Current Practice

CLINICAL PROGRESS

Cancer of the Breast

Early Diagnosis

A. P. M. FORREST,* M.D., CH.M., F.R.C.S.

British Medical Journal, 1970, 2, 465-467

Breast cancer is the commonest cause of death from malignant disease in women. Therapeutic advances have done little to improve its mortality, and emphasis has recently been placed on the need for earlier diagnosis. In practical terms this means presymptomatic diagnosis, or the discovery of a cancer of the breast before it has become obvious to the patient.

Rationale

There is no direct evidence that earlier diagnosis improves the absolute survival of patients with cancer of the breast. There is, however, good evidence that those breast cancers which are brought to light by screening programmes are smaller in size and associated with a lower incidence of axillary node metastases than those arising spontaneously.^{1,2}

The influence of delay in seeking treatment on the prognosis of cancer of the breast has been studied by Bloom.³ Contrary to popular belief, he found no relation between the duration of symptoms before treatment and survival rates. The explanation for this apparent paradox lies in the inherent malignancy of the tumour. Thus Bloom found that the histological grades of those tumours associated with long histories before presentation were lower (in other words, the tumours were less malignant) than in those with short histories. Further, within each histological grade, the length of time before treatment increased the number of more advanced cases.

Thus the relatively good survival rates of patients with long histories are due to a process of natural selection, only those with relatively favourable tumours being able to survive a long period between the time the tumour was discovered and treated.

Available Screening Methods

Clinical Examination

To be of value, examination of the breast must be performed systematically.⁴ A cursory "feel" of the breasts is useless; careful inspection and palpation are essential for the discovery of early breast lesions, and normally take about five minutes.

Mammography

Soft-tissue x-ray films of the breast of suitable contrast are taken with unfiltered x-rays of low kilovoltage on fine grain industrial film. Two views are usual—craniocaudal and lateral—but additional films of the axillary tail may be required. The examination takes 30 to 40 minutes. The tell-tale signs of early malignancy are a dominant soft-tissue lesion (classically irregular and spiculated), microcalcification (of "broken-needle" type), and hypervascularization. Two

modifications of conventional mammography are currently under study:

Photo-fluorography.—70 mm. miniature x-ray films, akin to those used for mass miniature radiography of the chest, may be used for mammography.^{5,6} The tube and camera are mounted on a motorized stand which can be rapidly rotated or adjusted for height. With the patient standing two views at right angles may be taken of both breasts in less than 10 minutes. Though less expensive and less time-consuming than conventional mammography, the standard of film is not as good. Interpretation can be improved by electronic variation of intensity and contrast.

Xeroradiography.—All breast tissue, including skin, can be portrayed on a selenium-coated charged metal plate by a single x-ray exposure. The image is transferred to paper or photographic film.⁷⁻⁹ Accentuation of the boundaries between tissues of different densities gives a bas-relief effect, which makes interpretation easy. Nevertheless, a greater exposure is required than for conventional mammography and the process of development is difficult to control.¹

Thermography.—The pattern of heat emissions from the surface of the breasts is recorded by an infra-red camera. This consists of a heat-sensitive detector (either indurium antimonide or a thermistor) and a transducer, which converts the impulses to electrical or visual signals. As the pattern of radiated heat from the skin is influenced by the vascularity and metabolism of the underlying tissues, an increase in temperature may point to an underlying neoplasm. More numerous or wider veins and an increase in venous temperature are other suspicious signs. Thermography is quick and both breasts can be scanned in under a minute. Cooling of the exposed breasts, however, to an ambient temperature of 20 to 22°C. for 10 to 15 minutes must precede the examination.

Accuracy of Methods

It is difficult to assess the "average" accuracy of the methods described above. The reported results may be tempered by the particular skills and beliefs of the clinician or radiologist and omit to mention whether the assessment has been carried out with or without access to the findings of other methods of examination. In this section I have tried to estimate, from such information as is available, the accuracy of the methods used in the diagnosis of established breast disease and in the detection of presymptomatic lesions.

Established Breast Disease

Reports from centres with special experience indicate that conventional mammography is a highly accurate method for the diagnosis of benign and malignant breast lesions (Table I).

The value of mammography and clinical examination was compared in Cardiff, as part of a study of over 2,000 mammograms (Table II).¹⁰ Both the clinician and the radiologist recorded their diagnosis without access to the findings of the other. The radiologist, however, did know the site of the

* Professor of Surgery, Welsh National School of Medicine, Cardiff.

lesion and was able to examine the breast to confirm that the lesion had been adequately shown by radiology. The study showed that the two methods are clearly complementary, the highest accuracy following their combined use. Mammography is best in the fatty glandular breast; clinical examination in the one that is fibrous and atrophic.

TABLE I.—*Diagnostic Accuracy of Mammography in Histologically Proved Lesions of the Breast*

	Benign		Malignant*	
	No.	% Accuracy	No.	% Accuracy
Egan ²⁰	241	97	179	91
Egan (collected) ²⁰	728	96	482	91
Clark <i>et al.</i> ²¹	1105	90	475	79
Hessler & Gershon-Cohen ²²	157	90	58	86
Friedman <i>et al.</i> ²²	543	91	233	81
Stewart <i>et al.</i> ¹⁰	352	86	263	92

*In the malignant group suspicious and possible malignancy has been included as well as unequivocal findings.

TABLE II.—*"Blind" Comparison of Clinical and Radiological Diagnosis of 144 Cancers (all histologically proved) and 335 Benign Lesions of the Breast¹⁰*

Method of Examination	% Correct Diagnosis	
	Carcinoma (144 Cases)	Benign Lesions (335 Cases)
Clinical	85	88
Mammography	92	92
Both	97	97

Little information is available yet about the accuracy of 70 mm.-photofluorography or xeroradiography in the diagnosis of established breast lesions. A recent survey carried out in Cardiff suggests that the former compares unfavourably with clinical examination.¹¹ Though we have found in over 400 patients that thermography is considerably less accurate than either clinical examination or conventional mammography,¹¹ others have reported a high incidence of correct diagnoses in established breast disease. Fifty-four of 57 cancers studied by K. L. Williams and his colleagues,¹² and 188 of 200 cancers studied by Gershon-Cohen,¹ had a discernible increase in surface temperature. Comparisons with mammography (Table III) and with clinical examination and mammography (Table IV) have been reported from the United States and Israel. In general, the accuracy of thermography compares favourably with that of the other methods, at least in the diagnosis of malignant disease, particularly when access to clinical data is allowed (Table V). The relatively high incidence of positive findings in benign disease—"false positives"—is to be expected, as 37% of breast dysplasias have increased skin temperature.¹ In the survey reported by

TABLE III.—*Comparison of the Accuracy of Thermography and Mammography in Patients with Histologically Proved Lesions of the Breast*

Examination	% Correct Diagnosis			
	Wallace and Dodd ²⁴		Isard <i>et al.</i> ²⁵	
	Carcinoma (69 Cases)	Benign Lesions (118 Cases)	Carcinoma (76 Cases)	Benign Lesions (190 Cases)
*Thermography	87	61	72	39
Mammography	77	78	82	61

*Note that "correct" thermography is positive in a cancer, and negative in a benign lesion.

TABLE V.—*Combined Results of Screening*

Method of Screening	Total No. Examined	Abnormal Findings Suspicious of Malignancy	% Biopsies	Cancer Detection Rate (1000 Screened)	Authors
Clinical	72,933	1.4	0.4	0.6	Pedersen ²⁶ ; Barnes <i>et al.</i> ¹⁷
Mammography	10,128	3.2	1.4	3.2	Witten and Thurber ²⁷ ; Stevens and Weigen ¹⁸ ; Wolfe ²⁸
Clinical and Mammography	13,154	1.0	3.9	1.4	Griesbach and Eads ²⁹ ; Irvine and James ³⁰
Thermography	1,924	7.3	3.1	1.2	Hoffman ³¹
Clinical and Thermography	2,523	13.5	0.6	0.4	Hitchcock <i>et al.</i> ³²

A. M. Lilienfeld and his colleagues¹³ thermography was found to be complementary to the other methods of examination, each method detecting different groups of cases.

These results suggest that in established breast disease clinical examination and mammography together have a very high degree of accuracy in diagnosing cancer. Despite the growing evidence that thermography also is another accurate method, this opinion is less widely based and requires confirmation before it is accepted for the early diagnosis of breast disease.

Presymptomatic Diagnosis

The findings of several isolated programmes for screening normal women—by clinical examination, mammography, and thermography—indicate that unsuspected tumours can be detected by these methods, particularly when they are combined (Table V). It is now also well recognized that mammo-

TABLE IV.—*Combined Accuracy of Clinical Examination, Thermography and Mammography in Histologically Proved Lesions in six Medical Centres*

	No. of Malignant Lesions	% Accuracy	No. of Benign Lesions	% Accuracy
Clinical examination	305	82.3	626	78.4
*Thermography "blind"	305	74.1	635	60.2
"with access"	297	72.1	629	79.8
Mammography	229	70.3	451	80.7

*Each thermogram was read twice at the participating hospital, "blindly" and "with access" to clinical data. Mammography was carried out according to the routine practice of the hospital.¹³

graphy plus clinical examination will detect more tumours than either alone. Nevertheless, the large number of suspicious findings is a considerable disadvantage, since they entail the further examination of many patients who ultimately prove to be free from disease.

As these surveys have been uncontrolled, they cannot tell us what the effect of screening has been on the mortality of breast cancer. The survey being carried out in New York by P. Strax and his colleagues is free from this criticism.^{2,14-16} In this survey about 31,000 women aged 40 to 64 years were chosen at random for clinical and mammographic examination of the breasts. This was performed when they entered the programme (initial screening) and at three annual intervals thereafter. A control group of similar size was also selected at random from the same population in which women received only their normal medical care. The initial, first, and second annual screenings have now been completed. Though the end-point of the study is a comparison of mortality, the following findings have been reported already:

(1) Of the women selected for screening 65% reported for their initial examination. Thereafter the fall-out was less, and 82% of those initially screened reported back for their first, and 78% for their second, annual examination.

(2) Initial screening detected rates of breast cancer which were higher (2.72 per 1,000) than in the control group (1.44 per 1,000). On subsequent annual examination the rates in the screened population fell to control levels.

(3) A total of 532 biopsies was recommended, and ultimately yielded 118 cancers. False-positive rates were high; 65% of 153 lesions suspected to be malignant by the clinician and 63% of 173 by the radiologist were finally proved not to be cancer. Conversely, only 10% of 249 lesions suspected to be benign on clinical

examination, and 2% of 57 lesions on radiological examination, were subsequently proved to be cancer.

(4) Both clinical and radiological examination are essential for satisfactory screening; 45% of cancers were discovered *only* by clinical examination and 34% *only* by mammography.

(5) Axillary nodes were more frequently negative in those whose cancers were detected by screening (70%) than in the control population (44%).

Conclusions

The key question "Does early detection of cancer of the breast improve survival?" will be answered by the New York survey. Nevertheless, it should be remembered that those whose cancers are detected by screening will be treated earlier than those who are controls. Hence their survival *from the time of treatment* will inevitably be longer. The study must therefore be continued until the prolongation of survival in the screened population exceeds the time by which treatment has been put forward on what may be a fixed time-scale.

Treatment of the Early Disease

J. IAN BURN,* F.R.C.S.

British Medical Journal, 1970, 2, 467-469

Whatever man's inhumanity to man, generally his humanity to woman is unquestioned. It is no wonder then that cancer of the female breast offends more than most and troubles our consciences by the affliction it causes.

The Past

If left untreated, cancer of the breast will kill. Reports of series of untreated patients make this abundantly clear,³³⁻³⁵ and before the Halsted era death from the disease was inevitable. After W. S. Halsted^{36, 37} and W. Meyer³⁸ independently introduced their operations of radical total mastectomy, succeeding decades witnessed increasing numbers of long-term survivors.³⁹ No one should doubt that treatment is justified, but we have to question the true efficacy of the methods at our disposal.

The introduction of safe, effective radiotherapy and dissatisfaction with the reported morbidity of the classical Halsted procedures resulted in radical surgery being challenged.⁴⁰⁻⁴² The 1950s thus saw wide acceptance of simple total mastectomy, in which the pectoral muscles were left intact and the axilla not dissected, combined with radical postoperative radiotherapy to the chest wall and regional lymph nodes. Also about this time, the advent of the modified radical mastectomy operation,^{43, 44} in which full dissection of the axillary nodes was achieved without removing the pectoralis major muscle, cast fresh doubts on whether the full radical procedure was justified. These variations in treatment were practised almost exclusively in the British Isles, and probably reflected a growing confidence in radiotherapy which at that time was not enjoyed by other countries.

In other European countries and America, far from decrying the Halsted mastectomy, surgeons were embarking on even more extensive radical surgery, believing any additional morbidity to be fully justified by the more certain eradication of all diseased regional lymph nodes.⁴⁵⁻⁴⁸ There were few proponents of extended radical mastectomy in this country.⁴⁹

Screening by any method is expensive, both in money and manpower—more so when one considers the possibility of a poor response (only 38% of women in Lewisham accepted a written invitation to attend a clinic¹⁷), the need to use more than one method of examination, and the high incidence of spurious findings which require full investigation and treatment. G. M. Stevens and J. F. Weigen¹⁸ have calculated that if every woman over the age of 40 in the United States were to have a mammogram annually every radiologist would be required to examine 20 mammograms each working day. C. R. Lowe¹⁹ estimated that a screening programme in England and Wales for the over-35s would require additional facilities for 8 million examinations a year at a cost of £800 to £1,250 per cancer discovered. Hence there is little justification for carrying out breast screening programmes until we have evidence that the prognosis of the disease is improved. Nevertheless, it must be stressed constantly that examination of the female patient—whatever complaint brings her to her doctor—is incomplete without thorough examination of the breasts.

The Present

Recent reports have questioned the propriety of even the more moderate methods of treatment.⁵⁰⁻⁵³ We now have to recognize that the principle of minimal intervention, even to the extent of limiting treatment to simple excision of the mass in the breast, has a growing number of advocates.

Some apparent credence is given to the pleas for conservatism in the treatment of all breast cancer. Firstly, it has been argued that occult distant metastatic foci always are present before the disease can be recognized clinically. In other words, there is no such clinical entity as early localized breast cancer and, therefore, radical measures are not justified. The second reason is that ablating the regional lymph nodes necessarily impairs the putative immune response and thus weakens the natural host-defence mechanisms. Primary treatment of the regional nodes is therefore harmful. The weakness of these two opinions is their manifest contradiction. Metastatic disease present almost from inception of the cancer denies the existence of competent local host-defence mechanisms. But if such mechanisms do exist they might reasonably be expected to contain the disease within the regional nodes for at least part of its life and thus enable it to be totally removed. In fact, the results of treatment suggest that the truth lies somewhere in between the two extreme points of view.

About a quarter of our patients will have genuinely early breast cancer when first treated. These are the patients in whom adequate therapy will enable them to live a normal life span with no further evidence of the disease. We now accept that 5-year and even 10-year survivals are not sufficient criteria of success, but 15-year survivals are more realistic.^{54, 55} After this, the expectation of life in treated patients is the same as that of a similarly aged group of the normal population. These patients are cured.

Why these survivors have disease genuinely confined to the region of origin is debatable. There has recently been prolific reawakening of interest in the immunological concepts of cancer control.^{56, 57} Not only do regional lymph nodes have an undoubted barrier function, but they probably play an

*Consultant Surgeon, Breast Unit, Department of Surgery, Royal Postgraduate Medical School, London W.12