

Is the page turned for radiotherapy in a combined approach with surgery? In view of the available randomized trials and the recent metaanalysis, a quick answer is yes. Indeed, both observed either no effect or even a detrimental impact on survival. Nevertheless, those trials were performed during the last three decades, a period of many improvements in the knowledge of the disease, in imaging procedure, in surgery and in radiotherapy. Preoperative radiotherapy may increase the resectability rate in well-selected patient: some groups are still advocating this approach for superior sulcus tumor whereas many phase II and some phase III trials are combining radiation with chemotherapy in a preoperative settings. The data available suggested a higher rate of pathological complete response but also a slight increase in morbidity. In contrast, postoperative irradiation improves the local control especially for stage III disease: this was clearly demonstrated by the Lung Cancer Study group trial, the MRC trial and the Feng trial. Furthermore, we should remember that the PORT metaanalysis suggested a differential impact according to the tumor extent: the negative impact of postoperative radiation disappeared for stage III disease (a similar observation was made by Dautzenberg et al). One possible explanation is that the therapeutic effect of postoperative radiotherapy compensated the negative impact due to a poor radiation technique (large volume, high daily dose, and cobalt machines...). Both approaches imply to use a modern radiation technique minimizing the risk of inducing severe life-threatening late effects: this is especially the case for postoperative radiotherapy due to the already loss of lung function due to the surgery and a long history of tobacco abuse. This is probably the place for a conformal radiotherapeutic approach.

The last issue concerns the management of patients after induction chemotherapy followed by surgery: the current approach is to reserve postoperative radiotherapy for incomplete resection or for persistent nodal disease. Probably, another important factor may be the presence or not of nodal capsular rupture. We are certainly lacking good data on the postresection management and outcome of those patients.

In conclusion, radiation has still its place for stage III disease in a combined approach with surgery and chemotherapy providing the use of an adequate radiation technique.

50. THE IMPORTANCE OF MODIFYING HYPOXIA IN RADIOTHERAPY

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51. BIOLOGICAL CONCEPTS OF BREAST CANCER: IMPLICATIONS FOR THERAPY

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The data from over 3000 breast cancer patients treated without adjuvant chemotherapy and followed-up for over 15 years were studied with two aims:

- 1) to analyze the relationship between tumor diameter and incidence of distant metastases during the 25 years after initial treatment. The threshold volume at which dissemination occurs can be estimated in each subset of patients and varies widely; it is inversely correlated with the histologic grade and the number of involved axillary nodes.
- 2) to investigate the impact of a residual tumor on distant dissemination. In patients with local recurrence, the incidence of distant dissemination is elevated. The analysis of the delay between the initial treatment and clinical emergence of the metastases shows that the excess of metastases corresponds to disseminations which are initiated after initial treatment and therefore originated from the residual tumor.

This conclusion was supported by the update of a controlled clinical trial comparing two adjuvant treatments: A) a chemotherapy by CMF or B) post-operative radiotherapy (RT) followed by immunotherapy with poly A - poly U. At 15 years the cumulative incidence of local recurrence and of distant metastases is significantly lower in the B group (42% metastasis-free survival in the RT group and 29% in the CT group $p=0.03$). This result seems to be due mostly to lower incidence of local recurrence.