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April 1994 Annual Report. Period 3/15/93-3/14/94

"Early Detection of Breast Cancer and Recurrence Using Near Infrared Time Resolved Spectrophotometry"

Contract No. DAMD17-93-C-3071

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The following techniques are employed to measure the optical absorption and scattering factors of breast tissue: 1) In year 1, a pulse time device in which light at lower power (50 μW) laser diode is employed. The time delay in light propagation from the input to output fiber optic couplers is related to the scattering factor and the measured rate of decay of emerging photons is related to the absorption factor. 2) Phase modulation (years 2 and 3), which is more convenient and rapid, measures the phase shift of a high frequency oscillating light of approximately the same power and wavelength used in the pulse time method. Here, there is direct reading of the time delay which is characteristic of the scattering power when low frequency oscillation is employed. Contrast agents may be used to increase the tumor detection sensitivity. For example, the absorption of porphyrins at 620 nm and indocyanine green at 860 nm, afford possibilities to follow the time course of tumor uptake of optical contrast agents. Histopathological confirmation of diagnosis will be obtained and correlated with the optical and MRI results. Both the imaging and optical data obtained from this proposed project will facilitate research on using the optical properties of breast tissue to screen for early stage cancer.

pulse time device, phase modulation, contrast agents, screen for early stage cancer 23

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ANNUAL REPORT

Contract:	**#DAMD17-93-C-3071**
Title:	**Early Detection of Breast Cancer and Recurrence Using Near Infrared Time Resolved Spectrophotometry**
Period:	**March 15, 1993 - March 14, 1994**
Princ. Inv.	**Lawrence Solin, MD**
Co-Investigators:	**Britton Chance, Ph.D.**
	Susan Orel, MD

INTRODUCTION

Preliminary data on human subjects indicates that the absorption factor (μ_a) and scattering factor (μ_s') of near infrared optical radiation (670-780 nm) are several hundred percent larger in tumor than in normal breast tissue. High consistency in the absorption factor (μ_a) (average value is 0.0213 $\pm$ 0.005 cm^{-1}) has been obtained in 12 examinations of 5 normal subjects, providing a baseline for tumor detection. Thus the increased blood content of the tumor relative to the breast tissue affords a physiological contrast agent.

Two techniques are to be employed quantifying optical absorption and scattering factors of breast tissue: 1) A pulse time device (Year 1, Table I) in which a laser diode emits two colors of red light at lower power (50 μW). Light is scattered by the tissue and is picked up by a sensitive and fast detector. The time delay in propagation from the input to output fiber optic couplers is related to the scattering factor and the measured rate of decay of emerging photons is related to the absorption factor. Thus, these two quantities can be determined from the time course of light emission from various portions of the breast. These factors would be selectively modified by the presence of tumor within the optical field. 2) Phase modulation (Years 2 and 3, Table I) measures the phase shift of a high frequency oscillating light between the source and detector. The time delay is characteristic of the scattering. This apparatus is more compact and portable than the pulsed time method, however, both are suitable for clinical use.

Collaboration with Dr. R. Lenkinski and Dr. M. Schnall is assured by our concurrent study of the same patients as those examined by gadolinium-enhanced MRI (Magnetic Resonance Imaging). Histopathological confirmation of diagnoses will be obtained and correlated with the optical and MRI results.

The set of data acquired by either phase modulation or the pulse time method can be combined directly to give localized values of absorption and scattering properties of tissue. Imaging the spatial distribution of the absorption and scattering properties of the breast tissue is expected to increase the sensitivity for detecting tumor.

EXPERIMENTAL METHODS / RESULTS OBTAINED

The experimental methods used in these studies follow those of Aim 1 which "complements needle biopsy procedure with a fast localized optical field that includes the suspected tumor and detection quantitates μ_s' and μ_a characteristics" (see Fig. 1 below).

PLANNED SCHEDULE OF STUDIES

Year	1	2	3
Method 2 (Pulse Time)	+	-	-
Method 3 (Phase Modulation))	-	+	+
Method 4* (Amplitude Modulation)	-	+	+
No. of Studies	120	120	120
Expected Malignant	30	30	30

*120 patient studies with this method are proposed. It is proposed that 50 of these be studied in Years 2 and 3 **(from p 243 of original application)**.

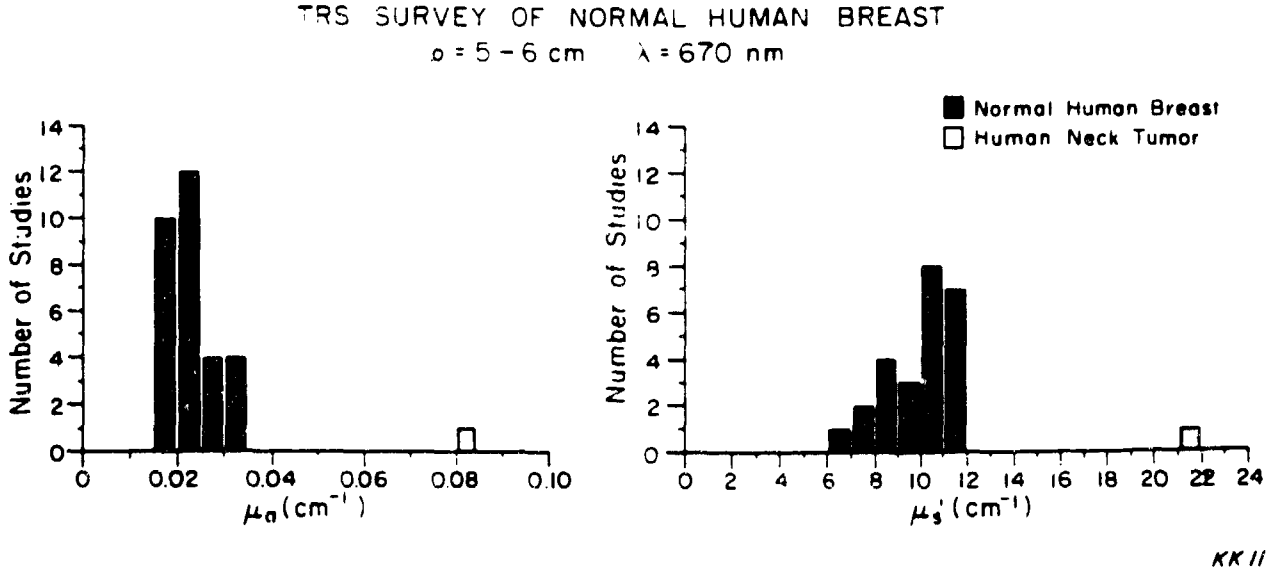

Figure 1. Histogram display (λ=670 mm of 22 observations of μ_a and μ_s' in a normal human breast over a wide ethnic and age population. It is seen that there is a tight clustering of both μ_a and μ_s' values for the normal breast. The characteristics of a human neck tumor are indicated to be widely separated from those of the normal human mammary.

Results of Studies

After 8.5 months of funding, we have studied 20 of 30 proposed patients and have decided to make 35 replicate studies of 20 patients at this time. A total of 700 breast observations, i.e., 35/patient of μ_a, and a total of 600 breast observations, i.e., ~37/patient of μ_s' at various locations (Nioka, S., et al 1994) are analyzed. Thus, a rigorous statistical analysis of these observations for these 20 patients is presented. The breasts contained tumors between 5 and 7 mm in diameter as determined by MRI gadolinium enhanced imaging. Figures 2 and 3 are intended to show the perturbation of μ_a, μ_s' values with respect to the control value Figure 1. The distribution of μ_a values is greater than in the normal breast as would be expected due to the tumor induced heterogeneity.

The values of μ_s' are significantly different from those of the control of Figure 1 which center around 5.5 cm^{-1} for the 20 tumor bearing breasts examined. This result is consistent with the data obtained under other support where the scattering of mitochondria in tumors appears less than other tissues, such as brain (breast adipose tissue has not yet been studied).

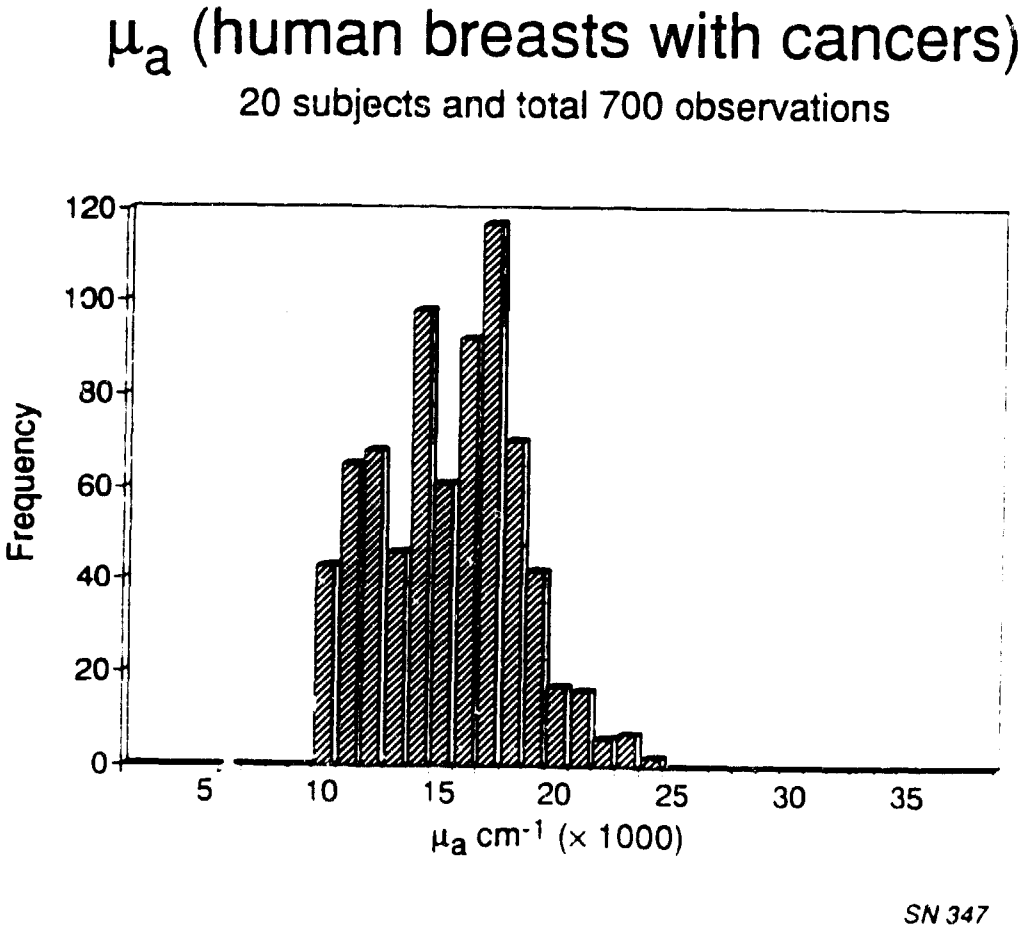

Figure 2. Distribution of μ_a values (times 1,000) for human breast with small tumors of the 20 subjects of this progress report.

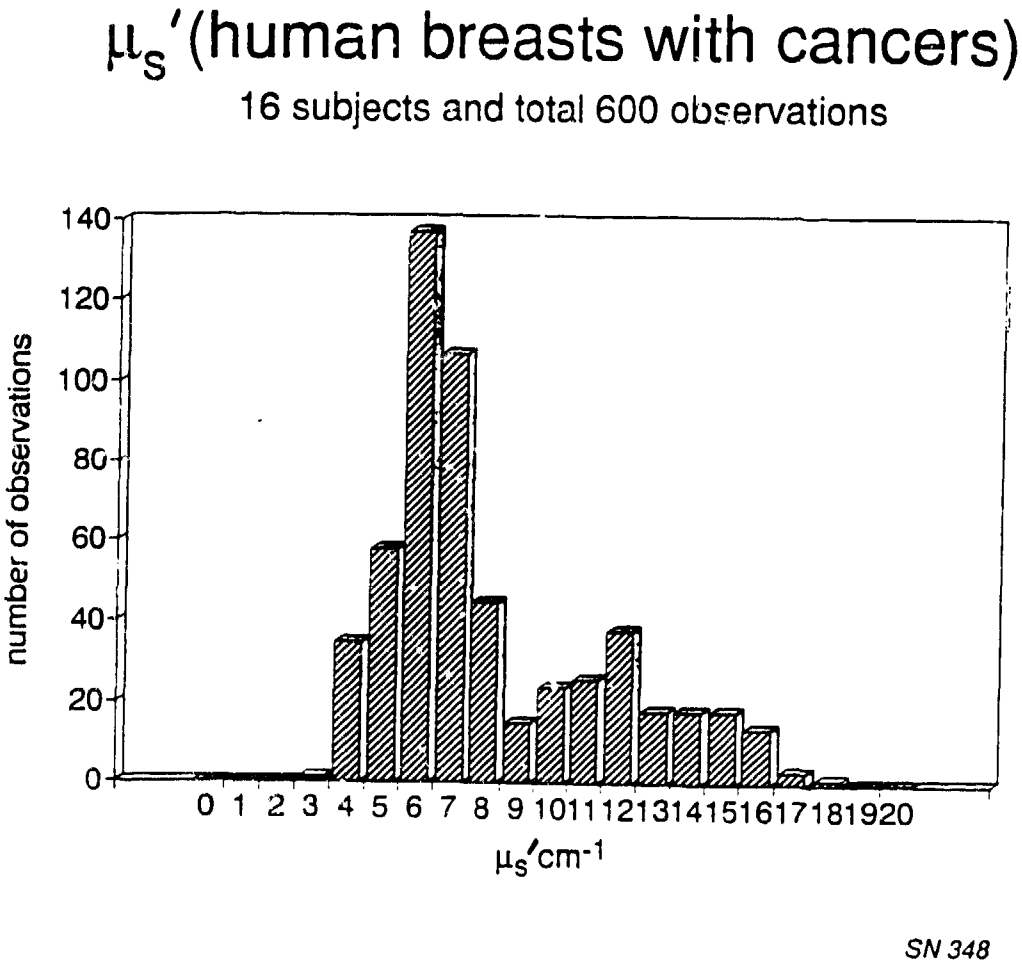

Figure 3. Histogram display of μ_s' values for human breast with small tumors of the 20 subjects of this progress report.

Thus we have achieved the goals of Aim 1.

Progress

The progress in Year 1 has been according to the proposed time table, namely the use of the pulse time method and we have been able to analyze 700 observations by TRS (time resolved spectroscopy) optical spectroscopy and imaging of tumor bearing breasts of 20 out of 30 patients studied at the date of reporting period (6/1/93 to 3/10/94; an interval of 8.5 months).

The protocol ensures that the breast studied is tumor bearing; candidates for surgical treatment were first studied by NMR/MRI using gadolinium chelate and then by the optical method, using as contrast, the absorption and scattering as proposed in the grant application. In this particular geometry, the patient is studied by MRI prone with the breast pendant. The MRI expected location of the tumor, as obtained from gadolinium contrast, is penciled on the breast and repeated optical scans of the tumor are taken with the TRS system. The data analysis has given both absorption and scattering values and

are given in the histograms of Figures 2 and 3 based on the data from the 20 patients so far studied. Tabular data are not needed in addition to the figures. See appended manuscript for further data and details.

Proposal for Year 2

The plan of studies for Year 2 includes the 10 remaining subjects of the 8.5 months of support of Year 1 and is according to the proposed schedule, Method 3, Phase Modulation and Method 4, Amplitude Modulation for the same number of tumors as studied in Year 1, i.e., 30. The patient group is from the same source as in this study, namely Dr. Susan Orel of Department of Radiology, Hospital of the University of Pennsylvania We expect the Phase Modulation studies to be more sensitive than TRS and the examination time will be shorter because of the faster response. In this case, the values of μ_a will be enhanced; phase modulation gives $\sqrt{\mu_s'/\mu_a}$ and data are obtained with two optical wave-lengths, usually 754 and 816 nm at which μ_s' is invariant and μ_a calculated, from which hemoglobin saturation is computed from known values of extinction coefficient.

Contribution to Decision Making

We have tabulated the data on μ_a and μ_s' from our patients as shown in Figures 2 and 3 and expect that further data will be even more refined and contributory to decision making. It is clear that a biomodal distribution is obtained in Figure 3 and may afford a decision criterion.

CONCLUSIONS

The conclusions of the studies of 20 tumor bearing breasts (700 measures for μ_a, and 600 for μ_s') indicate that the scattering factor may afford more sensitivity than absorption factor, under these conditions of observation, where low resolution imaging has been employed and the characteristics of the small tumor (5-7 mm diameter) may have been "diluted" out by the lack of imaging resolution. We expect to obtain greater sensitivity as the imaging ability is increased and as the phase modulation (Method 3) and amplitude modulation (Method 4) studies will be undertaken in Years 2 and 3 of proposed support.

REFERENCES

Nioka, S., Miwa, M., Orel, S., Schnall, M., Haida, M., Zhao, S. and Chance, B. (1994) Optical Imaging of Human Breast Cancer. ISOTT (Mainz, Germany) Adv. Exp. Biol. and Med. (P. Vaupel and D. F. Bruley, eds.) in press.

APPENDIX

Nioka, S., Miwa, M., Orel, S., Schnall, M., Haida, M., Zhao, S. and Chance, B. (1994) Optical Imaging of Human Breast Cancer. ISOTT (Mainz, Germany) Adv. Exp. Biol. and Med. (P. Vaupel and D. F. Bruley, eds.) in press.

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OPTICAL IMAGING OF HUMAN BREAST CANCER

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INTRODUCTION

Breast cancer has become one of the most serious epidemic diseases of middle aged women since the incidence has increased over the decade dramatically to one eighth or ninth of a woman's life time. Over thirty thousand woman die every year from breast cancer. Mortality can be reduced by early cancer detection. While X-ray mammography has been used to screen breast cancer currently, this technique has difficulty detecting breast cancer in some cases. The reasons are as follows: first, its detection ability has been restricted in some cases, as it is mainly sensitive to calcification, and is hard to distinguish between normal fibrotic tissue and cancer. Secondly for woman under the age of 35 years old, X-ray mammogram does not see through breast tissue with sufficient contrast, since young breast tissue is normally fibrotic. Thirdly X-ray radiation itself is carcinogenic, and frequent usage is not recommended. Recently, Magnetic Resonance Imaging has appeared to be a better technology than X-ray for new mammography (1), but it is more expensive and may not be used as a typical screening test at present. For these reasons, we are still seeking a better imaging technique to satisfy our needs for early breast cancer detection.

Despite the long history of the optical imaging technology, it has not been commonly used for breast cancer detection. Photon diffusion into the tissue makes a shadow of the object too obscure to use for imaging. The shadow imaging with continuous light (diaphanography) has been used in Asia, where average breast size is relatively smaller, but the shadow technique does not allow real imaging. Today, with new technologies, such as the time gated technique (2), long path diffusive photons are eliminated and therefore better images can be obtained. We have studied the ability of the time gated optical technique to human breast cancer.

We have chosen to develop the time gated optical technique for breast cancer detection for the following reasons. First, the breast tissue consists of a relatively low scattering media, namely fat, whose scattering coefficient is as low as 3 cm^{-1}. Second, the breast is located on a surface of the body and accessible to optical instruments. Thirdly, the time gated technique will allow selection of photons which have not diffused extensively (the extensively diffused photons are the ones which create obscure images). We selected 15 % of total photons, which relatively less diffused and arrived earlier than 85% of rest of photons. We emphasize not only possible improvement of sensitivity of detection by this time gated technique, but also high specificity of cancer detection by functional imaging. It creates an oxygen image through hemoglobin oxygenation, a blood volume image and a scattering image, and therefore can be helpful in interpreting the cell function of lesions.

Preliminary studies using time resolved spectroscopy (TRS) for characterizing tumors in the breast has been published elsewhere (2).

SUBJECTS AND METHODS

Thirty five women who had breast tumors detected by X-ray mammogram were subjects for the optical imaging. The age of the women spread from 30 to 84 years old. In them, 15 patients had lesions removed (lumpectomy operation). 20 patients had a single suspicious small tumor shadow in the mammography The tumor sizes are from 3 mm to 1 cm diameter. The post-operative scar tissue contains seroma, fibrotic scar as well as fibrocystic tissue, which was located initially. The size of the post-operative lesion is 2 cm to 5 cm in diameter. Approximately 30% of the patients have primary fibrocystic disease.

For the optical measurement, the breasts were compressed gently with two surface holders located parallel to each other (Figure 1). One surface holds an incident light guide and the other holds a light guide coupled to a detector, photomultiplier. In between the two light guides, time resolved spectra of the breast are acquired through transmittance mode. Then, the light guides are moved on the two surfaces 5 mm equally to obtain a two dimensional transmittance image. During the acquisition, light guide separation is fixed and constant.

Figure 1. The schema shows a set up for the optical breast imaging. The breast is gentry compressed with two surface holders located parallel to each other. One surface holds an incident light guide and the other holds a light guide coupled to a detector. In between the two light guides, TRS of the breast are acquired through transmittance mode.

A time resolved spectrometer (TRS) consists of two wavelength pulsed lasers, which emit lights at 780 and 830 nm, a photo multiplier (gallium arsenide), a time amplitude converter (TAC), a photon counting system, and data stored in a personal computer through an A/D converter. Time width of the pulsed laser light is 300 picoseconds through the TRS system and is used as an instrument function. This time resolution of the instrument function is good enough for human breast spectra to be used without deconvolution because the tissue spectra gained the half width more than 5 times larger than the instrument function. The two tissue spectra at the two wavelengths are acquired simultaneously by time sharing (delaying one pulse by 10 nanoseconds).

The two tissue spectra with wavelengths at 780 nm and 830 nm are analyzed to obtain absorption and scattering coefficients with a curve fitting program, which in principle, is based upon a diffusion equation using semi-infinite boundary conditions (Patterson and co-workers model) (3). Scattering coefficients are mainly calculated at maximum of photon arrival time in the equation. This requires 15 to 20 % of early arrival photons. The absorption coefficient is mainly calculated by the photon decay curve of the spectra in the equation, requiring 25 to 50 % of the early arrival photons. Hemoglobin saturation with oxygen (SaO_2) is calculated using the two absorption coefficients (4). As a presentation of blood volume, the two absorption coefficients are averaged. Scattering coefficients at two wavelengths are also averaged to yield a scattering image.

Three independent pieces of information are used to process three images from a set of measurements; the oxygen image is based upon hemoglobin saturation with oxygen, blood volume image from absorptions, scattering image from scattering coefficients. Once these three are calculated, they are fed into the image processing program, which translates the location of light guides on the breast surface as a pixel of the image. It therefore creates images of a 5 mm^2 resolution. Usually a 5 x 7 pixel image is acquired.

RESULTS

It is found that the ability to detect breast lesions by the time gated optical method depends upon the size of lesions, the thickness of the breast and contents of breast tissue (fat and fibrous tissue). Usually post-operative lesions can be seen in our optical images, but a small cancer mass of less than 1 cm in diameter is not detectable with 5 to 10 cm thick breasts. Here, we show 3 patients who have post-operative lesions with 4 optical images and MRI.

Case No. 1. The images shown in Figures 2 to 5 are from a 38 year-old patient whose cancer was removed one month previous (lumpectomy), and under pre and post radiation therapy, respectively. A 2 x 1.5 cm cyst is formed in the location, where a cancer mass was before operation (See MRI Figure 2, and 4 corresponding to optical images of Figure 3 and

Figure 2. MRI (lateral slice) of case 1, whose cancer was removed (lumpectomy) one month previously. This MRI was taken prior to radiation therapy (pre-radiation). The closed area shows the area that optical imaging was conducted (see Figure 3). Also note that a cyst 2 x 1.5 cm is seen in the location.

Figure 5). Light guide separation was 6 cm. The cyst had less oxygen level; O_2 saturation in Hb is 82% in the cyst and 85-87% in the surrounding tissue in pre-radiation (Figure 3-C). After radiation therapy, the size of the cyst became reduced and formed a heterogeneous fibrotic tissue (Figure 4). An overall lower O_2 level was observed in the same area in post radiation than in pre-radiation (Figure 5C as compared to Figure 3C), and similar heterogeneity was observed in the area where the smaller cyst is. The area where the cyst and fibrous scar tissue are located has less blood volume (less absorption (Figure 3-B,5-B)) and more scattering (Figure 3-A, Figure 5-A).

Figure 3. Optical images of case 1, under pre-radiation corresponding to Figure 2. A: scattering image. B: blood volume image C: oxygen image. Note that the cyst has low oxygen concentration than the surrounding tissue.

Figure 4. MRI of case 1, after a radiation therapy. The closed area shows the area that optical imaging was conducted (see Figure 5). The size of the cyst became reduced and formed a heterogeneous fibrotic mass due to the irradiation.

Figure 5. Optical images of case 1, post-radiation therapy, corresponding to Figure 4. A: scattering image. B: blood volume image C: oxygen image. The lesion is more scattering and contains less oxygen than the surrounding tissue.

Case No.2. The MRI and the optical image (Figures 6,7) is from a post lumpectomised cancer patient. She is 48 years old who has small to medium size breasts (light guide separation 4 cm). After lumpectomy, there is a 4.5 x 2.5 cm mass consisting of fibrotic scar tissue and cysts in the middle of her breast (Figure 6). The optical images were taken laterally covering between cysts and fibrotic tissues. The oxygen image shows that a part of the cyst has a low oxygen level indicating a quite heterogeneous profile (Figure 7-C). The oxygen level in the cyst capsule is particularly higher than the surrounding tissue. The blood volume image shows that the cysts have less blood volume (Figure 7-B). In addition, there is heterogeneity in the scattering images in the cysts as well as in the surrounding fibrotic tissue (Figure 7-A) constructing an image of scar tissue.

Figure 6. MRI of case 2, who has a large lesion after a lumpectomy. A lesion consists of cysts, fibrous scar tissue, and cysts.

Figure 7. Optical images of case 2. The images were taken from top-to-bottom (cardio-caudal) direction. A transmittance light was shed in the direction of indicated lines and between two lines (Figure 6). The line nearer to the nipple corresponds to the left line of each image. The right side of the images clearly show the lesion. Note that the lesion has a lower oxygen location, which scatters more than surrounding tissue, indicating a heterogeneity.

Case no.3. The patient is 52 years old and weighs 180 lbs. Her tumor in the breast is determined to be a cancer by biopsy. She already has gone through a lumpectomy followed by a radiation therapy (Figure 8).

The optical images (Figure 9) were taken with cardio-caudal direction. In the optical scattering image (Figure 9-A), there are two highly scattered masses, connected to each other by a capsule like structure. This capsule like structure has higher oxygen tension than those in the two masses (Figure 9-C). The two masses differ in blood volume (See Figure 9-B), one near the nipple has more blood volume than the other.

Figure 8. MRI (cardio-caudal direction) of case 3, post-lumpectomy. The closed area shows the area that optical imaging was conducted (see Figure 9).

Figure 9. Optical images of case 3, corresponding to Figure 8. A: scattering image. B: blood volume image C: oxygen image. There are two highly scattered masses connected to each other by a capsule like structure. This capsule has higher oxygen tension than in the two masses.

DISCUSSION

Clearly, we have demonstrated that the time gated optical imaging technique is capable of imaging a relatively large object. However, this technique does not yet clearly detect a small cancer (generally smaller than 1 cm), therefore we did not include those small tumors in this report. It is shown that the time gated imaging system is not yet as precise as X-ray mammography for lesions smaller than 1 cm in size. However it is certainly better than the current diaphanography in principle.

In the optical imaging technique, the main cause responsible for low resolution of image is photon diffusion. For the human breast image, conditions for the continuous wave technique (any technology which uses CW light or current diaphanography) are viable in breasts that are small, thin and fatty, and having tumors larger than 1 cm in diameter. Since the CW technique will not satisfy most of needs for early detection of breast cancers, we have developed a time gated photon imaging system to test feasibility for the purpose. Scattering and absorption images use only 15-20% and 40-50% of early arriving photons respectively, which therefore eliminates most of more diffusive photon, that create obscurity. The results show that the scattering image may have more clearer images of lesions than those used absorption (oxygen and blood volume images) because of narrower time windows for scattering images.

It is clear that this time gated system is not adequate to show a high contrast of lesions of less than 1 cm in size from surrounding tissue.The cause of low resolution comes from the many factors. First, although fortunately the breast contains substantial amounts of fat, whose scattering factor is low compared to any other tissue constituents, contrast between fat and fiber and tumor is not always substantial enough. Secondly, differences of oxygen tensions or blood volumes between those tissue components also may not be substantial enough. Thirdly, the technique we use here presents a number in a pixel as a mean value of a long tissue mass across the two light guides, and can not present a small lesion.

These problems can be solved by finding causes of obscurities. A more sophisticated image reconstructing technique such as inverse recovery technique (5), will better adapt photon diffusion characteristics into the image construction procedures. In addition, we will be able to obtain higher resolution images with a contrast agent, such as cardiogreen. which may accumulate in the lesions with permeable capillaries and more circulation. One of the optical techniques, the phased array system using phase modulation device will be expected to give better resolution, and will be suitable for detecting a small object (7). We are in the early stage of developing the optical imaging, and in the future attempts to improve substantially the quality of optical imagings will be pursued.

SUMMARY

Since an increasing number of breast cancers have been reported in recent years, there is a need for improving techniques for early detection of the breast cancer. Here we tested a time gated optical imaging technique as a tool for imaging human breast. Pulsed laser light at wavelengths of 780 and 830 nm are transmitted through human breast tissues and time spectra of the diffused light through the tissue are recorded over nanoseconds. Data from different locations are acquired and used to reconstruct a two dimensional image as a set of spectra in pixel form. The imaging consists of absorption and scattering coefficients, and the absorption coefficients at the two wavelengths are related to oxygen concentration and blood volume. The analysis of these coefficients is based upon the early arrival photons, therefore allowing construction of a better image than those from the current diaphanography. We demonstrate images of breast cancer, cysts created after lumpectomy, and consequences of radiation therapy. Results show that time gated optical imaging can image oxygen concentration in the cancerous and fibrotic breasts. Resolution of the imaging for smaller tumor size needs to be improved.

ACKNOWLEDGMENTS This work was supported in part by NIH grants CA 50766 and USAMRDC DAMD 17-93-C3071.

REFERENCES

1. Orel SG, Schnall MD, Livolsi VA, et al. MR Imaging of suspicious breast lesions with radiologic pathologic correlation. Radiology. in press.
2. Kang, KA, Chance B, Zhao S, Srinivasan, Patterson E, and Troupin T. Breast tumor characterization using near-infra-red spectroscopy. SPIE Proceeding. vol.1888. 1994. in press.
3. Chance B, Leigh JS, Miyake H, Smith D, Nioka S, Greenfield S, Finander M, Kaufman K, Levy W, Young M, Cohen P, Yoshioka H, and Boretsky R. Comparison of time resolved and unresolved measurements of deoxy hemoglobin in the brain. Proc. Nat. Acad. Sci. 85:4971-4975. 1988.
4. Patterson MS, Chance B, and Wilson B. Time resolved reflectance and transmittance for the noninvasive measurement of tissue optical properties. J. Appl. Optics. 28:2331-2336. 1989.
5. Sevick EM, Chance B, Leigh J, Nioka S, Maris M. Quantitation of time- and frequency-resolved optical spectra for the determination of tissue oxygenation. Anal. Biochem. 195:330-351. 1991
6. Schotland J, Haselgrove J, and Leigh JS. Photon hitting density. Applied Optics. 32: 448-453. 1993
7. Chance B, Kang K, He L, Wang J, and Sevick EM. Highly sensitive object location in tissue models with linear in-phase and anti-phase multi-element optical arrays in one and two dimensions. Proc. Natl. Acad. Sci. USA. 90:3423-3427. 1993.

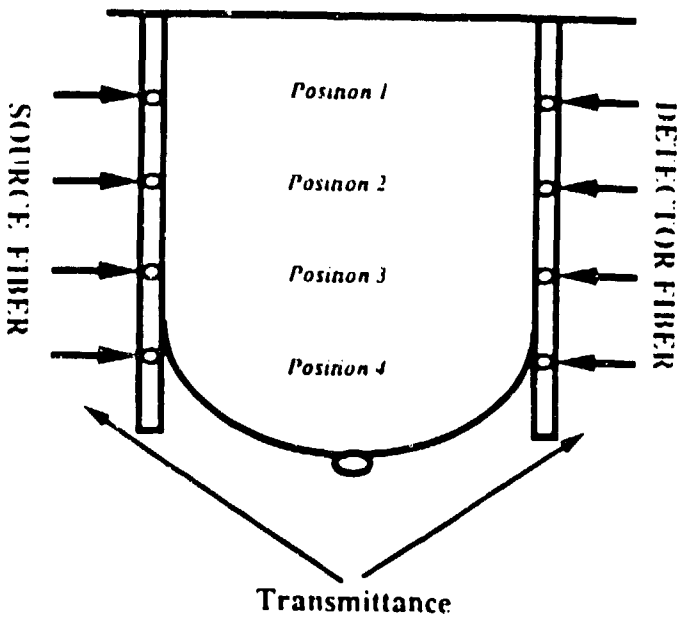
CHEST
Position 1
Position 2
Position 3
Position 4
SOURCE FIBER
DETECTOR FIBER
Transmittance

Figure 1

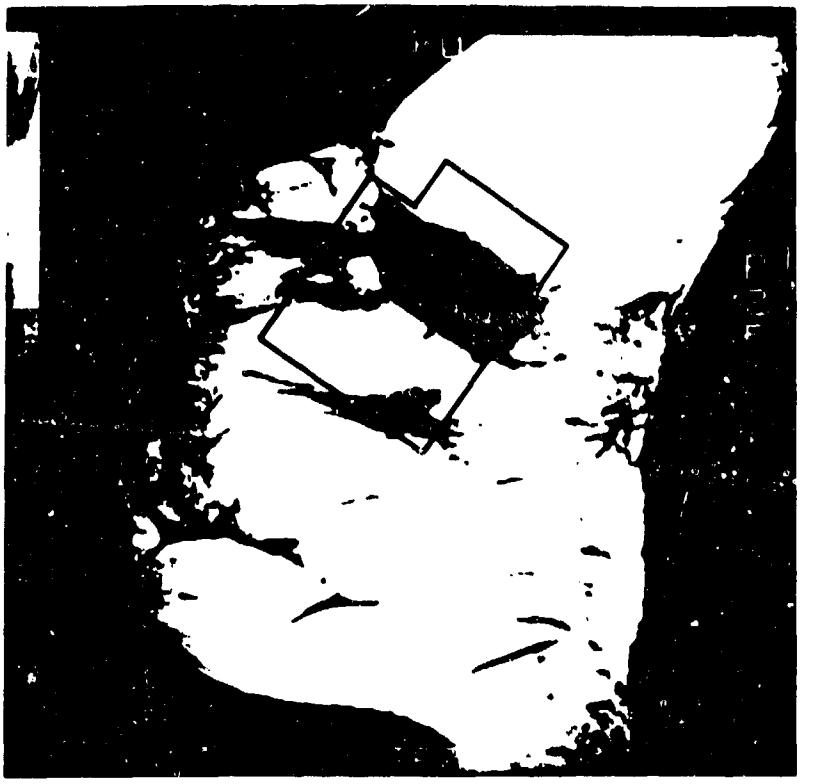

Fig 2

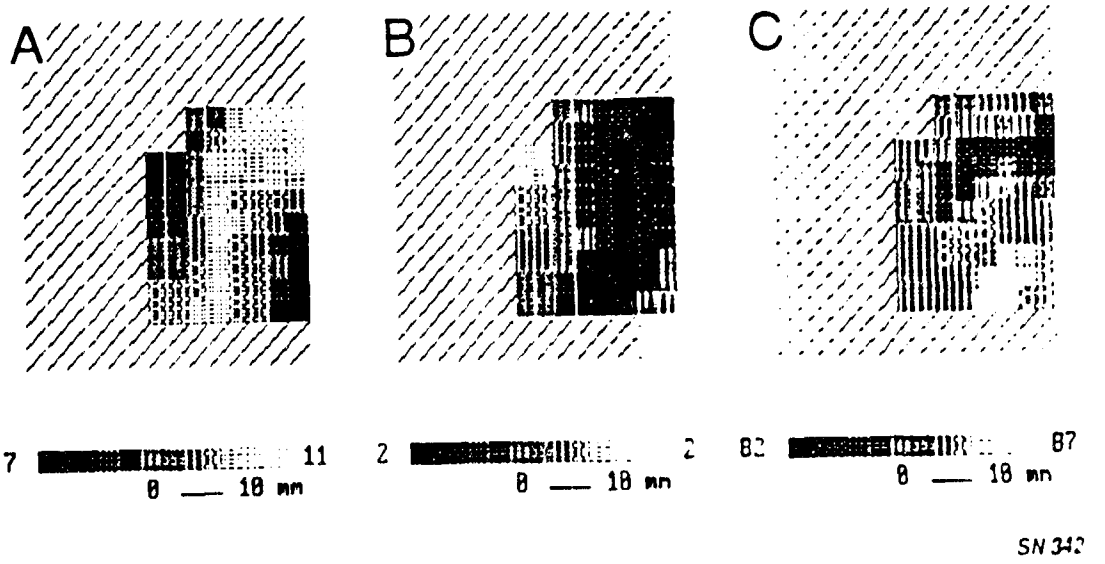

Fig 3

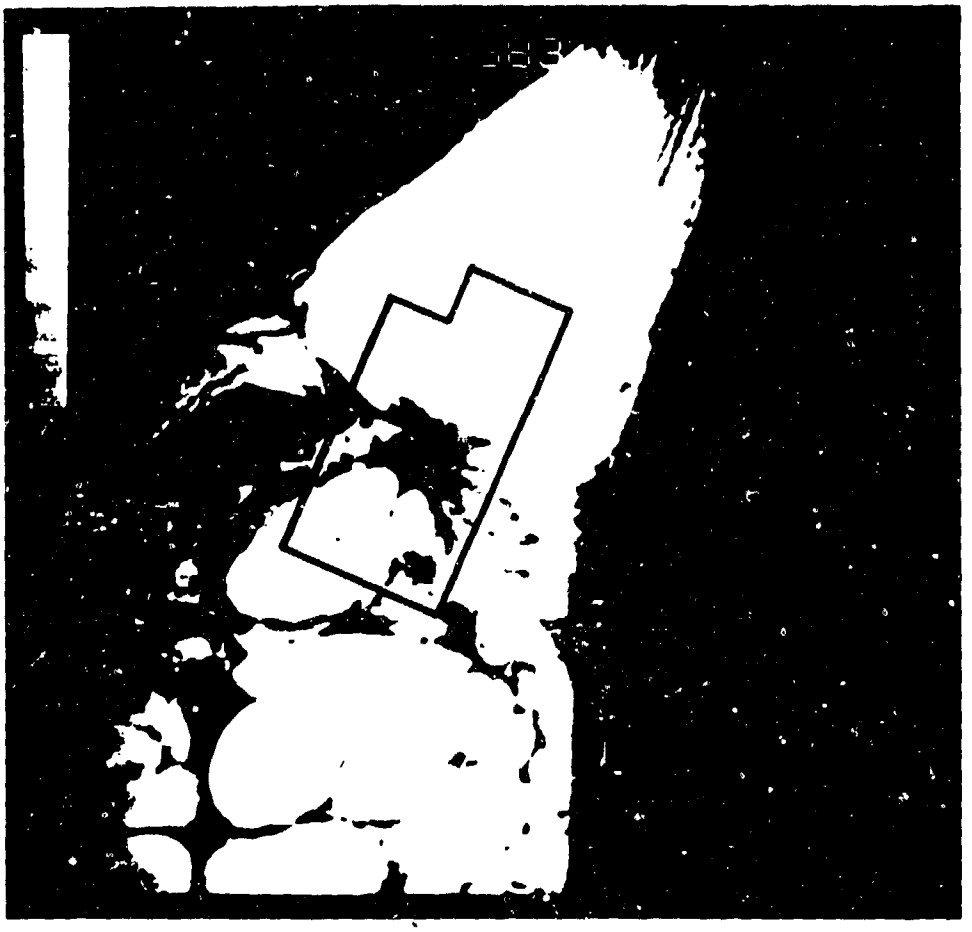

Fig 4

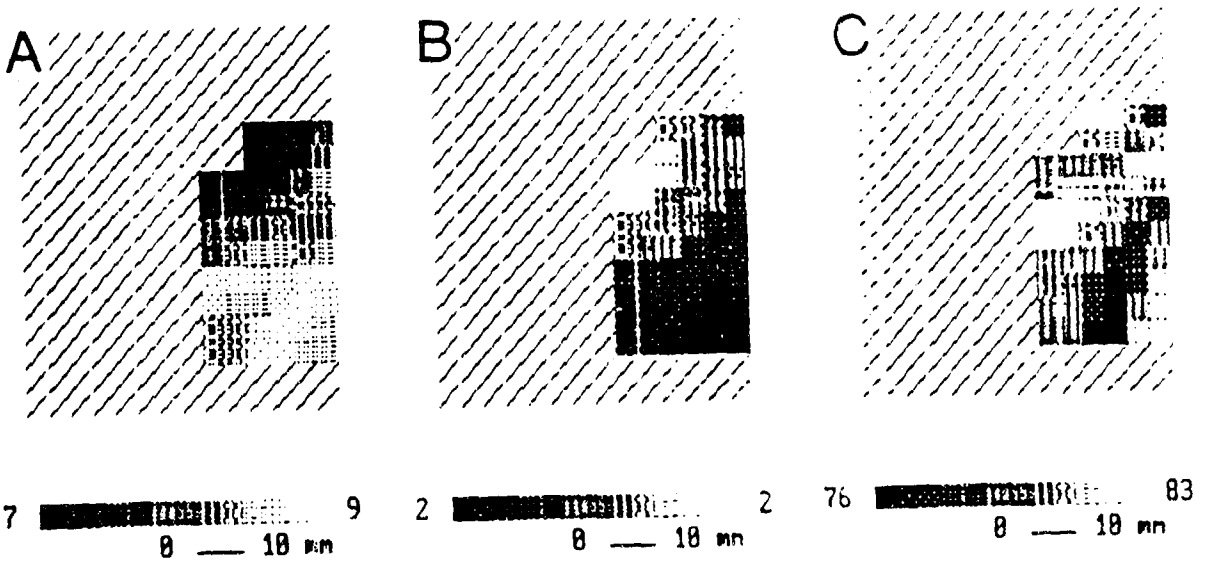

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Fig 5

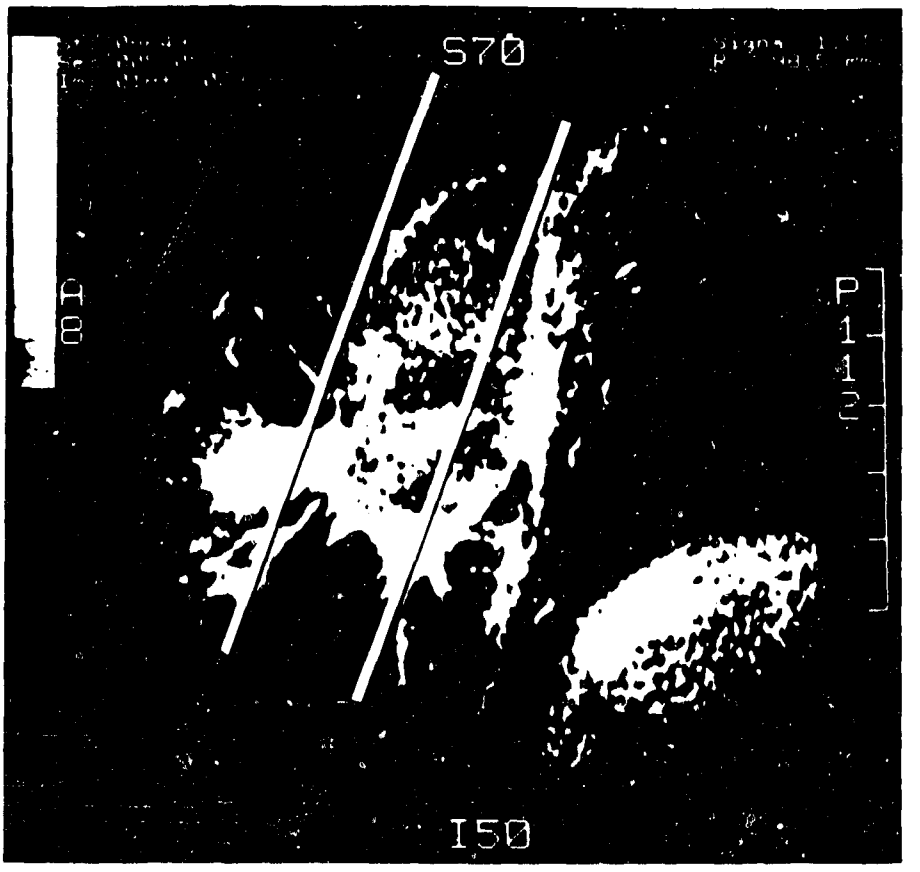
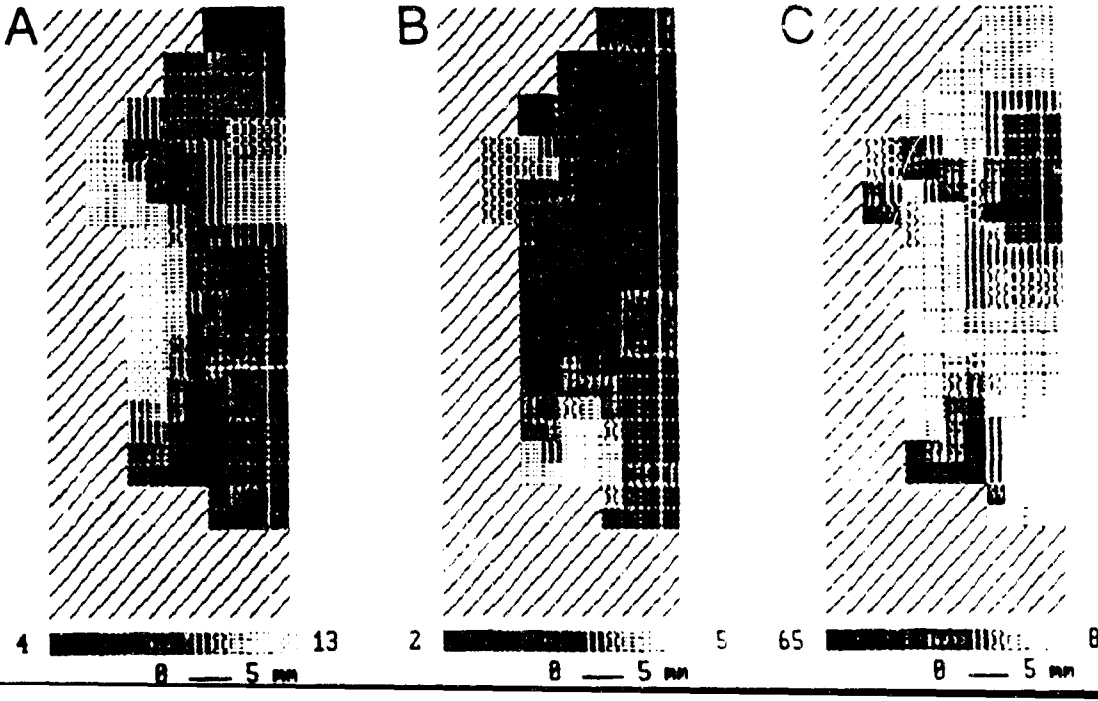


Fig 6

Fig 7



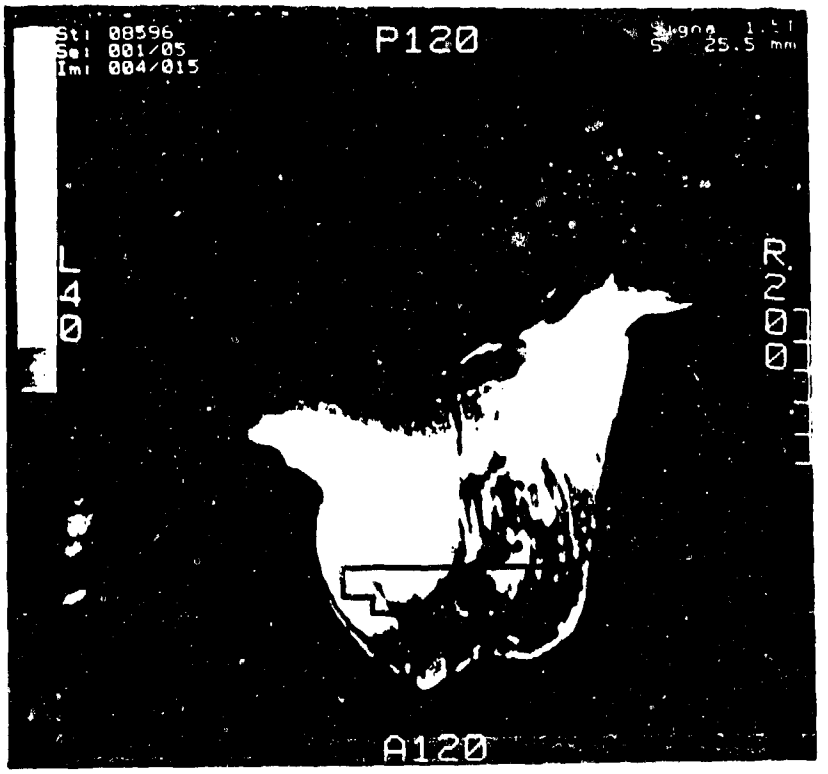


Fig 8

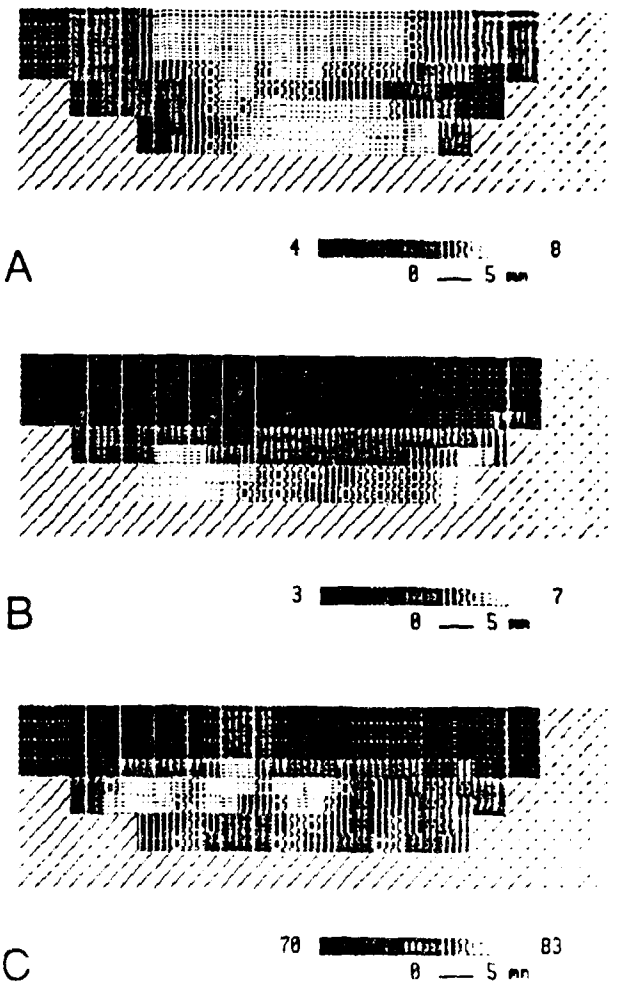


Fig 7