

cell polarization or necrosis and several new classifications have recently been proposed. Careful correlation of these classifications with other features of DCIS and, most importantly, development of invasive carcinoma and death from metastatic carcinoma following conservation therapy is of the utmost importance for development of future strategies for management of this heterogeneous lesion.

#### SY-2-2 Imaging of DCIS for Diagnosis and Treatment

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Before the widespread use of screening mammography DCIS was considered a relatively uncommon lesion, accounting for 0.8-0.5% of all breast carcinomas. In recent studies of patients undergoing mammographic studies without any clinical abnormality, DCIS accounts up to 15-20% of all breast cancers. Although clustered microcalcifications are a highly sensitive mammographic sign of DCIS, its specificity ranges from 10 to 35%. As a consequence, the number of diagnostic surgical biopsies for clustered microcalcifications has dramatically increased. Furthermore, the extent of DCIS cannot always be accurately predicted on mammograms. Therefore, the diagnosis and assessment of DCIS on mammograms are one of the most common and difficult challenges for the radiologist. The diagnostic accuracy of core needle biopsy for isolated clustered microcalcifications associated with DCIS is an issue that is still debated. More recently, several series reported contrast enhancement in DCIS up to 95% on dynamic MRI. Furthermore, the extent of contrast enhancement statistically correlated with the histopathologic analysis. If further studies confirm these results, dynamic MR could prove to be a useful tool for diagnosing and planning local treatment of DCIS.

#### SY-2-3 SY04 Ductal Carcinomas in Situ: Clinical Trials

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The treatment of DCIS is a source of perplexity and more and more cases are diagnosed as a result of the development of mammography and screening programs. A simple mastectomy will cure almost 100% of cases, the few failures being due to a small invasive carcinomas missed by the pathologist. However it is difficult to justify such a mutilating operation for DCIS that are often now very small lesions, while, invasive carcinomas are treated conservatively. But which conservative treatment and for which DCIS? First, what is the role of radiotherapy after a complete wide excision? Several national trials have started in Europe and also the EORTC 10853 and in the USA the NSABP B17 which early results have been published. In the EORTC trial Lesions up to 5 cm will have a complete excision and are randomized to: Radiotherapy to the whole breast 50 Gy (2 Gy  $\times$  25 in 5 weeks) or not. Strict guidelines are given for the quality of the excision, a quality control on site and a central review of histopathology are done. Ineligible cases are also registered. Thus we collect a large data base that will provide precious resources of clinical, pathological and biological information which enable markers of risk of relapse to be identified. This may lead to a more individualized approach to management of DCIS with some patients being treated with local surgery alone, other needing additional radiotherapy and some needing mastectomy. Soon it should be possible to treat DCIS on a basis of precise information for clinical trials rather than a result of clinical prejudice.

#### SY-2-4 DCIS: Quality Control of Conservative Treatment

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DCIS is diagnosed after two different clinical situations. Firstly, DCIS is suspected by microcalcifications on routinely performed mammography. Secondly, DCIS is — coincidentally — found in a breast biopsy performed for any symptomatic reason, usually being a breast mass or bloody nipple discharge. The situation of clinical occult microcalcifications poses the clinician for more difficult questions: how to diagnose the nature of the calcifications, do they represent only in situ carcinoma or also invasive cancer, what is the extent of the disease and consequently how to proceed to — and not jeopardizing — optimal treatment? For the diagnostic work-up a high quality two-directional mammography with magnification views should always be available. Concerning the microscopical diagnosis, stereotactic FNA-cytology is insufficiently reliable to establish the diagnosis of DCIS. Multiple stereotactic core biopsies enables the exclusion of a malignancy if there is a complete concordance between the mammographical appearance

and histological findings. Core biopsy does not give information about extent and infiltration. Furthermore, uncertainties exist about the risk of needle tract seeding, and spill in case of hemorrhage.

In the absence of core biopsy diagnosis, diagnosis has to be made after wire guided biopsy. The wire localization has to be very precise. This biopsy, aimed at diagnosis, has to be representative, and should not exceed a lump of 30-40 grams (4x4x4 cm). Per operative specimen radiography is mandatory, as is identification of the specimen for the pathologist. Frozen section histology is strongly discouraged. The pathologist should examine the specimen fully, inking of the margins is indispensable and the performance of multiple slides (2-3 mm) radiography is very helpful. For reliable exclusion of invasion and margin involvement, on average 10 slides have to be examined. If margins are close, or if there are any doubts on the completeness of the excision of the mammographical microcalcifications, a post-operative mammogram should be made, preferably 6-8 weeks later (there is no need for haste in DCIS!). As the treatment of DCIS is aimed at complete local excision, in case of presumed incomplete excision a re-excision, if indicated with a guide wire re-localization, has to be performed. Quality in the management of DCIS is only controlled within a dedicated "breast team": a radiologist with high quality mammography and localization equipment, a surgeon with knowledge of the biological nature of DCIS, a pathologist who is prepared to a complete work-up. In any case, local control should be comparable to that after total mastectomy: less than 10% chance of breast relapses (half of them invasive!) in 10 years.

### SY-3. Local Recurrences After Breast Conserving Therapy (September 11)

#### SY-3-1 Local Recurrences after Breast Conserving Therapy: Tumor Characteristics

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About 60% of invasive breast cancers are multifocal, of which approximately 15% have a very high multifocal tumor burden, usually of the intraductal type (extensive intraductal component; EIC), outside the invasive mass. On the other hand, about 40% of invasive breast cancers are unifocal, having no tumor foci beyond the index tumor. Optimal therapy may vary for these groups of cancers from breast-conserving surgery with or without local radiotherapy to mastectomy. This therapeutic choice is largely based on the expected amount of residual tumor left behind after an excisional biopsy.

Optimum pathology supported by specimen X-ray and high quality mammography is capable to predict the type and amount of potential residual tumor in most of the cases.

In a recent study on a series of 149 patients, the amount of DCIS within 1 cm from the invasive edge of the primary, and the size of margin-width around the primary turned out to be the most important factors in the assessment of residual tumor after an excisional biopsy. Therefore, at histologic evaluation the attention should be focused primarily on the assessment of the amount of DCIS around the invasive tumor and the relationship of these tumor foci to the margins.

An adequate pathologic evaluation of the margins requires a proper orientation of the specimen during handling by the pathologist.

#### SY-3-2 Local Recurrences after Breast Conserving Therapy: Therapeutical Factors

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Many risk factors for local recurrence after breast conserving treatment are connected with surgical procedure, irradiation dose and technique, adjuvant treatment. The purpose of our study is to report on the basis of the literature and of our experience, the role of some therapeutical factors in the occurrence of local recurrences. In the period 1980-1992 1574 patients with breast cancer (T < 3 cm) were treated with conservative treatment (surgery + radiotherapy) in our Hospital. Mean and median follow-up is 79 and 84 months respectively. The actuarial incidence of breast recurrences at 8 years was  $7.1 \pm 1\%$ . pT1 (1185 pts) vs. pT2 (374 pts):  $6.8 \pm 1.1\%$  vs.  $7.8 \pm 2\%$  NS. Negative margins (898 pts)  $6.1 \pm 1.6\%$  positive margins

(136 pts)  $8.6 \pm 3.7\%$ , margins unknown (540 pts)  $8.2 \pm 1.3\%$  NS. Boost dose (942 pts)  $5.5 \pm 1.2\%$  no boost dose (632 pts)  $8.6 \pm 1.4\%$  NS. Interval between surgery and radiotherapy  $\leq 6$  weeks (200 pts)  $9.5 \pm 2.6\%$ ; 7–12 weeks (580 pts)  $7.3 \pm 1.4\%$ ; 13–18 weeks (511 pts)  $7.0 \pm 2\%$ ;  $> 18$  weeks (283 pts)  $5.2 \pm 1.9\%$   $p = 0.03$ . No adjuvant ther. (1074 pts)  $8.5 \pm 1.2\%$ ; Adjuvant chemother. (178 pts)  $5.4 \pm 2\%$ ; NS Adjuvant hormonother. (322 pts)  $2.8 \pm 1.5\%$   $p = 0.0008$ .

### **SY-3-3 The Need for Boost Doses in Breast Conserving Therapy**

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Abstract not available.

### **SY-3-4 Impact of Local Control on Survival**

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It is generally accepted that most breast cancer deaths result from metastatic deposits already present at time of diagnosis, and that secondary metastases resulting from locally persistent or recurrent tumor foci play a subsidiary role. Unlike systemic therapies, adjuvant local treatment (radiotherapy or more radical surgery) can favorably influence survival only by preventing secondary metastases in the subgroup of patients having residual locoregional cancer but no viable metastatic deposits following initial surgery. Moreover, most risk factors for local failure also in themselves reflect metastatic risk. As a consequence of the above considerations, one might expect that 1) local failure should be a *marker* for subsequent metastases. 2) if more aggressive local therapies have a positive influence on survival, this effect will be both *small* and *delayed* in onset with respect to the effect of systemic treatments, and it may be difficult to demonstrate because of competing causes of death (including those related to the possible toxicity of treatment). This lecture will discuss the above aspects in the light of results from the literature, with particular emphasis on randomized clinical trials.