### Proffered papers

#### Breast cancer—local treatment

**ORAL** 

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#### DUCTAL CARCINOMA IN SITU (DCIS) OF THE MALE **BREAST: ANALYSIS OF 23 CASES**

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Material: From 1960 to 1990, 581 cases of male breast cancer (MBC) were reviewed in 19 Cancer Institutes in France. 23 (4%) were pure DCIS. The median age was 56.5 years (ext. 26-77). Five patients had less than 40 years (22%). Gynecomastia was found in 10 out of 23 patients (43%). Three had family history of B.C. According to TNM classification, we found 6 impalpable lesions (T0) discovered by serosanguineous nipple discharge, 7 T1, 6 T2, and 4 Tx.

Treatment: The surgery consisted of 3 lumpectomies, 16 modified, 2 subcutaneous and 2 radical mastectomies. 16 patients had axillary dissections and 6 irradiation on the chest wall.

Histology: All cases were pure DCIS: in 14 the subtype was clearly identified: papillary (4), papillary intracystic (3), mixed papillary and cribriform (3), comedocarcinoma (2), cribriform (1), apocrine (1).

Three patients had local recurrences: two occurred in the patients initially treated by lumpectomy alone: the first was again a DCIS, but the second was an infiltrating carcinoma; this patient died by metastases. The last relapse occurred on the chest wall in a patient treated by mastectomy. One patient developed a contralateral DCIS. Two patients developed a lung and kidney cancer respectively.

In the literature the rate of DCIS in man varies from 0 to 16%. The serosanguineous nipple discharge seems a frequent symptom, especially in young men. The main histologic subtype is papillary (pure or intracystic). Mastectomy is the treatment of choice.

#### PREOPERATIVE AND PATHOLOGICAL INDICATORS OF **EXCISION MARGINS POSITIVITY IN BREAST CONSERVATIVE SURGERY**

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Positive margins (PM) may have an important role in predicting intramammary recurrences after conservative treatment of breast cancer (BC). We analyzed a variety of preoperative and pathologic factors to determine their association with the occurrence of PM. 1148 BC cases observed from 1980 to 1994 were reviewed. All patients had undergone wide excision of the tumour and 1108 had axillary dissection. Age ranged from 23 to 87 (mean 56). pT category was pT1 in 908, pT2 in 225, and pT4b in 15 cases, respectively. pN category was pN0 in 799, pN1 in 309, and pNx in 40 cases, respectively. PM were observed in 94 (8.2%) cases (intraductal = 56, invasive = 38). PM were significantly associated with a variety of factors, namely: a) age < 40 years (13.4% vs. 7.6%, P = 0.03); b) microcalcifications vs. opacities at mammography (12.9%) vs. 6.6%, P = 0.001; c) pT2 vs. pT1 (11.5% vs. 7.3%, P = 0.04); d) pN1 vs. pN0 (11.6% vs. 7%, P = 0.01); e) extensive intraductal component (EIC) or multifocality (24.2% or 17.5% vs. 3.3%, P < 0.001). No association was found between PM and histologic type or grading, evidence of necrosis and inflammation, or type of tumour growth.

Our experience suggests that in younger patients with microcalcifications at mammography, T2, EIC and multifocality, a wider excision of the tumour is necessary to obtain tumor free resection margins.

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#### INFLUENCE OF LOCAL CONTROL ON SURVIVAL IN CONSERVATIVE TREATMENT OF BREAST CANCER

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Service de Radiothérapie, Hôpital Saint-Louis, 75010 Paris, France We have reviewed the evolution of our patients experiencing a local relapse after conservative treatment.

Population: 1183 pts have been treated with a combination of limited surgery and radiotherapy. 89 local relapses (LR) have been observed, for a 10-years local control rate of 83%. All the LR except two were invasive. 11% were inflammatory, 4 pts have metastasis at the time of LR diagnosis. Only 15 pts have had an axillary dissection, 10 pts with positive nodes. An extensive intraductal component was found in 46% of cases, vascular invasion in 35%. In 64% of cases, location of the LR was in the same quadrant as the initial tumor. 86% of the pts have been treated with a mastectomy; for 3 pts a second conservative treatment have been attempted; 45% of the pts have received chemotherapy.

Results: Survival for the whole population was 94% and 87% at 5 and 10 years. For patients experiencing a LR, 91% and 76% (P = 0.005). More metastatic disease occurred in the patients with a LR (36% vs 13%; P < 0.001). Due to the small number of patients, no prognostic indicators could be found: there is no influence of nodal status, site of relapse, type of salvage surgery or adjuvant chemo or hormonotherapy over long-term survival. However, early LR (before two years after initial tumorectomy) have a statistically worst prognosis than the others: survivals at 5 and 10 years were 81% and 57% for the early LR against 87% and 75% for late LR.

Conclusion: Local relapse after breast conservative treatment is an indicator for a future metastatic dissemination. Early local relapse seems to have an especially bad prognostic, and are good candidates for adjuvant chemotherapy.

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#### AXILLARY SURGERY CAN BE AVOIDED IN SELECTED BREAST CANCER PATIENTS: ANALYSIS OF 401 PATIENTS

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Until now axillary, dissection has been considered an integral part of breast cancer treatment and is routinely carried out even after the introduction of breast conserving surgery into clinical practice. However we believe that axillary surgery can be avoided in selected breast cancer patients. In this perspective we have analyzed 401 breast cancer patients who underwent breast surgery without axillary dissection from January 1986 to June 1994. In these patients axillary dissection was spared in consideration of some reasons, principally age, small breast cancer and previous contralateral tumor. 323 (81%) patients were in post-menopausal whereas 78 (19%) in pre-menopausal status and the mean age was 62.9 years (range 30-83). No patients had clinically involved nodes in homolateral axilla, and 312 patients (78%) had no palpable node. 216 out of 401 patients (53.6%) had a pathological tumor diameter ≤ 1 cm, 133 (33.6%) were between 1 and 2 cm, whereas 38 (9.5%) had a tumor size > 2 cm. The remaining 4 patients had no evaluable diameter due to previous incisional biopsy. The histological diagnosis was ductal infiltrating carcinoma in 188 cases (46.9%), associated to DCIS in 73 cases (18.2%) or to lobular infiltrating carcinoma (LIC) in 17 cases (4.2%). LIC was present only as histotype in 59 cases (14.7%). Breast conservative surgery was performed in 383 patients (95.6%) and only 18 patients (4.4%) underwent total mastectomy in consideration of the presence of extensive intraductal component. 257 patients (64.1%) received radiotherapy to the operated breast. In elderly patients an adjuvant hormonotherapy was preferred considering the hormonal receptorial status.

An accurate follow-up > 24 months was obtained in 209 patients (mean 46.5 months, range 24-93); 25 patients died, 12 for uncorrelated or unknown causes. 20 patients had distant metastases only and 2 patients had axillary and distant metastases syncronally. 27 patients had clinically axillary metastases as only and first site of metastatic disease: 21 patients underwent full axillary dissection showing pathological metastases in 17 cases. The mean number of metastatic nodes was 6 (1-32) and the mean diameter of the primary tumour in these metastatic cases was 16.8 mm. Only one case had a tumour diameter < 1 cm. The mean time of disease free interval was 29.1 months. 3 patients out of 26 were treated with radiotherapy to the axilla without surgery, and 3 patients were treated with hormonotherapy. All operated patients are disease free. Even if this study is not a prospective randomized trial, we can conclude that avoiding axillary dissection in small breast tumors and in elderly patients does not impair local control of disease and does not have a negative impact on long term outcome in selected patients.

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#### RECENT REFINEMENTS IN FREE FLAP BREAST RECONSTRUCTION: THE DEEP INFERIOR EPIGASTRIC PERFORATOR (DIEP) FREE FLAP ANASTOMOSED TO THE INTERNAL MAMMARY ARTERY

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By dissecting the perforating vessels of the deep inferior epigastric pedicle out of the rectus abdominis muscle, no muscle tissue has to be resected, as is done with the conventional Transverse Rectus Abdominis Myocutaneous (TRAM) Flap. Hereby, we avoid abdominal wall dysfunction and complications and still keep the advantages of the TRAM flap. The same skin paddle as with the TRAM flap can be safely prelevated on two or more perforating branches of the deep inferior epigastric vessels, which is then anastomosed to the internal mammary vessels. One total flap loss out of 15 free DIEP flaps occurred due to cephalic vein thrombosis. Abdominal wall function was evaluated in DIEP and TRAM flap patients.

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### ROLE OF BOOSTER DOSE TO THE TUMOR BED IN BREAST CONSERVATIVE TREATMENT—PHASE III STUDY

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Tumorecomy with axillary dissection followed by locoregional irradiation is the standard treatment of T1 T2  $\leq$  3 cm breast cancer. The optimum dose to the breast and the tumor bed remains controversial. To answer this question a phase III study was conducted in Lyon since 1986. Main criterias of inclusion were T1 T2  $\leq$  3 cm with free margins on the pathological specimen, age no more than 70 years.

Randomization was between two dose levels: Arm 1: whole breast irradiation 50 Gy/20 F/5 weeks (dose specified on the 95% ICRU isodose); Arm 2: same dose plus a boost of 10 Gy with electrons 9 or 12 Mev (isodose 90%).

First end point will be local recurrence. For this criterium, on the assumption of a 1.2 annual rate of local recurrence, in patients with boost, and a 2.4 rate in those not receiving boost, with an annual censured rate of 1%, at one side sent, a type 1 error equal to 5% and a power of 85%, a number of 1014 patients must be included in the trial.

Between 01/86 until 07/92, 1024 patients were enrolled in this trial. Randomization was performed with stratification on pTNM classification. The groups were comparable for know prognostic factors.

Results: The local relapse free survival after 5 years was 96.4% in the 60 Gy group (tested group) and 95.5% in the 50 Gy group (controlled group). The hazard ratio, adjusted for other prognostic factors was 0.31 (0.11 to 0.88-P = 0.028).

The disease free survival after 5 years was 86% in the 60 Gy and 82.2% in the 50 Gy group. The adjusted hazard ratio was 0.6 (0.38 to 0.96-P=0.037)

There was no significant difference for overall survival between the two groups.

Telangiectasis grade 1 were present in 6% in the 50 Gy group and 12% in the 60 Gy group.

This result suggests a trend in favor of the boost (60 Gy) in term of local control with a small and acceptable detrimental effect on cosmetic results.

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## AN ASSESSMENT OF THE PHYSICAL AND FUNCTIONAL MORBIDITY FOLLOWING DIFFERENT RADIOTHERAPY SCHEDULES FOR BREAST CANCER

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The aim of this study was to determine the physical and functional morbidity after treatment with a range of radiotherapy schedules for breast cancer. Case notes from all patients treated with radiotherapy at the Mount Vernon Centre for Cancer Treatment between 1984 and 1988 were examined (total number 1661). All patients who were well at the time of their last follow-up were asked to complete a questionnaire to assess the incidence and severity of symptoms. Analysis of data for patients treated in 1988 is as follows: a total of 181/208 (87%) questionnaires were returned with 177/208 (85%) suitable for analysis, 47% of patients reported pain in the breast or chest wall, 28% reported pain in the arm, 19% reported tingling in the arm, 27/177 (15%) swelling of the arm and 34% reported restriction of arm movement. These symptoms analysis of the remaining data is in progress. Patients may find this type of information useful prior to giving informed consent to treatment.

# A PROSPECTIVE TRIAL OF CONSERVATIVE SURGERY (CS) WITHOUT RADIATION THERAPY (RT) FOR EARLY-STAGE BREAST CANCER

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We performed a one-arm prospective trial, 1986-92, to test the hypothesis that RT can be safely omitted after CS in selected pts with early-stage breast cancer. Pts were selected to include unicentric, clinical T1 carcinomas with neither an extensive intraductal component nor lymphatic vessel invasion. We required histologically negative margins of  $\geqslant 1$  cm and pathologically negative axillary nodes. The trial was closed after the accrual of 87 pts when early stopping rules were met. Median pt age was 67 yrs (27-84). The cancer was detected by mammography alone in 76%. Median pathologic tumor size was 0.9 cm. All pts underwent re-excision with only 2 having evidence of residual cancer. The median total volume of resected breast tissue was 114 cm<sup>3</sup>. Median f/u is 56 mos for the 84 surviving pts. 14 pts (16%) developed a LR as their first site of failure. The average annual LR rate is 3.6% and the crude 3-yr LR rate is 8%. 4 pts developed distant failures for a crude 3-yr rate of 1%. In comparison, 45 pts fulfilling the trial's strict eligibility criteria but treated with CS + RT between 1983-86 had a crude 3-yr LR rate of 0% and a crude 3-yr DF rate of 4%. This data suggests that even with careful selection and surgical treatment, this group of pts is at substantial risk of LR following treatment with CS alone. More accurate predictors of LR following CS alone are needed.

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## DEFINITIVE RADIOTHERAPY (DR) FOR DUCTAL CARCINOMA IN SITU (DCIS): A RETROSPECTIVE MULTICENTRIC STUDY OF 110 PATIENTS

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Radiation Oncology Department of <sup>1</sup>Trento, <sup>2</sup>Varese, <sup>3</sup>Reggio Emilia, <sup>4</sup>Padova, <sup>5</sup>Mestre, <sup>6</sup>Aviano, <sup>7</sup>Treviso, <sup>8</sup>Milano S.Pio X, <sup>9</sup>Venezia, Italy Purpose: To evaluate the outcome of pts treated with Breast-Conserving Surgery (BCS) and definitive irradiation (DR) for Ductal Carcinoma in situ of the breast (DCIS).

Patients and methods: 110 cases (104 evaluable) treated between 1980 and 1990 have been collected in 9 Italian Institutions. All the cases were treated with BCS (quadrantectomy 78, wide excision 8, tumorectomy 18) and DR (median breast total dose 50 Gy, median boost dose 10 Gy).

Results: Median follow up time was 62 months (range 21–151). There were 6 (5.7%) failures in the breast. Neither nodal recurrences or distant metastases were observed. All the 6 patients were salvaged with mastectomy. Five metachronous controlateral breast tumors (2 invasive)