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Current Controversies in Cancer

In this new section of the journal, a controversial issue in oncology shall be discussed by three experts in the field. The first will put forward the argument in favour of the topic under discussion ("*Pro*"); the second will argue against the topic ("*Contra*"); and then both sides of the debate shall be brought together in the final editorial ("*Arbiter*"). Currently, there are many important questions which need to be discussed, particularly in clinical oncology, and it is hoped that, through debate and meaningful data, some answers might be reached. Our readers are encouraged to send their opinions to the *European Journal of Cancer* in the form of a "Letter to the Editor" to add to the debate.

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Is Routine Axillary Nodal Dissection Necessary in the Treatment of Breast Cancer?

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SURGEONS TREATING breast cancer are often given advice by medical oncologists suggesting that axillary surgery is unnecessary as part of primary treatment and that delayed surgery in recurrent cases is safe [1]. Before being drawn by this siren-like argument on to the rocks of therapeutic nihilism, it is important that several errors and omissions should be corrected.

AXILLARY TREATMENT DOES AFFECT THE PROGNOSIS

The work of the NSABP was cited as showing no apparent effect of delayed surgery on the prognosis [2]. In the NSABP trial B–04, patients with operable breast cancer and clinically uninvolved axillary nodes were randomised to one of three arms: radical mastectomy; total mastectomy and postoperative radiotherapy to the chest wall and gland fields; or total mastectomy alone [3]. Axillary nodal metastases were found in 39% of the radical mastectomy cases, but only 15% of the total mastectomy group developed relapse in the axilla requiring subsequent surgery. This was taken as evidence that some axillary disease remained occult, and furthermore the overall survival of all three groups was the same.

These conclusions have been vigorously questioned by Harris and Osteen [4]. They pointed out that 35% of the group randomised to total mastectomy alone actually had a limited axillary dissection. Furthermore, there was a relationship between the extent of axillary surgery and the need for subsequent clearance, 12% of those who had between one and five nodes removed compared with 0% of those who had six or more nodes resected.

The much larger Danish Breast Cancer Cooperative Group study, which was published in this journal, was not cited [5]. This study comprised 13851 patients who were deemed node-negative at the time of primary surgery. It was found that misclassification occurred when less than 10 nodes were examined and found to be negative. In the group of patients with 10 negative nodes there was a significantly better axillary recurrence-free survival and overall survival.

Similarly, in the Guy's Hospital wide excision trials, which compared radical mastectomy and radiotherapy with wide excision and radiotherapy, in which the axilla was undertreated, there were more axillary relapses and deaths from breast cancer in the group treated by wide excision [6].

AXILLARY DISSECTION AND LOCAL CONTROL

There is no argument that inadequate treatment of the axilla leads to an increase in rate of local relapse. Not only does this lead to an increase in distant recurrence but also to local morbidity. Axillary recurrence is not always amenable to surgical resection. It can produce skin recurrence and brachial plexus infiltration leading to intractable pain.

Such a complication is a rebuke to the surgeon who failed to treat the axilla and should be avoided whenever possible in patients with originally operable disease. The assumption that axillary relapse is a relatively benign complication is not borne out by those who have seen women dying with uncontrolled axillary disease.

Just because the majority of cases of early breast cancer can be treated by conservation, this is not an excuse for assuming that axillary surgery can be omitted. It should be remembered that all the trials which have shown breast conservation therapy to be as equally effective as mastectomy included axillary clearance as an intrinsic part of breast conservation [7].

It cannot be assumed that the more widespread use of systemic adjuvant therapies will obviate the need for axillary treatment either by surgery or radiotherapy. In the Danish Breast Cancer Cooperative Group Trials 82b and 82c, patients who had been treated by total mastectomy with node

sampling and were deemed to be at increased risk of relapse by virtue of tumour size (T3–4) or clinically node positive (N+) were randomised to receive axillary radiation or no further local treatment [8].

Premenopausal patients (1473) were all given adjuvant CMF and postmenopausal cases (1202) received tamoxifen. In both pre- and postmenopausal cases, there was a significantly increased axillary relapse rate in the non-irradiated group. Furthermore, the overall survival was significantly increased in the premenopausal irradiated group (68 versus 63%). It was concluded that adjuvant systemic treatment alone did not prevent locoregional relapse in high-risk cases.

Use of radiotherapy rather than surgery than surgery to treat the axilla can lead to an increase in morbidity. In the Edinburgh trial, 417 patients undergoing total mastectomy were randomised to have either an axillary clearance or sampling [9]. Those in the sampled group who had histological evidence of nodal involvement were given axillary radiotherapy. When this group was compared with the node positive group treated by clearance, there was a significant increase in reduced arm mobility, severe interference with daily activity and lymphoedema in the irradiated group.

AXILLARY NODAL STATUS AND PROGNOSIS

Despite a multinational billion dollar industry which has tried to replace pathological nodal status by other prognostic factors, usually related to the behaviour of the primary tumour, the pathologist still remains the most significant prognostic indicator. This information is now known by an increasing number of patients. Thus, the majority wish to know their likely prognosis and, if axillary staging has been inadequate, this will be a mission impossible. This latter aspect is often forgotten by doctors who have not appreciated that patients will have opinions and needs with regards to their future prognosis and treatment.

Finally, it may be argued that as more cases are diagnosed as a result of mammographic screening so they will have small (<1 cm) tumours with a good prognosis. A recent study from Guy's Hospital of 336 women with tumours up to 1 cm revealed that 31% had axillary nodal metastases [10]. Furthermore, patients with impalpable tumours and nodal involvement had a significantly worse prognosis than those who had palpable lumps with nodal involvement.

Of course, it has to be accepted that approximately half of the patients undergoing axillary surgery will have pathologically negative nodes. This does not mean that the operation was unnecessary, since the patient and her doctor will be better informed. Naturally, the procedure will be replaced as imaging techniques are able to indicate true negativity.

However, it will still be necessary to treat the axilla when there is pre-operative evidence of nodal metastases. Whether this should be by surgery or radiotherapy remains a moot point. What is most important is a multidisciplinary approach to treatment, with the surgeon playing an important role in both local treatment and staging.

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When a treatment has been painstakingly validated over many years—and when even longer has been required to convert practitioners at large to its use—there is understandable reluctance to welcome criticism of the approach in question. Times change, however, and the conventional wisdom of 1986 or 1991 may not prove equally valid in 1996. As suggested in the accompanying commentary (Fentiman, pages 1460–1461), multidisciplinary decision-making is an appropriate policy for the modern age; it is therefore entirely appropriate for medical oncologists to discuss the utility of a surgical procedure justified in large part by its impact on medical decision-making. Here I address the concerns expressed above in response to my recent review of routine axillary nodal dissection (RAND) [1].

The key point of the original article was not that RAND has become less effective as a prognostic exercise, but that the clinical decision-making value of nodal staging has declined substantially over the last decade. To reiterate the evidence for this view [1] here would be futile; suffice to say, however, that the simplistic 1980s rule-of-thumb "no nodes, no adjuvant therapy" is now virtually defunct. This partly reflects the growing realisation that such patients remain at high risk of premature death, and is especially relevant to older women in whom tamoxifen is likely to be prescribed whatever their nodal status. Even for younger women in whom chemotherapy is being considered, substantive adjuvant chemotherapeutic benefit is now recognised in node-negative cohorts [2]; preliminary results from the updated Early Breast Cancer Trial-