Estimating Fetal Age: Computer-Assisted Analysis of Multiple Fetal Growth Parameters[1]

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Regression models for predicting menstrual age based on real-time sonographic measurements of four fetal parameters (biparietal diameter, head circumference, abdominal circumference, and femur length), used alone and in combination, were developed in a cross-sectional study of 361 fetuses between 14 and 42 menstrual weeks. The head circumference and femur length were the strongest individual predictors of age. A number of combinations of fetal parameters, including the combination of head circumference and femur length, provided age estimates that were significantly better ($p = 0.05$) than those using any single parameter alone. It was also demonstrated that simply averaging individual age estimates in a given case could provide results that were not significantly different from those obtained by using the same parameters in a complex regression equation. The advantages and potential pitfalls of this system of fetal dating are discussed.

Index terms: Fetus, growth and development

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SONOGRAPHIC measurement of the fetal biparietal diameter (BPD) can provide a good estimate of fetal age in the first half of pregnancy (2 SD = ±7–10 days) (1, 2), but there is a progressive increase in the variability as pregnancy progresses, with a maximum variability of approximately ±3.6 weeks in the last six weeks of pregnancy (1, 2). For this reason, efforts have been made to predict fetal age from other fetal growth parameters such as the head circumference (HC) (3), abdominal circumference (AC) (4), and femur length (FL) (5, 6). However, the variability patterns in predicting age from these parameters used individually are similar to those obtained when BPD is used alone (3–7).

In another report we demonstrated statistically significant improvement in estimation of fetal age in the third trimester of pregnancy when two or more of these measurements are used in combination (8). This method resulted in a reduction in the variability of approximately 25 to 30%, as well as a reduction in the maximum errors that are observed when an individual parameter such as the BPD is used alone (8). In this study we expanded the original study population from 177 to 361 fetuses to evaluate this method of fetal dating throughout a broader range of gestational ages (14–42 weeks).

MATERIALS AND METHODS

The study group consisted of 361 middle-class Caucasian women from the Houston area. All of these patients had a history of regular menses, and knew unequivocally the beginning day of the last menstrual period. In all cases the first-trimester clinical findings were in agreement with the last menstrual period. Patients with maternal disease that might adversely effect fetal growth (*e.g.*, diabetes mellitus) were not included; similarly, patients with multiple gestations in this pregnancy were not included. In keeping with proper design of a cross-sectional study, each fetus was measured only once in gestation.

All examinations were performed by physicians using a commercially available linear array real-time ultrasound system with a 3.5-MHz focused transducer (ADR—Tempe, AZ). The techniques for measuring the BPD, femur length, head circumference, and abdominal circumference (Fig. 1) are described in detail elsewhere (2–5). Measurements of the BPD and femur length were made using electronic calipers. Circumference measurements of the head and abdomen were either made directly from Polaroid images using an electronic digitizer (Numonics Corp.) or by calculation from two diameters using the formula for the circumference of a circle ($D_1 + D_2 \times \Pi/2$); these methods have been shown to give equivalent results (9).

Regression models for predicting menstrual age from these parameters, both individually and in all possible combinations, were obtained by stepwise regression analysis (10). The regression analysis for the individual parameters included the linear, quadratic, and cubic terms of each parameter, and the stepwise regression for the combinations of parameters include the linear, quadratic, and cubic terms of the individual parameters as well as all the cross-products of these terms. For example, stepwise regression analysis of menstrual age as a function of all four parameters included the following terms: BPD, BPD^2, BPD^3, HC, HC^2, HC^3, AC, AC^2, AC^3, FL, FL^2, FL^3, BPD × AC, BPD × HC, BPD × FL, HC × AC, HC × FL, AC × FL. The optimal regression function chosen by this analysis is the one with the highest r^2 and

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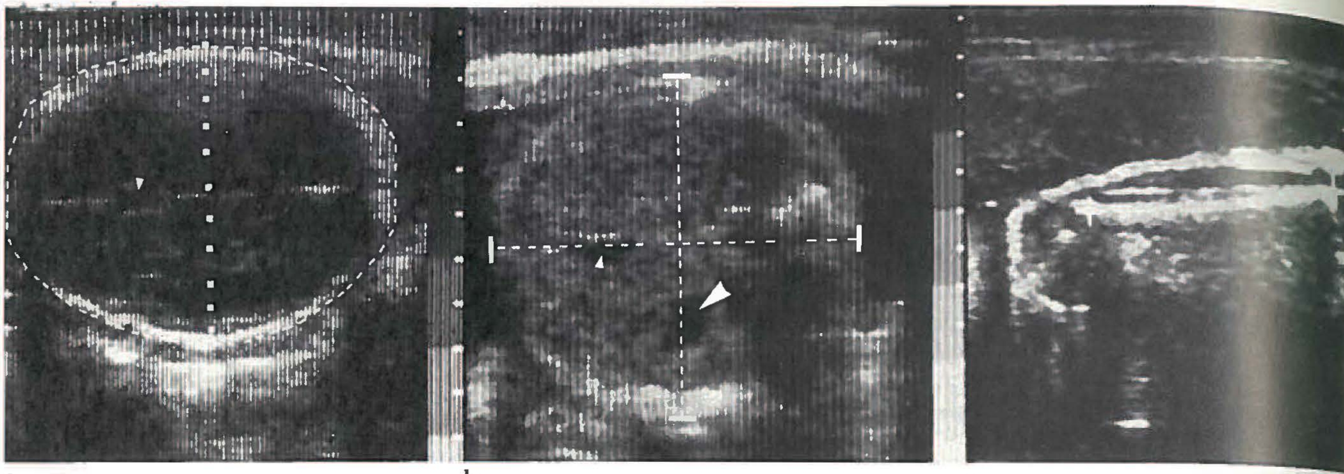
Figure 1



a. b. c.

a. Demonstration of the appropriate axial section of the fetal head for measurement of the BPD (broken squares in vertical axis) and head circumference (broken lines). The small arrowhead is a landmark thought to represent the cavum septi pellucidi.
b. Demonstration of the appropriate axial section of the fetal abdomen for measurement of the abdominal circumference. In this case circumference is calculated using the formula (D1 + D2) × 1.57. The small arrowhead indicates the umbilical portion of the left portal vein and the large arrowhead indicates the stomach.
c. Demonstration of the appropriate section for measurement of the femur length (+ indicates electronic caliper markers).

the lowest standard deviation, and the method requires that all terms in the regression equation be statistically significantly different from zero ($p < 0.05$).

The ability of various combinations of the individual parameters to predict menstrual age accurately was also evaluated by a simple averaging technique (8), which gives equal weight to each age estimate based on our previously published nomograms (2–5) for each parameter. For example, if all four parameters were to be evaluated as a group, individual estimates of age would be made based on BPD, HC, AC, and FL, and these four estimates would simply be added together and divided by four to provide a composite age estimate (8).

The efficacy of each individual parameter and various groups of parameters as estimators of fetal age was assessed by comparing the magnitude of the variability for each regression model, which is represented in this context by the standard deviation of the regression. The F test was used to determine if there were significant differences ($p = 0.05$) among the various models (10); each regression model was compared with every other regression model in this manner. This test was also used to determine if there were significant differences in the variability between the regression model and the simple averaging technique when both used the same individual parameters to produce a composite age estimate.

Finally, the 361 known menstrual age data points were divided into six-week intervals by age as follows: 12–17.99 weeks, 18–23.99 weeks, 24–29.99 weeks, 30–35.99 weeks, and 36–41.99 weeks. The regression models obtained from the stepwise regression analysis described in the preceding paragraph were then evaluated as predictors of menstrual age in the subgroups, to determine if there was any change in variability with increasing menstrual age. The results using the simple averaging technique in these intervals were also evaluated, and were compared with the results using the regression models to determine if there were significant differences within these age intervals.

RESULTS

The results from the stepwise regression analysis of menstrual age on the individual parameters and the combinations of parameters are summarized in TABLE I. The results using the simple averaging technique were not significantly different ($p < 0.05$) from those using the various regression models. The best results (as defined by the lowest standard deviation, the highest r^2 value, and the smallest maximum error) were obtained using all four parameters in combination (Fig. 2). The results using this model were significantly better ($p = 0.05$) than any of the individual parameters used alone, and were also significantly better than the combinations of *BPD and AC*, *BPD and HC*, *HC and AC*, and *BPD, HC, AC*. There were no significant differences, however, in the variabilities of the remaining combinations of parameters. It would appear from the magnitude of the standard deviations, the r^2 values, and the maximum errors that five of these regression models could be considered optimal models. These include the combinations of *HC and FL*, *BPD, AC, and FL*, *BPD, HC, and FL*, *HC, AC, and FL*, and *BPD, HC, AC, and FL*.

The variability in predicting menstrual age in the six-week subintervals using the individual parameters and the combinations of parameters is indicated in TABLE II. There was no significant difference between the variability among the optimal models within each subinterval, but the results using these models were significantly better than those using the best individual models. It appears from this analysis that the HC is the most accurate individual parameter in predicting age, a point that has also been observed recently by Law and MacRae (11). There was a progressive increase in variability with time between 12 and 30 weeks for all the individual parameters and groups of parameters, but no significant differences in variability were demonstrated when the variability for a given regression model between 30 and 36 weeks was compared with the variability for the same regression model during the period of 36 to 42 weeks ($p = 0.05$).

DISCUSSION

The variability in predicting menstrual age from any individual fetal measurement such as BPD, head circumference, abdominal circumference, or femur length is known to increase progressively throughout gestation, reaching a maximum variability of ±3.5 weeks in the third trimester of pregnancy (1–7). Our approach in this investigation, in contrast with a previous study limited to the third trimester, was to develop regression equations for predicting menstrual age

TABLE I: Regression Equations for Predicting Menstrual Age (MA) from Fetal Measurements (12–42 wks)

Fetal Measurements (cm)	Regression Equation	Standard Deviation (wks)	Maximum Error (wks)	R^2 (%)
BPD	$MA = 9.54 + 1.482\ (BPD) + 0.1676\ (BPD)^2$	1.36	5.1	96.7
HC	$MA = 8.96 + 0.540\ (HC) + 0.0003\ (HC)^3$	1.23	4.1	97.3
AC	$MA = 8.14 + 0.753\ (AC) + 0.0036\ (AC)^2$	1.31	4.6	96.9
FL	$MA = 10.35 + 2.460\ (FL) + 0.170\ (FL)^2$	1.28	4.9	97.1
BPD, AC	$MA = 9.57 + 0.524\ (AC) + 0.1220\ (BPD)^2$	1.18	3.8	97.5
BPD, HC	$MA = 10.32 + 0.009\ (HC)^2 + 1.3200\ (BPD) + 0.00012\ (HC)^3$	1.21	3.5	97.4
BPD, FL	$MA = 10.50 + 0.197\ (BPD)\ (FL) + 0.9500\ (FL) + 0.7300\ (BPD)$	1.10	3.6	97.8
HC, AC	$MA = 10.31 + 0.012\ (HC)^2 + 0.3850\ (AC)$	1.15	4.3	97.6
HC, FL	$MA = 11.19 + 0.070\ (HC)\ (FL) + 0.2630\ (HC)$	1.04	3.3	98.0
AC, FL	$MA = 10.47 + 0.442\ (AC) + 0.3140\ (FL)^2 - 0.0121\ (FL)^3$	1.11	3.8	97.8
BPD, AC, FL	$MA = 10.61 + 0.175\ (BPD)\ (FL) + 0.2970\ (AC) + 0.7100\ (FL)$	1.06	3.4	98.0
HC, BPD, FL	$MA = 11.38 + 0.070\ (HC)\ (FL) + 0.9800\ (BPD)$	1.04	3.2	98.1
HC, AC, FL	$MA = 10.33 + 0.031\ (HC)\ (FL) + 0.3610\ (HC) + 0.0298\ (AC)\ (FL)$	1.03	3.4	98.1
HC, AC, BPD	$MA = 10.58 + 0.005\ (HC)^2 + 0.3635\ (AC) + 0.02864\ (BPD)\ (AC)$	1.14	4.0	97.7
BPD, HC, AC, FL	$MA = 10.85 + 0.060\ (HC)\ (FL) + 0.6700\ (BPD) + 0.1680\ (AC)$	1.02	3.2	98.1

throughout the entire range of gestation using various combinations of parameters. The rationale for using more than one parameter is as follows: (*a*) the demonstration by other investigators that the use of a combination of parameters provides better results then a single parameter in estimating neonatal age by the Dubowitz examination (12), estimating fetal weight using ultrasound (13), determining fetal well-being with a biophysical profile (14), and predicting fetal age in the first trimester using ultrasound (15); (*b*) the fact that any of these parameters used alone may be limited not only by the biological variability but also by subtle technical problems that may be apparent only to the very experienced sonographer; (*c*) the observation that in a normal fetus any of these parameters may be generally larger or smaller than the mean value expected for the menstrual age, and that these discrepancies are not always in the same direction, *e.g.*, the fetus with a 75th percentile head size and a 25th percentile body size (16); and (*d*) routine measurements of BPD, head circumference, abdominal circumference, and femur length are now considered part of a standard ultrasound examination (17, 18).

The results in this study demonstrate that there is a significant reduction in the overall variability and the maximum observed errors when an optimal combination of parameters is used to estimate age instead of any single parameter. For example, if one chose to use the BPD alone to estimate age in place of using the optimal combination of four parameters, the overall variability as estimated by the standard deviation of the regression would be increased by 33% (1.02 vs. 1.36 wks), and the maximum observed error would be increased by 55% (3.2 vs. 5.1 wks). We feel the magnitude of these differences warrants routine use of this dating method.

TABLE II: Subgroup Variability in Predicting Menstrual Age Using the Regression Equations in TABLE I

Fetal Parameters	Subgroup Variability (±2 SD) in Weeks: 12–18 Weeks (N = 43)	18–24 Weeks (N = 69)	24–30 Weeks (N = 76)	30–36 Weeks (N = 95)	36–42 Weeks (N = 78)
BPD	±1.19	±1.73	±2.18	±3.08	±3.20
HC	±1.19	±1.48	±2.06	±2.98	±2.70
AC	±1.66	±2.06	±2.18	±2.96	±3.04
FL	±1.38	±1.80	±2.08	±2.96	±3.12
BPD, AC	±1.26	±1.68	±1.92	±2.60	±2.88
BPD, HC	±1.08	±1.49	±1.99	±2.86	±2.64
BPD, FL	±1.12	±1.46	±1.84	±2.60	±2.62
HC, AC	±1.20	±1.52	±1.98	±2.68	±2.52
HC, FL	±1.08	±1.34	±1.86	±2.52	±2.28
AC, FL	±1.32	±1.64	±1.88	±2.66	±2.60
BPD, AC, FL	±1.20	±1.52	±1.82	±2.50	±2.52
BPD, HC, FL	±1.04	±1.35	±1.81	±2.52	±2.34
HC, AC, FL	±1.14	±1.46	±1.86	±2.52	±2.34
HC, AC, BPD	±1.21	±1.58	±1.94	±2.60	±2.52
BPD, HC, AC, FL	±1.08	±1.40	±1.80	±2.44	±2.30

Figure 2

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NUMBER    ERROR(wks)
   2        -3.0        *
   5        -2.5        ***
   8        -2.0        ****
  16        -1.5        ********
  46        -1.0        ***********************
  64        -0.5        ********************************
  77         0.0        ***************************************
  67         0.5        **********************************
  42         1.0        *********************
  18         1.5        *********
   8         2.0        ****
   6         2.5        ***
   2         3.0        *

   *=2 cases
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A histogram of the residuals (*e.g.*, differences between actual age and predicted age) using the regression model based on all four fetal measurements (residuals rounded to the nearest half week).

The choice of parameters used to predict age in a given case will depend both on the philosophy of the sonographer and the number of technically satisfactory measurements obtained. For example, the data in TABLE I demonstrate that head circumference and femur length in combination provide age estimates that are not significantly different ($p = 0.05$) from those obtained using all four measurements in combination. One could argue justifiably that only these two measurements are needed to predict age; a similar argument could be made for the use of BPD and femur length in combination, but this case could be weaker because head circumference has a stronger relation to age than the BPD and is more shape independent. In our department we use all four measurements routinely, since BPD and abdominal circumference are already available because of their role in estimating weight (13). Another important feature of our results is that they provide information about the magnitude of overall variability and maximum errors that one can expect when certain measurements are technically impossible (TABLES I, II).

These regression models are easily

programmable into a microcomputer, so that one can choose the appropriate regression model for the number of technically satisfactory measurements one is able to make in a given case. Of equal interest, however, to the practitioner without microcomputer capability, is the fact that the simple averaging technique using these parameters in combination provides results that are not statistically different ($p = 0.05$) from those obtained when these parameters are used in the regression models described. To facilitate use of this method, the mean predicted values for all four parameters at a given menstrual age based on data from the patients in this study are presented in TABLE III. In using this table, individual age estimates are obtained by reading from right to left (*e.g.*, BPD 8.1 cm = 32 weeks; HC 29.7 cm = 31.5 weeks; AC 28.6 cm = 32.5 weeks; FL 6.2 cm = 32 weeks; composite age = 32 + 31.5 + 32.5 + 32/4 = 32 weeks). Although the use of these data in this way is not as mathematically correct as using tables in which menstrual age is the dependent variable, the results in our laboratory are virtually the same, and it obviates the need for four separate tables. This table has also proved to be very useful in evaluating growth patterns in fetuses in which the menstrual age is known unequivocally.

An obvious limitation of this system of fetal dating is that it will systematically overestimate age in fetuses that are symmetrically large for gestational age and will systematically underestimate age in fetuses that are symmetrically small for gestational age. If the clinical history suggests either of these possibilities, the multiple-parameter dating method cannot be expected to provide age estimates that are significantly better than those obtained using any single parameter. A second potential problem in using this dating system is including measurements of the BPD in cases in which there are extreme variations in fetal head shape, particularly dolichocephaly, which is usually encountered in breech fetuses, twins, or in cases with premature rupture of membranes (19–21). The cephalic index has been shown to be an effective way of detecting such extremes in head shape, and the BPD should not be included in the group of parameters for fetal dating when the cephalic index is outside the normal range (<70, >86) (22). A third potential problem with the composite age dating system is the case in which a single fetal parameter is disproportionately large or small based on a pathologic process in the fetus (*e.g.*, the femur length in a dwarf; the head circumference in cases of hydrocephaly or microcephaly; the abdominal circumference in macrosomia, ascites, or asymmetric growth retardation). One can avoid these pitfalls by evaluating body proportionality using certain body ratios that are relatively age independent (18). For example, if the anatomy of the head and femur are normal, and if the cephalic index demonstrates no extreme variation in head shape, the femur length/BPD ratio should be measured (FL/BPD × 100 = 79 ± 8) (23). If this measurement is abnormally low one should discard the femur measurement because of the possibility of dwarfism, and if it is abnormally high in a fetus with a normal head shape, one should probably discard the head measurements because of the possibility of microcephaly. If the femur length/BPD ratio is normal, one can then measure the femur length/abdominal circumference ratio (FL/AC × 100 = 22 ± 2) (24); if this measurement is low one should discard the abdomen measurement because of probable macrosomia, and if the measurement is high the abdomen should not be included in the composite age estimate because of possible growth retardation (24).

The advantages of using a microcomputer for evaluation of data from obstetrical sonograms have been outlined in several recent reports (25–27). The regression equations generated in

TABLE III: Predicted Fetal Measurements at Specific Menstrual Age

Menstrual Age (wks)	Biparietal Diameter (cm)*	Head Circumference (cm)†	Abdominal Circumference (cm)‡	Femur Length (cm)§
12.0	1.7	6.8	4.6	0.7
12.5	1.9	7.5	5.3	0.9
13.0	2.1	8.2	6.0	1.1
13.5	2.3	8.9	6.7	1.2
14.0	2.5	9.7	7.3	1.4
14.5	2.7	10.4	8.0	1.6
15.0	2.9	11.0	8.6	1.7
15.5	3.1	11.7	9.3	1.9
16.0	3.2	12.4	9.9	2.0
16.5	3.4	13.1	10.6	2.2
17.0	3.6	13.8	11.2	2.4
17.5	3.8	14.4	11.9	2.5
18.0	3.9	15.1	12.5	2.7
18.5	4.1	15.8	13.1	2.8
19.0	4.3	16.4	13.7	3.0
19.5	4.5	17.0	14.4	3.1
20.0	4.6	17.7	15.0	3.3
20.5	4.8	18.3	15.6	3.4
21.0	5.0	18.9	16.2	3.5
21.5	5.1	19.5	16.8	3.7
22.0	5.3	20.1	17.4	3.8
22.5	5.5	20.7	17.9	4.0
23.0	5.6	21.3	18.5	4.1
23.5	5.8	21.9	19.1	4.2
24.0	5.9	22.4	19.7	4.4
24.5	6.1	23.0	20.2	4.5
25.0	6.2	23.5	20.8	4.6
25.5	6.4	24.1	21.3	4.7
26.0	6.5	24.6	21.9	4.9
26.5	6.7	25.1	22.4	5.0
27.0	6.8	25.6	23.0	5.1
27.5	6.9	26.1	23.5	5.2
28.0	7.1	26.6	24.0	5.4
28.5	7.2	27.1	24.6	5.5
29.0	7.3	27.5	25.1	5.6
29.5	7.5	28.0	25.6	5.7
30.0	7.6	28.4	26.1	5.8
30.5	7.7	28.8	26.6	5.9
31.0	7.8	29.3	27.1	6.0
31.5	7.9	29.7	27.6	6.1
32.0	8.1	30.1	28.1	6.2
32.5	8.2	30.4	28.6	6.3
33.0	8.3	30.8	29.1	6.4
33.5	8.4	31.2	29.5	6.5
34.0	8.5	31.5	30.0	6.6
34.5	8.6	31.8	30.5	6.7
35.0	8.7	32.2	30.9	6.8
35.5	8.8	32.5	31.4	6.9
36.0	8.9	32.8	31.8	7.0
36.5	8.9	33.0	32.3	7.1
37.0	9.0	33.3	32.7	7.2
37.5	9.1	33.5	33.2	7.3
38.0	9.2	33.8	33.6	7.4
38.5	9.2	34.0	34.0	7.4
39.0	9.3	34.2	34.4	7.5
39.5	9.4	34.4	34.8	7.6
40.0	9.4	34.6	35.3	7.7

* BPD = −3.08 + 0.41 (MA) − 0.000061 MA^3; r^2 = 97.6%; 1 SD = 3 mm.
† HC = −11.48 + 1.56 (MA) − 0.0002548 MA^3; r^2 = 98.1%; 1 SD = 1 cm.
‡ AC = −13.3 + 1.61 (MA) − 0.00998 MA^2; r^2 = 97.2%; 1 SD = 1.34 cm.
§ FL = −3.91 + 0.427 (MA) − 0.0034 MA^2; r^2 = 97.5%; 1 SD = 3 mm.

this report are easily stored in instruments of this type, and the appropriate regression equation can be chosen for use based on the number of technically satisfactory images obtained. We anticipate that in the near future sonographers will make six linear measurements using electronic calipers (BPD, short and long axes of the head and abdomen measured outer to outer, and femur length). The computer will then analyze body proportionality (cephalic index, FL/BPD ratio, HC/AC ratio, FL/AC ratio) and will calculate age, weight, and weight percentile based on the appropriate measurements.

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