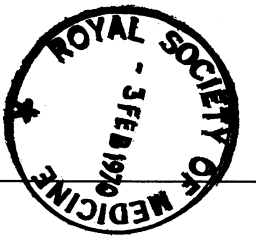

Section of Radiology

President J W D Bull MD

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Management of Early Carcinoma of the Breast [*Abridged*]

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A Controlled Trial of Conservative Treatment for Early Breast Cancer

Diagnosis

The first duty of a surgeon to a patient with a lump in the breast is to establish a definitive diagnosis as soon as possible. Even if meticulous interrogation and examination are practised, the accuracy of diagnosis is considerably enhanced by the use of mammography. From an experience of over 2,000 mammograms, Stewart *et al.* (1969) have reported from Cardiff that radiological examination of the breast had an overall accuracy of 93% for both benign and neoplastic conditions. In Table 1 the diagnostic accuracy of mammography and clinical examination has been compared in 144 cancers and 335 benign lesions, all proved histologically. Both mammographic and clinical diagnoses were recorded without the findings of the other being known. The accuracy of either mammography or clinical examination alone is approximately 90%, but when both methods are combined the accuracy is increased to 97%.

In our experience, thermography, using the AGA machine, does not approach this accuracy. As part of an investigation of diagnostic methods, a blind comparison of thermography with clinical examination and conventional mammography is being carried out. To date, thermography has compared unfavourably with these other methods of examination (Table 2). In this table the accuracy of thermography is given both for an agreed diagnosis and for the majority diagnosis of 3 observers, each of whom assessed the thermograms separately; considerable observer error is noted.

Even with the availability of these methods, histology is still the only certain method of diagnosis. This can be obtained on the day the patient attends the clinic by drill biopsy or, more simply, by needle aspiration. Our experience of the latter method, although small, is similar to that reported by others and gives an accuracy of diagnosis for cancer of around 70% (Table 3). However, it is important to appreciate that a negative aspirate does not rule out cancer.

Table 1
Accuracy of mammography and clinical examination in the diagnosis of 479 breast lesions all histologically proved (Stewart *et al.* 1969)

	Percentage of correct diagnoses	
	144 cancers	*335 benign lesions*
Mammography	92	92
Clinical examination	85	88
Both	97	97

Table 2
Accuracy of thermography compared with clinical examination and mammography in 41 histologically proved cancers of the breast and 138 lesions which were considered benign, either on histological or follow-up grounds

	Percentage of correct diagnoses	
	41 cancers	*138 benign lesions*
Clinical	93	91
Mammography	87	97
Thermography:		
3 of 3 observers	39	65
2 of 3 observers	54	86

Table 3
Reported results of needle aspiration biopsy

	Proved cancer		*Proved benign*	
Series	*No.*	*Percentage correct*	*No.*	*Percentage correct*
Gibson & Smith (1957)	53	82	24	100
Franzén & Zajicek (1968)	873	76	807	97
Cardiff	14	69	22	64

Operability
If a diagnosis of cancer is suspected, the next duty of the surgeon is to establish that the tumour is operable. This demands a diligent search for metastases. In our clinic this includes mammography of the other breast, X-ray of the skull, chest and pelvis (where bone metastases are frequently symptomless) and, if the tumour is medially placed, biopsy of an internal mammary node at the time of surgery. The yield, although small, is well worth while, as in the patient whose radiograph of the skull is shown in Fig 1 and who, as a result, avoided a mutilating operation. A strict discipline is necessary for screening patients for occult metastases, and this is aided by the use of a check list and the TNM system of classification[1].

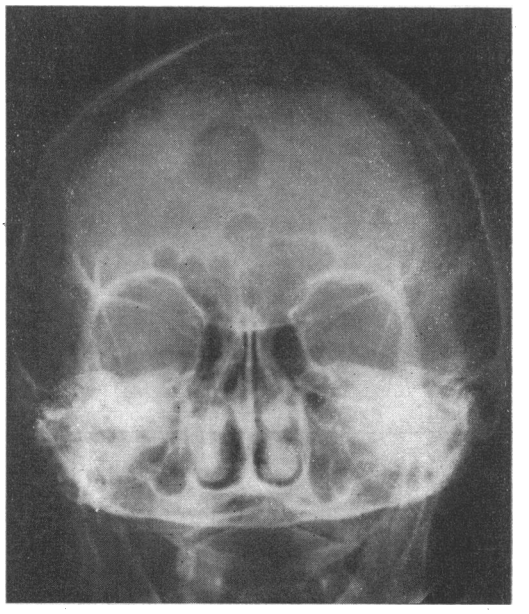

Fig 1 *Skull X-ray of a patient with a cancer of the right breast without palpable axillary lymph nodes*

Such investigations are time consuming and costly and cannot be carried out in all patients with lumps in the breast without increasing the anxiety of those with benign lesions. Hence the need for as accurate a diagnosis as possible *before* the patient comes to operation.

Treatment
It is over 60 years since Halsted described the radical operation for cancer of the breast. Yet we do not know whether this is or is not the operation of choice for the disease. Radiotherapists have similar doubts about the place of X-ray therapy as adjuvant treatment. There is, as a result, a state of uncertainty as to how breast cancer should be treated and many have reverted to what time may show to be inadequate methods of treatment. Doubts such as these can be resolved only if we recognize the importance of the controlled clinical trial as a therapeutic weapon.

It is our belief that the aim of treatment of primary cancer of the breast is to control the local manifestations of the disease with minimum mutilation and morbidity. This belief is based on the following considerations:

Controlled trials: Three key controlled trials have now been reported – from Copenhagen (Kaae & Johansen 1959, 1968), Cambridge (Brinkley & Haybittle 1967) and Manchester (Paterson & Russell 1959, Easson 1968) – in which standard methods of treatment have been compared randomly in large series of unselected patients. As a result, it can be concluded that:

(1) Simple mastectomy and X-ray therapy by the McWhirter technique give results equal to the most radical operations. Thus, Kaae & Johansen (1968) described identical survival and recurrence rates over ten years for 331 patients treated by simple mastectomy and X-ray therapy and 335 patients treated by an extended radical operation in which the breast and the axillary, supraclavicular and internal mammary nodes were removed surgically.

(2) Extension of local treatment beyond the breast and axilla confers no advantage over keeping such treatment in reserve until demanded by recurrence. Thus, Easson (1968) reports equal survival rates over ten years for 752 patients in whom the *initial* treatment was radical mastectomy alone (X-ray therapy being reserved for recurrence) compared with 709 patients in whom radical mastectomy was combined with postoperative X-ray therapy.

(3) Surgery and X-ray therapy are equally effective in treating involved nodes. This assumption is supported by the results of all three trials, but particularly by those from Copenhagen and

[1]Copies of the TNM check list used in Cardiff may be obtained from Professor Forrest, Welsh National School of Medicine, Cardiff

Cambridge, in which patients treated only by X-ray therapy to the nodal areas fared equally well as those in whom surgery or surgery plus X-ray therapy was used.

Incurability: It has long been recognized that the extent of the disease, in terms of axillary node involvement, is the best guide to prognosis (Cutler 1966). The greater the number of axillary nodes involved, the worse the prognosis (Pickren 1961). As a result of histological examination of all the axillary nodes in 204 mastectomy specimens, Auchincloss (1963) found that five-year survival was recorded only if involvement of the nodes was limited to the lower axilla. Lymphatic spread above the lower border of the pectoralis minor muscle was indicative of incurable disease. Local treatment, no matter how radical, cannot cure incurable disease.

Morbidity: The morbidity of local treatment of cancer of the breast is proportional to its extent. In a meticulous study of 252 patients (229 treated by radical and 23 by limited mastectomy) Eisenberg & Goldenberg (1966) found that morbidity, in terms of arm swelling, impairment of function and inability to resume normal activity, was greater with radical mastectomy than with the simpler operation (Table 4). Seventy-five of their patients had also been treated by post-operative radiotherapy and, of these, 43% had a severe reaction with blistering of the skin, severe nausea, weakness or fatigue. The Halsted operation carries a further disadvantage in that a woman without a pectoral muscle complains that she can no longer wear a swim-suit or a low-necked garment. Provided it does not compromise cure rates, preferable treatment is that which carries least morbidity.

Table 4
Morbidity of mastectomy (Eisenberg & Goldenberg 1966)

	Type of mastectomy	
	Radical (229 patients)	*Limited (23 patients)*
Swelling of arm (2·5 cm)	22%	0
Impaired arm function	24%	10%
Impaired activity	17%	10%
Altered attitude	62%	50%

Immune reaction: It is recognized that experimental animal tumours can provoke an immunological response in the host. Evidence that cancer of the breast in humans can do likewise is slender. Yet certain changes, characteristic of an immune response, do occur. These are lymphocytic infiltration (or the presence of plasma cells and 'immunoblasts' – large immature pyroninophilic cells) in the tumour and reactive hyperplasia (or sinus histiocytosis) of the local lymph nodes. These changes are related to the contour (Stewart *et al.* 1968) and histological grade (Hamlin 1968) of the tumour. They are also related to prognosis.

Patients with tumours of smooth contour (Lane *et al.* 1961), marked round cell infiltration (Berg 1962), enlargement (Cutler 1968) and sinus histiocytosis (Black 1965) of the regional nodes, have a relatively good prognosis compared with those in whom the changes are less obvious.

Disturbance of this response at the time of primary treatment, for instance by removal or radiation of normal nodes, may be contrary to the interests of tumour control.

Multicentric origin: As a result of examining whole breast sections of 157 breasts removed for cancer, Qualheim & Gall (1957) reported multiple tumour foci in 54% of cases. In 37% the unconnected tumours occupied opposite portions of the breast. Similar results were found by Stewart (1968, unpublished) in our laboratories. Fifty breasts, resected for tumour, were prepared by the large-section technique of Gough & Wentworth (1960): multifocal deposits were found in 38%. 'Lumpectomy' will leave residual tumour, therefore, in one-third of cases.

Cardiff Trial

As a result of these considerations, we have adopted a plan of treatment based on the following principles:

(1) Treatment by surgery or X-rays should be given only to sites of proved involvement: excess removal or irradiation of normal tissues increases morbidity but not cure.

(2) Because of the probability of multifocal origin, local mastectomy is the minimum acceptable operation for primary breast cancer.

(3) Surgical excision and X-ray therapy are equally effective methods of treatment for involved lymph nodes.

(4) Substantial axillary node involvement signifies incurable disease.

In accordance with these principles, our standard operation is a local mastectomy. This is performed through a transverse incision, which gives minimal tension and a relatively inconspicuous scar. The axillary tail is completely removed with two of three of the lower pectoral group of nodes which lie in close association to it. The axillary fascia is not disturbed unless palpable nodes are

present in the axilla, when one or two are removed for histological examination. A small piece of skin also is removed from the edge of the incision nearest to the excised tumour. Rapid return of function is encouraged by suction drainage, a minimum of dressings and early mobilization.

Subsequent treatment by radiotherapy is dictated by the histological state of the removed nodes and skin. If no metastases are present, no further treatment is given but normal lymphatic function is preserved. If the pectoral or lower axillary nodes are involved, radiotherapy is given post-operatively to the axilla alone by a course of treatment of 4,000 rads fractionated into ten separate treatments over three weeks using cobalt irradiation. This regime was adopted as there is now some evidence from animal experiments (Du Sault *et al.* 1958) and collected data from a number of treatment centres (Cohen 1966) that, in the case of mammary carcinoma, treatment on alternate days gives a better therapeutic ratio than daily treatment. Radiotherapy to the skin flaps, using a similar regime, is given only if the biopsy of skin contains tumour cells.

This plan of treatment is currently being compared randomly with a standard regime based on radical or modified radical mastectomy, by which the axilla is cleared of lymph nodes in all cases. In this group radical radiotherapy is given to the axilla, supraclavicular and internal mammary regions and chest wall if the axillary nodes and/or skin biopsy are positive. The total doses given are 4,000 rads to the chest wall, 3,500 rads to the supraclavicular and internal mammary fields and 4,000 rads to the axilla, fractionated over a period of four weeks. The chest wall and gland fields are treated on alternate days. The dose regime is based upon that of De Moor *et al.* (1961) which was shown to give a very low incidence of local recurrence following radical mastectomy.

No adjuvant endocrine or cytotoxic therapy is given to either group.

This trial, which started in September 1967, now includes 43 patients, of whom 22 have been allocated to the conservative and 21 to the radical groups.

Before being randomized into the trial, patients are staged carefully by a surgeon and a radiotherapist, according to the TNM classification. Only those patients with T1No, T1N1, T2No and T2N1 tumours are included. The tumour stage is recorded together with the mammographic findings and the results of the skeletal survey. The forms used are completed subsequently and include the details of surgical treatment and the plan of radiotherapy, if given. In addition, the detailed histological report of the tumour, the lymph node and skin biopsies are included. Estimations of urinary androgenic steroids and corticosteroids are being done in all patients.

In the assessment of the results, not only will survival and disease recurrence be analysed but the quality of life will be carefully documented. Provided there is no risk to the patient, a policy of treatment based on the principle that normal tissues should not be interfered with is both rational and desirable, and will save needless physical and mental scarring.

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