

Radiation therapy in breast cancer

Radiation therapy has been part of the treatment of breast cancer for many decades.

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Radiation therapy has been a part of the treatment of breast cancer since the early 1930s, and over time, through both careful review of results from what was initially an empirical practice, and later on from well-conducted randomised studies, a large body of data and experience has been built up to inform current evidence-based standards of practice in 2008.

Ionising radiation, when properly used, offers a highly localisable modality of therapy with the ability to preferentially kill tumour cells and spare normal cells. Simply put, to give radiotherapy (RT) safely and effectively, one must do the following:

- Aim it carefully (*planning*), to cover the volume that needs to be treated, and avoid as much as is possible what does not need to be treated.
- Give it slowly (*fractionation*) as a small daily dose building up to a total dose that has been shown to be biologically effective for the aim of the therapy. Fractionation exploits the fact that normal tissues have effective high capacity repair mechanisms for sublethal damage to cellular DNA, whereas tumour cells generally do not have competent repair capabilities. Over a fractionated course of RT (typically 25 - 30 treatments), the normal tissues in the irradiated volume sustain little severe acute or long-term damage, whereas any cancer cells generally receive lethal cumulative damage.

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In the management of potentially curable breast cancer, RT is most commonly given as an adjuvant for loco-regional control after definitive surgery, although rarely radiotherapy may be used as the definitive therapy. In the palliative setting, RT has a very useful and varied role in management of such problems as bone metastases, brain metastases and locally advanced symptomatic breast masses, to name a few.

In common with all specialties of medicine, RT is constantly evolving, so this review will look at some pertinent issues of change and progress in the two most common uses of RT in breast cancer.

Breast-conserving therapy

It has been known for 20 years that mastectomy is not needed for most early tumours, and with an increasing proportion of patients

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diagnosed on programmes of mammographic screening it has been estimated that currently up to 80% of patients presenting with early invasive cancer in the developed world could be treated with breast-conserving therapy (BCT).

A recent meta-analysis¹ confirmed that post-lumpectomy RT in stage 1 and 2 breast cancer reduces the 5-year local recurrence rate from 26% to 7% (Fig. 1). To improve this further, detailed studies of the reasons for local recurrence have shown the following:

- A high technical standard of planning and delivering the adjuvant RT is vital. In 2008 all patients are now treated with highly individualised 3D conformal radiotherapy (3DCRT). This has a double benefit in maximising efficacy and improving local control by ensuring homogeneous dose coverage of the breast by avoiding areas of underdose ('cold spots'), and at the same time eliminating areas of relative overdose ('hot spots') thus minimising normal long-term tissue toxicity (skin changes and fibrosis) which negatively affect cosmesis.
- It is important to give a 'boost dose' of RT to the lumpectomy site on completion of the RT to the whole breast. To accurately plan this boost volume the radiation oncologist needs full information about the preoperative clinical and radiological findings, the operative technique and findings, and detailed pathology reported in a standardised and systematic manner. This has reinforced the trend to close co-operation between breast surgeons and radiation oncologists and pathologists, preferably in a multidisciplinary forum. Perhaps the greatest advance in the management of breast cancer has been realised by the development of close co-operation rather than competition between the different specialties involved.
- The association between the pathological margin status of the lumpectomy specimen and risk of local recurrence after BCT has been shown conclusively so that it has become accepted that re-excision is the norm if margins are positive and should be considered if margins are close (<2 mm). An ongoing randomised controlled trial is examining whether or not the increased local recurrence risk of focally positive or close margins can be counterbalanced by increasing the boost dose, since further re-excision surgery is often technically difficult and it is seldom that any residual tumour is found in the re-excision specimen.
- There is now a large body of data showing that patients with infiltrating lobular cancer (ILC) do not have a higher risk of

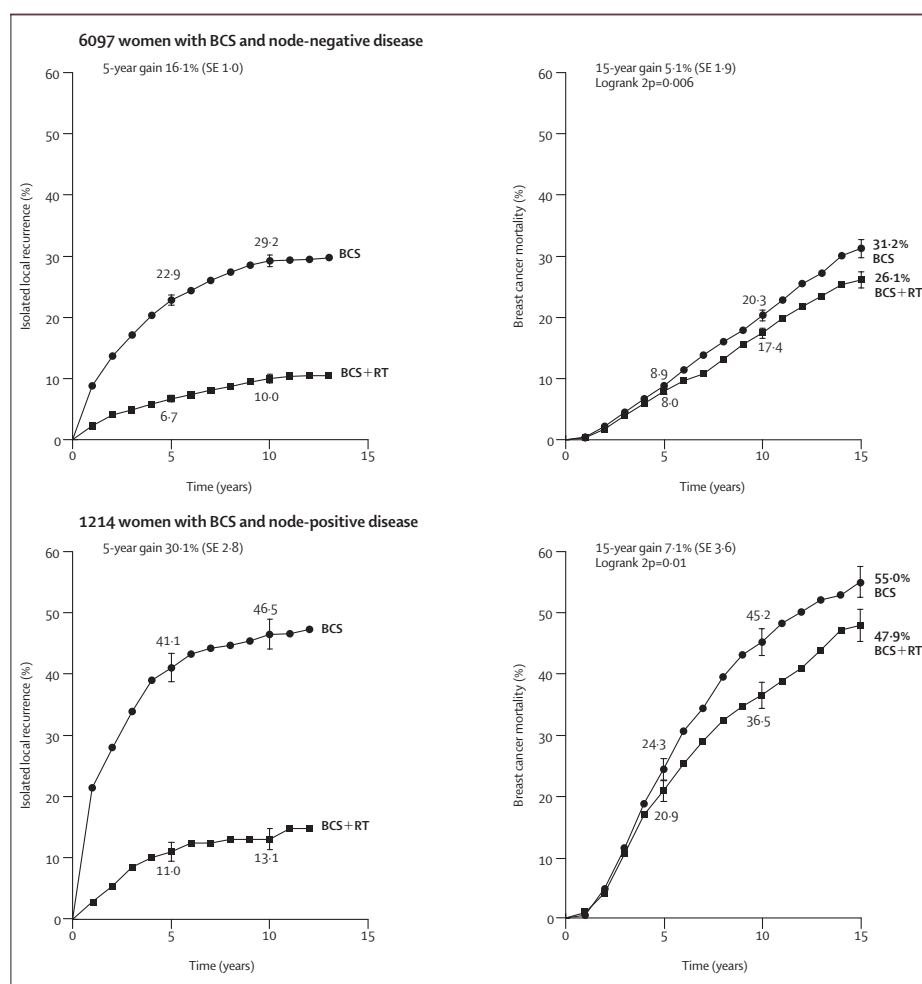


Fig. 1. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on local recurrence and breast cancer mortality – 15-yr probabilities. Data from 10 trials. Vertical lines indicate 1 SE.¹

local recurrence after BCT than patients with ductal cancer. ILC is known for multicentricity and it may be more difficult to visualise its true extent, which raised concerns about the use of BCT. A number of studies have reported 5-year local recurrence rates equal to those of patients with invasive ductal cancer as long as careful surgery and review of the pathology with re-excision, if necessary, is done. However, it is accepted that ILC is more often quite diffuse and that conversion to mastectomy may be optimal in these patients.

- Youngage (<35 years) has been shown to be an independent unfavourable risk factor for local control after BCT. The relative reduction in risk of local recurrence from adjuvant radiotherapy is constant in all age groups but the younger patient has a higher baseline recurrence risk. However, young age per se is not a contraindication to BCT, especially since nearly all younger patients now receive adjuvant systemic chemotherapy and hormonal therapy, which has been shown to reduce local recurrences by between 35% and 53%. Also, nowadays all patients get a RT boost to the tumour bed (as described above) and in the randomised trials proving the value of the RT boost to the tumour bed, the benefit was predominantly in the younger patients (<50 years), with little extra benefit in patients over 60. Essentially there is no cookbook approach in the younger patient and all options must be discussed with the patient.

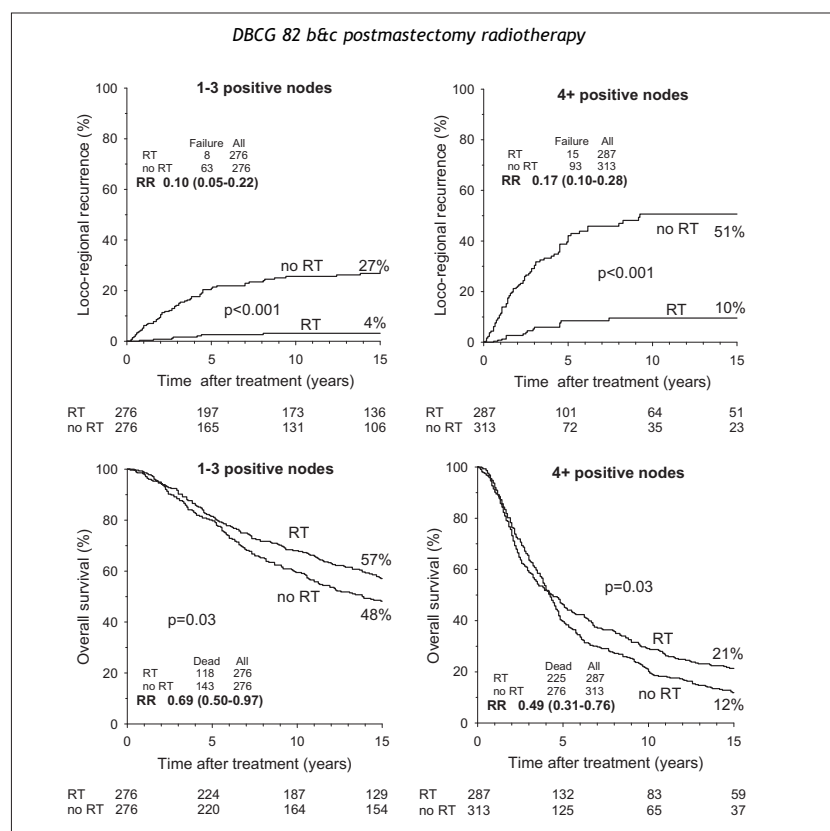


Fig. 2. Fifteen-year actuarial values and frequencies of loco-regional recurrence (LRR) and survival as a function of the number of positive nodes and post-mastectomy radiotherapy.²

Post-mastectomy radiotherapy

The role of post-mastectomy chest wall and regional nodal RT for locally advanced disease is well accepted. The 2005 update by the Oxford overview group¹ reviewed the long-term data from RCT of post-mastectomy RT and clearly demonstrated that at 15 years there was a 70% reduction in the rate of local recurrences in all patients irrespective of age, tumour characteristics, or administration of systemic therapy. What was also shown was an improvement in overall survival. The data show that for every 4 local recurrences avoided at 5 years, 1 breast cancer death was avoided. This is because local chest wall recurrences have a high propensity to seed systemically (50% occur with synchronous metastatic disease) and any effort to prevent local recurrence is very worthwhile.

The absolute improvement in local control depends on the baseline risk, with the highest gain for patients at high risk, hence the consensus that post-mastectomy RT is indicated in patients with 4 or more involved

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axillary nodes, T3 and T4 tumour stage, invasion of the pectoral muscle or positive surgical margins.

There is less consensus on the benefit of post-mastectomy regional RT for patients with early-stage disease (T1 T2, <LN). Theoretically these patients might have the highest breast cancer specific survival from eradicating locoregional disease because of a lower probability of spread beyond the regional lymph nodes.

A recently published update² (Fig. 2) of the large Danish randomised trial of post-mastectomy RT confirmed that the 15-year local control (27% v. 4%) and survival (57%

v. 48%) benefits were substantial after RT v. no RT in the 1 - 3 positive node group. The same order of benefit has been seen in the other randomised trials of post-mastectomy RT, and the Danish researchers make the point that there is now a need for review of the current guidelines for post-mastectomy RT.

Complications from radiotherapy

With the delivery of smaller fractions, the complications from radiotherapy have markedly decreased. However, problems

are seen. Acute problems, defined as during and up to 6 months after RT, include skin erythema, breast tenderness, mild tiredness, and occasional mild nausea. Late problems (>6 months post RT and usually 2 - 3 years or more) include skin telangiectasia, subcutaneous fibrosis and thickening, lymphoedema of the arm, lung fibrosis, brachial plexopathy, and secondary cancers.

References

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2. Overgaard M, Nielsen HM, Overgaard J. Is the benefit of post mastectomy irradiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 b&c trials. *Radiother Oncol* 2007; 82: 247-253.

In a nutshell

- In the management of breast cancer, radiotherapy is most commonly used in the adjuvant setting.
- Breast-conserving surgery and radiotherapy is a safe option for the majority of patients with a single lesion.
- Re-excision then radiotherapy should be considered if surgical margins are involved.
- Post-mastectomy radiotherapy reduced the local recurrence rate in all patients with nodal involvement, and especially with >4 axillary nodes involved.
- The acute complications seen from adjuvant radiotherapy are generally mild and transient.

Single Suture

Use a photo diet log for success

A study of eating habits of people on diet comparing the effects of written food diaries with taking a snapshot of each meal suggests that the photographic variety is the most effective. Food diaries track food consumption during weight loss programmes, but now people are using digital cameras to record their meals rather than laboriously writing everything down.

Lydia Zepeda and David Deal at the University of Wisconsin-Madison asked 43 people to record what they ate for one week in words and as pictures. When the volunteers were followed up, the photo diaries seemed to be the most effective. According to the authors, these photo diaries provided a powerful visual documentation of snacking, but also prompted participants to actually think hard about what they were about to photograph – and eat.

Written diaries are often filled in long after a meal – too late to help someone change their minds – and do not provide as powerful a reminder of the quantity and quality of the food eaten.

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