

A practical solution to combining dating and screening for Down's syndrome

Trish Chudleigh¹, Pam Loughna² and Tony Evans³

¹The Rosie Hospital, Cambridge University Hospitals NHS Trust, Cambridge, UK; ²Academic Division of Obstetrics and Gynaecology, Nottingham University Hospitals NHS Trust, Nottingham, UK; ³Division of Medical Physics, LIGHT Institute, University of Leeds, Leeds, UK
Corresponding author: Dr Trish Chudleigh. Email: trish.chudleigh@addenbrookes.nhs.uk

Abstract

The offer of combined Down's syndrome screening to all pregnant women in England requires accurate estimation of gestational age. The guidance issued by the British Medical Ultrasound Society (BMUS) in 2009 recommends dating by crown rump length (CRL) up to 13 weeks 0 days and by head circumference (HC) after this gestation. The guidance issued by the Fetal Anomaly Screening Programme (FASP) in 2010 states that combined screening for Down's syndrome is the recommended strategy. Combined screening requires the measurement of nuchal translucency, which should be performed when the CRL is between 45.0 and 84.0 mm. Uncertainty exists as to how best to combine the BMUS dating guidance and the FASP Down's syndrome screening guidance in routine practice. The solution proposed by the authors is to date the pregnancy by CRL up to and including 84.0 mm and to date using HC when the CRL is greater than 84.0 mm, irrespective of whether or not Down's syndrome screening is requested. Screening for Down's syndrome should be by combined screening when the CRL is between 45.0 and 84.0 mm. Where the CRL is greater than 84.0 mm, screening for Down's syndrome should be by maternal serum quadruple testing, performed after 14 weeks and two days.

Keywords: Down's syndrome screening, pregnancy dating, nuchal translucency, crown rump length

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Current best practice recommends that all pregnant women in England should be offered an ultrasound scan for pregnancy dating, ideally in the first trimester, and a screening test for Down's syndrome that has a detection rate greater than 90% for a screen positive rate that is less than 2%.

In 2009, the British Medical Ultrasound Society (BMUS) recommended a series of charts for ultrasound dating and estimation of fetal size in pregnancy.¹ This guidance has subsequently been incorporated into standards, guidelines and recommendations of other bodies, including the Fetal Anomaly Screening Programme (FASP). In a rapidly developing field such as antenatal screening, it is inevitable that the data presented by one publication do not dovetail perfectly with the data presented by a second publication, especially when separated by any significant period of time.

The introduction, nationally, of first trimester combined screening during 2010–2011 has highlighted the difficulties of incorporating into routine clinical practice two separate data sets that are scientifically robust but at variance with each other, namely those for dating (by crown rump length [CRL] and head circumference [HC]) and those for combined screening.

This article reviews the current issues and offers a pragmatic solution to departments wishing to provide a

workable and robust strategy for dating and Down's syndrome screening.

BMUS recommendations for dating

The BMUS guideline recommends that measurement of CRL should be used to date a pregnancy from 6 weeks + 0 days to 13 weeks + 0 days. From 13 weeks + 1 day to 25 weeks + 6 days the pregnancy should be dated by HC or femur length.

The data in the Robinson and Fleming publication² cover the gestational age (GA) range from 6 to 14 weeks and the error quoted is ± 4.7 days for the estimation of GA for any given CRL value. This compares with the ± 1.2 weeks uncertainty quoted for the HC-derived GA values and on that basis it may seem logical to assume that the use of CRL should be prolonged as far as possible into the pregnancy. However, within the Robinson and Fleming paper there are no values supplied for the actual number of measurements that were made at each gestation nor of the GA dependence of the standard deviation of the population. The general consensus is that fetal flexion alone makes it probable that the reliability of CRL will in fact decrease as

the pregnancy progresses, although there is a dearth of hard data to support this. Until such evidence emerges, a more pragmatic solution is needed.

The recommended equations for the calculation of gestational age are shown in Appendix 1. The CRL dating table in the BMUS guidance provides gestational age equivalents from 5 mm to 80 mm, i.e. 6 weeks + 0 days to 13 weeks + 6 days. For reasons discussed below, these data have now been extended to 84.0 mm, i.e. to 14 weeks + 1 day. Appendix 2 shows the gestational age equivalents, calculated from the same equation, from 5.0 mm to 84.0 mm.

It will be noted from Appendix 2 that a CRL of 69.0 mm is equivalent to a gestational age of 13 weeks + 1 day. Adherence to the BMUS dating guidance therefore indicates that HC should be used for pregnancy dating when a CRL of 69.0 mm or greater is obtained. The HC dating table is shown in Appendix 3.

FASP recommendations for combined screening

Current FASP guidance, as issued in December 2010, recommends that screening for Down's syndrome should take place between 10 weeks + 0 days and 20 weeks + 0 days and that combined testing is the recommended strategy.³ Combined screening combines the measurement of nuchal translucency (NT) and CRL with maternal serum levels of pregnancy-associated plasma protein A and free beta human chorionic gonadotrophin (β hCG).

Nuchal translucency measurement should be taken when the CRL is between 45.0 and 84.0 mm. Using the current BMUS 2009 dating formula, the gestational age window for NT measurement is 11 weeks + 2 days to 14 weeks + 1 day.

From 14 weeks + 2 days to 20 weeks + 0 days, the quadruple test should be offered. This test estimates Down's syndrome risk by measuring maternal serum levels of alphafetoprotein, hCG, estriol and inhibin-A. Reference to Appendix 3 indicates that this time window equates to an HC range of 101.0–172.0 mm.

Combined screening versus dating

FASP Down's syndrome screening requires the following:

- (1) Assessment of gestational age;
- (2) Assessment of the maternal age related risk for Down's syndrome, for the known gestational age;
- (3) Calculation of the gestational age related multiple of median values for the serum analytes;
- (4) Measurement of the size of NT relative to the CRL of 45.0–84.0 mm if combined screening is being performed.

BMUS dating requires the following:

- (1) Assessment of gestational age by CRL up to and including 13 weeks + 0 days, i.e. $CRL \leq 68.9$ mm;
- (2) Assessment of gestational age by HC from 13 weeks + 1 day, i.e. $CRL \geq 69.0$ mm.

In an ideal world the gestational age calculated independently from CRL and HC would agree exactly. Unfortunately evidence-based routine clinical practice does not support this premise as experience tells us that, even when perfectly measuring perfect images, the gestational age equivalents of a CRL and an HC are as likely to disagree (albeit by perhaps only one or two days) than agree. The issue becomes challenging after 13 weeks when we must use the CRL to calculate the NT related risk for combined screening but should use the HC to date the pregnancy. If the gestational age calculated from the two parameters differs, which is 'correct' and what, therefore, is the 'accurate' estimated delivery date?

Guidance

No data are available at the current time to provide an answer to the above. As pragmatic solutions are arguably more useful to busy ultrasound departments than a long wait for the definitive data set, we propose the following:

- (1) Where both dating and Down's syndrome screening are requested, and the CRL is between 45.0 and 84.0 mm, the pregnancy should be dated by CRL and combined screening performed.
- (2) Where both dating and Down's syndrome screening are requested, and the CRL is ≥ 84.1 mm, the pregnancy should be dated by HC.
 - (a) If the HC is ≥ 101.0 mm and the gestational age is ≥ 14 weeks + 2 days, date by HC. The CRL measurement should be ignored as it is > 84.0 mm. Quadruple screening can be performed.
 - (b) If the HC is < 101.0 mm and the CRL is > 84.0 mm, date by HC. If the gestational age as calculated from the HC is ≤ 14 weeks + 1 day, the woman should

Table 1 Range of CRL and HC measurements that should be used to date pregnancies and recommended screening method for Down's syndrome when requested

Parameter (mm)	Down's syndrome screening	Measure NT	Screening method	Parameter for dating and EDD
CRL 45.0–84.0	Requested	Yes	Combined	CRL
	Declined	n/a	n/a	CRL
CRL > 84.0 (do not use or report) use HC	Requested	No	Quadruple	HC
	Declined	n/a	n/a	HC
HC < 101.0 and CRL > 84.0	Requested	No	Quadruple (from 14 ⁺² weeks)	HC
	Declined	n/a	n/a	HC
HC 101.0–172.0 and CRL > 84.0	Requested	No	Quadruple	HC
	Declined	n/a	n/a	HC

CRL, crown rump length; HC, head circumference; n/a, not applicable; NT, nuchal translucency; EDD, expected date of delivery

be informed that the NT risk cannot be calculated from a CRL > 84.0 mm, even though the gestational age of her pregnancy, as estimated by the HC, lies within the gestational age window for combined screening. Combined screening is not an option but quadruple can be performed from 14 weeks + 2 days.

- (3) Where dating is requested but Down's syndrome screening is declined, one option is to apply the BMUS guidance and date by CRL up to 68.9 mm and by HC when the CRL is 69.0 mm and greater. Our recommendation is to use CRL to date all pregnancies up to and including a CRL of 84.0 mm, irrespective of whether or not Down's screening is requested. We accept the potential inaccuracies that larger CRLs may introduce into the dating process, but suggest that applying a single, simple dating strategy to all pregnancies is preferable as it is less confusing for all concerned.

The above guidance is summarized in Table 1.

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DECLARATIONS

The authors have no conflict of interest to declare.

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Appendix 1 Equations for the calculation of gestational age

Dating parameter	Equation for calculation of gestational age
CRL	$8.052 \times (\text{CRL} \times 1.037)^{1/2} + 23.73$
HC from BPD (outer to outer) and OFD	$\pi(\text{BPD} + \text{OFD})/2$
HC from ellipse	$\text{Log}_e(\text{GA}) = 0.010611\text{HC} - 0.000030321\text{HC}^2 + 0.43498 \times 10^{-7}\text{HC}^3 + 1.848$
FL	$\text{Log}_e(\text{GA}) = 0.034375\text{FL} - 0.0037254\text{FL} \times \text{log}_e(\text{FL}) + 2.306$

CRL, crown rump length; HC, head circumference; GA, gestational age; FL, femur length; BPD, biparietal diameter; OFD, occipitofrontal diameter

Appendix 2 Crown rump length (CRL) dating table

CRL (mm)	GA (weeks + days)		
	50th centile	5th centile	95th centile
43	11 + 0	10 + 3	11 + 5
44	11 + 1	10 + 3	11 + 6
45	11 + 2	10 + 4	11 + 6
46	11 + 2	10 + 5	12 + 0
47	11 + 3	10 + 5	12 + 1
48	11 + 4	10 + 6	12 + 1
49	11 + 4	10 + 6	12 + 2
50	11 + 5	11 + 0	12 + 2
51	11 + 5	11 + 1	12 + 3
52	11 + 6	11 + 1	12 + 4
53	11 + 6	11 + 2	12 + 4
54	12 + 0	11 + 2	12 + 5
55	12 + 1	11 + 3	12 + 5
56	12 + 1	11 + 3	12 + 6
57	12 + 2	11 + 4	12 + 6
58	12 + 2	11 + 4	13 + 0
59	12 + 3	11 + 5	13 + 0
60	12 + 3	11 + 6	13 + 1
61	12 + 4	11 + 6	13 + 1
62	12 + 4	12 + 0	13 + 2
63	12 + 5	12 + 0	13 + 3
64	12 + 5	12 + 1	13 + 3
65	12 + 6	12 + 1	13 + 4
66	12 + 6	12 + 2	13 + 4
67	13 + 0	12 + 2	13 + 5
68	13 + 0	12 + 3	13 + 5
69	13 + 1	12 + 3	13 + 6
70	13 + 1	12 + 4	13 + 6
71	13 + 2	12 + 4	14 + 0
72	13 + 2	12 + 5	14 + 0
73	13 + 3	12 + 5	14 + 0
74	13 + 3	12 + 6	14 + 1
75	13 + 4	12 + 6	14 + 1
76	13 + 4	13 + 0	14 + 2
77	13 + 5	13 + 0	14 + 2
78	13 + 5	13 + 0	14 + 3
79	13 + 6	13 + 1	14 + 3
80	13 + 6	13 + 1	14 + 4
81	14 + 0	13 + 1	14 + 4
82	14 + 0	13 + 2	14 + 5
83	14 + 0	13 + 3	14 + 5
84	14 + 1	13 + 4	14 + 6

GA, gestational age

Appendix 3 Head circumference (HC) dating table: calculated from outer to outer BPD and OFD measurement (after Altman and Chitty⁴)

HC (mm)	GA (weeks + days)		
	50th centile	5th centile	95th centile
80	12 + 4	11 + 3	13 + 5
85	12 + 6	11 + 6	14 + 1
90	13 + 2	12 + 2	14 + 4

(Continued)

Appendix 3 (Continued)

HC (mm)	GA (weeks + days)		
	50th centile	5th centile	95th centile
95	13 + 5	12 + 4	15 + 0
100	14 + 1	13 + 0	15 + 3
105	14 + 4	13 + 3	15 + 5
110	15 + 0	13 + 6	16 + 1
115	15 + 3	14 + 2	16 + 4
120	15 + 6	14 + 5	17 + 0
125	16 + 2	15 + 1	17 + 3
130	16 + 4	15 + 4	17 + 6
135	17 + 0	15 + 6	18 + 2
140	17 + 3	16 + 2	18 + 5
145	17 + 6	16 + 5	19 + 1
150	18 + 2	17 + 1	19 + 3
155	18 + 5	17 + 4	19 + 6
160	19 + 1	17 + 6	20 + 2
165	19 + 3	18 + 2	20 + 5
170	19 + 6	18 + 5	21 + 1
175	20 + 2	19 + 1	21 + 4
180	20 + 5	19 + 3	22 + 0
185	21 + 1	19 + 6	22 + 3
190	21 + 4	20 + 2	22 + 6
195	22 + 0	20 + 4	23 + 2
200	22 + 2	21 + 0	23 + 5
205	22 + 5	21 + 3	24 + 2
210	23 + 1	21 + 5	24 + 5
215	23 + 4	22 + 1	25 + 1
220	24 + 0	22 + 4	25 + 5
225	24 + 3	22 + 6	26 + 1
230	24 + 6	23 + 2	26 + 5
235	25 + 3	23 + 5	27 + 1
240	25 + 6	24 + 1	27 + 5

GA, gestational age