

EARLY DETECTION OF CARCINOMA OF THE BREAST*

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The breast is the most common site of primary carcinoma in women, breast cancer representing about 22% of all their malignancies. It develops in about 5% of all women, and when it does, only about 50% live for longer than 5 years.

Eminent authorities, using carefully controlled series of patients, have studied the long-term survival of breast cancer cases. International vital statistics have also been collected and analysed. The results have shown that there is an almost uniform and constant trend, the over-all survival figures showing either nil or only a very slight improvement throughout the years. Despite all the amazing and brilliant modern medical and surgical advances, and the acceptance and use for over 50 years of radical mastectomy or various modifications thereof by ever-increasingly well-trained surgeons, reinforced by powerful radiotherapeutic aids, the over-all survival rate for this terrible disease has not been improved to any substantial extent.

Many believe in the 'pre-determinism theory', which states that the eventual course of the disease is determined in the preclinical stages. Those who do may tend to adopt a pessimistic attitude, reasoning that the outcome will be the same irrespective of the treatment. The relation between the duration of symptoms and eventual survival is not always proportional. This is because of the varying pathology, growth rate, host resistance, etc. Sometimes those with a short duration of symptoms live a much shorter time than those with a longer history.

However, turning again to statistical evidence, it is found that there is a very close correlation between the duration of the disease and its stage of advancement. This, in turn, is reflected generally in the prognosis and survival rate; the shorter the time, the better the chance of survival. In 1957 Robbins and Gross, reporting on a review of clinical material from the Memorial Hospital in New York, found that in those patients whose delay in seeking treatment was less than one month from the time of discovery of the tumour, 45% had 'early cancers' (first stage, i.e. no axillary spread), whereas of those who delayed for longer than 12 months only 25% were 'early'.

The average survival rate of patients with untreated breast carcinoma is about 3 years, for treated breast cancer about 5 years, and for those in whom breast cancer was treated at the earliest possible time about 13 years.

It has been generally accepted by surgeons when dealing with carcinoma of the breast that the smaller the size of the tumour, the better the results. Patients with stage 1 carcinoma and a small tumour had a 74% 5-year survival, whereas those with large tumours had a 53% 5-year survival, treatment being the same in both instances. Thus the larger the tumour, the worse the prognosis; but the tumour size alone is not an infallible index of prognosis. When special cancer detection centres are used for periodic detection examinations, early asymptomatic breast

cancer discovered at these examinations and treated show a remarkable 5-year survival rate, much higher than for those patients whose breast cancers are found in a routine manner. Thus the importance of early diagnosis cannot be too strongly stressed, and it must be generally accepted that early recognition and treatment will very materially improve results.

However, the term 'early' must be very carefully defined, as it can mean different things to different people. 'Early' in the clinical sense could mean the presence of a palpable tumour with the recent onset of signs and symptoms. 'Early' to others could signify a tumour in its early stages before it has become clinically apparent.

Our principal aim in fighting this disease should therefore be directed towards finding and treating the early case; early especially with regard to the advancement of the disease, rather than early referable to the duration of symptoms. The ideal is to find not only the early clinically palpable tumour, but, better still, the tumour which has not yet reached this stage.

MEANS OF EARLY DETECTION

What present-day means have we at our disposal which could help achieve the above aim?

1. Improved education of medical practitioners and the general population.
2. Special early cancer detection centres.
3. Mammography.
4. Thermography.
5. Estimation of the hormonal content in the urine.
6. Cytological examination of cyst aspirate, nipple discharge and needle biopsy.

Improved Education of Medical Practitioners and the General Population

About half of all females with carcinoma of the breast reporting for treatment have had symptoms for longer than 7 months, and the average mean delay is calculated at around 7½ months.

When considering the causes of this extraordinary delay, factors relating not only to the patients but also to their medical practitioners should be considered. It is often found that the doctor is at fault in wrongly adopting a 'wait and see' policy, or in having too much confidence in his own ability to diagnose and to differentiate between various lesions.

The reasons for the patient delaying are numerous, some of the more common being ignorance, lack of financial means, hopefulness that the mass would 'go away', a false sense of security because of the absence of pain, and often paradoxically because of the fear that they might in fact have cancer.

Through every available method the population should be educated that carcinoma of the breast is not uniformly fatal, and that proper early treatment will cure the majority. Females over the age of 30 years should be taught to practise regular self-examinations, by means of observation, carefully comparing the breasts with the aid

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of a mirror, and by self-palpation. Physicians should be taught to regard every mass in the breast as malignant until proved otherwise.

Special Early Detection Centres

The public should be well aware of their existence, and should be made welcome to report for regular examinations. Here full and careful case history notes, including family history, should first be taken, followed by a thorough and careful examination. Then, when indicated, patients should be subjected to thermography and mammography examinations, and hormonal estimations should be carried out on their urine. Cytological services should also be available. At these centres the patients should be educated in all aspects concerning carcinoma of the breast.

These early detection centres may be confined solely to examination of the breast, but often they may be appropriately associated with early detection of carcinoma of the cervix and uterus, when regular examinations and special smears could be done at the same time.

In those areas where special detection centres have been established, statistics show that many early asymptomatic carcinoma cases are detected and treated, and that these show a remarkable 5-year survival rate, much higher than in those average patients whose breast cancers are found in the usual manner when reporting to a doctor after having developed symptoms or noticed the presence of a mass.

Mammography

Mammography, in experienced hands, and using the correct equipment, has today reached a very high degree of perfection, and can be of inestimable help in cases of breast pathology. It should be used by the clinician to obtain the maximum possible evidence, not only to determine the presence or otherwise of a breast lesion, but to give a greater knowledge regarding character and extent of the disease and thus aid towards a more positive diagnosis and facilitation of the planning of future treatment.

The following are the principal indications for performing mammography:

- (a) Mass screening of the population with no breast complaint. Carcinoma was found in about 3 cases/1,000 in postmenopausal women.
- (b) Where a strong familial history of carcinoma of the breast is present.
- (c) Following suggestive thermography.
- (d) Following suggestive hormonal studies of the urine.

It should also be done as a survey procedure when looking for a primary site of carcinoma, and the second breast should also be examined, either in a case with clinical signs of carcinoma in a breast, or following mastectomy for carcinoma of one breast. The procedure is valuable in large, pendulous breasts where physical examination of any accuracy is impossible.

Cases which present with symptoms or signs referable to the breast but without frank palpatory findings in the breast *per se*, such as retraction or eczema of, or discharge from, the nipple, suspicious skin changes such as areas of thickening, redness, retraction or flattening, or

vague symptoms referable to the breast, such as pain, discomfort, generalized tenderness or fullness, are eligible for mammography.

Any of the above signs may be the first indication of serious underlying disease, despite negative findings on palpation of the breast. Mammography may reveal pathology, or alternatively a negative mammogram affords considerable reassurance.

Mammography is invaluable in cases presenting with confusing palpatory findings such as a generally lumpy breast without any dominant nodule or gross fibrocystic disease of the breasts, in which a possible underlying carcinoma may be present; in cases in which the breast is too painful to examine properly; and in cases during pregnancy and lactation where either it is too difficult to examine properly, or the patient is in the first trimester and one wishes to avoid any operation or anaesthesia.

It helps in difficult cases to select the correct site, and/or to make sure that the correct site has been selected, and the intended mass correctly biopsied or excised, by taking 'before and after' pictures. It is also of help to estimate the response to therapy, for example following treatment for inflammation, irradiation for carcinoma or systemic or hormonal therapy.

It is very interesting to note that generally those carcinomas which are easy to detect on palpation may be difficult to find on X-ray, and vice versa.

Mammography is a time-consuming procedure, and therefore mass examination is not very practical. The radiation hazard is practically negligible if care is taken, and in expert hands an accuracy of between 80 and 98% can be obtained; but despite this, mammography should always only be regarded as a supplementary examination, and should never replace physical examination by an experienced clinician. It is certainly not a substitute for biopsy.

Thermography

The temperature record of a patient's illness is generally accepted as being important, and its use on a hospital chart is regarded as routine.

It was realized that if the oral temperature record could be so helpful, then the use of a very accurate and sensitive modern heat-measuring apparatus should prove to be even more so. The heat generated by the body is in the form of infrared rays, and in order to obtain a visible image of this infrared pattern of the body a method was needed to convert the emitted invisible waves into visible light. The availability of semi-conductor detectors made it possible to register infrared radiation with great speed and accuracy, and thus the way was opened to develop a machine for use in the medical field. Thermography machines are in use today and produce a thermogram record in a matter of a few minutes. Other variations of machines provide instantaneous observation on a cathode-ray tube similar to a television screen, and associated photographic equipment can produce pictures in these cases for clinical records.

Thermography, while used to examine any part of the body, is especially applicable to examination of the breast, and clinically has been used mainly in this field. When it was recognized that skin temperatures are generally elevated in areas overlying a malignant lesion, and not

solely confined to areas of inflammatory processes, their importance in the detection of carcinoma was realized.

Thermographic machines produce thermal images, and the clinical essence of the matter lies in the detection of departures from bilateral thermal symmetry. The method of operation is entirely passive, utilizing only the radiations naturally emitted by the skin itself. It is thus entirely safe and may be used freely without fear of discomfort or danger to the patient (Figs. 1-5).

Before examination, the area of the body to be photographed is exposed and allowed to cool off for at least 10 minutes at room temperature. In addition a fan may be employed, or the skin sprayed with alcohol to increase the cooling effect.

Apart from its diagnostic usefulness, thermography may also supply prognostic data. Malignant lesions have an associated wide range of skin temperature elevations. These may extend from zero to 4°C. Low temperature elevations appear to have a better prognostic implication than those with higher temperatures.

Thermographic results for a large series of cases are in general still being evaluated, but some authorities already claim a high degree of accuracy.

Benign lesions of the breast can also sometimes be associated with skin temperature elevation. Among these are included inflamed cysts, many fibro-adenomas (especially actively growing ones), some cases of proliferative epithelial hyperplasia and breasts in certain periods of glandular activity, e.g. during adolescence, pregnancy and lactation and with the use of anovulatory drugs.

In some circles it is felt that the relationship of a rise in skin temperature in non-malignant cases should be carefully studied in the hope that this may enhance our knowledge of breast physiology and perhaps help to determine the type of breast most likely to develop carcinoma.

Alteration of the tumour temperature can be produced by the administration of hormones or by hormone surgery. Most breast cancers coming to operation measure at least

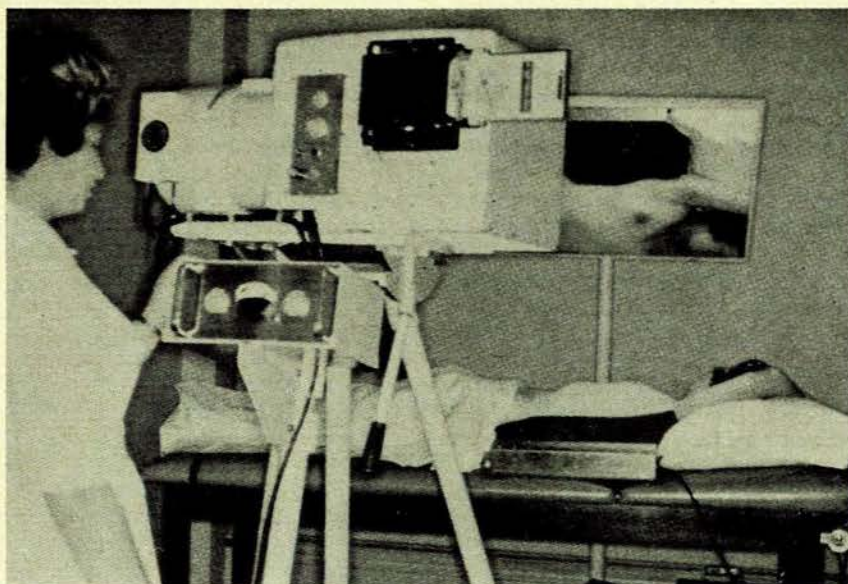


Fig. 1. A thermographic apparatus as currently used in examination of breasts. The patient is rotated slightly to the right so that the left breast lies flat against the chest wall. The radiation from the breast is then reflected into the apparatus by the front surfaced mirror above the patient. Lying on the table alongside the patient is the standard grey scale which is included with the scan of the patient.

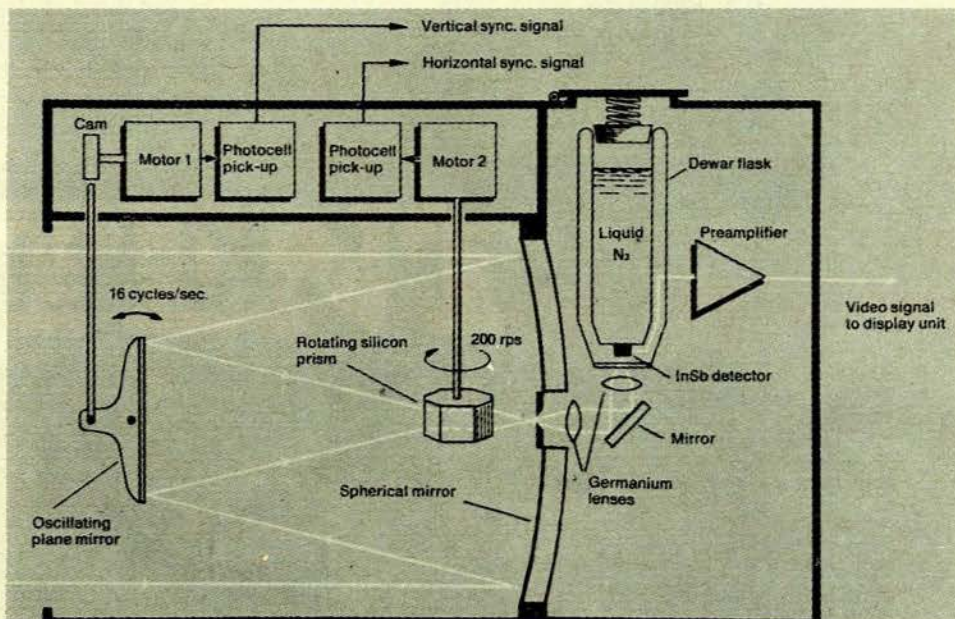


Fig. 2. Demonstrating the internal functioning of a thermogram machine. This system uses a spherical mirror to focus incoming infrared radiation on a plane mirror. The plane mirror tilts up and down to deflect the infrared signal vertically, and reflects the scanned beam to a four-sided prism. From the prism, the beam is optically focused on a crystal detector in the dewar where it is converted to low-level electrical signals; then the signals are amplified and transmitted to the display equipment. All the power required for the camera is transmitted from the oscilloscope via the connecting cable.

3 cm. in diameter, and this may represent a relatively advanced stage in the disease. Tumours smaller than this may be difficult to detect clinically, and it is especially in these cases that thermography may be of most help.

Another instance where it may be of great help is in deciding what actually constitutes a definite mass when palpating a very nodular breast. Most important, it may

prevent a small neoplastic area being missed in a breast dominated by larger lumps or cysts which disguise the underlying carcinomatous mass.

Thermography as a means of investigation is still in its infancy, and further clinical trials as well as research are needed before we can evaluate its true worth in the medical field.

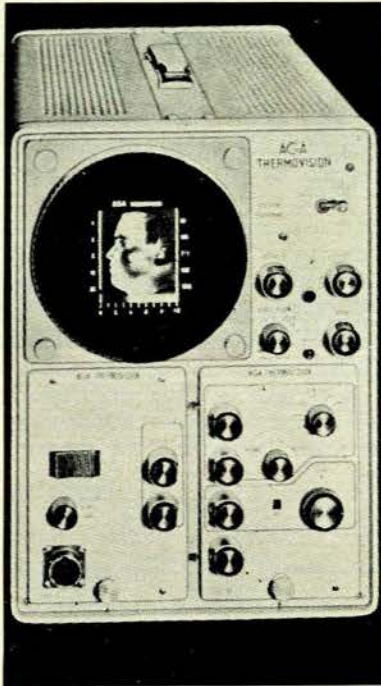


Fig. 3. A display unit of a thermographic machine showing the image, in this instance a face, displayed on a screen.

Estimation of the Hormonal Content in the Urine

Estimation of the hormonal content in the urine may be valuable in determining those cases likely to develop carcinoma of the breast.

The idea arose following investigations of the excretion of androgen and corticosteroid metabolites in the urine of patients with early breast cancer. These showed that the mean excretion of corticosteroid metabolites (17-hydroxycorticosteroids) and androgens (etiocholanolone) was subnormal, and when the results of the assays of these components were combined in a discriminating function, there was a negative discriminant in about half the patients, whereas this was a rare occurrence in normal women.

In an attempt to prove the above, the Department of Surgery at Guy's Hospital in London, in association with the Imperial Cancer Research Fund, undertook the 'Guernsey Trial', which is a prospective study of a normal population. Volunteers between the ages of 35 and 55 years were needed who would provide one complete 24-hour collection of urine, and who could subsequently be closely followed and not lost to follow-up. To achieve this ideal situation, a closed stable population was needed, and one that had a limited number of hospitals and doctors. The island of Guernsey in the Channel Islands, with only one hospital and 23 doctors, fitted the bill admirably. The help of two local newspapers and a local television service was enlisted, and a local nursing sister was employed on a full-time basis. Urine specimens, together with a completed questionnaire, were collected, and the urine was immediately stored at -20°C , and then flown to London laboratories for analysis.

Reliance was placed on the local Guernsey doctors and hospitals for further information, should one of these women subsequently develop carcinoma of the breast.

Over a period of 5 years, 24-hour specimens of urine were collected from 4,860 women in this age-group; 19 of these women have since developed carcinoma of the

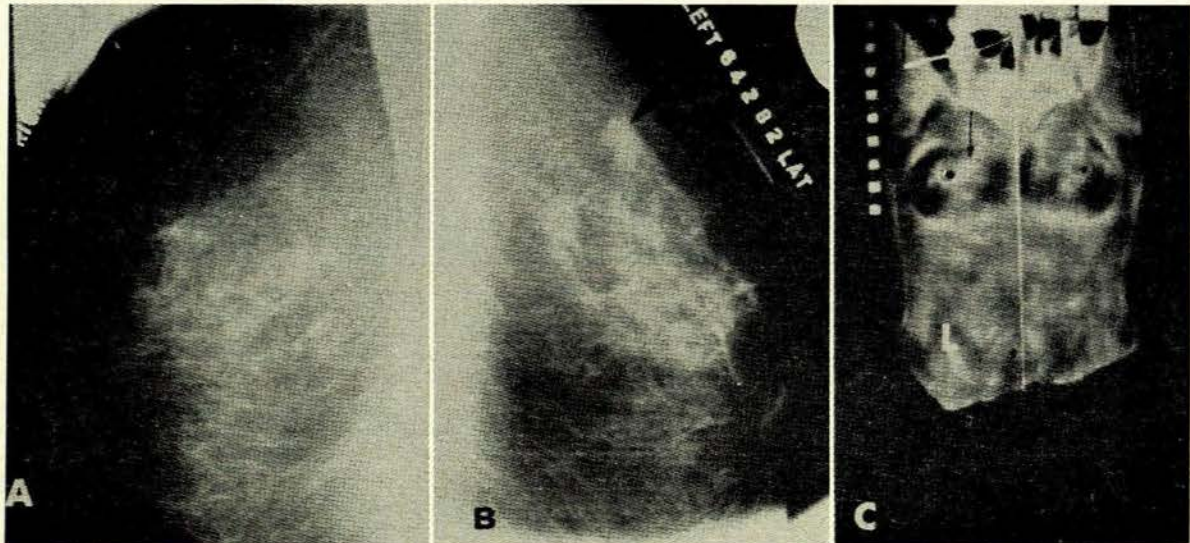


Fig. 4. A and B: Mammograms of the right and left breasts showing a carcinoma in the upper inner quadrant of the right breast. C: Thermogram of this patient showing a hot area of skin over the lesion in the upper inner quadrant which was 1.5°C warmer than a similar area of the opposite breast.

breast. In these cases it was found that the average time between urine collection and the development of carcinoma was 31 months, the shortest period being 3 months and the longest 61 months. Results show that in a substantial proportion of the cancer patients the hormonal excretion was abnormal. These, when carefully compared with controls, were shown to deviate further from the mean values than did the individual controls. This deviation was statistically significant.

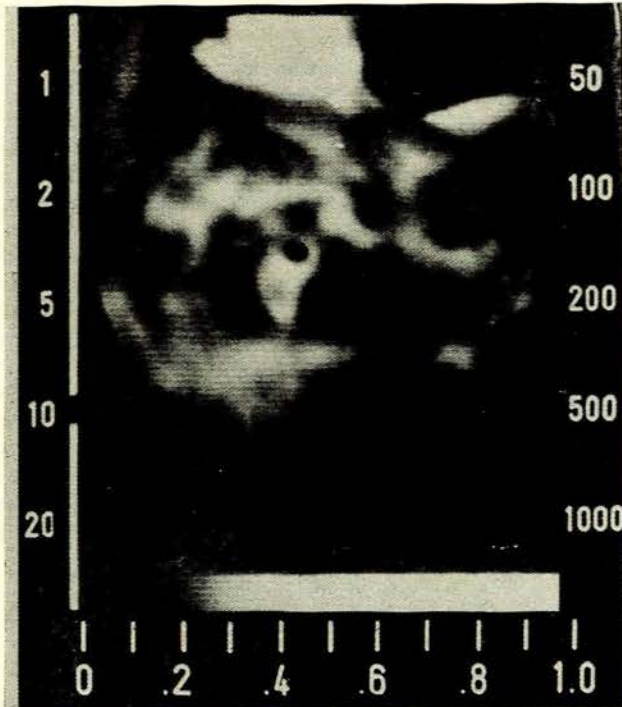


Fig. 5. In a thermogram, warm areas appear lighter than cold areas, and here the light area on the woman's right breast indicates an underlying tumour.

An important question is whether the tumour was already present but not clinically palpable at the time of collection of urine. Is the tumour the cause of the abnormal hormonal excretion in the urine, or does the abnormality possibly precede the onset of the tumour?

From these observations arises the possibility of using this method for screening the normal population. In this practical manner one would hope to identify women with a high risk of carcinoma of the breast, and then to subject them to very close observation and frequent examination.

Cytological Examination of Cyst Aspirate, Nipple Discharge and Needle Biopsy

If stress were placed, as is done in some modern clinics, on the cytological examination of all cyst aspirate and nipple discharge, the occasional early case of carcinoma could be diagnosed by this method. While this is commendable, it is most important to remember that a negative result does not rule out the presence of carcinoma, and care must be exercised to ensure that a formal biopsy is not neglected or delayed.

Similarly, with regard to obtaining a biopsy specimen by means of needle puncture of a mass in the breast, fairly accurate results can be obtained in experienced hands, but a negative result may not entirely rule out the possible presence of a carcinoma. It is probably far safer to obtain a biopsy specimen by means of an open incision.

The chief value of cytological examination lies perhaps in the positive case, when it will save 30 minutes normally spent on biopsy and frozen section. This may be of great importance in the poor risk case.

CONCLUSION

By the use of every possible additional investigatory means at our disposal more general information will be forthcoming, which may either help detect tumours in their preclinical stages, or provide in certain cases just that bit of more precise information which in turn may aid in selecting for each individual an earlier and more appropriate treatment, and which in the long run will result in considerably improved results for this prevalent and terrible condition.

It should be stressed that these new investigatory methods supplement our knowledge, and are by no means intended to supplant biopsy of specimens obtained by an open operation, which must remain our diagnostic mainstay.

An urgent plea is made for the early detection and early treatment of carcinoma of the breast. Financial expenditure in this respect would not only pay handsome dividends in alleviating human suffering, but must also result in a considerable long-term financial saving, because of the expensive and rather futile treatment required for the more advanced case.

SUMMARY

Primary carcinoma in women occurs most commonly in the breast; it develops in about 5% of all women. The survival rate is discussed relative to improvement over the past years, to the duration of symptoms, to the degree of advancement of the disease, to the size of the growth when first seen, and to whether the tumour was detected at a special detection centre or otherwise.

The principal aim in fighting this disease should be to find the early clinical case or, better still, the preclinical case. The present-day means at our disposal to achieve this aim are discussed in some detail. Every possible method should be utilized to find the earlier case, and to select for each individual case the most appropriate treatment. Considerably improved results, alleviation of human suffering and considerable long-term financial saving, can be expected. It is emphasized that, despite new investigatory methods, biopsy must remain the diagnostic mainstay.

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