NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Early and locally advanced breast cancer: diagnosis and management

Draft for consultation, March 2023

This guideline covers diagnosing and managing early and locally advanced breast cancer. It aims to help healthcare professionals offer the right treatments to people, taking into account the person's individual preferences.

This guideline will update NICE guideline NG101 (published July 2018).

Who is it for?

- Healthcare professionals
- Commissioners and providers of breast cancer services
- People with early and locally advanced breast cancer, their families and carers

What does it include?

- new recommendations on radiotherapy
- recommendations for research related to radiotherapy
- the rationale and impact section that explains why the committee made the 2023 recommendations and how they might affect services.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on effectiveness of different hypofractionation radiotherapy regimens. You are invited to comment on these new recommendations only. These are marked as **[2023].**

Recommendations shaded in grey are not part of this update and are given for context only. We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification. Rationale sections for these recommendations have not been included.

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.10 Radiotherapy

1.10.1 Use a radiotherapy technique that minimises the dose to the lung and heart. **[2018]**

1.10.2 Use a deep inspiratory breath-hold radiotherapy technique for people with left-sided breast cancer to reduce the dose to the heart. **[2018]**

For a short explanation of why the committee made the 2018 recommendations and how they might affect practice, see the rationale and impact section on radiotherapy techniques.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Radiotherapy after breast-conserving surgery

1.10.3 Offer whole-breast radiotherapy to people with invasive breast cancer who have had breast-conserving surgery with clear margins. **[2018, amended 2023]**

1.10.4 Consider partial breast radiotherapy as an alternative to whole-breast radiotherapy for women who have had breast-conserving surgery for invasive cancer (excluding lobular type) with clear margins and who:

- have a low absolute risk of local recurrence (defined as women aged 50 and over with tumours that are 3 cm or less, N0, ER-positive, HER2-negative and grade 1 to 2), **and**
- have been advised to have adjuvant endocrine therapy for a minimum of 5 years. **[2018]**

1.10.5 If partial breast radiotherapy (see recommendation 1.10.4) may be suitable for a woman, discuss the benefits and risks with them and reach a shared decision on its use. Topics to cover include that:

- local recurrence with partial breast radiotherapy at 5 years is equivalent to that with whole-breast radiotherapy
- the risk of local recurrence beyond 5 years is not yet known
- there is a potential reduction in late adverse effects. **[2018, amended 2023]**

1.10.6 When giving partial breast radiotherapy, use external beam radiotherapy. **[2018]**

1.10.7 Consider not using radiotherapy for women who:

- have had breast-conserving surgery for invasive breast cancer with clear margins **and**

- have a very low absolute risk of local recurrence (defined as women aged 65 and over with tumours that are T1N0, ER‑positive, HER2‑negative and grade 1 to 2) **and**
- are willing to take adjuvant endocrine therapy for a minimum of 5 years. **[2018]**

1.10.8 When considering not using radiotherapy (see recommendation 1.10.7), discuss the benefits and risks with the woman (see table 5) and explain that:

- without radiotherapy, local recurrence occurs in about 50 women per 1,000 at 5 years, and with radiotherapy, occurs in about 10 women per 1,000 at 5 years
- overall survival at 10 years is the same with or without radiotherapy
- there is no increase in serious late effects if radiotherapy is given (for example, congestive cardiac failure, myocardial infarction or secondary cancer). **[2018]**

Table 5 Benefits and risks of radiotherapy compared with no radiotherapy in the low risk group described in recommendation 1.10.7

-	Radiotherapy	No radiotherapy
Effect on local recurrence	On average, in 1,000 women, over 5 years local recurrence occurs in about 10 women, and does not occur in about 990 women	On average, in 1,000 women, over 5 years local recurrence occurs in about 50 women, and does not occur in about 950 women
Effect on survival	No difference in overall survival at 10 years	No difference in overall survival at 10 years
Risks	Possibility of short- and long-term adverse effects on the breast, and resulting cosmetic changes (such as skin soreness, changes to colour of skin, radiation fibrosis or stiffening of the breast tissue)	No short-term or long-term adverse effects on the breast, or cosmetic changes
Side effects	In this group of women at low risk, there is no increase in serious late side effects of radiotherapy (such as congestive cardiac failure, myocardial infarction or secondary cancer)	No side effects of radiotherapy will occur
Administration	Given at the treatment centre over a 3-week period for 5 days in each week, or a 1-week period for 5 days in that week	No need to attend the treatment centre for radiotherapy sessions

1.10.9 Consider adjuvant radiotherapy for people with DCIS following breast-conserving surgery with clear margins. Discuss the possible benefits and risks of radiotherapy (also see the section on surgery to the breast), and make a shared decision about its use. **[2009, amended 2023]**

For a short explanation of why the committee made the 2018 recommendations and how they might affect practice, see the rationale and impact section on radiotherapy after breast-conserving surgery.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Radiotherapy after mastectomy

1.10.10 Offer adjuvant postmastectomy radiotherapy to people with node-positive (macrometastases) invasive breast cancer or involved resection margins. **[2018]**

1.10.11 Consider adjuvant postmastectomy radiotherapy for people with node-negative T3 or T4 invasive breast cancer. **[2018]**

1.10.12 Do not offer radiotherapy following mastectomy to people with invasive breast cancer who are at low risk of local recurrence (for example, most people who have lymph node-negative breast cancer). **[2018, amended 2023]**

Dose fractionation for external beam radiotherapy

1.10.13 Offer a regimen of 26 Gy in 5 fractions over 1 week for people with invasive breast cancer having partial breast, whole breast or chest wall radiotherapy after breast-conserving surgery or mastectomy without regional lymph node irradiation. **[2023]**

1.10.14 Consider a regimen of 40 Gy in 15 fractions over 3 weeks for people with invasive breast cancer having partial breast, whole breast, or chest wall radiotherapy after breast conserving treatment or mastectomy when they:

- are having concurrent chemotherapy, or
- have a condition that increases sensitivity to radiotherapy, or
- have had implant–based reconstruction, or
- have any other factor that would mean having radiotherapy over 3 weeks is more acceptable (for example, people who experience high levels of fatigue). **[2023]**

1.10.15 When discussing the risks and benefits of the 2 regimens, follow the recommendations on communication and information in the NICE guideline on patient experience in adult NHS services.

1.10.16 Offer external beam radiotherapy, giving 40 Gy in 15 fractions over 3 weeks, for people with invasive breast cancer having regional lymph node irradiation, with or without partial breast, whole breast, or chest wall radiotherapy after breast conserving treatment or mastectomy.

For a short explanation of why the committee made the recommendation for research, see the rationale section on dose fractionation.

Full details of the evidence and the committee's discussion are in the evidence review for hypofractionation regimens

Breast boost following breast-conserving surgery

1.10.17 Offer an external beam boost to the tumour bed for people with invasive breast cancer and a high risk of local recurrence, following whole-breast radiotherapy. **[2009, amended 2023]**

1.10.18 Inform women of the risk of side effects associated with an external beam boost to the tumour bed following whole-breast radiotherapy. **[2009, amended 2018]**

Radiotherapy to nodal areas

1.10.19 Do not offer adjuvant radiotherapy to regional lymph nodes to people with invasive breast cancer who have histologically lymph node-negative breast cancer. **[2009, amended 2018]**

1.10.20 Do not offer people with invasive breast cancer adjuvant radiotherapy to the axilla after axillary clearance. **[2009, amended 2023]**

1.10.21 Offer adjuvant radiotherapy to the supraclavicular fossa to people with invasive breast cancer and 4 or more involved axillary lymph nodes. **[2009]**

1.10.22 Offer adjuvant radiotherapy to the supraclavicular fossa to people with invasive breast cancer and 1 to 3 positive lymph nodes if they have other poor prognostic factors (for example, T3 and/or histological grade 3 tumours) and good performance status. **[2009]**

1.10.23 Consider including the internal mammary chain within the nodal radiotherapy target for people with node-positive (macrometastases) invasive breast cancer. **[2018]**

For a short explanation of why the committee made the 2018 recommendation and how it might affect practice, see the rationale and impact section on radiotherapy to nodal areas.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Intraoperative radiotherapy

1.10.24 For guidance on intraoperative radiotherapy, see the NICE technology appraisal guidance on the intrabeam radiotherapy system for adjuvant treatment of early breast cancer. **[2018]**

Recommendations for research

The guideline committee has made the following key recommendations for research.

1 Effectiveness of 26 Gy in 5 fractions over 1 week regimen in people receiving concurrent chemotherapy or breast reconstruction

What is the effectiveness of radiotherapy given in 26 Gy in 5 fractions over 1 week compared to 40Gy in 15 fractions over 3 weeks in people with early or locally advanced invasive breast cancer who are offered concurrent chemotherapy or breast reconstruction?

For a short explanation of why the committee made the recommendation for research, see the rationale section on dose fractionation.

Full details of the evidence and the committee's discussion are in the evidence review for hypofractionation regimens

2 Effectiveness of 26 Gy in 5 fractions over 1 week regimen in people receiving nodal irradiation

What is the effectiveness of radiotherapy given in 26 Gy in 5 fractions over 1 week compared to 40 Gy in 15 fractions over 3 weeks in people with early or locally advanced invasive breast cancer who are also offered nodal irradiation?

For a short explanation of why the committee made the recommendation for research, see the rationale section on dose fractionation.

Full details of the evidence and the committee's discussion are in the evidence review for hypofractionation regimens

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice. They link to details of the evidence and a full description of the committee's discussion.

Dose fractionation

Recommendations 1.10.13 to 1.10.16

Why the committee made the recommendations

The committee noted that most centres use regimens of either 40 Gy in 15 fractions, or 26 Gy in 5 fractions. However, there was variation between centres in which regimen they used.

The evidence compared a number of different hypofractionation regimens, but the committee focused on the evidence from 2 randomised controlled trials (RCTs) that

compared the clinical effectiveness and safety, and a cost effectiveness analysis, of the 2 hypofractionation regimens that are established in current practice (40 Gy in 15 fractions over 3 weeks and 26 Gy in 5 fractions over 1 week). High to very low-quality evidence showed that the effects of both hypofractionation regimens were comparable, with no clinically important differences between treatment arms for all-cause mortality, breast cancer-related mortality or disease recurrence. Economic evidence showed the 26 Gy in 5 fractions as an effective use of NHS resources compared with 40 Gy in 15 fractions and supported its use in current practice. In addition the committee noted that, in their experience, most people preferred to attend radiotherapy appointments over the course of 1 week, rather than over 3 weeks for practical reasons related to fewer trips to the hospital (for example, reduced travelling time and costs, less time off work or from caring responsibilities). The committee recognised how the COVID-19 pandemic had also impacted current practice, and accelerated the change to implement the shorter 26 Gy in 5 fractions regimen.

However, the evidence did show that there was a higher incidence of outcomes related to adverse events at 5 years (such as normal tissue effects, and quality of life measurements related to swollen breasts and harder or firmer breasts) for people who were given 26 Gy in 5 fractions compared to 40 Gy in 15 fractions. The committee also noted that some people experienced increased levels of fatigue from the 5-day regimen, and this was harder to manage.

The committee agreed that in their experience, the 26 Gy in 5 fractions regimen is widely accepted by people, despite the higher incidence of adverse events. After taking into account the benefits of a shorter regimen and the impact of the adverse events, the committee recommended the use of 26 Gy in 5 fractions for people having partial breast, whole breast or chest wall radiotherapy after breast-conserving surgery or mastectomy.

However, the committee recognised that there are gaps in the evidence and there may be circumstances when a 40 Gy in 15 fractions treatment regimen would be more suitable than 26 Gy in 5 fractions. For example, the evidence did not consider the use of the 26 Gy in 5 fractions regimen in people receiving concurrent chemotherapy for breast cancer. The committee also noted that the number of

people who had undergone breast reconstruction surgery was small, and it was difficult to determine the most effective hypofractionation regimen for this group. The committee highlighted the importance of shared decision making for these groups and ensuring that people are aware of the benefits and risks of each treatment option. As such, the committee made a recommendation that 40 Gy in 15 fractions over 3 weeks should be considered for some groups of people, and that its use should be agreed between the person and their care team.

The committee discussed the eligibility criteria for some of the trials in the evidence and noted that people who received nodal radiotherapy were excluded from the main study populations. They highlighted that there are particular concerns around adverse effects such as lymphoedema for people who received regional lymph node irradiation. The committee acknowledged that future trials may report results for people who receive regional lymph node irradiation and a hypofractionated radiotherapy regimen and address some of these concerns, but until further evidence is available the 40 Gy in 15 fractions regimen should be used for this group.

Given the lack of evidence for people who are having concurrent chemotherapy and those who are having regional lymph node irradiation, the committee included two research recommendations. These should provide clinicians with an increased understanding of how effective the 26 Gy in 5 fractions regimen is for these groups in future.

How the recommendations might affect practice

The recommendations may reduce variation in practice, with most people being offered 26 Gy over 5 fractions rather than 40 Gy over 15 fractions. This is already current practice in many centres, and will not have a major impact for those centres. For places where 40 Gy in 15 fractions is used more routinely, these recommendations may increase the number of people who are offered 26 Gy over 5 fractions. This will reduce the treatment duration and reduce the costs associated with treatment.

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