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Contribution of nuclear medicine in early breast cancer: from ROLL (Radioguided Occult Lesion Localization) to I.A.R.T.[®] (Intra-operative Avidination for Radionuclide Therapy)

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The conservative surgery with axillary dissection and additional radiotherapy represents the treatment of choice for patients with early breast cancer. A standard course of whole-breast external-beam radiation therapy (EBRT) followed by a boost to the tumour bed generally require 5/7 week to complete. This can represent a logistical problem for many patients, particularly the elderly and those who reside a considerably distance from a radiation treatment facility. As alternative to the traditional treatment of radiotherapy, the intraoperative radiotherapy (IORT) has been recently proposed. This technique, although valid, is limited by two major points: i) the availability of a dedicated intraoperative linear accelerator, ii) a restricted field of irradiation which limits the management of positive surgical margins. The experience developed in our Institute with the ROLL technique and the radionuclide therapy with the avidin-biotin pre-targeting system lead us to the development of a new approach named I.A.R.T.[®] (Intraoperative Avidination for Radionuclide Therapy) capable to control recurrence as for EBRT and IORT.

The IART[®] procedure consists of two steps as follows:

Step 1: "avidination" of the anatomical area of the tumour with native avidin

The surgeon, intra-operatively, injects native avidin directly into the tumoural and peritumoural bed without margins and depth limitations. Avidin will percolate the tissue of the index quadrant as well as being drained by locoregional lymph nodes including internal mammary chain and upper clavicular nodes.

Step 2: targeting the anatomical area of the tumour by intravenous injection ⁹⁰Y-labeled biotin

The day after surgery, within 24 hours of the surgical intervention, Biotin-DOTA ligand, labelled with ⁹⁰Y, is administered i.v. as a slow bolus injection. Ten minutes before the i.v. injection of radioactive biotin, biotinylated human serum albumin (HSAbiot) is administered intravenously in order to chase the circulating avidin which has been adsorbed through the lymphatic system and entered into circulation and blocks the uptake of radioactive biotin in the liver and kidney where avidin accumulates.

It is clear from studies conducted to date that using IART[®], one can deliver radiotherapy as follows:

Targeted only in the region of "interest"

Sparing the vital organs, thereby minimising unwanted toxicity to these organs

With less damage and burn externally (cosmetic benefit)

Reduce hospital visits by up to a third (psychological [improvement in Quality of Life], and economic benefit)

Partially replace external beam radiation therapy (EBRT) time by a third (thereby making EBRT more easily available to other patients).

IART[®] offers several advantages over other currently available accelerated breast irradiation methods. Its main advantage is that it is potentially applicable to the majority of breast cancers, without limitation as to location, size or multifocality, as well as to many other solid tumours such as those of bladder, prostate and brain. The surgeon plays an important role in the procedure: having removed the tumour he/she chooses the exact sites to inject the avidin around the tumour bed, doing so under direct visual control. This aspect is relevant, since, irrespective of whether the tumour is close to the chest wall, nipple or axilla, avidin can be injected successfully, while these areas are generally contraindicated for other partial breast irradiation techniques.

Another advantage of IART[®] is that a dedicated linear accelerator and other sophisticated devices are not required, so the procedure can be carried wherever a nuclear medicine unit is present. Furthermore, since ⁹⁰Y-labelled biotin can be injected 16-24 h after avidin administration, the procedure can be used even if the nuclear medicine department is not close to the surgical unit. For example, ⁹⁰Y-biotin could be produced in a central radio-pharmacy and delivered within a few hours to surrounding hospitals. This would facilitate wider use of conservative breast surgery for breast cancer, which in many areas is not practiced because post-operative radiotherapy centres are unable to cope with the demand, or are too distant from patients' homes, and for a 5-7 week course this can present a serious obstacle.

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PET/CT in Lung Cancer and Oncology Guidelines - Has it Become a Must?

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