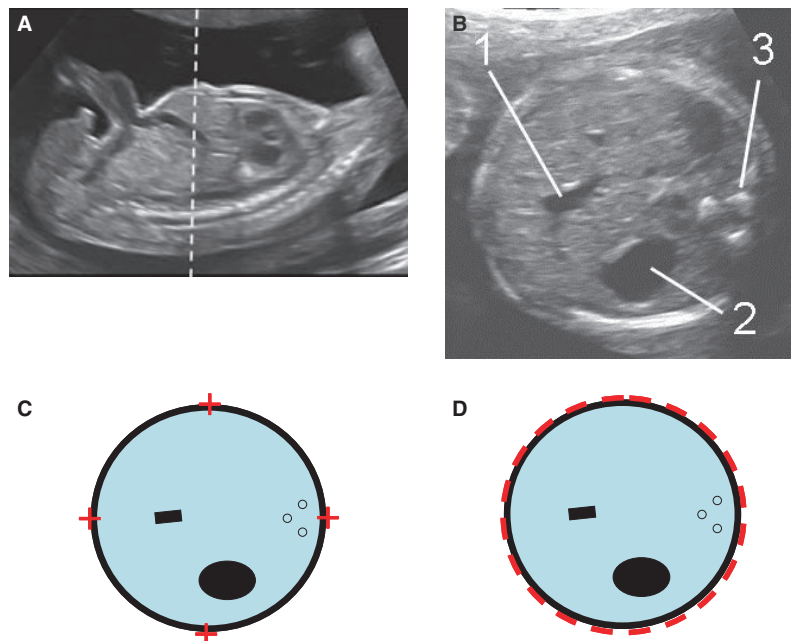

Figure 2. The level of the cross-section through the fetal abdomen for correct measurement (A). The image (B) is well magnified and the section is circular. The landmarks are seen with a short segment of umbilical vein in the anterior third (at the level of the portal sinus) (1), the stomach bubble is visible (2) and the spine (3) is lateral. Neither the bladder nor the kidneys should be visible. Callipers are placed so that their intersection is on the outer border of the body outline (skin covering) (C). When using the ellipse facility this should run along the outer border of the abdomen (D).

(skin covering). For the APAD, the intersection of the callipers should be placed from the posterior aspect (skin covering the spine) to the anterior abdominal wall. For the TAD measurement, the intersection of the callipers should be placed at 90° to the APAD across the abdomen at the widest point. Following this, the callipers are removed and, on the same still view, the AC is measured using the ellipse facility. The line of the ellipse should be placed on the outer border of the abdomen. The measurements of TAD, APAD and AC are repeated twice more on two newly acquired views. The AC is also calculated from the APAD and TAD measurements using the formula AC = π(APAD + TAD)/2.

The FL is the only measurement taken of the femur (Figure 3). To achieve this, a longitudinal view of the fetal thigh closest to the probe is taken with the femur as close as possible to the horizontal plane. The angle of insonation of the ultrasound beam is 90° with the full length of the bone visualised, unobscured by shadowing from adjacent bony parts. The femur should fill at least 30% of the monitor. The intersection of the callipers is placed on the outer borders of the edges of the femoral diaphysis (outer to outer) ensuring that the trochanter is not included in the measurement. This is repeated twice more on two newly acquired views.

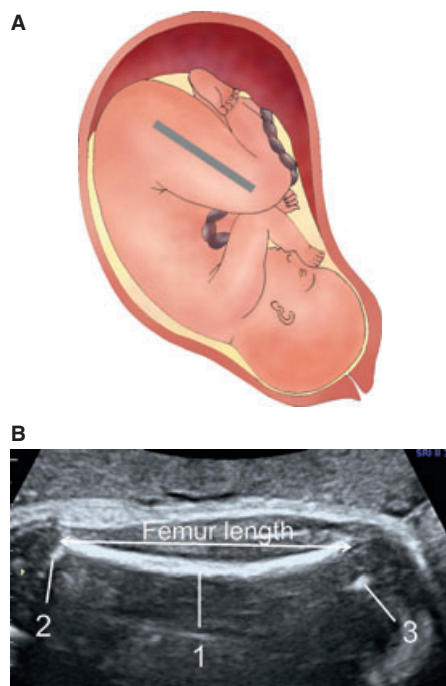At the end of the two-dimensional examination, ultrasonographers rate the quality of their images based on an image-scoring algorithm[16] (Table 1). Using this system, an image in the correct plane scores, for example, a maximum of 6 points for the head and abdomen. Images that do not score the maximum points are repeated until the best possible score is achieved.

Assessment of amniotic fluid

Amniotic fluid volume can be classified into broad categories; this appears to be a reliable measure in experienced hands, but is difficult to standardise. In this study, the ultrasonographers are first asked to record the amniotic fluid volume subjectively as: polyhydramnios, increased, normal, reduced, oligohydramnios, or anhydramnios. Following this, the Amniotic Fluid Index is measured objectively once (Figure 4). To achieve this, the uterus is divided into quadrants using the umbilicus as a reference (at $<20^{+0}$ weeks of gestation the uterus is divided into quadrants using the midpoint of the uterus). The probe is held longitudinally to the mother and at 90° to the floor. The deepest vertical pool in each quadrant that contains no fetal parts or umbilical cord is measured sequentially.

Presentation and placental localisation assessment

Fetal presentation and placental localisation are documented as they may affect fetal measurements. Fetal presentation is recorded in relation to the longitudinal axis of the mother as cephalic, breech, transverse or oblique. Placental position is recorded as fundal, high anterior, high posterior, high right lateral, high left lateral, low anterior, low posterior, low right lateral, or low left lateral.

Special clinical situations

Sometimes, the standard operating procedures described above cannot be followed. The most likely circumstances were anticipated and a protocol was prepared indicating the corrective action to take.

Difficulty in obtaining optimal measurements

Every effort is made to obtain the best possible measurements based on the guidelines above. However, the fetal position may on occasion be persistently unfavourable. In such cases, we ask the woman to return within 1 week for the scan to be repeated. If it remains impossible to obtain good quality measurements, then the best possible set of images is taken. The INTERGROWTH-21st Ultrasound Coordinating Unit will be made aware because the image score will be suboptimal in such cases.

Missing a scan appointment

If a woman misses an appointment, we always try to reschedule another within 1 week. If this is not possible, the

Figure 3. The level of the section through the fetal femur for correct measurement (A and B). Only the ossified diaphysis (1) of the femur should be measured. The greater trochanter (2) and distal ossification centre (3) should be avoided in measuring the femur length as this results in an excessive measurement.

Table 1. Image scoring criteria used for the standardisation exercise, based on Salomon et al.[16]

| Cephalic plane (max. 6 points)	Abdominal plane (max. 6 points)	Femoral plane (max. 4 points)
1 Symmetrical plane	1 Symmetrical plane	1 Both ends of the bone clearly visible
2 Thalami visible	2 Stomach bubble visible	2 Angle <45°
3 Cavum septi pellucidi visible	3 Umbilical vein one-third of the way along the abdominal plane (portal sinus)	3 Femur occupying at least 30% of image
4 Cerebellum not visible	4 Kidneys not visible	4 Callipers placed correctly
5 Head occupying at least 30% of image	5 Abdomen occupying at least 30% of image	
6 Callipers / ellipse placed correctly	6 Callipers / ellipse placed correctly	
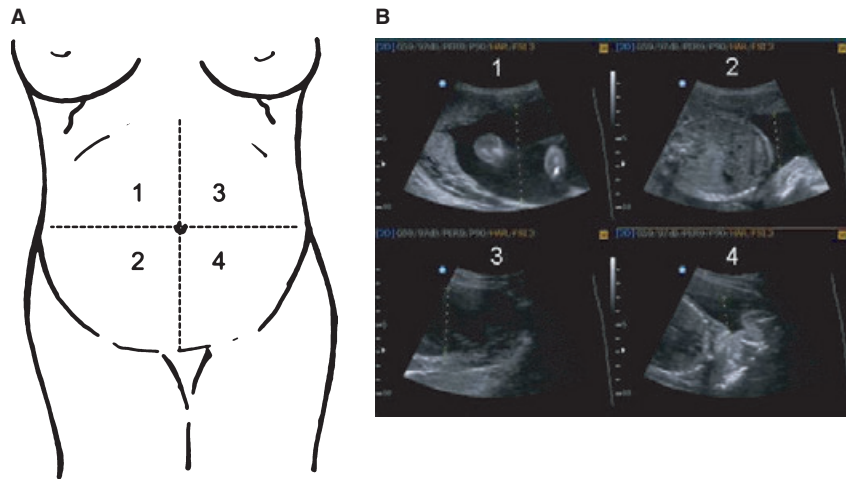
Figure 4. Amniotic Fluid Index (AFI) measurement. The uterus is divided into quadrants using the umbilicus as a reference (A). The probe is held longitudinally to the mother and at 90° to the floor. The deepest vertical pool in each quadrant (B) that contains no fetal parts or umbilical cord is measured sequentially.

next scheduled appointment in the 5-week cycle is kept and the missed appointment is not rescheduled.

Morphological abnormalities detected during an examination

A morphological evaluation is conducted in every centre at approximately 20 weeks of gestation. Any fetal abnormality diagnosed is then managed according to local clinical guidelines. If the woman continues with the pregnancy, she remains in the study until delivery; however, a full evaluation of the abnormality is conducted in the neonate and a specific data collection form is completed. Cases with predefined minor abnormalities that do not impact on fetal growth will be included in the data analyses at the end of the study, but all others will not.

Multiple pregnancy

In the unlikely event that a previously undiagnosed multiple pregnancy is detected at the time of a growth scan, the woman is advised that she cannot remain in the study. Appropriate clinical care is then arranged.

Discussion

In this paper, we have described the methodology used in the FGLS component of the INTERGROWTH-21st Project to acquire ultrasound-based, fetal biometric measurements. It should be read in conjunction with the corresponding papers on standardisation of CRL measurement[13] and ultrasound quality control[17] that also appear in this supplement. The methodology described represents a model for capturing, in a standardised manner for research purposes, fetal biometric data obtained by multiple ultrasonographers across different study sites.

Disclosure of interests
The authors declare they have no conflict of interests.

Contribution to authorship
All authors contributed to the paper and approved the final version. The first version of the INTERGROWTH-21st ultrasound protocol was prepared by AP and LS. AP revised the protocol based on feedback from the INTERGROWTH-21st Executive Committee and the other

authors. The protocol was discussed at the first meeting of the INTERGROWTH-21st Steering Committee Meeting, on 15–17 September 2008, and finally approved at the 2nd Steering Committee Meeting on 25–27 March 2009.

Details of ethics approval

The INTERGROWTH-21st Project was approved by the Oxfordshire Research Ethics Committee 'C' (reference:08/H0606/139) and the research ethics committees of the individual participating institutions and corresponding health authorities where the project was implemented.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. INTERGROWTH-21st Project: The Ultrasound Operations Manual. ∎

References

1 de Onis M, Garza C, Onyango AW, Martorell R. WHO child growth standards. *Acta Paediatr* 2006;450:1–101.

2 Villar J, Altman DG, Purwar M, Noble JA, Knight HE, Ruyan P, et al. for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st). The objectives, design and implementation of the INTERGROWTH-21st Project. *BJOG* 2013; DOI: 10.1111/1471-0528.12047.

3 AIUM Practice Guideline for the performance of an antepartum obstetric ultrasound examination. *J Ultrasound Med* 2003;22:1116–25.

4 Loughna P, Chitty L, Evans T, Chudleigh T. Fetal size and dating: charts recommended for clinical obstetric practice. *Ultrasound* 2009;17:160–6.

5 Sonographic examination of the fetal central nervous system: guidelines for performing the 'basic examination' and the 'fetal neurosonogram'. *Ultrasound Obstet Gynecol* 2007;29:109–16.

6 Chitty LS, Altman DG, Henderson A, Campbell S. Charts of fetal size: 2. Head measurements. *BJOG* 1994;101:35–43.

7 Chitty LS, Altman DG, Henderson A, Campbell S. Charts of fetal size: 3. Abdominal measurements. *BJOG* 1994;101:125–31.

8 Chitty LS, Altman DG, Henderson A, Campbell S. Charts of fetal size: 4. Femur length. *BJOG* 1994;101:132–5.

9 Snijders RJ, Nicolaides KH. Fetal biometry at 14–40 weeks' gestation. *Ultrasound Obstet Gynecol* 1994;4:34–48.

10 Bricker L, Neilson JP, Dowswell T. Routine ultrasound in late pregnancy (after 24 weeks' gestation). *Cochrane Database Syst Rev* 2008;4:CD001451; DOI: 10.1002/14651858.CD001451.pub3.

11 Robinson HP. Sonar measurement of fetal crown–rump length as means of assessing maturity in first trimester of pregnancy. *Br Med J* 1973;4:28–31.

12 Robinson HP, Fleming JE. A critical evaluation of sonar "crown–rump length" measurements. *BJOG* 1975;82:702–10.

13 Ioannou C, Sarris I, Hoch L, Salomon LJ, Papageorghiou AT, for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st). Standardisation of crown-rump length measurement. *BJOG* 2013; DOI: 10.1111/1471-0528.12056.

14 Royal College of Radiologists. *Standards for Ultrasound Equipment*. London: Royal College of Radiologists; 2005.

15 Økland I, Bjåstad TG, Johansen TF, Gjessing HK, Grøttum P, Eik-Nes SH. Narrowed beam width in newer ultrasound machines shortens measurements in the lateral direction: fetal measurement charts may be obsolete. *Ultrasound Obstet Gynecol* 2011;38:82–7.

16 Salomon LJ, Bernard JP, Duyme M, Doris B, Mas N, Ville Y. Feasibility and reproducibility of an image-scoring method for quality control of fetal biometry in the second trimester. *Ultrasound Obstet Gynecol* 2006;27:34–40.

17 Sarris I, Ioannou C, Ohuma EO, Altman DG, Hoch L, Cosgrove C, et al. for the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st). Standardisation and quality control of ultrasound measurements of fetal growth. *BJOG* 2013; DOI: 10.1111/1471-0528.12315.