

Award Lectures

FECS Pezcoller Award Lecture

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Sentinel lymph node biopsy and Intraoperative radiotherapy in breast cancer: a breakthrough?

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Twenty years ago we inaugurated a new trend in breast cancer surgery introducing the concept of the "lobectomy", i.e. that the excision of a mammary lobe, constituted by a ductal tree, might be the correct surgical treatment of breast cancer of limited size. This principle was based on the assumption that the intraductal spread of breast cancer is a common event and that the ductal tree from where the cancer originated is often extensively involved.

The original definition of lobectomy was for practical reasons modified into the term "quadrantectomy" to give the surgeons a clear anatomical description of the operation. A randomized trial, published 20 years ago, showed absolute identical survival rates between patients treated with quadrantectomy, axillary dissection and radiotherapy and patients treated with Halsted mastectomy. The Milan results were confirmed by other studies and breast conservation is now an accepted method of treatment of breast carcinoma. Hundreds of thousand of women with breast cancer have their breasts saved every year world-wide.

In the last decade our interest was directed to the possible avoidance of the axillary dissection in early breast carcinoma. In fact, following the development of imaging techniques that detect small, early stage primary carcinomas, it is increasingly noted that axillary dissection finds only healthy lymphatic nodes. Furthermore, it has been suggested that axillary dissection should not be viewed as a curative but mainly as a staging procedure for obtaining as much prognostic information as possible. The question is whether lymph node removal is always necessary in patients with a clinically negative axilla.

We demonstrated in a number of studies that the spread of breast cancer cells in the axillary nodes follows an orderly pattern and that the first level is first involved, skip metastases being present only in 1.5% of the cases.

These results were the premises to our approach to the sentinel node biopsy, a procedure which was first used in melanoma with good results. The sentinel node technique showed encouraging results in early studies on breast carcinomas. We designed a number of studies to address the need for axillary dissection in early breast carcinoma. First we showed in a study on 436 patients with small carcinomas (<1.2 cm in diameter) that axillary dissection may be avoided without significant risks, being the 5-year survival 98% in this series of patients.

Subsequently, we designed a study on 376 cases of breast carcinoma, which were treated with the sentinel node biopsy with a radio-tracer (Tc^{99}) which was immediately followed by a complete axillary dissection. The study showed an overall accuracy of 96.8%, a sensitivity of 93.3% and a specificity of 100%. There were a total of 12 false negative cases which represented 3.2% of all series and 6.7% of the cases with positive axillary metastases. An important multicentric study was conducted in the United States by Krag and others on 443 cases with similar results.

After these encouraging results we designed a randomized trial which was carried out in the years 1998 and 1999. We recruited more than 500 patients, who were randomized between routine total axillary dissection and elective axillary dissection, only in case of a positive sentinel node biopsy. The early results show that the sentinel node policy is able to detect the cases of positive axillary nodes in a percentage equal to that obtained with the routine axillary dissection.

Finally we showed that patients treated with the sentinel node biopsy only, without axillary dissection when the sentinel node was negative, and followed up for 1 to 5 years, showed no evidence of overt axillary metastases.

We conclude that probe-guided biopsy of the sentinel node is easy to apply, requires an easy surgical training and the whole procedure is associated to a low risk of false negatives.

We suggest that the technique should be widely adopted to stage the

axilla in patients with breast cancer with clinically negative lymph nodes. Large-scale implementation of the sentinel node technique will reduce the cost of treatment as a result of shorter hospitalization times and will also reduce indirect costs because motor compromise and lymphoedema as a result of axillary dissection will disappear.

The development of Intraoperative Radiotherapy was based on the evidence that local recurrences after breast conserving surgery occur mostly in the quadrant harbouring primary carcinoma. The main objective of post-operative radiotherapy should be the sterilization of residual cancer cells in the operative area while irradiation of the whole breast may be avoided.

We have developed a new technique of intraoperative radiotherapy of a breast quadrant after the removal of the primary carcinoma. A mobile linear accelerator with a robotic arm is utilized delivering electron beams able to produce energies from 3 to 9 MeV. Through a perspex applicator the radiation is delivered directly to the mammary gland and to spare the skin from the radiation the skin margins are stretched out of the radiation field. To protect the thoracic wall an aluminium-lead disc is placed between the gland and the pectoralis muscle.

Different dose-levels were tested from 10 to 21 Gy without important side effects. We estimated that a single fraction of 21 Gy is equivalent to 60 Gy delivered in 30 fractions at 2 Gy/fraction.

86 patients received a dose of 17-19-21 Gy intraoperatively as a complete treatment. The follow-up time of the 101 patients varies from 1 to 17 months (mean follow-up time 8 months).

The IORT treatment was very well accepted by all patients, either due to the rapidity of the radiation course in case of IORT as a whole treatment or to the shortening of the subsequent external radiotherapy in case of IORT as an anticipated boost. We believe that single dose intraoperative radiotherapy after breast resection for small mammary carcinomas may be an excellent alternative to the traditional postoperative radiotherapy.

ESTRO Award Lecture

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Positive aspects of irradiation accidents

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Considering the number of radioactive sources in use all over the world (both in industry and Medicine), irradiation accidents are exceedingly rare, as demonstrated by the main databases registering such cases: UNSCEAR, IAEA, REACTS (Oak Ridge, USA), the German group in Ulm and the Paris Institut Curie.

The precise causes of most accidents have been openly analyzed, allowing to reduce the risk of subsequent identical accidental exposures. In addition, a rapid retrospective overview shows that positive lessons could be drawn from such accidents:

1) Lessons for patient management: one should keep in mind that the first ever allogeneic bone marrow transplantations were performed in 1958, on scientists from Yugoslavia who had been severely irradiated in a nuclear Research laboratory. Apart from what was learned from such accidents for the management of severe aplasia, the treatment of superficial accidental exposures has also benefitted radiotherapy patients in certain specific situations.

2) Lessons for technology: The efforts to improve safety in nuclear plants are well known; the (successful) efforts to reduce the once-elevated risks when changing the therapeutic Cobalt 60 sources are less well known. Today, most irradiation accidents (by far) are related to misuse or loss of radioactive sources from industrial radiography sets. However, here again, various technological improvements significantly reduced the risks.

3) Lessons for Radiobiology; the need for more and more sophisticated biological dosimetry has led to studies allowing better understanding of the short and long-term effects of radiation on human cells. Analyses of samples taken in areas which were heavily accidentally irradiated also

helped to identify, in particular, the cardinal role of TGF beta and TNF alpha in the development of fibrosis and necrosis after irradiation.

4) Lessons for prevention of accidents in Radiotherapy: only three large-scale accidents involving external radiotherapy have been registered in the last decade, but deciphering the cause(s) of such problems clearly participated in the setting of demanding Quality Assurance programmes and strict national and international recommendations. Such open circulation of the information about these (fortunately rare) accidents appears to be one of the ways to improve Quality Assurance in Radiotherapy.