IORT, Intraoperative Radiation Therapy, is a type of radiation therapy in which radiation is delivered at the time of surgery. In breast IORT, the entire dose of radiation may be delivered during the single, intraoperative fraction, or an additional dose may be administered by external beam therapy postoperatively. Because the target and normal tissues can be clearly identified during surgery, IORT may increase targeting accuracy, thereby increasing dose to the target and reducing dose to critical structures. The shorter treatment time is more convenient for patients than the typical seven-week course of external beam therapy, likely increasing patient compliance. The single-fraction treatment should also greatly reduce costs to the healthcare facility.

ABOUT BREAST IORT

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USING AXXENT FOR IORT

The Xoft Axxent® Electronic Brachytherapy System® uses an electronic X-ray source instead of a radioactive isotope to deliver radiation to the breast from within a balloon catheter. The low energy and rapid dose fall-off of the electronic source permit treatment in typical operating rooms, with minimal shielding required. Lightweight and mobile, the system can be moved easily between multiple ORs. The source can be pulled back to dwell at multiple positions within the balloon, permitting customized dose distributions contoured to the shape of the target. Radiation treatment can be delivered in as little as 8 minutes. The small, flexible source and range of Xoft applicators also permit treatment of multiple non-breast indications, both intraoperatively and postoperatively.
My interest in developing a Xoft IORT protocol was derived from multiple sources. The reported pattern of recurrence of early breast cancer patients treated with whole-breast radiation therapy; favorable initial clinical results associated with other forms of accelerated partial breast irradiation (APBI), including the IORT data from overseas; and my clinical experience using Xoft to treat breast and endometrial cancers all influenced my interest in Xoft IORT.

What clinical data helped convince you to investigate breast IORT?

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Ivanov & Francescatti
For the past several years, reports of intraoperative breast single-fraction radiotherapy have been generated by Dr. Veronesi’s work in Milan, as well as the TARGIT trial that is accruing patients in both Europe and the United States. The preliminary results of these studies are quite favorable and deserve the attention of American breast surgeons.

Do you think breast IORT has the potential to affect the management of your patients?

Dickler
A certain segment of my patient population, mainly elderly patients who live a distance from our radiation center, elect to skip the radiation portion of breast conservation therapy (BCT). This is in spite of the fact that radiation has been shown to be an essential component of BCT and increases overall survival. My hope is that the option of IORT will decrease the number of patients who decide to be treated with surgery alone. This could lead to an improvement in breast cancer survival for this patient population.

Ivanov & Francescatti
Any method for the delivery of radiation treatment to the breast patient that can shorten the standard six-week course of treatment is a step in the right direction. Recently, APBI has significantly lowered treatment time. For the surgical community, in concert with radiation oncology, to be able to improve on this shortened course of treatment is very progressive. Breast IORT promises to be that mechanism for additional change.
How do you determine the best candidate for breast IORT?

Dickler When screening for IORT, I use the ABS/ASBS accelerated partial breast irradiation (APBI) selection criteria. These guidelines recommend APBI for patients with 3-cm or smaller tumors, tumors that do not involve the axillary lymph nodes, DCIS or infiltrating ductal cancers, and patients older than 50 years of age. At the time of the procedure, we also ensure that there is a skin-to-balloon distance of a minimum of 1 cm and that the balloon adequately conforms to the surrounding breast tissue via ultrasound.

Ivanov Clinically, breast IORT candidates should fulfill the criteria established for APBI by ABS/ASBS. However, a single-fraction breast IORT will increase the number of patients who might become candidates for APBI. One might ask how this is possible. A number of potential problems associated with the delivery of postoperative APBI can be negated with IORT, and specific surgical techniques can be employed at the operating table. For instance, problems of inadequate skin bridge often encountered in the postoperative patient can be addressed. In a similar fashion, concerns regarding non-targeted radiation to adjoining tissues (i.e., the chest wall, lungs and heart) can be obviated by placement of a temporary shield at the time of treatment.

Radiation is typically administered in multiple fractions of low dose. Will a single, higher-dose fraction have the same clinical effect?

Dickler The initial results from Europe are very encouraging. Although this data is from non-randomized trials, the results are comparable to whole-breast radiation therapy and other forms of APBI. I believe that giving a single fraction of radiation at the time of surgery will be advantageous because it will allow all the radiation to be delivered before any remaining tumor cells have a chance to grow. In addition, due to the dose distribution of the brachytherapy source, it will intensify the dose to the part of the breast at highest risk for recurrence.
IORT is a multidisciplinary approach. How does your institution arrange the coordination of treatment logistics?

Dickler

Dr. Ivanov and I work very closely together to determine which patients are the ideal candidates for IORT. All patients receive both radiation oncology and surgical consults before receiving any form of treatment for the breast cancer.

In comparison to other IORT products, what advantages do you see with the Xoft Axxent system?

Dickler

The mobile nature of the Xoft Axxent controller, the low energy/shielding requirements associated with the Xoft source, and the rapid fall of kV radiation all make it ideal for IORT.

Ivanov & Francescatti

The Xoft system is a practical solution to a very vexing problem that confronts the community hospital as well as tertiary hospitals. This is, of course, a multifaceted problem. Cost considerations are of paramount importance today, and the Xoft system provides hospitals with the ability to provide modern radiation therapy at a modest cost. Practically speaking, the system offers unparalleled advantages of versatility and mobility both in the OR and in other areas of the hospital.
Marianne H. of Illinois was the first patient to undergo IORT utilizing Xoft, Inc.’s Axxent® Electronic Brachytherapy System®. The new treatment was performed under the direction of Dr. Olga Ivanov, Medical Director for Little Company of Mary’s Comprehensive Breast Health Center, and Dr. Adam Dickler, Radiation Oncologist at Little Company of Mary Hospital, as part of a clinical trial at the hospital.

IORT delivers a concentrated beam of radiation to cancerous tumors while they are exposed during surgery. In Marianne’s case, the treatment goal was to deliver a complete dose of radiation therapy in the operating room at the time of her lumpectomy. When she awoke, she not only had her tumor removed, but had also completed her entire course of radiation therapy, which could normally take up to seven weeks.

“The fact that my treatment was done before I even woke up is beyond words,” says Marianne. “As Dr. Ivanov says, I came in with cancer, went to sleep, and when I woke up, I was completely done with my breast cancer.”

IORT is being evaluated for its potential to allow doctors to administer high doses of radiation to tumors without exposing nearby healthy organs to radiation. A single dose of intraoperative radiation may have as much effect on the tumor as 10 to 20 daily radiation treatments.

Using a miniaturized X-ray source that can deliver localized and targeted radiation treatment, electronic brachytherapy is designed to minimize radiation exposure to surrounding healthy tissue and enable physicians and treating professionals to remain in the operating room with the patient.

Marianne was able to leave the hospital on the same day as her surgery and IORT procedure, and attended a wedding just days later. “I danced at a wedding four days later to, of all songs, ‘I Will Survive.’ You’ve got to dance that dance. Since, I’m doing great, and I feel fine.”

“I want more women to know about this. I just can’t believe how lucky I was to have this type of procedure available to me in my community,” she added.

IORT: A PATIENT PERSPECTIVE

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Marianne H. (center) with Dr. Francescatti (left) and Dr. Ivanov (right).
TARGIT-A TRIAL SUMMARY


- Women aged 45 years or older with invasive ductal breast carcinoma undergoing breast-conserving surgery were enrolled from 28 centers in nine countries. Patients were randomly assigned in a 1:1 ratio to receive targeted IORT or whole breast EBRT.

- 1,113 patients received targeted IORT and 1,119 received EBRT. Of 996 patients who received the allocated treatment in the IORT group, 854 (86%) received targeted IORT only and 142 (14%) received IORT plus EBRT. 1,025 (92%) patients in the EBRT group received the allocated treatment.

- At four years, there were six local recurrences in the IORT group and five in the EBRT group. The Kaplan-Meier estimate of local recurrence at four years shows no significant difference in the conserved breast between the targeted IORT and EBRT groups.

- The frequency of any complications and major toxicity was similar in the two groups: for major toxicity, IORT, 3.3% (37 of 1,113) vs EBRT, 3.9% (44 of 1,119; p=0.44).

- Radiotherapy toxicity (RTOG grade 3) was lower in the IORT group, 0.5% (6 patients) than in the EBRT group, 2.1% (23 patients, p=0.002).

Conclusion: For selected patients with early breast cancer, a single dose of radiotherapy delivered at the time of surgery by use of targeted intraoperative radiotherapy should be considered as an alternative to external beam radiotherapy delivered over several weeks.

The TARGIT trial results clearly demonstrate the emergence of IORT and the major advance in cancer care.