Health technology description

Breast brachytherapy is considered in the literature as one of the options encompassed by the term accelerated partial breast irradiation (APBI). This covers interstitial or intracavity brachytherapy implants, 3-D conformal external beam radiotherapy (EBRT) or intraoperative radiotherapy techniques, all of which have the potential to shorten the conventional (whole breast) radiotherapy procedure from 5–7 weeks to a few days. In the absence of sufficient randomised trial data, guidance on patient selection based on observational evidence has been offered by the European Society for Therapeutic Radiology and Oncology.1

There are a range of brachytherapy techniques for the application of a radiation source (commonly iridium-192) into breast tissue. These include implanting multiple catheters into which the radioactive source is inserted and the placement of a single inflatable balloon catheter into the breast. The balloon provides a chamber which can contain the radioactive source material. Catheters usually remain in place for a few days and may be implanted intraoperatively or post operatively.

Epidemiology

Breast cancer is the most commonly diagnosed cancer in women in Scotland with around 4,000 new cases diagnosed each year. Age standardised relative 5-year survival is around 80%. In 2009, 1,002 deaths from breast cancer in women were recorded.2

Clinical effectiveness

The use of brachytherapy for breast cancer has been examined in two main clinical situations with the key outcomes being the prevention of recurrence, cancer-specific survival and cosmetic and quality of life measures. The sole use of brachytherapy may replace conventional whole EBRT which commonly follows surgery. Brachytherapy can also be used as a localised boost treatment following standard whole breast irradiation.

Key points

- NICE guidance states that brachytherapy as the sole method of adjuvant radiotherapy for breast cancer after local excision raises no major safety concerns, although the limited evidence on efficacy means that this procedure should only be used in the context of research. It should be noted that this guidance is based on evidence up to 2007. Two large randomised studies are currently in progress in the USA and Europe.

- No systematic review or randomised trial evidence was identified on the use of boost brachytherapy as an adjunct to conventional whole breast irradiation following surgery for breast cancer.

- More work on clinical effectiveness is needed before conclusions can be drawn on cost effectiveness.

- Brachytherapy as sole radiotherapy intervention following breast conserving surgery for patients with early non-invasive breast cancer

NICE conducted a rapid review of published evidence (up to November 2007) comparing the effectiveness of brachytherapy with the effectiveness of whole breast irradiation after breast conserving surgery.3

One RCT was identified. The study was conducted in Hungary between 1998 and 2004 in low-risk patients (as defined by tumour grade, size and surgical margins) (n=258), with early non-invasive breast cancers. There were no statistically significant differences identified between the interventions with respect to 5-year actuarial rates of local recurrence (5% versus 3%; p=0.50) or 5-year cancer-specific survival rates (98% versus 96%). In this low-risk group however, the study may have been underpowered to detect small differences in local recurrence rates.
In addition, around one-third of the patients randomised to brachytherapy received limited field electron beam therapy instead.

More patients in the brachytherapy group had excellent to good cosmetic results compared with those receiving whole breast irradiation (81% versus 66%; p=0.014). The NICE review also reported on a large non-randomised trial (n=398) which used case matched historical controls and found 5-year actuarial rate of cause-specific survival to be 97% for both interstitial brachytherapy and EBRT (p=0.34) in a low-risk population. Another non-randomised trial (n=144) with controls identified by retrospective chart review found local or regional recurrence (at mean follow up of 75 months) of 8% in the brachytherapy group and 5% in the EBRT group (p=0.23).

The NICE review also identified a large number of case series which had a wide range of follow-up periods from a few months to several years. Five of the largest were described in the review to highlight the range of technical issues experienced in the application of brachytherapy and the complications and clinical safety of the techniques.

Reflecting the paucity of randomised data which was identified, NICE issued the following guidance:

‘Current evidence on brachytherapy as the sole method of adjuvant radiotherapy for breast cancer after local excision raises no major safety concerns. Current evidence on its efficacy is limited in quantity and there is little information on long-term outcomes (5 years or more). Therefore, this procedure should be used only in the context of research, which should address control of local disease with a minimum of 5 years of follow-up.’

Two large randomised studies are in progress in the USA and Europe. Furthermore, a large international randomised trial comparing intraoperative radiotherapy (IORT), delivered by low energy x-rays, against external beam whole breast radiotherapy is in progress. However, this IORT technique (known in the USA as electronic brachytherapy) is not conventional brachytherapy and is outwith the scope of this review.

An additional literature search conducted to identify studies published since the NICE guidance identified two more recent systematic reviews of APBI using brachytherapy after breast conserving surgery, and several subsequent reports of mostly uncontrolled cases series.

A systematic review of comparative studies (2009) identified two RCTs and seven non-randomised studies of APBI compared with whole breast EBRT. All nine studies evaluated interstitial or external brachytherapy; the review found no comparative studies that used balloon brachytherapy or intraoperative APBI. Both RCTs were referenced in the NICE guidance (although one was excluded from the evidence summary). The seven non-randomised studies included the two comparative studies whose results were cited in the NICE guidance. All nine studies were judged to be of poor quality. The authors concluded that the available data on APBI compared with whole breast EBRT were insufficient to draw conclusions on their relative effectiveness. The additional literature search identified no other RCTs, and only one subsequently published non-randomised comparative study of APBI compared with whole breast EBRT.

The other systematic review included phase I and II studies (2008). This did not identify any studies not already included in the NICE guidance evidence review and/or included in the aforementioned systematic review of comparative studies. The additional literature search identified several reports of subsequent follow-up data for several of the uncontrolled phase I/II studies and case series that were included in the existing reviews and several reports of additional uncontrolled studies mostly of adjuvant brachytherapy following breast conserving surgery.

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**Boost brachytherapy as an adjunct to conventional whole breast irradiation following surgery for breast cancer**

APBI is a treatment option following whole breast irradiation after surgery to provide a localised boost dose of radiation to the site of excision and adjacent breast tissue. Brachytherapy is one method of applying this additional radiotherapy. No systematic reviews were identified on the effectiveness of breast brachytherapy in this clinical context.

A supplementary search identified very few data all from uncontrolled case series. Serial publication of follow-up data, and duplicate publication (including subsets from the same series and single-centre data from multicentre studies) is very common, making it difficult to determine the exact number of unique studies.
Clinical Safety

A review described the adverse events findings from registry and case review data of patients who had intracavity balloon catheter brachytherapy. The proportion of cases recording the following adverse events was highlighted:

- overall symptomatic seroma formation rate 12.7%
- fat necrosis 2%
- infection 4–9%
- persistent pain 2%
- significant telangiectasia (small, dilated blood vessels on the skin) 5%
- acute skin reaction 12%
- hyperpigmentation 16%
- treatment-related rib fracture 3% (although these patients were menopausal or had osteoporosis)
- balloon catheter rupture 1%

The NICE review also highlighted that in a case series subcutaneous fibrosis occurred in 32% of patients treated with interstitial brachytherapy and 11% of patients treated with balloon brachytherapy. Oedema in 3–6% was also recorded as a key safety finding in some case series.

Cost effectiveness

A review identified two cost-effectiveness studies. The first compared the incremental cost effectiveness of a range of APBI methods with whole breast irradiation for oestrogen receptor positive post menopausal women with early stage breast cancer. The model used assumed all APBI methods to be equally effective. The authors concluded that 3-D conformal external beam techniques were the most cost effective and that intracavity brachytherapy was not likely to be cost effective.

The second study examined societal costs (integrating medical and non medical/patient costs) of eight different whole breast irradiation schedules and APBI treatment regimens used to treat early stage breast cancer and concluded that brachytherapy-based regimens were about twice the cost of external beam and whole breast irradiation strategies.

Equality and Diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the six equality groups defined by age, disability, gender, race, religion/belief and sexual orientation.

The Evidence Note process has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on www.healthcareimprovementscotland.org

About Evidence Notes

For further information about the Evidence Note process, see www.healthcareimprovementscotland.org

To propose a topic for an Evidence Note, email evidencenotes.qis@nhs.net

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network (formally eLibrary) http://www.knowledge.scot.nhs.uk, or by contacting your local library and information service.
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