Materials and Methods: A patient of breast cancer and viral hepatitis B carrier developed elevation of GOT, GPT after one cycle of CMF. The biopsy showed viral hepatitis. This was the first patient who developed reactivation of hepatitis after chemotherapy. Later on, in 1999 a patient of breast cancer developed drastic change of GOT op to 1430 U/mL, GPT up to 2140 U/mL, Bilirubin up to 7.3 mg% after chemotherapy. All these confirmed the importance of monitoring liver function test (LFT) during chemotherapy for patients of HBV carrier. Since then routine HBsAg was screened in every patient before received chemotherapy at SYSCC. During chemotherapy, liver function was followed periodically for HBV carrier. Once GOT, GPT elevated to over 100u/mL, HBV DNA and liver biopsy were performed.

Results: Among the patients who developed reactivation of hepatitis B, 18 were breast cancers. All 18 patients were proved by histology and HBV DNA. Some of the patients has also a liver histology of drug effect. All the hepatitis B were treated by lamivudin successfully and chemotherapy was resumed after improved liver function test and was completed in every patient safely.

Conclusion: For cancer treatment, it is necessary to be careful for hepatitis carrier, since reactivation of hepatitis B may result in fulminant course. Reactivation of hepatitis B can be treated safely with lamivudin if we carefully monitor the LFT change. After the control of hepatitis, the chemotherapy can be completed safely.

303 POSTER

Lymphedema of upper extremities after treatment for cancer of breast: incidence and risk factors analysis

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**Purpose:** Lymphedema is the most significant complication of the locoregional management of breast cancer. Therapeutic procedures such as lymph node dissection, and/or radiation therapy cause local damage of the axillary lymphatic system. The overall incidence of post-mastectomy lymphedema that dependent on the criteria and follow-up period is varied, but is about 15–20% in USA. The study wants to evaluate the incidence and risk factors of arm lymphedema in patients receiving surgical treatment for breast cancer in central Taiwan.

Materials and Methods: In 2002, we retrospectively analyzed 571 patients received treatment for breast cancer at Changhua Christian Hospital between Jan, 1994 and Dec, 2000. The arm lymphedema was defined as at least 2 cm difference in circumference compared with the untreated limb at measured points. In lymphedema patients, we calculated the circumference, calculation volume and edema ratio (=excess volume/normal side volume).

**Results:** In total 571 patients, 8.1% (46/573) patients met the criteria of lymphedema. In MRM group, the lymphedema incidence was 8.35% (40/479), 20.86% (29/139) in MRM with radiotherapy, 3.24% (11/340) in MRM without radiotherapy. In breast conserving group, the incidence was 7.23% (6/83), 9.23% (6/65) in BC with R/T, 0 (0/18) in BC without R/T. The only significant risk factor for lymphedema is radiation therapy esp high dose (>5000 cgy). The mean time to arm edema was 22.1( $\pm$  20.9) months.

**Conclusion:** Radiotherapy was the predominant risk factor for arm lymphedema in patients receiving surgical treatment for breast cancer. Further prospective study is necessary to determine the accurate incidence of arm lymphedema in patients with breast cancer.

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Changes in sensitivity related to sectioning the intercostobrachial nerve during axillary dissection for the carcinoma of the breast

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Background: Side-effects of axillary surgery, primarily those relating to changes in sensitivity (e.g. pain, anesthesia, hypo- and paresthesia in the axilla, numbness of the arm), appear due to section of the sensitive intercostobrachial nerve (IBN), and may be a cause of significant discomfort in patients treated surgically for the carcinoma of the breast. The advantage of preservation of IBN to diminish sensory symptoms, has been evaluated prospectively in this study.

Material and Methods: Ninety-four patients undergoing axillary dissection for the carcinoma of the breast, hospitalised and operated at the Department of Surgery of Institute of Oncology and Radiology of Serbia in Belgrade, in the period from April 2001 to August 2002, were recruited

to this study, and followed prospectively for the period of three months. The patients were divided into three groups, according to the surgical interventions of IBN: in first group, the nerve is preserved; in second, the main trunk is preserved and peripheral branches are divided; in third group, the nerve is sectioned. Clinical testing to evaluate changes in tactile sensitivity and pain, using standard neurological methods, were conducted during the immediate postoperative period (4–7 days), after one month and after three months from the surgery. A statistical analysis using chi-square test, factorial analysis and the means of percentage has been applied to these results.

Results: Out of ninety-four patients, IBN has been preserved in 35 cases, while in 20 patients only peripheral branches have been preserved and in 39 of them, nerve has been sectioned. The greatest changes in sensitivity were found in the group of patients with the section of nerve trunk. The less intensive alterations were presented in the group with preservation of peripheral branches of the nerve. The least presence of pain, numbness and paresthesia, although also being presented, has been reported in the group with the preservation of the nerve. The incidence, intensity and the lasting of these changes, significantly increase with sacrifice of IBN (p<0.001 by the chi-square test).

Conclusions: The preservation of IBN during the axillary surgery for the carcinoma of the breast, is strongly recommended in cases where the nerve is not involved by lymph nodes, and where this preservation does not compromise a control of the disease from oncological point of view.

305 POSTER

Angiosarcoma of the breast: a propos three cases

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**Background**: Angiosarcoma of the breast is rare, the overall prevalence being around 5 per 10,000. In the last two years, however, three breast angiosarcoma cases were diagnosed in the 2nd Department of Pathology, Semmelweis University Budapest. We call attention to the likely increase of its incidence and the caution necessary in the follow-up of patients undergoing breast conserving surgery and radiotherapy.

Patients and Findings: Case 1. A 67 years old female patient developed invasive ductal carcinoma in her left breast and underwent breast conserving surgery in 1992. She received radio- and chemotherapy. In 1996, she presented with upper extremity malignant melanoma, which was excised. In 2001 haemorrhagic skin lesions of the left breast occurred, but several cytological examinations failed to prove malignancy. In 2002, left mastectomy was decided for a large mass in the breast parenchyma. High grade angiosarcoma was diagnosed. Later, contralateral axillary and breast, lung and skin metastases developed. At present she is undergoing chemotherapy. Case 2. A 69 years old female patient underwent breast conserving surgery in 1993 for invasive ductal carcinoma of her right breast. The operation was followed by radio- and chemotherapy. In 2000, she was operated for a benign tumor of the left breast. In 2002 she presented with a mass in the right breast. Preoperative cytology suggested a mesenchymal tumor. Wide local excision was performed. The tumor proved to be a low grade angiosarcoma. In November, 2003, a mass was found in the right breast on control mammography. Fine needle aspiration cytology revealed the recurrence of the angiosarcoma. Case 3. A 84 years old female patient underwent breast conserving surgery and radiotherapy for invasive breast carcinoma in 1997. In 2003 left mastectomy was performed for a large, exulcerated tumor, which proved to be intermediate grade angiosarcoma originating from the skin of the left breast. She died 4 months following the operation, after haemorrhage from the recurrent angiosarcoma.

Conclusion: With the increasing frequency of breast conserving surgery, the incidence of secondary breast angiosarcoma is likely to increase proportionally. Both primary and secondary breast angiosarcomas are aggressive, with high metastatic potential. Early diagnosis and radical surgery may extend survival time. Effective postoperative therapy is still to be established.

306 POSTER

Changes to the axillary vein are associated with an increased risk of breast cancer-related lymphoedema

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Aim: This study aims to prospectively evaluate the effect of axillary node clearance (as part of breast cancer treatment) on the axillary vein, and to investigate associations between the changes observed and risk of developing lymphoedema.

**Methods:** A total of 70 women were studied prior to breast cancer surgery to include a Level II or Level III axillary clearance, and at 3 and 12 months post-operatively. Arm volume was calculated from sequential circumferential measurements. Doppler U/S was able to provide information

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on venous anatomy, vein wall movement with the respiratory cycle and blood flow within the vein.

Results: Lymphoedema (>10% relative arm volume increase) was observed in 16% of cases at 3 months and 11% at 12 months. There was a significant reduction in the 'pulsatility' of venous flow in the lymphoedema group compared with the rest. Vein wall movement was significantly reduced following surgery, but this did not correlate with arm swelling. Obvious stenosis of the vein was demonstrated in 10% of cases and was associated with an increased risk of lymphoedema, but was also observed in the absence of arm swelling.

Conclusions: Axillary node clearance may cause changes in the axillary vein, with a significant association between altered flow and risk of lymphoedema. Venous stenosis can be observed in the absence of arm swelling, reinforcing the multi-factorial nature of this condition.

307 POSTER

Late cardiac and pulmonary complications in breast cancer patients after adjuvant chemo-radiotherapy – 5-years follow-up

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**Aim:** The aim of the study was to evaluate late myocardial and pulmonary damage in breast cancer patients, after mastectomy and adjuvant sequential chemo-radiotherapy.

Material and Methods: Forty seven women with stage II and III breast cancer, mean age 47 years, had mastectomy and sequential chemoradiotherapy. In 40 patients (pts) chemotherapy with antracyclines and in 7 — without antracyclines was administered. Radiotherapy included chest wall and regional lymph nodes, the specified dose was 45–50 Gy/2 Gy. The high resolution computed tomography (HRCT) of the lungs, electrocardiography and echocardiography were performed after a mean time of 17 months, then, after a mean time of 33 months and finally, after a mean time of 65 months. The third examination was possible in 37 pts because of progression of the disease and death in 10 pts.

Results: LUNGS: The first examination (after 17 months) revealed no changes in 24 pts (51%). There were fibrotic changes in lung apex in 19 pts and 19 parietal fibrosis. In the second examination (after 33 months) the normal findings were observed in 24 patients (51%). A tendency to regression in parietal areas was observed (p=0.031). In third examination (after 65 months, 37 pts), the same percentage of pts - 51% had no lung injury. The lung fibrosis was observed in 14 and parietal - in 13 pts. Twelve of parietal fibrosis observed in third examination persisted without any evolution (no progression, no regression), only 1 progressed. All these changes were discrete and asymptomatic and parietal fibrosis were invisible in chest X-ray. HEART: In first examination 7 of 47 pts had abnormal echocardiogram (ventricular dilatation, abnormal Left Ventricular Ejection Fraction). All of them received antracyclines. In 5 of them echocardiographic defect were asymptomatic and reversible at the time of second examination, in 2 - moderate toxicity was noted. The analysis of isodose distribution in all 7 cases excluded radiotherapy as a factor influencing toxicity, but the type of echocardiographical changes suggested that antracyclines could cause injury. After 65 months, no new cardiac complications were observed and the improvement in echocardiography in 6 patients was observed (1 patient died because of disseminated disease).

**Conclusions:** Modern postoperative radiotherapy caused no clinically significant lesions in lung and heart during 5 years of observation. Clinically important myocardial changes, observed in 2 pts, seemed to be caused by antracyclines, but not by radiotherapy.

308 POSTER

The influence of trastuzumab and chemotherapy combined treatment on valvular, systolic and diastolic cardiac function in metastatic breast cancer patients – 30 months follow up

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**Purpose:** to assess long-time cardiotoxic risk of treatment with trastuzumab and chemotherapy in metastatic breast cancer patients.

Patients and methods: 29 patients: 12 treated with combination of trastuzumab 2 mg/kg 1-weekly and chemotherapy consisting of docetaxel 75 mg/m² and cisplatin 75 mg/m² every 3 weeks and 17 treated with combination therapy of trastuzumab and cisplatin or vinorelbine or capecitabine were evaluated clinically, by ECG and by Doppler echocardiography at baseline (I), in 2nd (II), 4th (III), 6th (IV) month of chemotherapy and up to 2.5 year follow-up (V) thereafter. Valvular function, resting left ventricular ejection fraction (LVEF), LV and LA diarneters, diastolic and systolic LV function were determined. 20/29 patients were

anthracycline pre-treated to median cumulative dose 380 mg/m<sup>2</sup>, 5/29 of patients were irradiated previously to chest wall.

Results: trace mitral insufficiency (MI) was observed at baseline in 12 patients, in 2 patients MI was moderate. During treatment there was progression of pre-existing MI from trace to moderate in 4 patients. A new significant MI occurred in 2 patients. MI did not progress in 8 pts and two cases of baseline significant MI did not show important progression upon observation. 3 pts presented trace aortic insufficiency (AI) at baseline, one of them progressed during follow-up. No statistically significant changes were found for mean left ventricular ejection fraction (LVEF): I – 66%, II – 67%, III – 68%, IV – 67%, V – 68%, mean LV end-diastolic diameter (LVED) I – 44 mm, II – 46 mm, III – 46 mm, IV – 46 mm, V – 47 mm, mean isovolumetric relaxation time (IVRT) I – 93 ms, II – 91 ms, III – 86 ms, IV – 87 ms, V – 93 ms, mean LA diastolic dimension (LA) I – 36 mm, III – 38 mm, III – 36 mm, IV – 37 mm, V – 36 mm. In three cases asymptomatic moderate global hypokinesis was observed (EF – 49–59%).

Conclusion: echo-doppler imaging during trastuzumab and chemotherapy combination treatment revealed progression of mitral and aortic regurgitation in some patients. The changes of other parameters do not substantiate an important deterioration of LV systolic and diastolic function. The results of three-years follow-up will be presented.

909 POSTER

Appropriate solution selection at the administering epirubicin hydrochloride to the breast cancer patients

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Backgrounds and Objectives: Epirubicin hydrochloride (Farmorubicin®) is one of the key drugs in the treatment regimen for the breast cancer patients. In Japan, we had normally used the powder type because of easy to stock. From September 2002, when the pharmacists started to prepare the anticancer drugs at the time of building of teamwork system supporting the breast cancer patients, we have chosen to use the Farmorubicin RTU® (ready to use). Then the frequency of vascular pain during the administering the drug and vasculitis has been increased. This narrative experiments made us the chance to consider the cytotoxicity of epirubicin in order to avoid angiitis and soft tissue damage. Following 3 factors: pH, osmotic pressure, titrable acidity are considered to affect onset of angiitis and vasalgia. There is difference of pH between RTU (pH 2.5–3.5) and powder (pH: 4.5–6.0). The purpose of this study is to select the best solution in order to administer vesicant safely via peripheral in order to minimize risk of soft tissue damage.

**Methods:** Osmotic pressure, titrable acidity and pH of solution with epirubicin actually used in the clinical setting were measured. Five kinds of solutions (normal saline, 5% glucose, distilled water, 2 hypotonic solutions) with or without 2 kinds of pH epirubicin (RTU or power) were chosen and measured, respectively. We have aimed at the dexamethasone (Decadron®) to minimize the risk of those adverse events.

Results: Osmotic pressure of RTU was lower rather than powder type. The difference in the titrable acidity among the combination of solution and two kinds of epirubicin was estimated quite tiny. So then, the pH of solution was mostly concerned with onset of anglitis. Both in the cases we selected 0.9% sodium chloride and 5% glucose solution, the pH of the Farmorubicin RTU® increased from 3.5–4.0 to 6.0–6.2 by adding Decadron® 8 mg, which was not observed the onset of deposit during 24 hours. On the other hand, pH of freeze-dried Farmorubicin® plus Decadron® 8 mg increased until 6.9–7.1, which was onset of deposit. We have started to use the combination of Farmorubicin RTU® and Decadron® at the administration of FEC regimen for breast cancer patient from May 2003, we have only one case with anglitis and vasalgia among 24 patients underwent FE(75–90)C chemotherapy.

Conclusions: Farmorubicin RTU® is considered to be easy to use and safety for medical staff at the view of the preparation of agents. But the frequencies of the angiitis and vasalgia have been increased because of lower pH. To minimize the risk of tissue damage, this study puts forward a suggestion that the regimen combined Farmorubicin RTU® with Decadron® should to be selected especially at the treatment via peripheral vessels.