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Concurrent Radiotherapy and Trastuzumab in Early-stage Breast Cancer – A Prospective Single Institutional Experience

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Background: To evaluate the early and late heart and skin toxicities, as well as the efficacy of concurrent adjuvant trastuzumab-radiotherapy for breast cancer (BC), particularly in the case of internal mammary chain (IMC) irradiation.

Materials and Methods: Prospective study of 173 patients treated between 06/2003 and 03/2009 by concurrent trastuzumab-radiotherapy for non-metastatic BC. Left ventricular ejection fraction (LVEF) was assessed at baseline, before and after radiotherapy and then every 4–6 months. All toxicities were evaluated using CTCAE v3.0. Survival data were defined as the time from the histological diagnosis of BC until occurrence of the event. Loco-regional recurrence free- and alive patients were censored at the date of their last known contact. Survival and interval rates as well as their confidence interval (CI) were calculated by the Kaplan–Meier method.

Results: Median age was 52 years [25–83]. Previous adjuvant anthracycline-containing chemotherapy was administered in 157 patients (90.8%). All patients received trastuzumab every three weeks (8 mg/kg in the first infusion followed by 6 mg/kg) at the median dose of 6020 mg [1285–29180] for a median duration of 12 months [2–62]. 88 patients (50.9%) presented with left-sided BC. The IMC was irradiated in 134 patients (77.5%).

Acute skin toxicity was acceptable with 132 (76.3%) grade 1, 32 (18.8%) grade 2 and 6 (3.5%) grade 3 skin reactions. Esophagitis occurred in 18 patients (10.4%): 14 (8.0%) grade 1; 3 (1.7%) grade 2, and 1 (0.5%) grade 3. Out of 172 patients with assessments after 12 months, late telangiectasia grade 1–2 occurred in 14 patients (8.5%), local pain grade 1 in 23 patients (14.0%) and grade 2 in 4 patients (2.4%), fibrosis grade 1 in 31 patients (18.0%) and grade 2 in 8 patients (4.6%).

Out of 156 patients with LVEF assessments after completion of the radiotherapy, 5 patients (3.2%) experienced a reversible grade 2 left ventricular systolic dysfunction.

Median follow-up was 52 months [17–88]. Loco-regional control at 48 months was 95% CI95% [91;98]. Overall survival at 48 months was 98% CI95% [95;100].

Conclusions: In this prospective study of BC patients treated with trastuzumab and radiotherapy with, in most cases, anthracycline-based chemotherapy and IMC irradiation, both the rates of abnormal LVEF and skin toxicity were deemed acceptable with excellent local control.

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Preliminary Results Following Hypofractionated Irradiation in Breast-conserving Therapy

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Background: Over the last several years there has been renewed interest in hypofractionated adjuvant radiotherapy (RT) in breast cancer patients treated by conservative surgery in the light of radiobiological and clinical evidence. We present our experience regarding preliminary outcomes of a hypofractionated RT schedule.

Materials and Method: Between October 2007 and October 2009 80 women with early breast cancer were treated by 42.75 Gy/15 fractions over 5 weeks. This treatment involved three fractions per week (Monday-Wednesday-Friday). All patients received an additional boost dose to the tumor bed of 8.55 Gy in 3 fractions using 6 MV photons. Acute radiation toxicity was the principal endpoint. Cosmetic appearance including changes in breast appearance together with breast shrinkage/hardness/swelling was assessed. Methods of evaluation were photos (before and after the end of RT treatment at one/three/six month intervals), ultrasound examinations (before and after the end of RT treatment) and mammograms (three/six months and one year after RT).

Results: The median follow-up time was 24 months. In order to score radiation toxicity, patients were evaluated according the RTOG scoring system for radiation reactions at the end of treatment and 3, 6 and 12 months after treatment). At the end of RT RTOG grades 0, 1, 2 for acute skin toxicity were: 56/80 (70.0%), 19/80 (23.8%) and 5/80 (6.3%) respectively. After 3 months RTOG grades 0, 1, 2 were 64/80 (80%), 14/80 (17.5%) and 2/80 (2.5%). After 6 months RTOG grades 0, 1 were 72/80 (90.0%) and 8/80 (10.0%) respectively whereas after 1 year they were 78/80 (97.5%) and 2/80 (2.5%). Breast shrinkage and breast hardness were the most common changes especially in patient with large breast volumes. An excellent to good cosmetic outcome (i.e. no change in breast

appearance) was observed in 90% of patients. There wasn't local or distant recurrence in any patient during this limited two years follow up.

Conclusions: Preliminary results (skin reactions and cosmetic appearance) from this study are consistent with published data that support the use of shorter fractionation schedules in early breast cancer patients after breast conserving surgery, in terms of cosmesis and effectiveness in local control. However a median follow-up of 2 years is too short to allow assessment of all the potential late normal tissue effects. This study is still on going to estimate late radiation morbidity for final evaluation.

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Role of Simultaneous Integrated Boost IMRT in Carcinoma Breast

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Background: Breast conservation has been widely accepted in treatment of women with early stage breast cancer. The most common adjuvant radiation strategy after BCS, consists of irradiation of the whole breast using two tangential photon beams in 5–6 week period, with doses of 1.8–2.0 Gy/fraction to a total dose of 50 Gy followed by boost irradiation by electrons and/or photons up to a total dose of 60 Gy, resulting in total duration of 7–8 weeks. With this technique there may be appreciable dose inhomogeneity within the irradiated volume and dose to lung heart and contralateral (C/L) breast can be high. IMRT can shorten the overall treatment time by integration of the additional tumor bed boost significantly. In patients with node-negative invasive breast cancer or carcinoma in situ treated by BCS, postop whole breast RT with SIB-IMRT is a good option with the aim to minimize the target dose inhomogeneities and to provide differential dosing to the whole breast and the resection cavity. The sequential boost is eliminated as the overall treatment course is shortened by giving greater dose per fraction to the resection cavity. This retrospective study reports our experience of SIB IMRT in terms of radiation toxicity, cosmetic outcome and local control in cancer breast.

Material and Methods: 12 patients of cancer breast stage I-III treated with SIB IMRT after BCS between March to December 2010 were analyzed for normal tissue dose and corresponding toxicities with a follow up of 6 months. Virtual simulation done and CTVs for breast, cavity and normal structures were contoured on Eclipse planning system. Dose prescribed was 50 Gy/25# to PTV breast and 60 Gy/25# to PTV cavity and inverse planning IMRT done.

Results: Mean 95% PTV_{breast} and PTV_{cavity} 49.8 and 59.2 Gy respectively. No hot spots found inside PTVs. V_{40 Gy} of heart in left breast patients ranged from 1–7% and mean dose 12.8 Gy for the whole group. The mean dose to the ipsilateral lung, total lung, C/L lung and C/L breast were 18.1 Gy, 13.0 Gy, 2.5 Gy and 3.2 Gy respectively. The treatment was completed in scheduled 5 weeks without any interruption. Acute skin toxicity of RTOG grade I in 6, grade II in 4 and grade III in 2 patients were observed. At a follow up of 6 months 3 patients had induration and tenderness at lumpectomy site. The breast cosmeses were excellent in 90% of case. No pulmonary toxicity was seen.

Conclusion: The overall treatment time was reduced by SIB IMRT about a week with favorable acute toxicity profile. Longer follow up is necessary and larger number of patient to be taken for the study to assess the ultimate cosmeses, late toxicity and locoregional recurrence.

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Benefit of Different Radiation Boost Dose Based on Surgical Margins – Single-institution Experience on 2 173 Patients Treated with Radiotherapy After Breast-conserving Surgery

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Background: Local recurrence (LR) of breast carcinoma (BC) is reduced by whole-breast radiotherapy (RT) after breast-conserving surgery (BCS). There is no a worldwide consensus about the effective dose of radiations to prescribe, especially for what concerns the boost after the irradiation of the whole breast. The aim of this study is to validate the use of different doses of RT boost based on surgical margins.

Materials and Methods: A total of 2 173 infiltrating BC treated with BCS and adjuvant RT in our institution between 1987 and 2007 were retrospectively reviewed. A median dose of 50 Gy was prescribed to the whole breast. A 10 Gy boost was prescribed in case of surgical margins