

the EBCTCG<sup>1</sup> overview has shown, the effects of radiotherapy are proportional: the relative risk reduction is constant and independent from the currently available predictors of locoregional failure. The same observation were made in patients who received adjuvant medical treatment, in whom the relative benefit from radiotherapy was the same as in those who did not had these treatments.

Based on these evidence, the decision to avoid radiotherapy in an individual patient at low risk of recurrence can only be a shared decision. It should rely on the estimated long-term risk of recurrence without radiotherapy, the potential impact on survival of leaving residual disease, the risk of complications and long-term sequelae related to the modalities of radiotherapy, and the economical, social, and psychological constraints of treatment.

Further research should be encouraged to identify specific biological predictors of disease progression and response to radiotherapy.

## References

- [1] EBCTCG. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and on 15-year survival: an overview of the randomised trials. *Lancet*, December 2005 (in press)

22

Invited

### Who needs more?

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The need for more aggressive treatment, like delivering a higher radiation dose or re-excision, is dependent on the risk of local recurrence. Previous trials in breast conserving therapy demonstrated that increasing radiation dose will reduce the local recurrence rate. Similarly, it is shown that adding adjuvant systemic therapy to breast conserving therapy also reduces the local recurrence rate; the impact of hormonal adjuvant hormonal treatment being similar to the adjuvant chemotherapy regimens. Similarly patients who have a free margins after tumorectomy have less recurrences.

To avoid overtreatment one should base the decision upon well established prognostic factors for local recurrence like: age, the younger the patients the higher local recurrence, in patients with incomplete resection a higher local recurrence is seen and some other factors like grading, tumor size, etc. Despite these well-known clinical factors, it is still difficult to predict which patients will recur; therefore high radiation doses will be given to patients < 60 years and patients with a microscopically incomplete excision of the primary tumor. To avoid over-treatment further studies with micro-arrays and proteomics are urgently needed to individualize the radiation dose for this patients-group. Preliminary results demonstrated that predicting a local recurrence with a genetic profile based upon micro-array data are encouraging and may be of help in selecting the appropriate individual treatment regimen.

23

Invited

### Impact of delaying radiotherapy in early breast cancer

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Postoperative breast radiotherapy (RT) is a major tool in preventing local recurrence after surgery, and mainly in breast conservative approaches. Higher is the local recurrence risk (LRR), higher is the beneficial impact that RT may have on long-term breast cancer mortality [1]. The infinite delay (absence) of RT has a definitive impact on local control as shown by randomized trials. However, the definition of which delay is acceptable after local surgery is a matter of debate as results are based only on observational studies. The effect of delay has been also studied for other tumours and there is convincing evidence that in fast growing tumours such as head and neck, cervix carcinomas, and grade III-IV gliomas such delay is important in terms of local control [2-3]. There is also a convincing rationale based on theoretical studies to support this assertion [3-4].

The same principles may be applied to breast cancer. The mean impact of the delay of RT does not take into account patient and tumour variability, and tumour heterogeneity. For fast-growing breast tumours, a delay of 1-2 months can have a significant adverse effect on the outcome. Also, in mathematical models it has been considered that tumour growth following surgery is likely to be faster than undisturbed growth due to improved oxygenation [3]. Huang et al [2] on the basis of 21 observational clinical studies found that the LRR is higher when the delay after surgery is longer than 8 weeks. Similar considerations may apply to delays introduced during the RT delivery (increase of the overall treatment time) as was analysed in an extensive recent review [5]. The prolongation of the overall RT time could be compensated by additional treatment fractions.

These considerations do not take into account the delay of RT related to the introduction of systemic treatments before, during, or after RT.

Long debates on the optimal sequencing of systemic treatments and RT have been launched in the two last decades. However, the only reported randomised trial [6] included a small number of patients and rather favoured the sequence chemotherapy and then radiotherapy to decrease the incidence of distant metastases. The same approach has been favoured by observational studies [7] and some randomised trials comparing the sequence chemotherapy-RT with early RT [8]. This presentation will be based on theoretical and clinical considerations.

## References

- [1] Early Breast Cancer Collaborative Trialists' Group. *Lancet* 366: 2087-106, 2005.
- [2] Huang J et al. *J Clin Oncol* 21: 555-63, 2003.
- [3] Wyatt RM et al. *Phys Med Biol* 48: 139-55, 2003.
- [4] Mackillop WJ et al. *Int J Radiat Oncol Biol Phys* 34: 243-50, 1996.
- [5] Hermann T et al. *Strahlenther Onkol* 181: 65-76, 2005.
- [6] Recht A et al. *N Engl J Med* 334: 1356-61, 1996.
- [7] Benchalal M et al. *Cancer* 104: 240-50, 2005.
- [8] Arriagada R et al. *Acta Oncol* 44: 458-66, 2005.

24

Proffered Paper Oral

### Impact on the cosmetic outcome of concurrent administration of adjuvant chemotherapy and radiotherapy after breast-conservative surgery: Differences between patient's and doctor's view

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**Purpose:** In 1996, a multicenter randomized study comparing after breast-conservative surgery, sequential versus concurrent adjuvant chemotherapy (CT) with radiation therapy (RT) was initiated (ARCOSEIN study). After a median follow-up of 6.7 (4.3-9) years, we decided to prospectively evaluate the late effects and cosmesis satisfaction of these two strategies.

**Methods and material:** After breast-conserving surgery with axillary dissection, patients were treated either with sequential treatment with 6 courses CT first followed by RT (arm A) or CT administered concurrently with the same normofractionated breast RT (arm B).

With structured questions, 214 patients (107 in each arm) rated their satisfaction considering cosmesis, the difference in overall appearance, and specific changes of the breast. Late toxicity (LENT/SOMA scale) and cosmesis were blinded to treatment and assessed by a radiation oncologist by a qualitative scale and another semi-qualitative and semi-quantitative evaluation.

**Results:** Subcutaneous fibrosis (SF), telangiectasia (T), skin pigmentation (SP), and breast atrophy (BA) were significantly increased in arm B. Patient's cosmesis satisfaction was not statistically different between the two arms with 92.6% of good results in arm A and 86% in arm B ( $p=0.72$ ); although patients have found more important differences in the treated breast in arm B than in arm A, with 28.8% vs 14.3% of bad results, respectively ( $p=0.0015$ ).

Physician's prospective assessment found less favorable cosmesis results with concomitant treatment than with sequential one, with 40% and 15% of unsatisfaction, respectively ( $p=0.0014$ ) using a semi-quantitative and qualitative scale; The use of a subjective 5-point scale found also a worse physician's cosmesis satisfaction in arm B than in arm A ( $p=0.0013$ ).

**Conclusion:** Following breast conserving surgery, the concurrent use of CT with RT is significantly associated with an increase incidence of grade 2 or greater late side effects.

Rating of cosmesis is also subjective. Patients' satisfaction with cosmesis is greater than the doctors' for concomitant radiochemotherapy in breast cancer, and is not only determined by radiation late effects. Physician found a worse cosmesis outcome for concomitant radiochemotherapeutic arm.