patients. We evaluated the stage migration effect on prognosis by comparing the outcome of "SLN-N0"patients to N_0 breast cancer patients that were treated in the "pre-SLN" era.
Method: Two groups of patients were evaluated: a prospective cohort of 245 consecutive patients that were staged as N_0 based on pathologic assessment (HE and IHC-staining) of the SLN, and a cohort of 182 patients treated before 2000 for unifocal cancers and staged as N0 based on axillary lymph node dissection (ALND) specimens. Patients who had chemotherapy (in the SLN group) and patients who would nowadays have had chemotherapy (in the ALND-group) were excluded. Median follow-up was 4 years for the SLN-group and 9 years for the ALND group.
Results: The SLN group and the ALND group were comparable for tumor size, the proportion of high grade cancers and the proportion that received hormonal therapy.
2- and 4-year cumulative overall survival was 95 and 91% for the ALND group and 98 and 93% for the SLN group (P=ns). 2- and 4-year disease free survival was 93 and 86% for ALND-group and 97 and 91% for the SLN group (P = 0.1)
Conclusion: Stage migration appeared to have an effect on prognosis. Although not statistically significant, patients who were staged as N_0 based on SLN assessment seemed to have more favorable disease free survival.

2086 POSTER

Clinical implications of the MDR1 1236C>T polymorphism: influences on doxorubicin pharmacokinetics and myelosupression in Asian breast cancer patients

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Background: This exploratory study aims to identify predictive biomarker polymorphisms in the ABCB1 gene and their relation to doxorubicin pharmacokinetics and pharmacodynamics in Asian breast cancer patients undergoing adjuvant chemotherapy.
Methods: Patients (N = 32) who have had curative surgery for histologically confirmed Stage I to III breast cancer were recruited. Doxorubicin was administered at 60 mg/m^2 and cyclophosphamide at 600 mg/m^2 every 3 weeks. DNA was extracted from the blood lymphocytes for analysis of the 1236C>T, 3435C>T and 2677G>T/A polymorphisms in the MDR1 gene. The incidence of treatment related toxicities were recorded. The nonparametric Mann-Whitney U test was used to detect significant differences between paired groups and the Kruskal-Wallis test to assess genotypic-phenotypic correlations.
Results: The median age was 48.5 years (range 31.2−66.8). Majority were Chinese (84%); 12.5% Malays and 3.1% were Eurasian. Patients harboring the reference genotype for the 1236C>T polymorphism were found to have significantly lower exposure levels to doxorubicin compared to patients who were heterozygous [CC vs. CT, AUC0-inf/dose/BSA(h*m-5): 10.95±3.9 vs 22.10±5.7, P = 0.0001] or carried the homozygous variant allele [CC vs. TT, AUC 0-inf/dose/BSA(h*m-5): 10.95±3.9 vs 19.01±5.8, P = 0.011]. The exposure levels for doxorubicinol were also significantly lower in patients who had the reference genotype when compared to the patients who were heterozygous [AUC 0-inf/dose/BSA(h*m-5); 7.04±2.6 vs 11.60±3.4, P = 0.011] or of the variant genotype [AUC 0-inf/dose/BSA(h*m-5); 7.04±2.6 vs 11.59±4.1, P = 0.019]. The presence of at least one T allele was associated with an approximately 5-fold odds ratio of developing grade 3/4 febrile neutropenia [CC vs CT+TT; OR = 4.8, 95% CI; 0.5 to 45.5]. No significant correlations were observed between 3435C>T and 2677G>T/A polymorphisms and pharmacokinetics of doxorubicin and neutropenia.
Conclusions: The present exploratory study showed that the 1236C>T MDR1 polymorphism may influence doxorubicin pharmacokinetics and is a potential predictive biomarker for severe myelosuppression in patients on adjuvant chemotherapy. Accrual is ongoing.

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Saline instillation into the cavity after conservation surgery for breast cancer is a safe way of improving cosmesis

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Background: To demonstrate that saline instillation is a safe and simple procedure for volume replacement after wide local excision in breast surgery.
Materials and Methods: We performed a pilot study over a 12 month period at the Chase Breast Unit. 106 patients who underwent wide local excision for breast cancer had saline instilled into the surgical cavity at the time of wound closure. This was to maintain the volume and shape of the breast after removal of significant amounts of tissue. 75 mg of local anaesthetic (10 mls Ropivacaine hydrochloride 7.5 mg/ml) was added and included in the volume. We measured the volume instilled and monitored the wound and breast post-operatively at 1 week, 2 weeks and 3 months. As is our normal practice, all patients had peri-operative antibiotics.
Results: The volume of fluid instilled varied between 30–180 mls. The weight of tissue removed was in the range of 12–116 gms. The fluid was retained within the cavity. However, in one case the wide local excision cavity unexpectedly communicated with the axillary clearance cavity and all the fluid was evacuated spontaneously through axillary suction drain with a resultant visible reduction in the volume of the breast. There were no complications of saline instillation. In particular, there was no early or late infection in any of the 106 patients. None of the patients reported any additional discomfort or pain. There were no visible abnormalities apart from a subjective enhancement in the shape and volume of the breast. This improvement in shape and volume was maintained for the entire length of assessment (3 months).
Conclusions: Saline instillation is a simple and safe method of replacing volume after removal of significant amounts of breast tissue. Surprisingly, the benefits seem to persist. We are now proceeding to fully evaluate this technique in a formal prospective trial.

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Efficacy in terms of local control, cosmetic outcome and late toxicity in 536 women treated with interstitial brachytherapy boost for breast conserving therapy

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Background: The aim of this study is to report local control, cosmetic outcome and late toxicity in women with early breast cancer treated with brachytherapy boost after external beam irradiation following breast conserving surgery.
Materials and Methods: During 1980–2000, 536 women received tumor bed boost with brachytherapy after external beam radiation therapy. The median pathological T size was 3 cm and the lymph nodes were positive in 198 (37%) women. Adjuvant chemotherapy was given to 228 women while 85 received adjuvant hormonal therapy. Three hundred and eighty three women were treated with low dose rate brachytherapy (LDR) to a dose of 15−20 Gy and 153 received high dose rate brachytherapy (HDR) to a dose 10 Gy (optimised) in single fraction. The median follow up for the entire group was 52 months.
Results: Actuarial 5 year local control rate was 90% for LDR group and 92% for the HDR group. Cosmesis at the last follow up was good or excellent in 83% women. Post radiation worsening of cosmesis was observed in 11.5% women and was similar in the 2 boost groups. Moderate to severe late breast sequelae were observed in 22% women in the HDR group and was significantly higher 12% in the LDR group (p = 0.002). Fibrosis was the most common late sequelae of radiation and 14% women had moderate to severe fibrosis in HDR group as compared to 7% in the LDR group (p = 0.01). Other late sequelae included breast oedema observed in 6% women in the HDR group and 4.5% women in the LDR group.
Conclusion: The local control was comparable for LDR and HDR brachytherapy boost. Type of tumour bed boost did not have a significant impact on worsening of cosmetic outcome. The late breast sequelae were however significantly higher in women treated with single fraction HDR implant.

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Clinical impact of upfront adjuvant AI therapy on the early risk of recurrence

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Background: In postmenopausal women (PMW), most early breast cancer (BC) is hormone-dependent (HD), with a very heterogeneous natural history. During the first 2 years post surgery, there are more distant metastases (DM) events than locoregional or contralateral BC events. DM account for approximately 75% of all recurrences in patients taking