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(87%) reached surgery, of these 6 obtained a complete pathologic response (pCR), 42 had a partial response (PR), 48 had no change (NC) and 1 had progressive disease (PD). Thirteen did not go to surgery.

Median survival for the entire study 7.4 years.

The 3-year survival for patients treated in the first half-part of the study was 52% vs 82% for patients treated in the latest half-part. Survival according to response did not show a consistent pattern, 3-year survival for CR, PR and NC was 54%, 73% and 76%, respectively.

Conclusion: Changes in treatment modalities available through the millennium, is reflected in an increase in survival. As surgery mainly was performed as early as possible response at surgery was not reflected in survival.

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### Treatment of the axilla in locally advanced breast cancer

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**Background:** A retrospective analysis of women treated for locally advanced breast cancer (LABC) with local regional radiotherapy with or without neo-adjuvant chemotherapy and/or surgery focusing on axillary control.

**Materials and Methods:** All consecutive 131 patients diagnosed from January 1990 to December 2005 treated with local regional radiotherapy were reviewed. Treatment consisted of 50 Gy in 25 fractions of 2 Gy to the breast and regional lymph node areas and a boost of 20 Gy in 2 Gy fractions to the primary tumour area in 7 weeks. 80% of the patients had lymph node metastases. 46 patients received an axillary, 4 a supraclavicular and 1 an infraclavicular boost because of gross nodal involvement.

40 patients received irradiation only (IR) (1 of whom received breast irradiation only). 34 received neo-adjuvant chemotherapy without surgery (NC) and 57 patients received neo-adjuvant chemotherapy with surgery (NCS) before irradiation (33 wide local excision, 24 mastectomy) of whom 5 did not receive regional lymph node irradiation.

Of the whole cohort 89 patients (68%) did not receive axillary surgery, all of these patients were irradiated to the axillary lymph node region except for 1 patient. In the **IR** group 2 patients were treated with an axillary lymph node dissection (ALND). In the **NCS/NC** groups 36 were treated with an ALND and 4 with a sentinel node (SN) procedure, axillary lymph node irradiation was omitted in 5 of them. Median follow up was 65 months for the entire cohort.

Results: The 5-year local control rate was 76.9% (IR), 61.9% (NC) and 90.4% (NCS) in favour of the neo-adjuvant chemotherapy with surgery group (p-value = 0.004). The 5-year regional control rate was 94% in all groups (p-value 0.919). There were 7 regional recurrences, 4 in the supraclavicular fossa (IR: 1, NC: 1, NCS: 2) and 3 in the axillary region (1 in every group). 5 year axillary control rate was 100% for the 42 patients treated with ALND/SN and 98% for the remaining 89 patients (not significant).

Conclusion: Best outcome is achieved in terms of local control for the trimodality treatment consisting of neo-adjuvant chemotherapy, surgery and loco-regional irradiation in patients with locally advanced breast cancer. The data suggest that in these patients omitting ALND/SN did not influence axillary recurrence rate.

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#### Trends in advanced breast cancer in a developed Asian society

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Introduction: Although the overall incidence of breast cancer in Singapore is about one-third that of Western countries, the incidence of advanced breast cancer, including locally advanced breast cancer and metastatic breast cancer, is more common. It was observed in countries where nationwide mammographic screening was introduced, that breast cancers were being detected at an earlier stage. Singapore introduced nationwide mammographic screening in January 2004; going by previous observations, we would expect the incidence of advanced breast cancer to decrease following this. We therefore examined the trends in advanced breast cancer over a 8-year period, spanning a period before and after the introduction of nationwide breast screening.

**Materials and Methods:** A retrospective review of the breast cancer database from our institution, a tertiary hospital, from 1<sup>st</sup> January 2001 to 31<sup>st</sup> December 2008 was performed. Two thousand two hundred

patients were diagnosed with breast cancer during this period. Standard clinicopathological parameters were analysed.

Results: The incidence of advanced breast cancer had not changed significantly over the years, and ranged from 25% to 30% of all cancers (including ductal carcinoma-in-situ) diagnosed. Patient factors that correlated significantly with advanced breast cancer included older age, Malay ethnicity, nulliparity and a positive family history of breast cancer. High tumour grade, the presence of lymphovascular invasion (LVI), hormone receptor negativity and HER2 positivity were also significantly correlated with advanced breast cancer. On multivariate analysis, only Malay ethnicity, older age and the presence of LVI predicted for advanced breast cancer. Interestingly, among Malays, advanced breast cancer was more common among younger women. Tumour grade and LVI, but not hormone receptor or HER2 status, correlated with advanced breast cancer in Malays.

Conclusions: The incidence of advanced breast cancer has not decreased despite the introduction of breast cancer screening. In an earlier publication on breast cancer trends in our institution from January 2001 to December 2004, we had reported that Malays were more likely to present with advanced breast cancer. This has remained unchanged in recent years. Our study suggests that efforts to increase breast cancer awareness and early diagnosis should be directed towards Malay women, who are more likely to present at an advanced stage.

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# The use of vertical rectus abdominis myocutaneous flap for post-mastectomy defect cover of large breast tumours

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Background: Primary chemotherapy is the mainstay of therapy for advanced breast cancers, but surgery is still needed for local control in selected patients. In such cases, the post-mastectomy defect is often too large to allow for primary skin closure. Split skin grafts were previously used, but in recent years, our institution has moved towards using the vertical rectus abdominis myocutaneous (VRAM) flap. We present our results

**Material and Methods:** This is a retrospective review of 13 patients who underwent a VRAM flap from 1<sup>st</sup> January 2008 to 30<sup>th</sup> September 2009. We reviewed clinicopathological parameters and various surgical outcomes.

Results: Thirteen patients with T4 tumours underwent VRAM flap following mastectomy. Median age was 61 years (range 33 to 86 years old). Nine were Chinese and 4 were Malays. Median tumour size at the time of presentation was 100 mm (range 30 to 150 mm); all had skin involvement. Nine patients (69.2%) received primary chemotherapy, but either had no clinical response or progressively enlarging tumours. At the time of surgery, 7 patients (53.8%) had fungating tumours and 5 patients had clinical chest wall involvement. All patients underwent mastectomy and axillary clearance. It is our usual practice for the Plastics team to begin raising the VRAM flap concurrent with the mastectomy. The mean total time taken for both procedures was 279 minutes. Two patients developed major post-operative complications. One developed a haematoma, which required emergency haemostasis on the same day. Another developed partial flap loss, which required surgical debridement. There were three minor complications; one of the elderly patients suffered from functional decline post-surgery and received inpatient rehabilitation. Two patients had superficial wound infections which resolved with intravenous antibiotics. None of our patients had an incisional hernia. Median hospital stay was 10 days (range 6 to 40 days). Radial resection margins were clear in all 13 cases, although there was deep margin involvement in 3. Most patients

were started on adjuvant therapy within 3 weeks of surgery.

Conclusions: Our review shows that the VRAM flap is a good option for coverage of a large post-mastectomy defect. There are few flap-related and minimal donor-site complications and a shorter hospital stay compared to skin-grafting. The recovery route to adjuvant therapy is short with a robust flap much more able to withstand the rigours of radiotherapy.

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## Synchronous and metachronous bilateral breast cancer: one or two entities?

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**Background:** The aim of this study is to compare histopathological and clinical characteristics of synchronous and metachronous bilateral breast cancer (BBC).

Materials and Methods: We analyzed the data for 64 BBC pts registered during three years in Daily Hospital for Chemotherapy, Institute

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for Oncology and Radiology of Serbia. We defined synchronous bilateral breast cancer (SBBC) as cancer diagnosed in both breasts at the same time or within a 3 months period of diagnosis of the first tumor. In metachronous BBC (MBBC) second cancer is diagnosed more than 3 months after the first one. We had both breast specimens available for 20 SBBC and 23 MBBC pts, for 21 pts there was only one breast specimen.

Results: Out of a total of 64 pts, 48% (31 pts) suffered from synchronous and 52% (33 pts) from MBBC. Median age at diagnosis was 59.3 in SBBC group. In MBBC group median age at first diagnosis was 51.4 and 58.7 for contralateral BC diagnosis, with the median period from first to second BC of 79 months. 84% of SBBC pts were postmenopausal, compared to 55% in the MBBC group. In a group of SBBC, 52% of tumors were found to be lobular and 32% were ductal carcinoma. In a group of MBBC frequency of ductal and lobular carcinoma was similar, 42% of ductal and 40% of lobular. One MBBC patient had both-side tubular carcinoma. Same HP results in both breasts were found in 85% of SBBC and only 48% of MBBC. 70% of SBBC were hormone receptor positive, comparing to only 43%in MBBC group. 16% of SBBC were manifested as inflammatory breast cancer (IBC). In MBBC group, 15% of first and 39% of second malignancy were diagnosed as cancer mastitis. Initial metastases (stage IV) were more frequent in SBBC group, 32%, compared to 12% in MBBC. In SBBC group 8 pts out of 21 (38%) without initial metastasis had a disease progression during follow-up, with a median DFI of 28 months. In MBBC progression was detected in 28% (8/29) pts with a median DFI 34 months after the second BC

Conclusions: Our study showed that SBBC is more frequent in postmenopausal women, presented more often as hormone receptor positive lobular carcinoma with same HP findings in both breasts. MBBC are usually presented as IBC without distant metastasis. BBC is definitely an unusual clinical entity and because of its atypical and complex presentation patients with bilateral breast cancer require compound and individualized treatment.

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## Re-irradiation for recurrent breast cancer – a second curative approach

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**Background:** Repeat radiation is a rarely used and with caution performed treatment strategy. We investigated the efficacy of a second adjuvant radiotherapy series in case of recurrent and surgically removed breast cancer.

Patients and Methods: Forty-four patients were treated from 1993 to 2003 with modified radical mastectomy or local excision and postoperative re-irradiation for recurrent breast cancer. The median age was 58 years (range 33–76 years). The median exposure due to pre-radiation was 50.4 Gy. Postoperative re-irradiation was conventionally fractionated with single doses of 1.8–2.0 Gy to a median total dose of 60 Gy including regional lymphatics in 17 patients (39%) to a total dose of 50 Gy. In case of close or positive margins, local radiofrequency hyperthermia was offered as additional modality leading to a concurrent application in thirty patients (68%). Further adjuvant treatment consisted of chemotherapy (n = 20, 46%) and/or hormonal therapy (n = 14, 32%).

Results: After a median follow-up of 44 months (range 3–92 months) higher graded late toxicity (≥G3) according to CTC 2.0 and LENT-SOMA was not observed. The estimated 5-year local control rate reached 62%. Additional hyperthermia for patients at higher risk for local failure resulted in 67% local control. Furthermore, a total dose of ≥60 Gy given with photons was associated with complete local control (n = 14). The estimated 5-year overall survival and disease-free survival rates were 52% and 48%, respectively. The overall survival improved to 65% when supraclavicular +/-parasternal nodes were also covered by radiation portals.

Conclusions: Up to now, the available data are limited or heterogeneous. Thus, we present a single institution series including only patients with at most microscopic positive margins (R0-1) and sufficient follow-up. Our study reveals that postoperative re-irradiation with a median total dose of 60 Gy can be performed with acceptable toxicity. The local control rate is encouraging and translates into improved long-term survival for almost every other patient. It might be speculated whether additional hyperthermia compensates for positive margin. However, long-term local control depends on manifold and overlapping parameters which can not be isolated evaluated due to sample size. Therefore, the relevance of hyperthermia as well as the impact of irradiation of regional lymph nodes on long-term control need further investigation.

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### Metastatic disease

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Platinum-based chemotherapy in triple-negative metastatic breast cancer: results of the Institut Curie experience with cisplatinum and ifosfamide

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Background: Although recent experimental data strongly suggest that platinum-based chemotherapy (PBCT) could improve triple-negative breast cancer (TNBC) outcome, clinical data are missing in this specific subgroup of patients. In the present study, we reviewed clinical outcome in patients with metastatic TNBC treated with PBCT.

Patients and Methods: We conducted a retrospective analysis of the patients treated between 2000 and 2008 at Institut Curie, Paris, France. 146 female patients, with metastatic breast cancer who received PBCT, were eligible for this study. 93 (63.7%) of them had TNBC. 115 patients (78.8%) received PBCT after more than one line of CT (median 2, from 0 to 6). Mean age was 49 year (range from 29 to 76), median number of delivered CT-cycles was 4.2 (1–9). 123 of 146 patients received cisplatinum (CDDP), the other received carboplatin. The main combination used was CDDP-lfosfamide N = 118 (80.8%). We analysed overall response rate (OR), OS, PFS, prognosis factors for OS, and safety, for TNBC versus non-TNBC.

**Results:** Median follow-up was 44 months. For the whole population, median OS and median PFS were 11 months and 5 months respectively. OR was 33.3% in the TNBC group, versus 20.8% for the others, p=0.1 Median response duration was 8 versus 7 months (NS). Median OS and median PFS were statistically improved in the patients responding to CT: 25 months (PR) versus 7 months (PD), p < 0.001, and 12 months (PR) versus 3.5 months (PD), p < 0.001 respectively. No difference was observed for OS, PFS and response duration between TNBC and others. Other prognostic factor for worse OS was visceral metastasis sites (p < 0.001). One patient died from sepsis during aplasia, one other developed CDDP-related grade 3 renal failure. 15 patients had to switch to carboplatin because of unacceptable CDDP-related side effects.

Conclusions: In this series, PBCT tend to increase response rate in metastatic patients with TNBC compared to non-TNBC patients, but did not translate into a significant improvement for PFS and OS. Tolerance was acceptable. Longer observations and further analysis are warranted. Prognosis of metastatic TNBC remains poor and new targeted therapies are needed.

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Individually dose-adjusted treatment with epirubicin and paclitaxel with or without capecitabine as 1st line treatment in metastatic breast cancer. A randomized multicenter trial

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**Background:** Epirubicin, paclitaxel and capecitabine are effective drugs in the treatment of breast cancer. In the present trial, patients previously untreated with chemotherapy for metastatic disease were randomized to a combination of epirubicin and paclitaxel (ET, epirubicin 75 mg/m²; paclitaxel 175 mg/m², q3w) alone, or with the addition of capecitabine (TEX, epirubicin 75 mg/m²; paclitaxel 155 mg/m²; capecitabine 1650 mg/m²x14, q3w). Primary endpoint was time to progression (TTP) with a prolongation from 6 to 8.5 months being a significant clinical improvement.

**Material and Methods:** 287 patients were randomized to either ET (n = 143) or TEX (n = 144). Doses for each of the drugs were adjusted (escalated/de-escalated) according to predefined levels individually in relation to toxicity. If treatment was discontinued due to side effects