

Radiotherapy for breast cancer

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Introduction

Previous overviews, such as that conducted by the Early Breast Cancer Trialists Collaborative Group (EBCTCG 2002) [1] have demonstrated an absolute reduction in breast cancer deaths following post-operative radiotherapy; however, this was partly offset by an increase in non-breast cancer deaths after long term follow up. More recent studies, including patients treated with megavoltage therapy and conventional fractionation schedules, have however demonstrated a larger survival advantage without showing detrimental effects on cardiac events. Furthermore, new studies suggest a relative and absolute survival benefit from radiotherapy treatment particularly for patients with low to intermediate risk disease, challenging current consensus on the indication for post-operative radiotherapy, which is more conservative in North America compared to, for example, France. The recent meta-analysis from the EBCTCG demonstrated that the improvement in local control also has an impact on survival by reducing the breast cancer mortality rate. In general, one can state that avoidance of four local recurrences results in the avoidance of one breast cancer death [2].

Breast conserving therapy

Recently there has been increased discussion about the need for whole breast radiotherapy following breast-conserving surgery. Vinh-Hung and Verschraegen conducted a pooled analysis of 15 randomised trials involving 9422 patients in which breast radiotherapy was compared with no radiotherapy following breast conserving surgery [3]. They concluded that omission of radiotherapy resulted in a large increase in breast recurrences by a factor of three. Further, mortality data from a pooled total of 8206 patients in 13 trials revealed a relative risk of mortality of 1.086 if radiotherapy was omitted; in other words, a 8.6% relative excess mortality.

Two recently published randomised trials from Sweden and Germany also came to the conclusion that, even in low risk node negative, older patients (45–

75 years), breast-conserving surgery alone is insufficient treatment. These findings are also in line with retrospective series such as that published by Rapti and colleagues who analysed the mortality data from the Geneva cancer registry for stage I breast cancer patients. The recent meta-analysis from the EBCTCG demonstrated that the improvement in local control and impact on survival in breast conserving therapy is similar as seen by postmastectomy radiotherapy (see below).

Margins, young age and boost in breast conserving therapy

In a population based study, Kroman and colleagues looked at the mortality effects of breast conserving therapy with breast irradiation compared with mastectomy in patients under 50 years of age in Denmark between 1982 and 1998. There was no difference in survival between patients receiving breast conserving therapy and mastectomy. However, patients younger than 35 years treated with breast conserving therapy had a significantly increased risk of local recurrence compared with patients aged between 45–49 years.

This negative effect of younger age, and furthermore, tumour positive margins, on local control has also been reported in a number of retrospective studies.

In a detailed analysis of the results of the EORTC ‘boost versus no boost’ trial, which included 5569 patients with early stage breast cancer, only young age (<40 years) and the boost dose were independent factors related to local control [4]. For patients aged 35 years or younger, the local control rate was 82%, whereas for patients over 60 years the figure was 97%. The trial randomised patients following a complete local excision and 50 Gy irradiation to the whole breast to either no further irradiation or a boost of 16 Gy to the tumour bed. For patients 40 years or younger the boost decreased the local recurrence rate from 20% to 10% at 5 years [5]. Recent information therapy on long term follow up has shown that giving a boost dose after whole breast irradiation further reduces the local

recurrence rate by a factor of two, not only for young patients but also for older patients (Bartelink, JCO, in press).

Post-mastectomy radiotherapy

The effect of post-mastectomy radiotherapy has been the subject of evaluation in a number of studies, particularly looking at the potential benefits in early stage disease. Van der Hage and colleagues [6] reviewed the effect of chemotherapy and radiotherapy on the local control and survival of patients entered into three EORTC randomised trials. The beneficial effect of radiotherapy on local control translates into a significant reduction in the risk of death by half for patients with one to three tumour positive lymph nodes, whereas for patients with four or more positive lymph nodes the addition of radiotherapy reduces the local recurrence rate by a factor of two, but this had no significant impact on the overall survival.

These findings confirm those of Van de Steene and colleagues who looked in detail at a number of objective parameters from 36 randomized radiotherapy trials included in the EBCTCG meta-analysis [1]. In trials with the highest crude survival (80%), radiotherapy produced a 20% reduction in the odds of death. In trials with poor prognosis patients, the benefit from radiotherapy decreases. In the analysis of individual trials the greatest reduction in mortality ratio was seen for patients with no to three positive nodes compared to patients with four or more nodes.

In a retrospective comparison of mastectomy patients who had received doxorubicin-based chemotherapy, Woodward and colleagues [7] compared 470 patients who had been irradiated to 1031 patients who had not. Although the irradiated group generally has worse prognostic features, post-mastectomy irradiation led to a lower rate of loco-regional recurrence in all subsets, including patients with T1 or T2 tumours and one to three positive nodes (10 year loco-regional recurrence rates of 3% versus 13%, $P = 0.003$).

More clarification is urgently needed to define the patients who will benefit most from post-operative radiotherapy, particularly in the intermediate risk group with T1–2 N1 disease. In particular, whether all fields or just the chest wall require treatment.

Chest wall irradiation in combination with breast reconstruction

Breast reconstruction should not preclude women from optimal oncological treatment if chest wall

radiotherapy is indicated. Reports on series of breast reconstruction using either autologous tissue or implants have illustrated that, with careful attention to surgical technique, excellent aesthetic results with a low reconstruction failure rate can be achieved in combination with radiotherapy.

Conclusion

Radiotherapy in breast cancer treatment increases the local control rate by a factor of three to four, following mastectomy or breast conserving surgery. For breast conserving therapy, an additional 16 Gy leads to a further doubling of the local control rate. For all patient groups, a greater local control translates into improved survival rates, especially in patients with earlier stages of the disease.

Conflict of interest statement

None declared.

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