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When the use of breast conservation in Europe was still in its formative stages, local tumour excision was introduced during the 1960s as an adjunct to radical radiotherapy in order to allow local control to be achieved more reliably with lower doses [1,2]. Subsequently, the notion that conservative surgery might be considered a ‘radical’ operation was suggested by Veronesi and associates [3], and the National Surgical Adjuvant Breast and Bowel Project (NSABP) popularised the concept of microscopically ‘clear’ excision margins in their B-06 Trial [4]. As a consequence since the 1980s breast-conserving therapy is generally no

longer thought of in terms of ‘primary radiotherapy’. Surgeons have largely abandoned excisional biopsy in favour of wider excisions, with the intention of obtaining negative margins, and radiotherapy is now sometimes deferred for months to allow the timely administration of cytotoxic chemotherapy. Despite incontestable evidence from multiple randomised trials that breast irradiation dramatically reduces the rate of ipsilateral breast tumour recurrence (IBTR) by a factor of approximately 4-fold [5–8], the question continues to be raised as to whether or not breast irradiation can be dispensed with altogether, at least in a subset of favourable patients.

The benefits and disadvantages of breast irradiation have been extensively discussed in the two position

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papers by Rolf Sauer and Arne Wallgren that constitute the present debate [9,10]. The main advantage of breast irradiation resides in the prevention of IBTR, the principal disadvantages being those of cost and inconvenience, and to a lesser extent the acute and (uncommon) late toxicity. Enthusiasm for preventing IBTR at all costs is also tempered by two additional considerations: first, a survival advantage has not thus far been conclusively demonstrated in trials randomising patients to receive or not to receive breast irradiation; second, since most patients do not recur even without breast irradiation, it might be more 'efficient' to reserve radiotherapy for the treatment of patients who suffer IBTR after conservative surgery alone, as most such patients could be presumed to be candidates for a second breast-conserving procedure. Although there are hints from individual trials, as pointed out by Sauer, that patients randomised to receive breast irradiation may tend to have fewer distant metastases [5,6], Wallgren rightly mentions that these differences could at least partially be explained by detection bias. Even though it is now clearly established that IBTR is an unfavourable prognostic event [11], and recent analyses of failure data are consistent with the notion that IBTR is sometimes the source of distant dissemination [12], it must be conceded that overviews of data from the randomised conservation trials do not demonstrate a clear survival benefit from preventing IBTR, either using radiotherapy or total mastectomy [13].

The most cogent arguments in favour of breast irradiation are therefore those based upon the possible direct consequences of local failure: namely the psychological burden of such an event, the threat of breast loss, and the potentially increased risk of uncontrolled local-regional disease. Published experience has not confirmed the hypothesis that a large majority of patients recurring after conservation surgery will be able to keep their previously unirradiated breasts. Despite the intention to favour conservative salvage surgery, data from prospective trials indicate that breast loss is the consequence of IBTR in a substantial percentage of cases, even in patients not having had breast irradiation [5,14]. Moreover, little is known regarding the long-term results of conservative salvage surgery and salvage radiotherapy. In addition, data from randomised trials suggest that the 4-fold greater IBTR rate resulting from omission of breast irradiation exposes patients to a significantly greater risk of uncontrolled local-regional cancer. In the Scottish Conservation Trial, 3–4 times as many patients treated without initial radiotherapy had local-regional relapse uncontrolled by subsequent treatment [6], and in the NSABP B-06 Trial the risk of recurrent cancer on the chest wall was approximately six times greater in patients treated by initial lumpectomy without radiotherapy, relative to those having had breast irradiation [7]. Thus, breast irradiation cannot be

omitted in unselected patients without significantly decreasing the percentage of patients who will survive free from uncontrolled local-regional disease and with the breast preserved.

Neither of the authors advocates immediately abandoning breast irradiation as standard treatment for the majority of conservatively operated patients with invasive cancers, and both accept the notion that low-risk groups must exist that do not substantially benefit from the security provided by radiotherapy. Wallgren argues that more than two-thirds of patients could theoretically be spared breast irradiation, including those who would not have recurred without it, and those who recurred despite it. This argument, of course, might be applied to any 'adjuvant' treatment, be it local or systemic. It could also be applied to surgery, arguing that in patients receiving systemic treatment and radiotherapy, an operation might be of benefit in only a minority of patients. This latter hypothesis, however, has yet to be addressed in a prospective, controlled trial.

Both Sauer and Wallgren emphasise the difficulty encountered in defining low-risk patients appropriate for conservation surgery alone, including the question as to what constitutes an acceptable IBTR rate. Selection criteria will include older age (lower limit?), small tumour size (how small?), nodal negativity, favourable morphological features (no extensive intraductal component or lymph vessel invasion, non-lobular histology, low grade), wide excision margins (how wide? segmental or quadrant resection?), and perhaps receptor positivity (allowing tamoxifen therapy) [15]. Such criteria currently describe a minority of patients, but in a mammographically screened population low-risk cases should be commonly encountered. It remains to be proven in prospective studies that favourable subgroups can be consistently defined with IBTR rates less than 1–2% per annum without resorting to atypically large resections and extremely time-consuming pathological evaluations. Moreover, it is likely to remain unclear whether or not such practices can be exported outside of major centres of expertise.

Wallgren implies that, if patients knew the 'truth' about how small the statistical chances of benefit were, they would often elect not to receive radiotherapy. Although cultural differences may account for some variability in patient attitudes, North American studies suggest that most patients would be very reluctant to forego breast irradiation, even when the perceived benefit is extremely small or even non-existent [16,17]. Thus, the arguments regarding cost-benefit analysis are likely to be of more interest to governmental health resource planners than to breast cancer patients. If tendencies in North America are indicative, the latter interest group is likely to have increasing influence on future practices in the coming years. Clinical research in breast cancer has inexorably led towards more and more comprehensive

therapies, based on the (questionable) notion that even a small risk reduction is worthwhile, once it has been proven to be ‘statistically significant’. Research aimed at restricting the use of a standard treatment such as breast irradiation goes against this trend, in that it can at best produce oncological results that are ‘only a little worse’, in exchange for a reduction in cost (including morbidity) and inconvenience. The difficulty in conducting such research is illustrated by the recent experience of the European Organization for Research and Treatment of Cancer (EORTC) Breast and Radiotherapy Cooperative Groups, whose trial randomising low-risk patients to receive or not to receive breast irradiation was closed after recruiting less than 10 patients during the almost 2 years following its inception. It is difficult to generate enthusiasm amongst clinicians for research that does not promise a better result, and patient participation in such studies is problematical.

So is breast irradiation worthwhile? Considering the excellent overall results currently obtained, one hardly dares not to answer in the affirmative. At this beginning of the twenty-first century, it must be admitted that whole-breast radiotherapy remains the (almost) uncontested standard of care after conservation surgery for invasive cancer. But like Wallgren, this author believes that the future will bring some changes in the unselected, systematic use of this modality. A recent report describes a 5-year IBTR rate of only 1% in patients receiving standard breast-conserving therapy for screen-detected cancers in the Manchester area [18]. In a certain sense these outstanding results are disconcerting, as such a high level of control implies that more than 90% of the patients would not have recurred locally even if they had not received radiation. There is clearly room for truly localised treatment of selected patients with favourable presentations of breast cancer, as early tumours are often small and unifocal. It is to be hoped that improvements in our ability to identify such cases, including modern imaging techniques, will allow the safe development of simplified treatment approaches for selected patients.

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