NICE National Institute for Health and Care Excellence

Intrabeam radiotherapy for treating early breast cancer Decision aid: user guide and data sources

Role of the decision aid

Recommendation 1.5 of the NICE technology appraisal guidance on Intrabeam states that clinicians wishing to do Intrabeam radiotherapy should ensure that patients understand the uncertainties about the procedure and inform them about alternative treatment options. They should provide patients with NICE's written information on the evidence of the risks and benefits of the range of treatment options available as an aid to shared decision-making.

Deciding between external beam radiotherapy (EBRT, called simply external radiotherapy [ERT] in the decision aid) and Intrabeam involves a trade-off between the probability (but not certainty) of avoiding the need for post-operative radiotherapy, against uncertainties about the effectiveness of Intrabeam. People facing the decision should also take into account the possibility of other adverse effects. The decision aid presents the available information fairly and accurately.

Developing the decision aid

The decision aid was developed by pharmacists in NICE's Medicines and Technologies Programme, technology appraisal specialist staff and members of the appraisal committee. Comments were obtained from consultees on the technology appraisal guidance, including a breast cancer support charity.

Sources of data

The decision aid text reflects the conclusions of the appraisal committee (see the summary of the appraisal committee's key conclusions). Most of the data are taken from the TARGIT-A study (Vaidya et al. 2014) and derive from the TARGIT-A pre-pathology stratum, in which Intrabeam was delivered during the initial surgery (n=2,298). Data on breast fibrosis were taken from Sperk et al. (2012), a report from 1 German treatment centre participating in TARGIT-A (n=109). References to each section of the decision aid are given in table 1.

Median follow-up in TARGIT-A was 2 years and 5 months. To address the issue of follow-up, the TARGIT-A authors compared the 5-year Kaplan–Meier estimates of local recurrence in the conserved breast and overall mortality. These data have been used in the decision aid. All quantitative data have been presented using a common denominator (events per 100 women) with positive and negative framing, in line with guidance on presenting risk in NICE's guideline on patient experience in adult NHS services.

Table 1: References to each section of the decision aid

Page	Section	Evidence
1	What are the options?	The description of EBRT) is taken from NHS Choices; see www.nhs.uk/conditions/radiotherapy/what-happens/ (accessed 16 April 2018). The statement about how EBRT and Intrabeam compare reflects the committee discussion, paragraphs 4.9 and 4.10. The committee agreed that it is not possible to confirm that there is an overall survival benefit with Intrabeam compared with EBRT. It acknowledged that Intrabeam has not been proven to be non-inferior to EBRT and could have a higher risk of local recurrence. The statement about the availability of Intrabeam reflects technology appraisal guidance recommendations 1.1 and 1.2 and repeats NICE's information for the public. The text relating to patient selection for Intrabeam reflects technology appraisal guidance recommendation 1.4.
2	The choice for you	The possibility that no radiotherapy might be an option for some people reflects current practice and NICE's guideline on early and locally advanced breast cancer.
2	How do the benefits and drawbacks of EBRT and Intrabeam compare?	See the committee discussion, paragraph 4.4 and the summary of key conclusions. In TARGIT-A, EBRT was delivered in an average of 23 fractions, longer than the 15 fractions delivered in established clinical practice in the NHS. The radiation doses administered with EBRT ranged from 40 grays to 56 grays in TARGIT-A, whereas established clinical practice in the NHS is a dose of 40 grays. The committee concluded that some doubt remained about the generalisability of the trial data to NHS clinical practice. It concluded that length of follow-up in the trial was too short to show reliably the clinical effectiveness of Intrabeam compared with EBRT for the incidence of local recurrence. The possibility that partial breast radiotherapy might be an option for some people reflects current practice and NICE's guideline on early and locally advanced breast cancer.

Page	Section	Evidence
3	How long is the radiotherapy treatment?	The description of EBRT is taken from NHS Choices (accessed 16 April 2018). In TARGIT A, 21.6% of people in the pre-pathology stratum who were randomised to Intrabeam also had EBRT.
3	How good is the treatment at preventing the cancer coming back?	In the TARGIT-A pre-pathology stratum, the 5-year Kaplan–Meier estimated cumulative risk of local recurrence was 1.1% (95% confidence interval [CI] 0.5 to 2.5) in the EBRT group and 2.1% (95% CI 1.1 to 4.2) in the Intrabeam group, p=0.31. See the committee discussion, paragraphs 4.7 and 4.8. The committee considered the difference in Kaplan–Meier estimates of local recurrence and its 95% CI calculated using the conventional method. It noted that, using this method, the absolute difference between 5‑year Kaplan–Meier estimates for local recurrence in the pre-pathology group is 1% and the 95% CI is −0.68 to 2.68. The committee noted that the CI around the absolute difference in local recurrence at 5 years is wide, and that the upper end of the interval is higher than the pre-specified non-inferiority margin of 2.5%. The committee acknowledged that the rate of local recurrence in TARGIT‑A was low in both treatment groups, and that longer follow-up of patients is needed to provide more long-term data and less uncertain results. The committee considered that the criterion for non-inferiority was not appropriately defined. This meant that the trial was underpowered and the results could not be considered robust enough to determine whether Intrabeam is non-inferior to EBRT in terms of local recurrence. The committee therefore concluded that the non-inferiority of Intrabeam compared with EBRT in terms of local recurrence is unproven.
4	What would my options be if I have local recurrence of my cancer?	See the committee discussion on the potential benefits of Intrabeam, paragraph 4.2. If there is local recurrence after breast-conserving surgery and EBRT, this is usually treated by mastectomy. However, for some patients, brachytherapy may be a suitable breast-conserving treatment instead of mastectomy. If there is recurrence after treatment with Intrabeam, further breast-conserving surgery and EBRT still remain a theoretical treatment option.

Page	Section	Evidence
4	What is the chance of dying from breast cancer or other causes?	In the TARGIT-A pre-pathology stratum, the 5-year Kaplan–Meier estimated cumulative risk of death from breast cancer was 2.7% (95% confidence interval [CI] 1.5 to 4.6) in the EBRT group and 3.3% (95% CI 1.9 to 5.8) in the Intrabeam group, p=0.72. The 5-year Kaplan–Meier estimated cumulative risk of death from other causes was 4.4% (95% CI 2.8 to 6.9) in the EBRT group and 1.3% (95% CI 0.7 to 2.8) in the Intrabeam group, p=0.016. See the committee discussion on the overall survival results from TARGIT−A, paragraph 4.9. The committee agreed that, because the patient baseline characteristics in the trial did not include cardiovascular risk factors, it is not possible to confirm that there is an overall survival benefit with Intrabeam compared with EBRT.
4	How likely is the radiotherapy to damage other parts of my body?	No definite evidence is available to compare the risk of radiation toxicity to other organs. The decision aid reflects the committee discussion on the potential benefits of Intrabeam, paragraph 4.3.
4	How likely am I to get fatigue?	No definite evidence is available to compare the risk of fatigue. The decision aid reflects the committee discussion on the potential benefits of Intrabeam paragraph 4.3.
5	How likely am I to get short-term skin reactions?	No definite evidence is available to compare the risk of short-term skin reactions. TARGIT-A reported rates of more serious radiotherapy-related skin complications (0.8% with EBRT and 0.2% with Intrabeam). These data have not been represented in the decision aid because they relate to the whole trial population rather than only the pre-pathology stratum; the rates quoted are crude event rates, not Kaplan–Meier estimates like the other outcomes; and the denominator is the whole intention-to-treat population. Of this, 9% of the Intrabeam group and 8% of the EBRT group withdrew or did not receive their allocated treatment.

Page	Section	Evidence
5	How likely am I to get longer-term changes to my breast?	In the report by Sperk et al. (2012) the incidence of LENT SOMA scale grade II to grade III fibrosis was 18.4% in the EBRT group (n=55), 5.9% in the Intrabeam-only group (n=34) and 37.5% in the Intabeam plus EBRT group (n=20). In univariate analyses, the difference between Intrabeam-only and Intabeam plus EBRT was statistically significant (p=0.008), but the difference between Intrabeam-only and EBRT was not (p=0.163).
6	Other things to think about	The technology appraisal guidance recommends that Intrabeam should be used only in conjunction with NHS England specified clinical governance, data collection and submission arrangements (see section 6 of the technology appraisal guidance).

References

Sperk E, Welzel G, Keller A, et al (2012) Late radiation toxicity after intraoperative radiotherapy (IORT) for breast cancer: results from the randomized phase III trial TARGIT A. Breast Cancer Research and Treatment 135: 253–60

Vaidya J, Wenz F, Bulsara M, et al (2014) Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. Lancet 383: 603–13

