

node recurrence. Furthermore, radiotherapy is not devoid of risks or side-effects and should therefore be reserved for forms presenting an important risk of recurrence, in other words, forms which already present an important risk of relapse on the chest wall.

5. Conclusion

Radiotherapy is widely used in breast cancer treatment. Nevertheless, data on its long-term benefit are missing and some of its indications are not universally agreed upon.

Like an evidence-based medicine, radiotherapy should be used in cases where a beneficial effect has been proved. Targets and doses should be chosen according to data from randomised trials or sufficient proof of benefit leading to a consensus. Thus, if postoperative radiotherapy in conservative procedures is indicated, boost usefulness needs to be confirmed. In the same way, axillary nodes and internal mammary chain irradiation must be justified by long-term results before these techniques are widely used. Chest wall radiotherapy has been proved to reduce local recurrences without benefit on overall survival. Chest wall irradiation must be limited to high-risk patients.

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Arbiter

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Irradiation for breast cancer treatment has a very prominent place whatever the specific aim of this treatment: to cure the patient locally (without any further recurrence in the conserved breast or in the chest wall) or generally (without any distant recurrence). Three tumour types are focused on in current practice:

- Small tumours are those which can be treated by first-line conserving surgery (provided they are unicentric and without any widespread ductal carcinoma *in situ* (DCIS)). We have to divide them between two subgroups of low and high risk of local and/or distant recurrences. Irradiation of the breast and of nodal areas does not have the same impact on local risk of recurrence and of death in these two subgroups.

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- Large tumours are those which cannot be treated with immediate conserving surgery because their size would cause too high a risk of local relapse. In cases of neoadjuvant medical treatment (chemotherapy or hormonal therapy) irradiation is mandatory in the subsequent conserving procedure. On the contrary, in cases of immediate mastectomy, irradiation has to be discussed as to whether it will improve local and distant control of the disease.
- Locally advanced breast tumours have a very high risk of local or metastatic recurrence. Thus, it is easy to consider herewith that irradiation will be systematic whatever the type of surgery used and the medical adjuvant or neoadjuvant treatment applied.

Therefore, whatever the tumour type, three modalities are concerned: surgery with or without irradiation or irradiation alone. The choice will have to be based upon an analysis of risk factors of local and distant recurrence.

1. Risk factors of local recurrence

They have been widely analysed and the results can be summarised according to the publication of Standard Options and Recommendations (S.O.R.) for non-metastatic breast cancer from the French National Federation of Comprehensive Cancer Centers [1]. The weight of each prognostic factor can be modulated according to its statistical predictive value (Table 1).

2. Risk factors of distant — metastatic — recurrence

The same methodological analysis of the literature draws us to consider S.O.R. of non-metastatic breast

Table 1
Prognostic factors of local recurrences

Clinical factors	
Young age less than 35 years	+++
Premenopausal status	++
Tumour size	++
Breast volume	±
Pathological factors	
Involvement of tumour margins + DCIS	++++
High SBR grading	+++
Peritumoral emboli	+++
Involvement of tumour margins	+++
Tumour size	++
DCIS	±
Insufficient treatment	++++

DCIS, ductal carcinoma *in situ*; SBR, Scarff Bloom Richardson Grading.

Table 2
Prognostic factors of metastatic disease

Clinical factors	
Young age less than 35 years	+++
Tumour size	+++
Nodal involvement	+++
Premenopausal status	++
Age older than 70 years	++
Pathological factors	
Tumour size	+++
Nodal involvement	+++
Number of involved nodes (≥ 4)	+++
High SBR grading	+++
Peritumoral emboli	+++
Involvement of tumour margins	++
Nodal capsular effraction	±
Absence of DCIS component	±

DCIS, ductal carcinoma *in situ*; SBR, Scarff Bloom Richardson Grading.

cancer as a guide for indication of adjuvant local and general medical treatment (Table 2).

3. Irradiation and breast conserving procedures

3.1. Irradiation after immediate breast surgery

From published data, the debaters put forward the same argument, namely that irradiation after immediate breast conserving surgery decreases the rate of local relapse to a significant extent. Nevertheless, we do not know the real impact of local recurrence on metastatic risk. If overall survival is identical whatever the risk of recurrence in the National Surgical Adjuvant Breast and Bowel Project (NSABP)-06 trial [2] and in a Swedish trial [3], Cutuli stresses the fact that early local recurrence could worsen overall survival. Nevertheless, we do not have a specific trial focusing on this point. Furthermore, the meta-analysis of Early Breast Cancer Trialists' Collaborative Group (EBCTCG) [4,5] does not analyse the impact of radiotherapy on survival according to conserving surgical procedure alone. It shows results whatever the type of surgery: lumpectomy or radical mastectomy.

3.2. Exclusive irradiation

This procedure of conserving treatment is not commonly used, except in some locally advanced tumours treated with neoadjuvant medical treatment when the metastatic risk is much higher than the local risk. This is the case for inflammatory breast carcinoma and for elderly women with locally advanced breast cancer. Nevertheless, if local conserving surgery can be carried out after the reduction of tumour burden, it has to be proposed because it will decrease the risk of local failure.

In these cases of very poor prognostic tumours, improvement of survival can only come from improvement of medical therapies [6].

4. Irradiation and modified radical mastectomy

Unlike a local relapse in a conserved breast, a recurrence on the chest wall has a worse prognosis, due to a very frequent — immediate or delayed — association with metastatic disease. All the authors agree with the fact that post-mastectomy radiation therapy decreases the rate of local relapse. But in terms of survival benefit, EBCTCG analysis [4] does not show a real benefit from irradiation; nevertheless the trials involved in this meta-analysis are heterogeneous and the technical procedures of irradiation are now obsolete. Two recent trials from Denmark and British Columbia clarify this point.

Despite these relative insufficiencies of medical adjuvant treatment, we can assume that postmastectomy irradiation improves local control and that survival is also statistically improved.

In the two trials involving premenopausal women, irradiation was found to improve local control and survival whatever the prognostic factors of local and distant failure [7,8].

In postmenopausal women [9], improvement of relapse-free and overall survival is also seen for every subgroup of patients with high nodal involvement.

But both authors comment upon the potential cardiotoxicity of chest wall irradiation in cases with anthracycline adjuvant chemotherapy although, at the moment, no trial has answered this question.

The meta-analysis conducted by Whelan and colleagues [10] reports 18 trials that involved 6367 pre- or postmenopausal women who were treated with modified radical mastectomy and had pathological nodal involvement. Adjuvant systemic treatment was given in each trial, with chemotherapy and/or hormonal therapy. This study shows that loco-regional irradiation reduces the risk of any recurrence (odds ratio (OR): 0.69; 95% confidence interval (CI): 0.58–0.83), local recurrence (OR: 0.25; 95% CI: 0.19–0.34), and mortality (OR: 0.83; 95% CI: 0.74–0.94).

5. Irradiation of nodal areas

The question of axilla irradiation depends upon the level of nodal involvement. After a level I and II axillary dissection, irradiation of the axillary apex and supraclavicular area can be performed in cases of high nodal involvement ($>4 N^+$). It will decrease the recurrence risk on the supraclavicular field and perhaps overall survival. Concerning internal mammary chain irradiation, we can not assess its definitive usefulness. If there

is a significant decrease in regional recurrence, a survival benefit can not be demonstrated in patients irradiated specifically on lymph node areas. In the last meta-analysis by Whelan and colleagues, patients were irradiated on the chest wall and on the internal mammary chain in most of the trials [10]. However, there is no specific trial published on that topic. A European Organization for Research and Treatment of Cancer (EORTC) trial (protocol 22922/10925) is currently trying to analyse in a randomised phase III trial ‘the role of internal mammary chain and medical supraclavicular lymph node chain in stage I–III breast cancer’. Furthermore, sentinel node mapping with lymphoscintigraphy would provide an opportunity to further evaluate the internal mammary chain treatment, either surgical or radiotherapeutic [11]. Thus, the question of internal mammary chain irradiation is still open to evaluation.

Finally, the last meta-analysis from EBCTCG published in 2000 analyses the 10-year and 20-year results from 40 unconfounded randomised trials of radiotherapy involving 20 000 women. It takes into account all the published trials, whatever the types of surgery and irradiation, nodal involvement or medical adjuvant treatment.

Breast cancer mortality is reduced particularly after the second year of follow-up; there was a reduction of 13.2% (standard error of the mean (SEM) 2.5) in the annual death rate from breast cancer.

In conclusion several assertions can be made and are recognised by the two debaters:

- Breast irradiation is mandatory after conserving surgery, whatever the tumour size.
- Chest wall irradiation has to be carried out in cases of high risk of local recurrence.
- Internal mammary chain (and supraclavicular area) is efficient in cases of high risk of regional recurrence and it probably improves metastatic-free and overall survival. The level above which the irradiation can be avoided has to be determined.
- Irradiation of the axilla can be reduced.
- Prevention of loco-regional recurrence improves survival in case of high-risk metastatic disease.
- Modern technical approaches must be applied to avoid cardiopulmonary toxicity.
- The timing of irradiation in relation to adjuvant chemotherapy is not yet clear for patients treated or not by conserving procedures.

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