

without any additional foci outside the primary (non-multifocal tumors), radiation therapy theoretically may be avoided after the complete resection of the tumor. In some other patients with multifocal tumors, both type and quantity of the expected residual tumor should direct the total dose of radiation, or a decision for re-excision. For some remaining patients with widely spread and high tumor burden, mastectomy might be the optimum approach instead of breast conserving therapy [7–8].

Our studies on tumor distribution show that approximately 50% of invasive ductal carcinomas have a limited extent, that is, they are localized processes: "breast carcinomas of limited extent" (BCLE) [9]. These tumors could be regarded as the proper candidates for breast-conserving therapy and a subset of those may be the candidate for breast-conserving surgery without radiotherapy. A BCLE is defined as having no tumor foci (in situ, invasive or lymphatic) beyond 1-cm from the edge of the dominant mass.

- Such tumor should first be selected by state-of-the-art mammography. Magnification views should be performed as a routine to rule out suspicious microcalcifications and densities as signs of possible multifocality beyond the edge of the index tumor.

- The tumor should then be excised with a macroscopically free margin of approximately 2-cm of which the outer 1-cm microscopically tumor free.

The histologic evaluation of the surgical margins is a critical part of the assessment of any patient being considered for breast-saving therapy. This should include the inking of the specimen, the use of specimen mammography before and after the sectioning of the specimen and the generous sampling of the area of microcalcifications and margins. Pathologists should be trained to assess the expected type and amount of residual tumor in the remainder of the breast as either none to minimal, moderate, or massive, using the quantitative involvement of the biopsy margins as a guideline. This information is essential in guiding the further choice of management of, respectively, either local radiotherapy only, re-excision with or without radiotherapy, or mastectomy.

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## Optimization of follow-up

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What are the worries and problems of a patient after optimal locoregional and adjuvant systemic treatment of her breast cancer? Where should we take care of?

1. The fear of disease relapse.
2. Recovery.
3. Long-term sequela of treatment.

**Ad 1:** The fear of recurrence can be divided into the fear of loco-regional recurrence, distant dissemination and second new primaries.

The prognosis after the detection of locoregional recurrence (LRR) is mainly related to the initial tumour parameters (grade, size, nodal status),

the interval between primary treatment and detection, and the extent of the relapse: the smaller the relapse, the better the prognosis. The prognosis is independent of primary local treatment (ie. mastectomy or breast conserving therapy). About 3/4 of the recurrences are detected either by routine physical examination or by mammography (after BCT). These findings may be a rationale for regular follow-up for the early detection of LRR: this follow-up may be more intensive for patients at high risk for LRR (younger, bad risk tumours) and less intensive or even none for patients at very low risks.

According to the well known randomised trials performed in Italy 10–15 years ago, and evidence from many retrospective studies, there is currently no role for so called "early" detection of distant disease by routine tests (imaging, biochemistry): early treatment (= treatment for asymptomatic but apparent distant disease) appears to have no impact on survival. However, times are changing:

- Better imaging tools are emerging: PET-scanning, CT-PET scanning, MRI.
- More sensitive serum markers, also with the help of proteomics.
- Better systemic treatments, particularly Taxanes and new hormonal agents (Aromatase inhibitors, pure oestrogen blockers) and other receptor blockers (Trastuzumab), leading to improvement in survival for patients with disseminated disease.

These new developments warrant new studies in which, for some groups of patients, intensified follow-up with the new tests and subsequent optimal treatment may lead to better survival. Breast cancer survivors do have an on average twofold increased risk (0.7% per annum, lifetime) for a second primary breast cancer, justifying screening by annual mammography. Indirect evidence suggests that there is no benefit of annual mammography over mammography every two years in women over the age of 60 years. For younger women with a family history, suspected or even to be related to a BRCA1/2 mutation, MRI screening is an option.

**Ad 2:** Recovery has different domains for which we should have attention: the physical, psychological, social (family life, work), financial and esthetical domain. Evidently there will be interaction between these domains. The level of impairment of the different domains should be assessed at different time points, particularly after ending initial therapy (surgery, radiotherapy, chemotherapy), and addressed when these events are debilitating. Unfortunately, till date reliable and reproducible measuring instruments in this respect are lacking, in the sense that certain interventions are meaningful, except aesthetic recovery by immediate or delayed breast reconstruction and early physiotherapies. So, no universally applicable reach to recovery interventions are at hand. Nevertheless, according to most patient wishes, major attention should be given to psychological and social rehabilitation.

**Ad 3:** The most frequent sequela of treatments are: pain (dysaesthesia), ipsilateral shoulder function impairment, lymph oedema, fatigue, impairment of cognitive functions, oestrogen withdrawal effects (hot flushes, libido, vaginal complaints, osteoporoses) and some rare late effects of radiotherapy. The possibility that these effects could emerge should be communicated to the patient. Further, the level of these impairments should be assessed regularly and treated in a timely and adequate fashion (ie. lymph oedema, osteoporoses). The Breast Clinic should have protocols for each of these sequela and the possible interventions, and the patient should be aware of these protocols.

Much debate exists on who should do the follow-up: a surgical oncologist, a radiation oncologist, a medical oncologist, a nurse-practitioner/oncologist, a general or family practitioner or all together? From the patients point of view there are 4 important issues: commitment, knowledge (experience), continuity, accessibility.

It is not that much important who is doing the follow-up, unless these aspects are met. This may well depend on the preference of the patients, her age, the stage of the primary disease, the initial treatments. It is of great importance that the patient is informed and educated in an honest way on the sense and nonsense of follow-up. Further she should know who is the primary person she can refer to in case of emerging uncertainties. An individualized follow up programme should be discussed and agreed with the patient: nurse practitioners as well as oncological specialists from the same breast team should be part of this programme. There is nothing like a universally applicable policy; nor outpatient clinic visits every 3 months with every specialist with all kind of tests for years and years, neither sending the patients away 2 or 3 years after primary treatment.

A last, but important point of the value of follow-up is the prospective registration of the whereabouts of the patients, enabling analyses of treatment results and audit.