

National Institute for Health and Care Excellence

Multiple Technology Appraisal (MTA)

INTRABEAM Radiotherapy System for the adjuvant treatment of early breast cancer [ID 618]

Responses to consultees and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

| Section | Consultees | Comments | Action |
|-----------------|--------------------------------------|--|-----------------------|
| Appropriateness | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement Scotland | Yes | Comment noted. |
| | Carl Zeiss | Yes, it is appropriate since the technology improves health and quality of life. | Comment noted. |
| | Breakthrough Breast Cancer | It would be appropriate to refer this topic to NICE for appraisal. | Comment noted. |
| Wording | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |

| Section | Consultees | Comments | Action |
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| | Healthcare Improvement Scotland | Yes, although I would take out 'or locally advanced' breast cancer as the evidence to date is really looking at early breast cancer. | Comment noted. Workshop participants agreed, given the evidence base from the TARGIT-A trial, the remit should be amended to people with 'early operable breast cancer'. |
| | Carl Zeiss | Yes, it does reflect the issues. | Comment noted. Workshop participants agreed, given the evidence base from the TARGIT-A trial, the remit should be amended to people with 'early operable breast cancer'. |
| | Breakthrough Breast Cancer | The wording of the remit does reflect the issues of clinical and cost effectiveness about this technology that NICE should consider. | Comment noted. Workshop participants agreed, given the evidence base from the TARGIT-A trial, the remit should be amended to people with 'early operable breast cancer'. |
| Timing Issues | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement Scotland | Not urgent - evidence not mature. | Comment noted. |
| | Carl Zeiss | A positive guidance would increase access for patients the technology in more NHS hospitals. | Comment noted. |

| Section | Consultees | Comments | Action |
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| | Breakthrough Breast Cancer | <p>Patients receiving radiotherapy for primary breast cancer are required to attend hospital five times a week for three to five weeks. This is very disruptive to a patient's life and means that a return to normalcy after breast cancer treatment is delayed. In addition, attending hospital daily can be expensive for some patients as they may incur costs of petrol or public transport and parking costs. For patients who live far away from the hospital, they may have to arrange to stay near the hospital while they are having radiotherapy treatment. This causes further disruption and means that patients may be away from their homes and families for extended periods of time and may need to make arrangements regarding childcare or caring for other relatives.</p> <p>Prompt implementation of this technology may mean that patients will be able to avoid attending hospital on a daily basis and resume their normal lives much faster. Implementation of this technology may also be beneficial to older breast cancer patients who may in some cases be frail and find travelling to hospital every day is very difficult. This is important as breast cancer is more common among older women with more than 80% of breast cancers being diagnosed in women over the age of 50 (1).</p> <p>Breast Cancer: UK Incidence Statistics – Age (2009), Cancer Research UK, http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/incidence/#age</p> | Comment noted. |

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| Additional comments on the draft remit | Association of Breast Surgery | <p>The proposed Health Technology Appraisal is both relevant and timely since there is level I evidence available from a randomised controlled trial (TARGIT Trial) and a further more updated publication is awaited later this year. The comments below relate to the draft appraisal:</p> <ol style="list-style-type: none"> 1. The objective should be 'To appraise...' 'for the adjuvant treatment of early breast cancer' and not for locally advanced breast cancer. 2. Population: Breast cancer patients with early operable breast cancer – not locally advanced. 3. Other intra-operative techniques (eg: EIOT Trial – intraoperative radiotherapy with electrons), should also be considered to ensure objective comparison of available technology. 4. The INTRABEAM device would only be used for breast cancer treatment at present, in the UK. 5. The proposed remit and scope meets stated aims of NICE. 6. This novel approach to adjuvant radiotherapy has the potential to make a significant impact on health-related benefits, by avoiding the cost, inconvenience and morbidity of external beam radiotherapy in a selected patient group. 7. It could be considered through the MAT process or as an update to the previous NICE guidance on partial breast radiotherapy (2008). | <p>Comments noted. The remit and scope have been amended to people with 'early operable breast cancer' only.</p> <p>The use of other intra-operative techniques was discussed at the scoping workshop. It was not considered that these techniques should be included as comparators because they are not currently in use in clinical practice. It was not considered that their use was sufficiently comparable for them to be included as interventions alongside INTRABEAM.</p> |

Comment 2: the draft scope

| Section | Consultees | Comments | Action |
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| Background information | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement Scotland | Accurate information. Paragraph 2, I'd recommend changing to say '.....adjuvant treatment which <i>includes</i> radiotherapy, hormone therapy, chemotherapy <i>and biological therapy</i> after removal of the primary cancer by surgery.' | Comment noted. The background of the scope has been updated to reflect the use of biological therapies as an adjuvant treatment option. |
| | Healthcare Improvement Scotland (Consultant in Oncology) | Tumour bed boost is not used only in 'people with high risk of local recurrence. The EORTC boost trial shows a benefit all age groups although the absolute benefit in patients > 60 years is only modest. I suggest : , 'using a linear accelerator ,commonly supplemented with an external beam external beam tumour bed boost' | Comment noted. The background of the scope has been updated to reflect this issue. |
| | Carl Zeiss | Yes | Comment noted. The background section has been updated to account for comments from other consultees. |
| | Breakthrough Breast Cancer | The background information appears to be accurate. | Comment noted. The background section has been updated to account for comments from other consultees. |
| The technology/ intervention | Society and College of Radiographers | There are a number of different technologies that provide intra-operative treatment- this is just one. | Comment noted. The use of other intra-operative techniques was discussed at the scoping workshop. It was not considered that their use was sufficiently comparable for them to be included as interventions alongside INTRABEAM. |
| | Association of | No comment | No actions requested. |

| Section | Consultees | Comments | Action |
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| | Breast Surgery | | |
| | Healthcare Improvement Scotland | Yes | Comment noted. |
| | Healthcare Improvement Scotland (Consultant in Oncology) | No comment | No actions requested. |
| | Carl Zeiss | Yes | Comment noted. |
| | Breakthrough Breast Cancer | The description of the technology appears to be accurate. | Comment noted. |
| Population | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement Scotland | As said previously, I would not include locally advanced disease in the scope of this review. | Comment noted. The remit and population have been amended to people with 'early operable breast cancer'. |
| | Healthcare Improvement Scotland (Consultant in Oncology) | It is not appropriate to consider Intrabeam in the context of locally advanced breast cancer where there is skin involvement and whole breast external irradiation with full dose to skin would be required. The assessment should be confined to early breast cancer | Comment noted. The remit and population have been amended to people with 'early operable breast cancer'. |
| | Carl Zeiss | Yes | Comment noted. Following the scoping workshop the remit and population have been amended to people with 'early operable breast cancer'. |

| Section | Consultees | Comments | Action |
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| | Breakthrough Breast Cancer | The population appears to be appropriately defined. | Comment noted. Following the scoping workshop the remit and population have been amended to people with 'early operable breast cancer'. |
| Comparators | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement Scotland | Yes | No actions requested. |
| | Healthcare Improvement Scotland (Consultant in Oncology) | External beam radiotherapy without or without tumour bed boost | Comment noted. |
| | Carl Zeiss | Yes, the external beam radiotherapy with linear accelerator is the currently used NHS comparator. At present, Brachytherapy treatment is not routinely used for early breast cancer in the UK. | Comment noted. |
| | Breakthrough Breast Cancer | The comparator appears to be appropriate. | Comment noted. |
| Outcomes | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement | Yes | Comment noted. |

| Section | Consultees | Comments | Action |
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| | Scotland | | |
| | Healthcare Improvement Scotland (Consultant in Oncology) | Ipsilateral local recurrence rate instead of 'rate of recurrence' and this should be the primary outcome measure with health related QOL should be secondary outcome measure | Comment noted. Workshop participants agreed to amend the outcome 'rate of recurrence' to 'ipsilateral local recurrence rate'. |
| | Carl Zeiss | Yes | Comment noted. |
| | Breakthrough Breast Cancer | <p>The outcome measures currently include overall survival and progression free survival which are not the most important outcomes for radiotherapy treatment. The aim of radiotherapy in the primary setting is to reduce the likelihood of the breast cancer recurring. The role of radiotherapy in the breast cancer treatment pathway is not to save or extend life. While overall survival is important, the rate of recurrence is a more immediate outcome measure for this technology.</p> <p>Rate of recurrence, adverse effects of treatment and health-related quality of life are all appropriate outcome measures for this technology.</p> | Comment noted. Workshop participants agreed that ipsilateral local recurrence rate is an important outcome, and noted that overall survival will be linked to the aforementioned measure. |
| Economic analysis | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement Scotland | The time horizon needs to take into account that the evidence shows that there is a constant annual local recurrence rate of ipsilateral breast cancer for over 20 years | Comment noted. The scope states that the time horizon for an appraisal should be sufficiently long to reflect the differences in costs and outcomes between technologies being compared. |
| | Healthcare | No comment | No actions requested. |

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| | Improvement Scotland (Consultant in Oncology) | | |
| | Carl Zeiss | No comments | No actions requested. |
| | Breakthrough Breast Cancer | No comment. | No actions requested. |
| Equality and Diversity | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare Improvement Scotland | I'm not aware of any reason why this proposed remit and scope would result in any of these consequences. | Comment noted. |
| | Healthcare Improvement Scotland (Consultant in Oncology) | No comment | No actions requested. |
| | Carl Zeiss | There are no equality issues. | Comment noted. |
| | Breakthrough Breast Cancer | The scope does not appear to promote discrimination. | Comment noted. |
| Innovation | Society and College of Radiographers | No comment | No actions requested. |
| | Association of Breast Surgery | No comment | No actions requested. |
| | Healthcare | The technology is undoubtedly innovative. If proven to be non- | Comment noted. These aspects of |

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| | Improvement Scotland | <p>inferior to the comparator (once mature data is available) it offers potential benefits in reduced hospital visits, travel etc.</p> <p>The technology would, however, not replace external beam treatment in all cases. Any benefits would therefore have to be offset against the costs of the infrastructure, equipment, staffing etc required to deliver this form of therapy in addition to that required to deliver external beam therapy.</p> | innovations should be included in submissions to NICE. |
| | Healthcare Improvement Scotland (Consultant in Oncology) | The technology is innovative but the follow up of the RCT comparing it to external beam irradiation is too short to assess whether the impact on local control is a 'step change'. | No actions requested. |
| | Carl Zeiss | <p>Yes it could be considered as a step-change. The standard treatment lasts for 6 – 7 weeks after surgery. With the single treatment of the technology the patient will have an improved quality of life. The results of the Targit A (Vaidya et al.) trial are available and show the above mentioned benefits.</p> <p>No, there are no other substantial health-related benefits that are unlikely to be included in the QALY calculation.</p> | Comment noted. These aspects of innovations should be included in submissions to NICE. |
| | Breakthrough Breast Cancer | Radiotherapy for breast cancer is currently given five times a week over a three to five week period. Although these appointments are short, they can be very disruptive to the patient's life. These appointments can incur costs in terms of parking and petrol as well as delaying returning to work or other normal aspects of a patient's life such as caring for family. In addition, for patients living in remote areas, travelling to and from hospital every day is not possible and they will need to make arrangements to stay overnight near the hospital meaning that they are away from their homes and families for long periods of time and are unable to carry on with their lives. Some breast cancer patients may be considered too frail to travel to and from hospital every day. | Comment noted. These aspects of innovations should be included in submissions to NICE. |

| Section | Consultees | Comments | Action |
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| | | INTRABEAM radiotherapy is to be given during surgery and may mean that patients are able to avoid attending daily radiotherapy appointments. This will allow patients to move on from breast cancer treatment sooner than previously and regain some normalcy in their lives. In addition, giving INTRABEAM radiotherapy during surgery instead of at numerous outpatient appointments would free up capacity within the NHS. | |
| Other considerations | Society and College of Radiographers | Further research and longer patient follow-up data is required for intra-operative treatments to be routinely used outside of the trial setting (recommendations from published papers). | Comment noted. Workshop participants were aware that TARGIT-A trial includes a multi-year follow-up period, and that researchers involved in the TARGIT-A trial will be exploring the use of a registry to follow patients in the longer-term. |
| | Carl Zeiss | <p>There are other indications outside breast cancer which are currently investigated in clinical trials (e.g. spine metastases, colorectal cancer, brain metastases). The technology can be used therefore in other types of cancers in the UK and would increase the usage of the device.</p> <p>Any other subgroups of people in whom the technology is expected to be clinically effective are: breast cancer in men; patients with breast cancer in the event of local recurrence or a new primary in the site of the original tumour or other part on the affected side would open the opportunity for breast salvage; additionally, patients with co-morbidities not offered standard radiotherapy after breast conserving surgery would benefit from a single fraction of IORT.</p> | <p>Comment noted. Attendees at the workshop discussed whether INTRABEAM was likely to be used for other indications outside of breast cancer. It was considered that currently use would be restricted to breast cancer except as part of clinical trials.</p> <p>Attendees discussed whether it was appropriate to specify any subgroups of people such as those not currently suitable for external beam radiotherapy. It was agreed that the evidence base available did not permit specification of these groups within the scope. Evidence for subgroups may be included in a submission for NICE.</p> |
| | Breakthrough | NICE Technology Appraisal 112 on hormonal therapies for the | Comment noted. NICE Technology |

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| | Breast Cancer | adjuvant treatment of early oestrogen-receptor positive breast cancer (2006) is listed as a related guideline. Implementation of INTRABEAM radiotherapy does not appear to impact on a patient's ability to receive hormone therapy as an adjuvant treatment nor is its use restricted to patients with or without hormone receptor positive breast cancer. It is therefore not clear why this technology appraisal has been listed as a related guideline. | Appraisal 112 was listed as a related guideline given its wider relevance to treating patients with early breast cancer. |

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Royal College of Nursing
 Royal College of Radiologists
 Breast Cancer Care
 Marie Curie Cancer Care
 Department of Health