Material and methods: From 1994 to 2002, the medical records of 1078 female patients with breast cancer were examined in order to identify those with histopathologically positive axillary lymph nodes and extranodal tumor spread (n=301, 28%). Ninety-one (30%) out of 301 patients were identified as having ⩽3 lymph nodes involved and 70% of patients 4 or more lymph nodes. Patients were postoperatively treated with adjuvant irradiation. Irradiation was given to the breast (n=160) or thoracic wall (n=141) up to a total dose of 50 Gy (range, 46–54 Gy). Regional irradiation was given to patients with ⩾4 positive axillary lymph nodes. Chemotherapy was administered to 70% (n=210) patients, hormonal therapy to 53% (n=160) and combined systemic treatment to 26% (n=78) patients.

Results: The median observation time was 34 months (range, 2–99). The median age of the patient population was 58 years (28–84 years). In 91% of patients more than 10 axillary lymph nodes were removed. Of the 28 (9.3%) patients with a recurrence, 6.6% had an isolated local relapse, 1% experienced a regional failure (isolated axillary, 0.7%; isolated supraclavicular 0.3%) and 1.7% had a simultaneous local and regional failure (local+supraclavicular, 0.7%; local+axillary, 1%). Subsequently 27% of patients experienced distant failure.

Conclusion: Isolated axillary failure is uncommon among patients with positive axillary lymph nodes and extranodal spread. Balancing the risks and benefits of adjuvant radiotherapy, we conclude that axillary irradiation should not routinely be given following an adequate axillary dissection.

322 POSTER

Long-term radiation sequelae after breast conserving therapy in women with early-stage breast cancer treated with 2.5 Gy per fraction

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Background: Breast irradiation after lumpectomy is an integral component of breast-conserving therapy (BCT). An optimal fractionation schedule for breast irradiation has not been uniformly accepted world wide and altered fractionations are discussed. We examined retrospectively late toxicity of a 22-day fractionation schedule (2.5 Gy per fraction to 55 Gy, 4×/wk, without additional boost).

Patients and Methods: Between 1988 and 1993 1662 patients with early-stage breast cancer (pT1-2, pN0-1, cM0) were treated with adjuvant radiation therapy (85% with 6 MV photons) using 2.5 Gy single fraction size to a total dose of 55 Gy, 4×/week. During their last follow-up visit late toxicity was assessed in 345 relapse free women using the LENT-SOMA criteria (mean follow-up 9 years, range 6.5–13 years).

Results: Moderate and severe toxicity (grade 2; grade 3 and 4) were observed as follows: pain (14%; 2%), breast edema (2%; 0%), breast fibrosis (41%; 10%), telangiectasia (7%; 10%), arm edema (1%, <1%), atrophy/ retraction (22%; 8%), skin ulceration (<1%; 0%). Six percent of women were using pain medication at the time of follow-up and 4% were regularly undergoing lymph drainage treatments.

Conclusion: The LENT-SOMA criteria are a useful tool for assessing radiation induced late toxicity after BCT using 2.5 Gy fraction sizes to a dose of 55 Gy. In this study population, late radiation effects do occur not infrequently. However, in the majority of patients they are asymptomatic when scored using the LENT-SOMA criteria.

323 POSTER

Post-mastectomy adjuvant internal mammary lymph node irradiation – benefit and cardiac toxicity: an Indian experience

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Background: Worldwide there is no consensus as to whether post-mastectomy internal mammary node (IMN) irradiation should or should not be used in medial or central quadrant **(m/c)** breast cancer patient.

Aim of study: The present study was aimed to evaluate the benefit of inclusion of ipsilateral IMN field during post-mastectomy adjuvant radiotherapy in axilla positive m/c tumor and to analyze the cardiac effect amounting from radiation of this additional anatomical area.

Material and method: After simple mastectomy with level I/II axilla dissection, IMN radiation was considered only in m/c disease with axilla involvement. Out of total 1068 patients receiving post-mastectomy radiation in Cobalt-60, 203 cases had axilla positive m/c disease and were studied between June 1995 and November 2002. Of these 203 cases, 94 Pt.s (Left breast cancer in 43) received IMN radiation. Remaining 109 Pt.s (Lt breast = 55) did not receive IMN. Total dose was 45 Gy/20 fractions/4 wks. All patients received 6 cycles of adj. chemotherapy (FAC or AC). All patients had CT-based treatment planning in 3D TPS to optimize the IMN coverage. Volume of heart irradiated and dose received were quantified individually from integral DVH. Cardiac effects were studied by ECG, CXR, Doppler Echocardiogram at the start of radiation, on completion and then 6 monthly. TMT and 24 hr. Halter monitor were done in selected cases.

Summary of result: In a median duration of F.U. of 39 months, 4 patients had chest wall recurrence – 2 received IMN and 2 did not. **IMN recurrence was observed in none whether received IMN radiation or not.** Regarding **cardiac effects**, 2 out of 43 **left** breast patients receiving IMN developed constrictive percarditis, 3/43 had LV dysfunction (EF<50%), 3/43 had congestive failure and no toxicity in 55 Lt breast cases not receiving IMN ($p<0.001$). So significant late cardiac toxicity was observed in 8/43 Lt breast IMN-treated and in 0/55 Lt breast IMN not treated cases ($p<0.001$). It was also absent in Rt breast radiation **even if received IMN**. Analysis of compiled integral DVH data revealed 50% heart volume was exposed to 22–25 Gy in IMN treated vs. 8–10 Gy in IMN not treated Lt breast patients.

Conclusion: In centers equipped with only Cobalt 60 and with no facility of IMRT or electron, addition of IMN portal is not justifiable at least in left breast cancer even in axilla positive medial quadrant disease as it may invite fatal late cardiac toxicity *without any additional gain* in loco regional control.

324 POSTER

Pulsed dose rate peri-operative brachytherapy (PDR BT) as an interstitial boost in conservative treatment (BCT) of breast cancer. Preliminary results

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Background: Reduced risk of local recurrence in patients treated with BCT including a boost dose to the tumor bed in addition to whole breast irradiation (EBRT) was confirmed in a large randomized trial. In practice, the extent of boost tumor volume may be incorrect if the tumor bed is determined using clinical parameters. The intra-operative implantation of BT catheters allows for decreasing the risk of "geographical miss" in determining the target volume. Despite its favourable radiobiological features, PDR BT has rarely been used in breast cancer. We present here our early experience with this method employed as an interstitial boost.

Material and Methods: A total of 40 consecutive T1–3N0–1M0 breast cancer pts (4 pts with T2–3 tumor after prior chemotherapy) who underwent BCT between 05/2002 and 08/2003 were analyzed. Breast sparing surgery consisted of primary segmenetectomy (27 pts) or reexcision after excisional biopsy (13 pts), full-axillary sampling in all but 2 pts with negative sentinel node, immediate tumor cavity reconstruction, and intra-operative BT tube placement. Peri-operative PDR BT of 15 Gy (1 Gy/pulse/h) was administered with Paris system rules and volume optimization technique using BT planning system PLATO. BT was followed by whole breast EBRT after the final histology had been obtained.

Results: Tube implantation (mean 9, range 5–13) prolonged time of surgery by no more than 20 minutes. Two-plane implant was used in 38 pts (95%) and one-plane in the remaining 2. BT started the day after implant placement in 38 pts and was delayed by 1–3 days in 2 pts. Temporary peri-operative breast infection in one reexcised case and fat necrosis in another one were the only side effects observed. The median period between BT and whole breast EBRT was 12 days (range, 10 to 31). Subsequent breast EBRT was abandoned in 3 pts (7.5%) including one pt with multiple pathological factors implying the superiority of mastectomy, one with final histology of LCIS and one with no malignant tumor; all these pts were diagnosed by fine needle aspiration cytology.

Conclusions: Peri-operative PDR BT with tube implantation at the time of surgery is a safe and convenient boost method. In some pts therapeutic strategy has to be verified after the final histology is obtained. Therefore, this approach necessitates careful pt selection and preoperative histological diagnosis.

325 POSTER

The effect of exercise program on the fatigue of cancer under external radiotherapy

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Cancer fatigue is the commonest complication during and after cancer treatment, especially radiotherapy. It is possible that exercise with its physical and emotional effects might be useful in reducing cancer fatigue. This study was intended to convey the effects of the scheduled exercise program on the fatigue of cancer patients under radiotherapy and to compare it with a control group. The experimental group was trained for four weeks; the first week before the program; the second and third weeks were the exercise week when the subjects were required to have exercises for 20 minutes each day followed by a 10 minute bed rest and deep slow

breaths, with their eyes closed. Fatigue was scaled in a summarized scale of 0–10. The control group did not received any treatment but their fatigue was measured daily. The results indicated that both groups experienced mild fatigue during the first week before the program with no significant difference between them. After treatment, the control group experienced sever fatigue and the experimental group experienced mild fatigue; the difference was significant. It was concluded that jogging/aerobic exercises can reduce fatigue.

326 POSTER

Intraoperative Radiotherapy (IORT) for primary breast cancer treatment

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Purpose: Presenting the technique and evaluating first results with the intraoperative application of a tumor bed boost irradiation (IORT) in breast conserving therapy.

90% of all local recurrences occur near the primary tumour location. Several authors have demonstrated the benefit of a boost irradiation to this region additional to percutaneous radiotherapy of the whole breast for local tumor control in breast conserving therapy.

This boost can be applied by several means but the "geographic miss" of the primary tumor location is considerably high. The intraoperative application of this boost offers the unique possibility to visualise and control the irradiation to this region of interest and by that completely avoiding the problem of "geographic miss". Moreover percutaneous radiotherapy can be shortened by the anticipation of this boost and results demonstrate no significant concomitant increase in postoperative morbidity. This procedure has now been applied in over 500 cases at our special dedicated unit since 10/1998. So far 200 patients have been evaluated over a 30 months follow up, with no local recurrence after IORT.

Conclusion: Experience with intraoperative radiotherapy (IORT) in breast conserving therapy (BCT) for primary breast cancer demonstrates the efficiency and safety of this high quality boost in over 500 cases during a 5 year period.

327 POSTER

Use of clipping to guide radiation boost planning for breast conservative therapy of the early breast cancer

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Purpose: Lumpectomy and quadrantentomy followed by radiation therapy are well established locoregional management of early breast cancer that has gained popularity in Japan. It is important to use boosting after whole breast irradiation for the finding of microscopic tumor in the margin, because most of mammary recurrences after breast conserving therapy develop from the tumor bed (or close to surgical margin).

Materials and Methods: One hundred and ten patients were treated with conservative surgery and irradiation for stage 0, 1, and 2 breast carcinoma between October 1996 and October 2003. Their ages ranged from 30 to 73 years old, and tumor sizes were from 0 to 35 mm. Indication of the boost is the finding of microscopic tumor in the margin, close margin, and unknown margin. We use the titanium clips, which length are 5.2 mm, because surgical clips around the resected area are helpful in planning the boost. The setting points of the surgical margins are three; close point of the nipple, bilateral half points of the distant of the nipple in the tumor bed.

Results: These distances between surgical scar and clips were 0–6.2 cm (mean 2.1 cm).It is easy to find these surgical clips at using the simulating film, ultrasoud, chest X-ray, and CT. Twenty three patients were setting this technique, and three of them were boosting after finding at the simulating film. Usually the boost dose is 1000 cGy given at the rate of 200 cGy per fraction, and the electron energy should be one that reaches the deepest part of the tumor area with the 80 to 85% isodose line. The clinically marked boost area encompassed the surgical clips adequately in 20 patients, 8 by 8 cm and 10 by 10 cm fields were placed on the breasts. The function of a boost in radiotherapy is to give a higher dose to the primary tumor bed than to the surrounding tissue. We have no severe complication of these clips.

Conclusion: To accurate the localization of the boost irradiation field, the titanium surgical clips were placed at the margin of the tumor bed of the breast cancer, in 110 patients. The conserving surgical scar is often a poor indicator for the location of the underlying tumor bed. Our presented methods is useful for easy setting the boost irradiation field and to maximize target definition.

328 POSTER

Intraoperative radiotherapy (IORT) as a boost in patients with early breast cancer

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Background: External beam radiotherapy (EBRT) of the whole-breast after breast-conserving surgery with a total dose of 45–50 Gy is the gold-standard in patients with limited stages of breast cancer. Most in-breast recurrences appear in close vicinity to the tumor-bed of the reference tumor. Therefore this area is often provided by a boost in routine practice, but no standard technique has been established. The boost dose is applicated either by different EBRT-techniques, by brachytherapy or by intraoperative radiotherapy (IORT). Since february 2002 in our department IORT is delivered in breast cancer patients by a mobile miniature X-ray source (Intrabeam™).

Materials/Methods: From February 2002 until October 2003 seventy patients with early stage breast cancer were treated by IORT after breast-conserving surgery. 45 of them had the IORT-treatment as a boost before consecutive EBRT. Median age was 63 years (43.1–86.5). The median tumour size was 14 mm (6–45). Definitive pathology results showed ductal-invasive histology in 18 patients, lobular-invasive histology in 13 patients, mixed histology in 10 patients, tubular-invasive histology in 2 patients, medullar histology in 1 patient and mucinous histology in 1 patient. IORT treatment time was 20 minutes (18.6–48.8). In most cases a spherical applicator with a diameter of 4.5 cm was chosen (3.0–5.0). Intrabeam™ is producing low energy X-rays, which can be applicated in an isotropic dose distribution to the tumor-bed. Therefore a single high-dose (20 Gy) can be applicated on the applicators surface reaching the wrapped breast tissue up to a tissue depth of 1.5 cm. After wound-healing all IORT-patients were treated by homogenous external-beam radiotherapy of the whole breast with a total dose of 46 Gy.

Results: Treatment was tolerated well by all patients without any skin necrosis. Three patients had wound healing problems, two showed skin erythemas °II after IORT, which disappeared without any delay. After a maximum follow-up of 20 months patients had good cosmetic outcome without any significant late effects. One patient had to be treated by secondary mastectomy because of multifocality and one patient developed cervical lymph node metastases 2 months after breast conserving surgery. In both cases additional EBRT was omitted. One other patient presented with multifocally relapsed disease with several skin metastases 10 months after IORT plus EBRT and died 4 months later.

Conclusions: IORT with the Intrabeam system is a comfortable, effective method to deliver a single high-dose to the tumour-bed as a boost. After breast-conserving surgery, the resection cavity can be ideally irradiated intraoperatively by short-distance X-rays. A miss of the target, as it happens often during external beam course, can be avoided.

Thursday, 18 March 2004 16:00–17:30

PROFFERED PAPERS

Hereditary cancer

329 ORAL

Risk of breast recurrence in relation to BRCA1/2 mutation status following breast-conserving surgery and radiotherapy

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Background: *BRCA1* and *BRCA2* germline mutations are associated with a strong risk of breast cancer, which may preclude breast-conserving treatments in carriers. We investigated whether mutation status was influencing the rate of breast recurrence following breast-conserving treatment (BCT) with surgery and radiotherapy.

Patients and Methods: *BRCA1* and *BRCA2* genes were screened for germline mutation in 131 patients (with 136 breast cancers) with a family history of breast and/or ovarian cancer, treated with BCT. Tumor features, breast recurrences (BR) and contralateral breast cancer (CBC) rates of *BRCA* mutation carriers were compared to those of non-carriers with a family history. The 131 pts. with familial history were matched to 261 pts.