QUANTITATIVE MEASUREMENT OF OPTICAL PARAMETERS IN NORMAL BREASTS USING TIME-RESOLVED SPECTROSCOPY: *IN VIVO* RESULTS OF 30 JAPANESE WOMEN

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ABSTRACT

Previous investigation has proved time-resolved spectroscopy to be applicable to measurement of optical parameters in the human breast. To increase knowledge of these properties *in vivo*, the optical parameters of healthy breasts were measured using time-resolved reflectance spectroscopy. A time-correlated single-photon counting method was used to obtain time-response curves for the breasts of 30 Japanese women. Values of μ_a (absorption coefficient) and μ_s' (transport scattering coefficient) were analyzed by fitting the curves to the diffusion equation. The relationships of optical parameters to age, body mass index (BMI), thickness of the breast, number of pregnancies, and menstrual status were examined. The μ_a and μ_s' ranged from 0.0024 to 0.0078/mm and from 0.63 to 1.08/mm, respectively. The values of μ_a and μ_s' showed a high correlation with age and BMI, respectively. The range of the optical parameters of the healthy breasts was determined. These properties may be strongly influenced by changes in tissue components related to aging, menstrual status, and so on. This optical information will contribute to the investigation of photon migration in the human breast.

Keywords time resolved spectroscopy; breast; optical parameters; absorption coefficient; transport scattering coefficient.

1 INTRODUCTION

Recently, the concept of time-resolved spectroscopic technique was used to measure optical path lengths in living tissue by Chance et al.[1] In time-resolved spectroscopy (TRS), the pathlength distribution of detected photons is obtained directly by measuring the intensity of light (number of photons) in the time domain.

Light passing through living tissue is influenced by both absorbing and scattering phenomena. It is important to understand these phenomena when determining the optical properties of various tissues and producing optical images. The absorbing and scattering phenomena are expressed as absorption coefficient μ_a and transport scattering coefficient μ_s' respectively. The analytical solution of a diffusion equation lets us know the values of μ_a and μ_s' in limited situations.[2] We investigated the applicability of TRS measurement to obtain the optical parameters (μ_a and μ_s') of tissues with finite geometries such as the breasts, and could quantify the parameters with errors of less than 10%.[3]

The human breast consists of glandular tissue, fatty tissue, and so on. The proportion of these tissues varies with age, menstruation, and other factors. The TRS measurement provides us with "average" information concerning the optical properties of various components in the breast *in vivo*. The optical parameters of the breast may reflect the proportion of component tissues. In the current study, we measured the optical parameters of 30 normal breasts and examined the relationship between age or other factors and optical parameters to increase our knowledge of the optical properties of the human breast.

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2 MATERIALS AND METHODS

2.1 SUBJECTS

TRS measurements were performed in normal breasts of 30 Japanese women aged 23 to 74. The characteristics of the subjects are summarized in Table 1. Their breasts were clinically healthy on the measured side. Three women had a present or past history of breast cancer on the contralateral side, but on the measured side showed no abnormal findings in both the x-ray mammogram and ultrasound examinations.

2.2 TRS MEASUREMENT

The time-response curves of the subjects' breasts were measured in a darkened room after obtaining their informed consent. The measurements were carried out on various menstrual days from 3 to 33 days for 15 premenopausal subjects, and 2 months to 29 years after last menstruation for 15 menopausal or postmenopausal subjects.

Figure 1 shows the experimental setup, which has been described in detail elsewhere.[3] Briefly, a picosecond light pulser (PLP) using a semiconductor laser emitted a train of pulses at a wavelength of 753 nm. Pulses irradiated the breast through a fiber collimator 1.8 mm in diameter. The diffusely reflected light was collected at a distance (D) of either 30 or 40 mm from the input site and guided to a microchannel plate photomultiplier (MCP-PMT) using a fiber optics bundle 3.0 mm in diameter. Then a time response curve was obtained using a time-correlated single-photon counting method. The measurement was completed at a peak count of 5000. The full width at half maximum of instrument function was less than 140 ps. An observed response and an instrument function are demonstrated in Figure 2.

During the measurement, the breasts were slightly compressed to the thickness (T) shown in Table 1 and fixed with a black holder. The measuring position was on the center of the compressed breast and at a distance of more than 25 mm from the chest wall to avoid a boundary effect. It took a few minutes to obtain a time-response curve.

The observed time-response curves were deconvolved with the instrument functions using the

Table 1 Subject characteristics.

Variable	Mean±SD
Age (years)	48.9±14.3
BMI (kg/m^2)	22.2±3.0
No. of pregnancies	1.8±1.3
T (mm)	43.2±4.8

Note: BMI, body mass index; T, breast thickness.

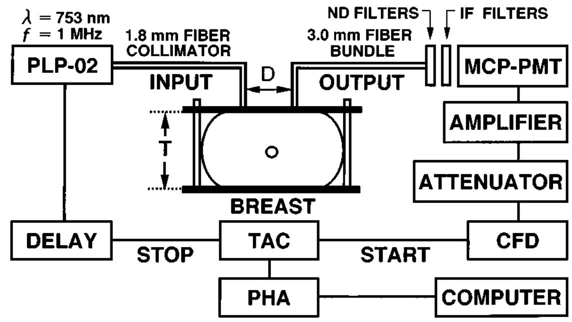

Fig. 1 Block diagram of the apparatus for measuring optical parameters in the breast. PLP, picosecond light pulser; MCP-PMT, microchannel plate photomultiplier tube; CFD, constant fraction discriminator; TAC, time to amplitude converter; PHA, pulse height analyzer.

Bayesian deconvolution procedure. We obtained the values of μ_a and μ_s' by fitting the deconvolved curves into the diffusion equation solved analytically by Patterson et al.[2] using the simplex method. The values of μ_a and μ_s' are expressed in a $\log_e$ scale.

2.3 STATISTICAL ANALYSIS

We examined the relationship between subject characteristics and optical parameters of the breasts. The relationship between age, body mass index (BMI), breast thickness (T), number of pregnancies (0, 1, 2 and ⩾3), menstrual status (0 =premenopausal women with regular menstrual cycle from 25 to 40 days, regular menstrual status, and 1=menopausal or postmenopausal women without regular cycles, irregular menstrual status), and optical parameters were studied using Pearson's moment correlation coefficients and multiple regression analysis (stepwise method).

We divided 22 women whose x-ray mammograms were available into two groups according to

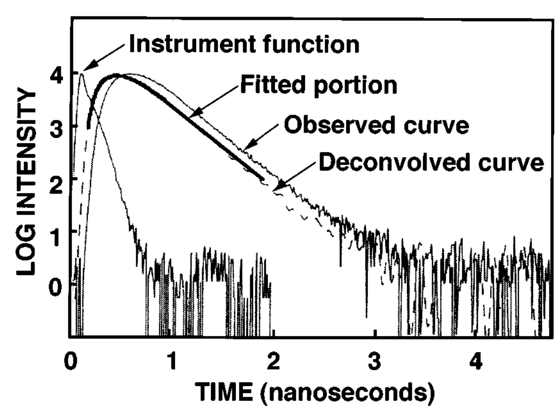

Fig. 2 Time-response curve observed in the normal breast of a 45-year-old Japanese woman. The observed curve is deconvolved with an instrument function (earliest curve).The deconvolved curve (second peaked broken curve) is fitted into the diffusion equation in the range shown as a thickened line.

mammographic pattern to make rough estimates of breast components; DY or P2, and N1 or P1, according to Wolfe's classification.[4,5] The N1 breast is composed primarily of fat. The P1 breast is composed mainly of fat and has prominent ducts occupying up to 25% of the breast. The P2 breast has prominent ducts occupying more than 25% of the breast. The DY breast is characterized by poorly defined sheetlike regions of densities without visible ducts. Comparison among the groups was performed using the Student t test after checking equality of variance by the F test.

3 RESULTS

A mean value $\pm$ standard deviation of μ_a was 0.0046 ± 0.0014/mm and a mean value $\pm$ standard deviation of μ_s' was 0.89 ± 0.13/mm at a wavelength of 753 nm. The frequency distributions of μ_a and μ_s' values are shown in Figure 3. The lowest values of μ_a (0.0024/mm) and μ_s' (0.63 /mm) were observed in the breasts of 68- and 74-year-old women in postmenopausal periods, respectively. On the other hand, the highest values of μ_a (0.0078/mm) and μ_s' (1.08/mm) were observed in the breasts of 28- and 47-year-old women with regular menstrual cycles, respectively. Figure 4 demonstrates the relationship between age, menstrual status, and optical parameters.

As shown in Table 2, the optical parameters were significantly correlated with age, BMI, and menstrual status, but not with the thickness of the compressed breast and number of pregnancies. We could not find a significant correlation between menstrual day and optical parameters in 15 premenopausal cases (Pearson's coefficients: 0.279, $p = 0.315$ for day versus μ_a', 0.262, $p = 0.345$ for day versus μ_s'). There was a significant correlation between μ_a and μ_s' values (Pearson's correlation coefficient: 0.671, $p<0.001$).

Menstrual status correlated highly with age (Pearson's correlation coefficient; 0.830, $p<0.001$), so we excluded menstrual status from the variables in multiple regression analyses because of collinear-

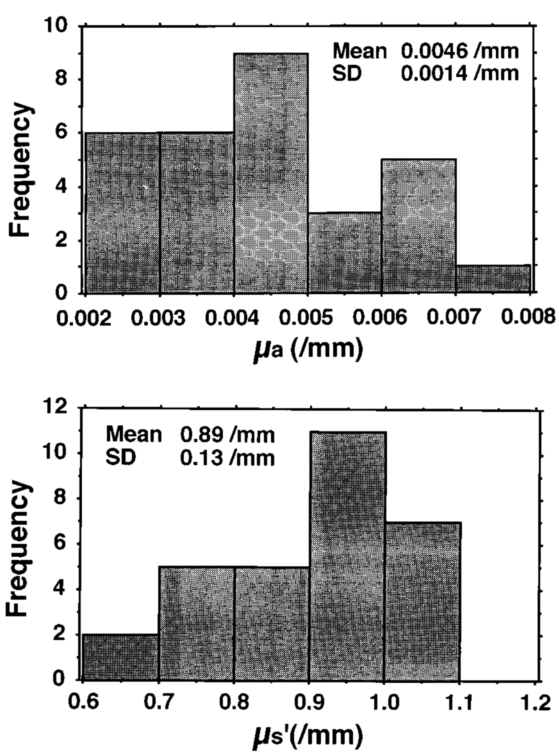

Fig. 3 Frequency distribution of μ_a and μ_s'.

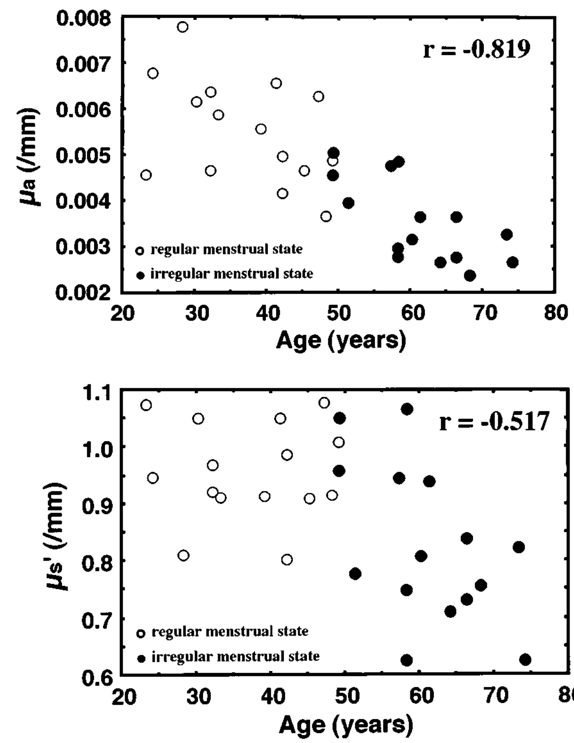

Fig. 4 Relationship between age and optical parameters. Open circles show women with a regular menstrual cycle. Closed circles indicate menopausal or postmenopausal women without a regular menstrual cycle. The "**r**" denotes Pearson's coefficient.

Table 2 Correlation between subject characteristics and optical parameters in the breast.

Variable	μ_a	μ_s'
Age	−0.819***	−0.517**
BMI	−0.717***	−0.682***
T	−0.251	−0.045
Preg.	0.134	0.260
Mens.	−0.716***	−0.481**

Note: BMI, body mass index; T, breast thickness; Preg., no. of pregnancies; Mens., menstrual status. All values are Pearson's correlation coefficients. ***$p<0.001$, **$p<0.01$.

ity. Table 3 shows the results of these analyses. Age, BMI, and number of pregnancies were significant variables for explaining the μ_a value, and BMI and number of pregnancies were significant for the μ_s' value. Age and BMI in particular contributed highly to the respective values of μ_a and μ_s'.

After confirming no significant differences in subject characteristics and optical parameters between the subjects with and without x-ray mammograms, we compared the group with the DY or P2 pattern and that with the N1 or P1 pattern. This result revealed significant differences in age, BMI, and μ_a value (Table 4). The values of μ_a were higher in breasts with the DY or P2 pattern than in those with the N1 or P1 pattern.

4 Discussion

There was a wide range in μ_a values. The lowest μ_a value of the breast was about one-third of the highest one and was approximately equal to the μ_a of water at a wavelength of 750 nm.[6] The highest value of μ_a was observed in the breast of a 28-year-old woman with a regular menstrual cycle. The higher μ_a values observed in young women may be explained by the greater content of fibroglandular tissue in the mammographically dense breasts.

In fact, the μ_a value was negatively correlated with both age and BMI and was statistically higher in the group with the DY or P2 mammographic pattern. It is impossible to discuss these factors separately because of the interrelation of age, menstrual status, body weight, and mammographic pattern.[7–11] However, all of these factors have an influence on the tissue component of the breasts. Both aging and menopause are strongly associated with replacement of glandular tissue with fatty tissue.[12,13] In general, women with high BMI have an abundant subcutaneous fat layer. Breasts with an N1 or P1 pattern have a higher proportion of fatty tissues and a lower proportion of dysplasia and glandular tissue.[7] Adipose tissue has a lower metabolism and a smaller blood (hemoglobin) volume. Because the main absorber in the breast is hemoglobin in the near-infrared wavelength, the proportion of the fatty tissue has a strong influence on the μ_a.

Table 3 Regression of optical parameters on subject characteristics.

Variable	μ_a	μ_s'
Age	−0.603***	NE
BMI	−0.353**	−0.732***
T	NE	NE
Preg.	0.225*	0.362**
Adjusted R^2	0.752	0.563

Note: BMI, body mass index; T, breast thickness; Preg., no. of pregnancies; Mens., menstrual status. Values are standardized multiple coefficients. NE: not entered. ***p<0.001, **p<0.01, *p<0.05.

Table 4 Differences in subject characteristics and optical parameters related to mammographic patterns.

	Wolfe's classification	
Variable	DY/P2 (N=13)	N1/P1 (N=9)
Age (years)	41.8±10.0	61.3±9.0***
BMI (kg/m^2)	21.5±2.9	24.5±2.2*
T (mm)	42.5±5.3	44.9±4.4
μ_a (/mm)	0.0054±0.0014	0.0035±0.0009**
μ_s' (/mm)	0.91±0.12	0.83±0.11

Note: BMI, body mass index; T, breast thickness. Values are expressed as the mean ± SD. Unpaired t tests were performed after checking the equality of variance with the F test. ***p<0.001, **p<0.01, *p<0.05.

The range of μ_s' values was not as wide as that of the μ_a values. The μ_s' values were related weakly with age, BMI, and menstrual status. Fat cells have coarse and scarce intracellular structures and fatty tissue has few intercellular vessels. So, scattering phenomena occur less frequently in fatty tissue. Because age does not contribute to the explanation of the μ_s' values, the abundance of subcutaneous fat tissues rather than the fatty replacement of glandular tissues influences the μ_s' values.

Obstetrical and lactational history is one of the important factors correlated with the onset and progression of breast involution.[11] Pregnancy accelerates the replacement of glandular tissue with fatty tissue in the breast. However, we unexpectedly found a weak positive correlation between the number of pregnancies and optical parameters.

The thickness of the breast during TRS measurement revealed no significant correlation with the optical parameters. This fact probably means that the boundary condition was negligible. Although the breast volume may be related to the breast component, the thickness of the compressed breast seems not to express the breast volume exactly because of its elasticity.

Peters et al. reported *in vitro* studies on optical properties of the breast components.[14] Their findings that adipose tissues had lower μ_s' values than glandular tissues at a wavelength of 700 nm support our results. However, their results of μ_a values are inconsistent with ours, probably because of the lack of hemoglobin-related information for *in vitro* studies.

In conclusion, we investigated the range of the optical parameters of healthy breasts. The optical properties range widely and probably depend on the proportion of component tissue. This information is believed to be useful in fundamental experiments to obtain optical images of the breast.

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