

- Title** Assessment of intraoperative radiotherapy (IORT) in breast cancer
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Aim

The medical questions of this assessment focus on intraoperative radiotherapy (IORT), in women undergoing lumpectomy (breast-conserving surgery) and adjuvant radiotherapy for early breast cancer, in order for it to be refunded by the National Health Insurance. IORT was compared to standard whole-breast irradiation.

Conclusions and results

In conclusion, the available data are not mature enough to demonstrate that IORT is useful in adjuvant conservative breast cancer treatment in comparison with standard external whole breast irradiation. As a consequence, at this stage, the elements are not gathered to support IORT payment by National Health Insurance.

Long-term data from clinical and medico-economic studies are needed to prove clinical utility of the IORT in early breast cancer.

1. Conditions of this irradiation treatment

The implementation of IORT has a main impact on hospitals, as multidisciplinary timing and organisation are mandatory to mobilise the teams. In France, as radiation protection measures require patient monitoring by the operators out of the operating theatre during the irradiation, specific equipments should be in place. Furthermore, the IORT procedure which needs to be performed with precaution increases the global operating time by about 1 hour.

For breast cancer, literature confirms the feasibility of IORT in an operative theatre on well-selected patients especially on the small tumor size except in cases linked to anatomical elements (tumor closed to skin, small mammalian volume). Anesthetical and hospitalisation procedures are not modified in case of IORT.

No updated guidance (quality assurance) on procedures for carrying out IORT has been published at the time this report was written.

2. Risk-benefit ratio

The non-inferiority of this technique compared to whole-breast external radiotherapy used as adjuvant to lumpectomy has not yet been demonstrated in the 2 ongoing randomised and comparative clinical trials.

In particular, long-term data that is at minimum 5 and 10 years post-irradiation concerning local recurrence and survival were not available for TARGIT-A trial, using Intrabeam® device. Total breast irradiation has to be added secondary to IORT for a substantial proportion of cases (15% in a major clinical trial and up to 20% in other studies) with the aim to prevent loss of patient chances regarding pejorative histo-pathological data on tumor and sentinel nodes examination.

Moreover, no study has presently validated IORT as tumor bed radiation boost followed by total breast external beam radiation in patients with higher recurrence risk; this situation is likely to constitute a second medical indication.

IORT safety data, though not exhaustive in the 2 randomised and comparative clinical trials, or coming from studies with a lower level of evidence, report less cutaneous toxicity than with external beam radiation. However, complications of residual breast tissues (subcutaneous fibrosis) or collections (seroma, hematoma or more particularly cystosteatonecrosis) appear frequently. The collections require sometimes interventions of aspiration or biopsy (5 to 11%) to examine a potential recurrence if resorption did not occur.

Long-term (cardiac and pulmonary) toxicity cannot be wholly evaluated because of the current short follow-up.

It is to note that none of the foreign Agencies recommends IORT in this indication (3 available reports).

3. Eligible population for IORT in claimed indication

This issue concerns all accelerated partial-breast irradiation techniques (APBI) and focus on which patients are the best candidates for this irradiation mode taking into account the unique dose benefit and loco-regional recurrence risk. The suitable patients are identified by a low risk of recurrence according to current known risk factors specified by American (ASTRO 2009) and European (GEC-ESTRO 2010) recommendations on APBI (i.e. respectively tumor size T1 ≤20 mm or T2 ≤30 mm, woman older than 51 or 60 years; invasive ductal carcinoma, with oestrogen-receptor, N0M0).

But, at the time this report was prepared, no guidelines advocated the use of IORT in breast cancer. In France, Cancer Institute (INCa) emphasises that IORT should be reserved for clinical research as other APBI techniques.

The consultation of professional bodies during this assessment has revealed a debate about this technique on several issues:

- a controversy exists on the merits of the technique in breast cancer due to lack of perspective development in the overall concept of accelerated partial breast irradiation (APBI) and absence of tumor and sentinel nodes pathological data at the moment the IORT is performed;
- some practical disparity was noticed between the ten centres equipped in France with regard to patient selection criteria (age) and modalities to switch from exclusive IORT to boost, complemented by postoperative external beam irradiation.

Recommendations

HAS recommends eventually that IORT is performed exclusively in the context of clinical research in breast cancer.

Methods

Medical assessment questions have been grouped within 3 themes:

1. evaluation of conditions for achieving an IORT process (environment, technical platform, multidisciplinary organisation, risk management [anaesthetic, infectious, radiation protection, logistics/ technical] experience and training of professionals);
2. clinical benefit/risk ratio of the IORT in comparison with standard external breast irradiation;
3. population eligible for IORT treatment, with the highest standards in terms of risk factors in the current state of knowledge.

The assessment method used in this report is based on:

- a critical analysis of data from the selected literature identified through a systematic search;
- gathering the viewpoints of relevant stakeholders (National Professional Boards of the medical and health professional domains, as well as national instances and patient associations of the domain).

The conclusions of this assessment are reviewed by the National Commission for the Assessment of Medical Devices and Health Technologies and then validated by the HAS Board.

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