BrachyBytes

The Role of IORT in Breast Cancer Treatment

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Intraoperative radiation therapy (IORT) is a method of partial breast irradiation treatment delivery being studied in phase III trials that reduces treatment from five days of postoperative delivery to one intraoperative treatment. The potential advantages of IORT are clear, particularly the increased convenience for patients.

However, many physicians feel a number of issues need to be addressed before widespread adoption will occur. In addition to data with limited follow-up, there are questions surrounding selection of patients without complete pathologic assessment, a lack of treatment planning, a lack of image-confirmed target coverage and potential difficulties with OR logistics.

Radiation oncologist Douglas Arthur, MD, outlines current IORT techniques and shares his views on the emerging modality, including the need for more data before IORT can be adopted as a standard of care.

Describe the three techniques for delivering IORT.

IORT is the reduction of accelerated partial breast irradiation (APBI) from 5 days of postoperative treatment delivery to one intraoperative treatment. The three techniques currently available differ in target coverage, dose profile and surgical technique.

The first technique, known as ELIOT, uses intraoperative electrons as its radiation source. After the lumpectomy, the tissue is surgically arranged so the desired target is pulled together in a flat plane to ensure an even dose can be delivered and that skin is spared. Shielding placed deep to the target tissues is used to protect underlying structures. A mobile accelerator (there are three currently on the market) is then swung into place and 21 Gy is delivered to the target in one fraction. OR delivery time has been reported as approximately 30-40 minutes.

A second method involves a device called Intrabeam, which uses a 50 Kv energy source delivered via a reusable solid state applicator that is placed into the cavity. Like IORT with electrons, the treatment dose is 21 Gy, but because of the energy source used, there is great variation of dose across the 1 cm target. The surface dose is usually 20 Gy, with 5-7 Gy being delivered to a depth of 1 cm. OR delivery time for this technique has been reported as approximately 20-35 minutes.

The third technique—electronic brachytherapy (Xoft)—has been reported to take less than 10 minutes of OR delivery time. It utilizes a disposable balloon applicator and an x-ray source, and has similar dose distribution properties as Intrabeam.

What data are available to support these techniques? What are your thoughts on the current body of research?

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The IORT data are slowly maturing. There are two prospective randomized trials that have been performed with early data, or yet to be published data. There is strength in the fact that it is Phase III data, but the difficulty is that we do not yet have enough follow up to make significant practice changing conclusions. From the Targit-A trial (Intrabeam), we have one published

paper with a median follow-up that is undisclosed but is expected to be between two and three years, and a more recent abstract presentation of outcomes with a median follow-up of two years and five months. The ELIOT (intraoperative electrons) data has a median follow-up of 3.5 years as reported from a patient cohort that was treated off-protocol, as well as one abstract presentation from their randomized trial that reports follow-up of greater than five years, although it has yet to be published. To my knowledge, Xoft does not have any current trials underway to further our knowledge of intraoperative treatment with electronic brachytherapy.

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It is important to note that IORT is sufficiently different than APBI with intracavitary brachytherapy that we need to make sure we have strong data before we adopt this as a standard of care. We should remember that the establishment of intracavitary brachytherapy as a partial breast treatment technique, whether it is with a balloon or a strut-based device, was founded on a progression of data and experience documented in the published literature that defined the target as 1-2 cm beyond the cavity and determined a dose distribution that would be effective while yielding low toxicity. However, the IORT techniques bring a new set of concepts that should be thoroughly investigated before widespread adoption. Additionally, each of the three IORT techniques incorporate different surgical techniques and contrasting dose distributions, making it difficult to strengthen the data by combining experiences. If we begin to see 5-year data with acceptable in-breast disease control rates and low toxicity, then we can start to gain confidence in this modality.

Although follow-up is limited, what kinds of outcomes are being reported in the early data?

The ELIOT data, when evaluating their entire spectrum of treated patients, is beginning to show a difference with in-breast control rates. The reported 5-year ipsilateral breast recurrence rate was 5.3%, compared to 0.7% for whole breast irradiation. In addition, a higher rate (12%) of fat necrosis is being reported.

We also have to consider that this group of patients included people who were potentially not good candidates for intraoperative electron therapy. However, as we remember that the target definitions and dose distributions differ with IORT, it does not mean these patients would necessarily be inappropriate for intracavitary brachytherapy. Since we are starting to see a difference in outcomes with IORT, we should be prompted to move forward cautiously with an eye on the data. Perhaps we will learn that the group of patients that are appropriate for IORT is smaller than the group that can be treated safely and effectively with intracavitary brachytherapy.

What are the biggest weaknesses of these techniques? In your opinion, will these issues prevent the widespread adoption of IORT?

There are two main issues with IORT. The first is patient selection. There is no other area within the field of radiation oncology where we make treatment decisions without complete pathologic data available to us except in the rare, individual case when it is not possible. The second issue is the lack of confirmation that the target is actually being identified and dosimetrically covered appropriately, another aspect of radiation treatment delivery that is avoided in our specialty. These two issues are difficult to correct and raise questions regarding how this may impact outcomes.

Do you plan to introduce IORT at your institution?

We do not presently have plans to implement IORT at VCU. As a group we share the concerns discussed above. Presently, we have decided to focus our clinical research efforts on reducing the treatment time for post-operative intracavitary brachytherapy rather than opening a new protocol on a competing technique. We are enrolling on a multi-institutional phase II trial (principal investigator – Dr. Atif Kahn) using intracavitary brachytherapy that is moving us towards 2 treatment fractions and completing APBI in 2 days.

Does IORT have a role in the management of early-stage breast cancer? If so, what role does it play, and what (if any) concerns do you have?

In my opinion, I do not think we have clearly defined a role at this time. I have no doubt that a role will be defined, but more follow up on outcome data is needed to help us understand IORT patient selection and whether there is a better IORT technique for subgroups of patients.

Dr. Arthur is a professor and vice chairman of the radiation oncology department at Virginia Commonwealth University's Massey Cancer Center in Richmond. His clinical and research interests include brachytherapy, management of breast and genitourinary malignancies, and soft tissue malignancies.

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