mastectomy by Patey utilizing electrocautery which performed processing of surgical wound (all surface of wound) by 0,15% sterile solution of sorbent's suspension "Sillard-P" before application of suture. 1-group consist of 18 patients. 2-group (control group) consist of 60 patients which underwent radical mastectomy by Patey utilizing electrocautery without of wound processing.

Results: The existence of seroma in 1-group was short duration and disappeared on 5-th day. In 91% of cases just 3-times puncture was performed. In 8,3% patients had seroma duration about 3 week, which can be explained as not qualitative processing of axillary's region by sorbent's suspension. 85% of patients in control group had seroma with duration about 2 week.

Conclusions: Processing of surgical wound by 0,15% "Sillard-P" suspension preventing seroma, decreasing of seroma volume and duration, improve breast cancer patient's quality of life and decreasing in patient's day.

686 POSTER

Sentinel node biopsy in breast cancer: are there differences according to the time of radioisotope injection?

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Introduction: Lymphoscintigraphy is essential for a highly accurate sentinel node (SN)mapping and biopsy. There have been reports supporting the isotope injection in the morning of the surgery and others defending the previous day injection. At our institution we got logistic advantages with the day-before procedure. Nevertheless, we do not know whether this fact results in misidentification or higher number of SN. We compare the results of two groups of patients, trying to assess the differences between them.

Methods: We studied a series of 105 consecutive patients with cN0 breast cancer, submitted to the SN procedure, from Jul/99 to Jan/01. Sixty-one received the same-day injection (group A) and 44 received the isotope the day before surgery (group B). We used a combination technique, with peritumoral Tc99m sulphur colloid injection, subareolar Patent Blue V dye injection and gamma-probe detection. Statistical significance was assessed using Chi-Square and Mann-Whitney tests.

Results: The two groups are similar according to patient and tumor characteristics. There were no statistical significant differences in the studied variables between the two groups. Although, the results seem to be somewhat better in the day before injection group of patients. Lymphoscintigraphy showed hot spot's in 91.8% of group A and 95.5% in group B patients (p=ns). The mean number of hot spot's was 1.4 in group A and 1.6 in group B patients (p=ns). The mean number of excised sentinel nodes was 1.39 in group A and 1.45 in group B patients (p=ns).

Conclusions: These two distinct schedules for radioisotope administration yielded similar results. However, our institutional logistics prompted us to definitely choose the day before injection.

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Factors determining locoregional control and late sequelae in patients with locally advanced breast cancer (LABC) managed with radiotherapy (RT) as the primary locoregional treatment

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Introduction: RT plays an important role in the management of LABC, yet its clinical efficacy still remains far from satisfactory. The aim of this study was to evaluate retrospectively factors determining local control and late sequelae in a large series of consecutive LABC patients managed with RT as the primary locoregional treatment.

Material and methods: The records of 261 primarily inoperable LABC patients treated between 1991 and 1997 at two institutions: Medical University of Gdansk, Poland and Velindre NHS Trust, Cardiff, UK were analysed. All patients received megavoltage RT to the breast with two tangential fields, whereas the adjacent lymph node areas were irradiated using customised fields. Due to a large scale of RT doses and fractionation schedules, normalised total dose (NTD) was calculated for all patients using a linear quadratic model. In 241 patients RT constituted the only local treatment and the remaining 20 patients were subsequently subjected to mastectomy. Most patients received chemotherapy and/or endocrine therapy prior or after RT.

Results: Within the median follow-up of 37 months, locoregional recurrence occurred in 95 of 251 evaluable pts (38%). Three-year and five-year locoregional-free survival rates were 59% and 48%, respectively. At multivariate analysis of variables predicting the risk of locoregional relapse, inflammatory carcinoma ($p<0.01$; RR 1.96), T4 disease ($p=0.01$; RR 2.58) and involvement of supraclavicular lymph nodes ($p=0.04$; RR 1.99) were the most significant clinical factors, whereas response to RT ($p<0.01$; RR 1.52) and NTD ($p<0.01$; RR 0.75) were the most important therapeutic factors. Increasing the total dose to the tumour by 10 Gy was associated with an average 25% reduction of local relapse. Thirty nine patients (16%) experienced late radiation sequeale. Multivariate analysis showed that radical mastectomy performed after RT was associated with the reduced risk of arm oedema ($p<0.01$; OR=5.0), whereas neoadjuvant chemotherapy decreased the risk of subsequent teleangiectasia ($p<0.01$; OR=0.4).

Conclusions: Due to large heterogeneity of LABC pts, judicious tailoring of RT, particularly in terms of dose prescribing, is essential to increase the chance of locoregional cure. Therapeutic gain, however should be weighed against the increased risk of late complications.

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Improved cosmetic outcome by use of 3D-conformal boost RT and remodeled conserving surgery for early breast cancer

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Purpose: To evaluate factors determining cosmetic outcome, survival and failure pattern in patients treated with breast conserving therapy for early breast cancer.

Methods: From 2/1992 to 5/1999, 219 women with early breast cancer underwent breast RT with various technique of boost RT following various technique of breast conserving surgery. Median age of all pts was 44 ys old (range 20-67 ys old) and 170 pts were on premenopausal status. 159 pts underwent quadrantectomy and surgical defect was remodeled with fat reapproximation since 1996. All received tangent whole breast RT with total dose of 50.4 Gy in 28 fractions followed by a boost RT to the tumor bed, 10-15 Gy. Breast only was irradiated in 169 pts and breast and regional nodal area were irradiated in 50 pts. Technique for a boost RT to tumor bed included electron in 45 patients, Ir-192 HDR brachytherapy in 12 pts, 3D-conformal RT in 116 pts and 2D-photon in 6 pts. 20 pts with Tis did not receive a boost RT. 100 patients received chemotherapy concurrently with RT. Median follow-up was 44 mos with a range 3-112 mos. Cosmesis was determined by the physician and patients, scored to be excellent, good, fair and poor.

Results: 194 pts were alive without disease at the last follow-up. 5 pts (2%) failed in the breast; 2 salvaged by MRM, 1 salvaged by MRM and CT, 1 alive with disease after MRM and 1 alive with disease, on CT at the last follow-up. 12 pts (5%) developed distant metastasis. 5 yr overall and disease free survival were 94%, 95% respectively. Factors determining the survival include nodal involvement, presence of EIC, lymphatic invasion, number of node involved and multifocality. Chemotherapy was not a factor determining the survival but group of patients who received nodal RT showed poorer survival. 168 pts were scored for the cosmetic outcome at their last follow-up; 114 pts (68%) scored as excellent, 46 pts (27%) as good and 8 pts (5%) as fair.

Conclusion: The group of patients who received a boost RT with 3D-conformal and who underwent remodeled BCO showed much improved cosmetic outcome (excellent group was increased from 20% to 70%).

689 POSTER

The benefit of individualized custom bolus in the postmastectomy radiation therapy: Numerical analysis with 3-D treatment planning

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Purpose: With the improved survival rate of patients with breast cancer by postoperative chemoradiotherapy, meticulous radiotherapy techniques to

minimize side effects became more important. To reduce the dose to lung and heart in the case of chest wall irradiation using an appositional electron beam, we used an individualized custom bolus which was accurately designed to compensate the difference of chest wall thickness. The benefits were evaluated by comparing the normal tissue complication probabilities (NTCPs) and dose statistics with boluses to those without boluses.

Methods: Boluses were made and the effects were evaluated for ten patients treated with the reverse hockey stick technique. Electron beam energy was determined in order to irradiate 80% of the prescription dose to the deepest lung-chest wall boarder, which was usually located at the internal mammary lymph node chain. An individualized custom bolus was made to compensate the chest wall thinner than the prescription depth by accurately measuring the chest wall thickness at 1cm2 interval on the planning CT images. Second planning CT was obtained overlying the individualized custom bolus to each patients' chest wall. 3-D treatment planning was performed using ADAC-Pinnacle3 for each patient with or without bolus. NTCPs based on "the Lyman-Kutcher" model were analyzed and the mean, maximum and minimum doses for heart and lung were computed.

Results: The average NTCPs in the ipsilateral lung were reduced from 80.2 ± 3.43% to 47.7 ± 4.61% when individualized custom boluses were used, which shows statistically meaningful reduction ($p < 0.01$). The mean lung dose also was reduced about 430 cGy from 2757 cGy to 2327 cGy. The reduction of NTCP and the mean lung dose appeared to have statistically meaningful correlation since 'p value' was < 0.01. The NTCP in the contralateral lung as well as the heart were 0% even in the case of no bolus due to the small effective radiation volumes, mean value 4.4% and 7.1% respectively.

Conclusion: The use of an individualized custom bolus in the radiotherapy of postmastectomy chest wall reduce the NTCP of ipsilateral lung about 30-35%, which can increase the complication free cure probability of breast cancer patients.

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Salvage peroperative hdr or PDR brachytherapy for chest wall or infraclavicular recurrence of breast cancer in post mastectomy patients - a feasibility study

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Introduction: For patients with a local recurrence of post mastectomy breast cancer after external beam radiation (EBRT), we investigated the feasibility of fractionated salvage HDR or PDR brachytherapy (BT).

Material and methods: Thirteen patients with a local recurrence after EBRT and 1 patient without previous EBRT were treated between 1996 - 2000 in the age of 37 -85 years (mean 59 years). For 11 patients it was the second or third local recurrence. The mean previous EBRT dose was 58 Gy (range 42 - 62 Gy) and the mean EBRT- BT interval was 42 months. Local recurrence was resected and the tumor bed was marked with surgical clips. Mean 7 plastic tubes were implanted to the target during the surgery. After CT based 3D inverse BT planning a mean dose of 29 Gy (10 -40 Gy) was applied to the target shaped reference isodose. Two patients received additional EBRT (40 and 50 Gy).

Results: After a mean follow up of 12 months (range 1-33 months) we observed 7 out of 14 patients without signs of local progress or recurrence. Seven patients had a local recurrence or progress after a mean interval of 6 months (range1-18 months). However, in 8 out of 14 cases we observed later a systemic progress. No RTOG III or IV side effects were developed. All 7 patients with a local control have a good cosmesis.

Conclusions: For patients with local recurrences in previous irradiated field salvage peroperative Brachytherapy seems to be offering a meaningful chance for local control and/or better quality of life.

Metastatic breast cancer

691 POSTER

Health-related quality of life (HRQL) in women with HER2-positive metastatic breast cancer: effect of treatment with trastuzumab (Herceptin) plus chemotherapy versus chemotherapy alone

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Purpose: The addition of Herceptin (H) to chemotherapy (CT) produces significant benefits in women with HER2-positive metastatic breast cancer (MBC), including a survival advantage (Slamon DJ et al, NEJM 2001;344:783). We have reported previously that HRQL is stable in women treated with H monotherapy and improves in those who respond (Cobleigh MA et al. JCO 1999;17:2639). HRQL generally worsens in women treated with CT. We have compared HRQL in patients with HER2-positive MBC treated with H+CT or CT alone in a pivotal phase III trial.

Methods: The pivotal trial included 469 patients, of whom 400 completed an HRQL questionnaire (EORTC QLQ-C30) at baseline and on one or more subsequent occasions at 8, 20, 32, 44 and 56 weeks. These 400 patients had been randomized to receive either H+CT (208 pts) or CT alone (192 pts). CT consisted of either doxorubicin (epirubicin in 36 women) and cyclophosphamide or paclitaxel. HRQL improvement or worsening were defined as a >/=10 change in scores (range 0-100) from baseline in each of 6 preselected domains: global QL, physical, role, social, and emotional functioning, and fatigue. Changes of <10 were defined as stable HRQL.

Results: Baseline scores were similar in the H+CT and CT groups. At 32 weeks, global QL, physical functioning and fatigue showed statistically significant improvement ($P<0.05$) over baseline scores in the H+CT group. In contrast, scores in these domains deteriorated in the CT group. Statistically significantly higher proportions of patients in the H+CT group reported improvement in global QL (51 vs. 36%, p=0.003) and in fatigue (52 vs. 42%, p=0.03) than in the CT alone group. Higher proportions of patients in the H+CT group also reported improvement in physical (37 vs. 29%, p=0.08) and role functioning (29 vs. 21%, P=0.08), but these were not statistically significant. Interestingly, the proportions of patients in the two groups that reported worsening were similar, but significantly fewer patients in the H+CT than in the C group had stable scores for global QL (9 vs. 21%, P=0.0003) and social functioning (11 vs. 19%, P=0.03).

Conclusions: The addition of H to CT did not cause the proportion of patients reporting worsening HRQL to increase. In contrast, significantly more patients experienced improvements in global QL and fatigue when treated with H+CT than when treated with CT alone. (Supported by Genentech, Inc.)

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Older (age >60 years) patients obtain survival benefit from herceptin plus chemotherapy

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Background: Entry to the pivotal phase III trial that demonstrated that adding Herceptin (H) to chemotherapy (C) (doxorubicin/epirubicin and cyclophosphamide [AC] or paclitaxel [T]) as first-line therapy for HER2-positive metastatic breast cancer (MBC) improves response rate (RR) (50% versus 38%, p=0.003) and survival (odds ratio, 0.80, p=0.046) was not restricted by age. Methods: We conducted a retrospective exploratory analysis to determine the influence of age on clinical benefit from H in this trial. Results: Of the 469 patients enrolled in the pivotal phase III trial, 360 (77%) were aged <60 years and 109 (23%) >60 years. Although baseline patient characteristics were similar between the 2 groups, patients aged >60 years had a worse baseline Karnofsky Performance Status (score <80, 41% vs 30%), higher initial nodal burden (>4, 52% vs 34%), longer disease-free interval from adjuvant therapy (26 vs 20 months), more frequent prior exposure to hormonal therapy (71% vs. 54%), and less frequent adjuvant exposure to anthracyclines (31% vs. 40%). Outcomes are shown below.

Response rate (<60 years): C alone, 33%; H + C, 52%
Response rate (>60 years): C alone, 28%; H + C, 44%
Survival (<60 years): C alone, 23 months; H + C 26 months
Survival (>60 years): C alone, 24 months; H + C 19 months

The survival benefit obtained by adding H to C in patients aged >60 years was statistically significant (odds ratio: 0.64 95% CI: 0.41-0.99).