Measurement of Breast Volume by Ultrasound During Normal Menstrual Cycles and With Oral Contraceptive Use

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The volume of the human breast was measured by ultrasonographic methods with good reliability and reproducibility. Variations in breast volume of up to 36% were encountered with weekly measurements during the course of seven normal menstrual cycles. Oral contraceptives containing 35 to 50 μg ethynyl estradiol and amounts of norethindrone varying over a range of 0.4 to 2.5 mg/day and used for six cycles did not produce dose-related changes in breast volume as compared with untreated control subjects, but the sensitivity of the experiment was reduced by notable individual variation and relatively small sample sizes. ***(Obstet Gynecol 66:538, 1985)***

Surprisingly little attention has been paid to quantitative measurements of breast volume, although gross end-organ effects due to changes in the hormonal environment are of considerable interest. Simple linear or planimetric[1] measurements are of little value; methods attempting to use displacement of water[2,3] or actual casts[4] are confounded by the variable shape of the chest wall; phototopographic techniques involve costly and unusual equipment. As sonography has already been used for estimations of volume of the thyroid[5] and gravid and nongravid uterus,[6–8] it appeared reasonable to apply this technique to measurement of the volume of the human breast.[9]

Materials and Methods

Sonography was performed in an air-conditioned room using digital gray scale static scanners* using 3.5-mH transducers (medium focus). Each breast was scanned in transverse section (and in longitudinal section also in the first phase of this investigation) in supine position with 20- to 35-degree rotation sufficient to center the breast being examined to be symmetric. Support was provided on the posterior aspect of the chest to maintain a stable position.

Transverse scans were performed at 1-cm intervals starting above the breast and proceeding caudally to a level below the breast until no breast tissue was encountered. Longitudinal scans were performed laterally from the midline at 1-cm intervals until no breast parenchyma was recognized sonographically, usually at the midaxillary level. Conventional radiographic films were used for recording. The areas of the sections were measured (by the same individual) on an Electronic Digitiser* and volumes were estimated from the sum of the areas measured at 1-cm intervals. The breast area was measured from the posterior aspect of the dermis to include the subcutaneous layer, mammary layer, and sonographic retromammary space (not the radiographic retromammary space), and excluding the pectoral muscle (Figure 1). The posterior boundary of the breast was defined by the fascia covering the pectoral muscles, anterior boundary by the posterior border of the dermis, and on the sides by the sonographically recognizable breast edge.

Young women volunteers were used in both the methodologic and drug studies. The initial studies of reproducibility, carried out in 14 women, consisted of three consecutive daily (or every other day) measurements in the early follicular phase of the menstrual cycle. The technique was tested further by performing consecutive transverse and longitudinal scans of each

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* Numonics Corp., Lansdale, PA.

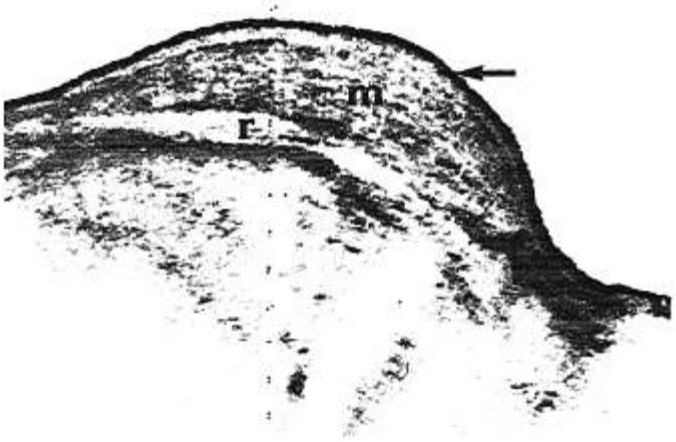

Figure 1. Transverse scan of the breast. m = mammary layer, r = retromammary space, straight arrow = dermis, curved arrow = lateral edge of the breast.

breast in 18 normal subjects. Serial measurements in the course of normal menstrual cycles were performed at weekly intervals in seven women. Finally, 22 women initiating the use of oral contraceptives were randomly assigned to one of the three agents that differed chiefly in the quantity of the progestational agent: Ovcon-35 (35 μg ethynyl estradiol) and 0.4 mg norethindrone; Ovcon-50 (50 μg ethynyl estradiol and 1.0 mg norethindrone) and Norlestrin 2.5 (50 μg ethynyl estradiol and 2.5 mg norethindrone). Differences observed among the three regimens are most likely to be associated with the large (6.25-fold) range in progestational exposure. In the last two regimens the estrogen exposure was identical. A control group of 15 cycling women who elected to use barrier contraceptives or none at all served as controls. Breast volume measurements were carried out in the premenstrual week of control or pretreatment cycles and during the last week of oral contraceptive therapy after two and six cycles of use.

For the three consecutive longitudinal volume measurements, the standard deviation of the three was calculated as the measure of variance, and these data were ordered by magnitude of breast volume. The statistical comparison of the transverse versus the longitudinal procedures for volume determination was performed by calculating the correlation coefficient of the two sets of measurements. The control and contraceptive-user groups were compared with respect to breast volume as a percentage of initial value by analysis of covariance.[10] This analysis was performed for the intervals zero to two, two to six, and zero to six months. Weight change was treated as a covariate to eliminate bias due to the effect of weight gain on volume increase.

Results

Reproducibility was tested by performing a transverse-slice volume measurement on three occasions within one to two days of each other in the early follicular phase of the cycle. The standard deviation for each set of three measurements per breast was calculated. There were five individuals with a breast volume of 130 cm^3 or less, and the mean standard deviation of the triplicates was 6.3 cm^3. In seven individuals the breast volume ranged from 151 to 300 cm^3; the mean SD of triplicates was 19.9 cm^3. In two instances the volume was about 700 cm^3 and the average SD was 35.3 cm^3. Overall, the mean standard deviation of the triplicates was 8% of the actual breast volume, a reproducibility satisfactory for most clinical purposes.

The study of reliability consisted of making sonographic slices through the breast tissue in both the transverse and vertical direction at 1-cm intervals. The study was performed in 18 individuals. Comparison of the volume derived from transverse versus vertical slicing yielded a correlation coefficient of 0.97, a highly satisfactory proof of reliability.

Volume determinations were carried out at weekly intervals in normal menstrual cycles, with the first measurement during the first three days of the cycle. In three of the seven women there was no detectable change in volume during the cycle. In the four others the change from maximum to minimum volume was 16, 25, 28, and 36%, respectively, with almost identical volume changes in the left and right breast. The minima were always in the second or third cycle week. Changes of this magnitude are unequivocally detectable by the ultrasound procedure.

Table 1 shows mean breast volumes of oral contraceptive users for intervals zero to two, two to six, and zero to six months as a percentage of the value at the beginning of the respective interval. For example, the value of 94% for the control group in the first interval indicates an average decrease in volume of 6% from baseline, and 109% in the second interval indicates a 9% increase from month 2 to month 6. Table 2 gives a

Table 1. Breast Volume as a Percentage of Initial Value*

Group	First interval (V_2/V_0)	Second interval (V_6/V_2)	Total interval (V_6/V_0)
Control	94 ± 15 (15)	109 ± 23 (14)	104 ± 36 (14)
Ovcon 35/0.4	110 ± 30 (7)	114 ± 34 (5)	122 ± 13 (6)
Ovcon 50/1.0	113 ± 34 (10)	88 ± 18 (10)	100 ± 36 (10)
Norlestrin 50/2.5	94 ± 11 (5)	90 ± 17 (4)	100 ± 23 (8)

V_0 = initial volume; V_2 = volume at two months; V_6 = volume at six months.

* Values given are for the mean ± S.D. The number of subjects is indicated in parentheses.

Table 2. Analysis of Covariance for Breast Volume as a Percent of Initial Value, Adjusted for Weight Change*

	First interval (V_2/V_0)		Second interval (V_6/V_2)		Total interval (V_6/V_0)	
	Unadjust	Adjust	Unadjust	Adjust	Unadjust	Adjust
Control vs Ovcon 35®	0.10	0.20	0.50	0.50	0.20	0.20
Control vs Ovcon 50®	0.05	0.10	0.05	0.05	0.50	0.50
Control vs Norlestrin®	0.50	0.50	0.10	0.20	0.50	0.50

V_0 = initial volume; V_2 = volume at two months; V_6 = volume at six months.
* None of the adjusted P values attain statistical significance.

statistical comparison of the treatment groups versus control with and without adjustment for weight change during the respective interval. Control versus Ovcon-50 reaches statistical significance in both the first and second intervals, but with adjustment for weight change none of the contrasts are significant at the $P = .05$ level.

These comparisons were also examined using volume change per month as the unit, with essentially identical results.

Discussion

The advantage of a beta-scanner is its ability to obtain images of large areas such as the breast, gravid uterus, or abdomen, and to use the stepped-up volume technique for calculation of volume. The sonograms were performed on a compound beta-scanner, which is widely available but being replaced for most conventional applications by high resolution real time equipment. The technical problems include those associated with a part of the body that varies in shape and size at different examinations. Reproducibility of ultrasonic technique is achieved by using the same settings on the machine for all tests on the same patient. It is easier to examine the small breast as compared with the large breast; operator skill and experience are necessary for consistent results in handling a part of the body that changes in shape on contact with the transducer. This could be avoided by the use of automated breast scanners that rapidly scan the entire breast at intervals as small as 1 mm, making a more accurate calculation of breast volume possible. Automated breast scanners, either of the immersion or water-bath type, coupled to videodiscs, videotapes, and microprocessors will allow selection of multiplanar sections and separations of the scan planes with storage.[11,12]

Direct water path scanning techniques in which the patient is placed in the prone position with the breasts suspended freely and completely immersed in a water tank are superior to contact methods.[12] Advantages of automated scanning are greater consistency and reproducibility of images, ability to obtain multiplane, high resolution, rapid, sequential whole breast images, and reduction of operator variability.[13] The use of such equipment should greatly simplify and improve the accuracy of breast volume measurements in the future.

Determinations of breast volume during the normal menstrual cycle reflected the individual variability that is consistent with clinical experience. In those women who did show changes during the cycle, the degree of change was substantial—up to 36% in one case in this small series—attesting to the reality of the premenstrual alterations that are commonly described. These findings are consistent with the water-displacement measurements of Ingleby.[4] Breast volume measurement should therefore prove useful in quantitating at least one feature of the premenstrual-tension syndrome.

While changes in breast size during the use of oral contraceptives are often mentioned, they relate most often to women in the postadolescent years whose maturation process is accelerated by a hormonal exposure more intense than that arising from endogenous sources. However, some degree of mastalgia occurs in a small percentage of adult women reporting side effects in clinical trials, and it was the authors' hope that this event could be quantitated and perhaps related to the estrogenic and/or progestational exposure. Milligan et al[3] have shown, by water-displacement methods, a progressive rise in breast volume during contraceptive-controlled cycles, while a small number of control cycles appeared to show a decline in volume around cycle days 9 to 17.

The data of the present breast-volume study do not demonstrate a statistically significant effect of the progestogen (norethindrone) incorporated in these oral contraceptives, even though a sixfold range of dosage was examined. However, the sensitivity of the experiment was relatively low, due in part to the small numbers involved and in part to individual variation in response of approximately 25%—a factor that will have to be considered in all studies of breast volume. An average change of 30% compared with control ($N = 15$) would have been required for an effect in the ethynyl estradiol 50 μg-norethindrone 1 mg group ($N = 10$) to be statistically significant, and a change of 40% for control versus 50 μg ethynyl estradiol-noreth-

indrone 2.5 mg ($N = 5$), because of the small group size. (A test group with $N = 70$ would be required to detect a change of 20% with a power of 0.8 and an $\alpha = .05$ or an $N = 100$ in both groups for a 10% change.) Thus, the authors' studies do not provide a definitive answer to this question. Additionally, a comparison of the effects of a progestational agent with and without concomitant estrogen would be of interest in view of the relationship of progesterone receptors to prior estrogenic stimulus. The effect of incremental estrogen dosage could be studied in a similar manner.

Together with the qualitative information on breast structure provided by ultrasonographic as well as mammographic techniques, useful noninvasive methods for studying endocrine effects on mammary tissue appear to be at hand.

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