fluorescence and chromogenic in situ hybridisation and immunohisto-chemistry.

Results: We observed that at the genetic level, lesions from the same patient displayed remarkably similar patterns of genetic aberrations (Spearman's correlations 0.55−0.89; p < 0.00001). All CLLs, low grade DCIS, LN and their matching invasive carcinoma harboured gain/amplification of 1q31−32 and loss of 16q12, 16q21 and 16q23. In addition to the aberrations found in CCLs, in situ and matching invasive components displayed additional genetic aberrations at 16 p13.3, 13q34, 20q13.33, 11q13.1-q14.1, 17q25.3, 19 p13.3, 7 p22.2, 8q24.3, 9q34.3, 14q32.33, 5 p15.33 and 10q25.3 and losses on 10q22, 8 p, 11q24−25, 15q11.2, 17 p11.2, 9 p11.2 and Xq. Amplification of cyclin D1 was detected by CISH in ILCs and their matching LN and FEA lesions.

Conclusion: Our results provide strong circumstantial evidence to suggest that CCLs are the earliest morphologically identifiable non-obligate precursors of more advanced lesions in the LNGBN family and that that loss of 16q and gain 1q are the earliest genetic changes in this family of lesions that lead to the activation of the 'luminal' pathway.

5176 POSTER

Can we use age-dependent changes of enzymes activity in benign disease as poor prognostic factors?

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Background: Mastopathy – benign disease of a breast, developed by a hyperplasia (by pathological growth) of a tissue gland. Risk factors for breast cancer are age, hormones level modification of the females and benign disease, such as mastopathy. It is known the direct interaction between metabolism of thymidine – precursor of DNA and rate of proliferation processes. Thus, as marker of proliferation was choosed any enzymes of thymidine exchange – thymidine kinase (TK) and thymidine phosphorylase (TP). Moreover TK correspond to the index of cellular proliferation.

The aim – to compare activity of TK and TP in blood serum of healthy women, patients with mastopathy and breast cancer from I to IV stages.

Materials and Methods: Blood serum of healthy persons, patients with mastopathy and patients with cancer of mammary gland. Age of surveyed groups 40−60 years. The activity of TK was defined by radioisotop method, TP – spectrophotometrically.

Table. TK and TP activity healthy women and women with pathology

Diagnosis	Healthy women	Mastopathy	Breast cancer			
			$T_1N_0M_0$	$T_2N_0M_0$	$T_3N_1M_0$	$T_4N_2M_x$
	n = 16	n = 32	n = 17	n = 22	n = 52	n = 39
Thymidine kinase (nMol/mg*h)	3.14±0.55	3.58±0.29	3.82±0.01	3.98±0.03	4.28±0.28	4.94±0.14
Thymidine phosphorilase (nMol/mg*h)	23.76±2.30	17.82±2.0	19.80±0.66	18.48±1.01	15.18±1.98	9.90±0.70

p < 0.05

Results: In comparison with healthy group (table), the level of TP activity was reduced at mastopathy. Upon $T_1N_0M_0$ the activity is TP is lower than normal (like mastopathy), but TK activity was enhanced that can be responsible for some increase in DNA biosynthesis in case of such pathology. The obtained dates about the increase of TK activity and decrease of TP activity at a mammary gland cancer according to a stage of cancer. This shift (simultaneously increasing of TK and decreasing of TP) indicates about more intensively proceeding processes of a proliferation at tumour pathology.

Conclusions: Thus, a similar metabolic displacement during mastopathy and breast cancer may be one of the endogenous factors of malignancy. The biochemical test of determination of TK and TP activity in blood serum of patients with mastopathy, we propose to use in early diagnostic of breast cancer.

5177 POSTER

Intraoperative ultrasound guided occult lesion localization in early stage breast cancer surgery

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Objective: Different methods are used in detecting non-palpable breast lesions. We present our experience in intraoperative ultrasound guided occult lesion localization in early breast cancer surgery.

Methods: Retrospective analysis of clinical, surgical, pathological and oncological data on 168 patients with non-palpable breast cancer lesions treated in University Surgical Hospital Split, Croatia, within five years time period. 88 (52%) patients had their lesions preoperatively labelled with blue-dye or hook wire, and intraoperative ultrasound hand-held probe was used in localizing occult breast lesion in other 80 (48%) patients. Definitive surgical and adjuvant treatment was carried out due to pathological findings.

Results: All the patients had their non-palpable breast lesion detected and surgically removed under local or general anesthesia. Tissue specimen obtained using intaroeprative hand-held ultrasound probe was easier to localize and surgically assessed. In the same time such tissue specimen was much more accurate to temporary and definitive pathological findings. Operative time was shortened using intraoperative US but without statistically singnificance. There were no intraoperative or postoperative complications due to detection method used.

Conclusions: Intraoperative ultrasound guided breast surgery allows detecting of occult early breast cancer lesions with high accuracy and safety.

5178 POSTER

Is mammographic breast density a breast cancer risk factor in women with BRCA mutations?

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Background: Increased mammographic breast density is well-recognized as a breast cancer risk factor in the general population. However, it is unclear whether it is a risk factor in women with *BRCA* mutations. We present the results of a correlative study investigating the relationship between breast density and breast cancer incidence in women with *BRCA* mutations.

Methods: The study population consisted of women ages 25 to 65 with *BRCA1* or *BRCA2* mutations enrolled in a single-centre high-risk breast cancer screening trial of annual breast mammography, MRI, and ultrasound, and semiannual clinical breast examination. Using a computer-aided technique (Cumulus), quantitative percentage density (PD) was measured for each participant on her first study mammogram by a single investigator blinded to the clinical outcome. For women with prior breast cancer, the contralateral breast was used for density measurement.

Results: Between 11/97 and 03/08, 462 women (mean age at first study mammogram = 44; 245 with *BRCA1* mutations and 217 with *BRCA2* mutations) were screened and 50 breast cancers were diagnosed (33 invasive ductal, 1 invasive lobular, 1 microinvasive, 3 DCIS with microinvasion, 12 DCIS only). Density was not measured in 40 women of whom 4 developed cancer (2 invasive ductal, 1 invasive lobular, 1 DCIS) because the baseline mammogram could not be digitized or located. Mean PD (± SD) for the 376 women who did not develop breast cancer was 34% (23) compared to 31% (21) for 46 women who developed cancer (p = 0.51, two-sample Wilcoxon rank sum test). Logistic regression model of breast cancer incidence and PD revealed an odds ratio of 0.99 (± 0.01) for a 1-unit increase in PD (p = 0.44).

Age-adjusted odds ratio for a 1-unit increase in PD was 1.00 (±0.01, p = 0.83). Results were similar when *BRCA1* and *BRCA2* mutation carriers were analyzed separately, as well as when women who developed DCIS without invasion were excluded from the analysis.

Conclusions: Increased mammographic breast density is not associated with higher breast cancer incidence in women with *BRCA* mutations. Therefore, breast density should not be considered a factor for these women in decision-making regarding prophylactic surgery or chemoprevention.

5179 POSTER

"Competition on Clinical Mass Spectrometry Based Proteomic Diagnosis" based on serum protein profiling for the detection of breast cancer

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Background: Detection of breast cancer at early stage can increase a patient's five-year disease-free survival rate. Mammography is currently the gold standard for screening purposes. This method is non-invasive and highly specific but low sensitivities have been reported. Especially for younger women with a familial or genetic predisposition mammography

sensitivity is only 40% and for women over 50 years 79.8% (interval screening).

A specific and more sensitive alternative to the mammography could be the use of proteomic biomarkers. By comparing the protein patterns in serum of patients with breast cancer with those of control persons, the differential proteins that are most discriminating for both patterns can be identified.

Methods: In a randomized block design pre-operative serum samples obtained from 115 breast cancer patients and 116 controls were used to generate MALDI-TOF protein profiles. The MALDI-TOF spectra generated using WCX magnetic beads assisted mass spectrometry (Ultraflex) were smoothed, binned and normalized after baseline correction. From these, a set of 76 cases and 77 controls spectra were defined as a calibration set. The remaining 39 cases and 39 controls were set-aside as validation set.

Results: Using the data obtained from this experiment, our department organized an international comparison to evaluate in-depth statistical bioinformatic methodology for high-dimensional protein profiles, namely "Competition on Clinical Mass Spectrometry Based Proteomic Diagnosis". For this collaborative data analysis project, we distributed the calibration dataset to invited participants, and asked them to construct a diagnostic classification rule for allocation of future patients. Upon receipt of their descriptions on chosen methodological approach and data analysis on the calibration data, we provided the validation set. The results were subsequently published in a special issue of SAGMB. http://www.bepress.com/sagmb/vol7/iss2/.

Conclusions: Comparing the serum protein patterns of patients with breast cancer with those of controls resulted in a recognition rate of 86%, a sensitivity of 88% and a specificity of 84%.

The different classification models showed consistent results (80%), which allows this method as promising for early recognition of breast cancer.

Competitions such as these can serve the useful role of providing standards against which new methods should be assessed and allow critical reflection by both clinicians as well as statistical methodologically on the development and application of biostatistical informatics for proteomic spectrometry.

For a next step the described procedure should be validated in patients at risk for breast cancer and in a population screening setting.

5180   POSTER

The differences of prognostic factors and pattern of failure between invasive micropapillary carcinoma and invasive ductal carcinoma in breast cancer: matched case-control study

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Background: Invasive micropapillary carcinoma (IMPC) is known for its high incidence of axillary lymph node metastasis, recurrence and distant metastasis. We designed this study to identify the differences of prognostic factors and pattern of failure between IMPC and invasive ductal carcinoma (IDC) in patients with breast cancer.

Method and Materials: We identified 72 patients diagnosed as IMPC during 1999 to 2007 at the Samsung Medical Center. These patients were matched with 144 controls who diagnosed as IDC at the same period. Exact matches were made for age ($\pm$3 years), pathologic tumors and node stages, and treatment methods. Other variables were compared using Fisher exact test and the χ^2-test. Kaplan-Meier product-limit methods were used to assess overall survival, loco-regional recurrence free survival and distant metastasis free survival.

Results: The median follow up was 45 months (13 to 116) in IMPC and 50 months (16 to 122) in IDC. There were no significant differences in the side of breast, primary tumor locations, extensive intraductal component, histologic grade, hormone receptors and percentage of chemotherapy and hormone therapy recieved between two groups. But, lymphovascular invasion (LVI, p < 0.0001), extracapsular extension (ECE, p < 0.0001) and high nuclear grade (p = 0.032), which are well-known prognostic factors, were more frequently detected in the IMPC group.

There was no significant difference in the overall survival after surgery between two groups (p = 0.192). But, the 5-year recurrence free survival after surgery showed significant differences as 68.1% in study versus 81.2% (p = 0.049) in control. During follow-up, the treatment failed in 15 patients (20.8%) in the study group and 26 patients (18.1%) in the control group. In first site of recurrence analysis, loco-regional recurrences developed in 11 patients (15.3%) of the former and 8 patients (5.6%) of the latter, in contrast, distant metastasis developed in 5 patients (6.9%) and 22 patients (15.3%), respectively. Therefore, in survival analysis, there were no differences in the distant metastasis free survival (78.1% versus 79.1%, p = 0.847), but 5-year loco-regional recurrence free survival was statistically significant between two groups (93.3% versus 79.1%, p = 0.0026).

Conclusion: Our study showed that, in a matched case-control study, IMPC group was associated with LVI, ECE, and high nuclear grade. And IMPC group showed more loco-regional recurrence compared with

IDC group, but not for distant metastasis. Further prospective studies are necessary to confirm these results.

5181   POSTER

Ultrasound-guided radiofrequency ablation of early breast cancer in a resection specimen

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Background: The trend towards less invasive local treatment of breast cancer has led to studies evaluating minimally invasive techniques to locally eradicate tumours. Radiofrequency ablation (RFA) is a minimally invasive thermal ablation technique. We performed an ex vivo study to determine the feasibility of this promising technique and evaluated the histological findings.

Materials and Methods: Radiofrequency ablation was performed of invasive ductal carcinoma – diagnosed by core needle biopsy – in postmenopausal women, after the surgical procedure (lumpectomy or mastectomy). A needle was placed in the centre of the tumor using ultrasound guidance. Subsequently, the tumor was ablated for a period of 12 minutes. Pathologic evaluation of the specimens was performed using conventional hematoxilin-eosin (HE) staining as well as cytokeratin 8 staining and NADH diaphorase to assess cell viability.

Results: Twenty patients with an average age of 66 years (range 51−78) were included in this study. The mean tumor size was 12 mm (range 7−23). Ex vivo RFA resulted in complete cell death in 17/20 lesions. In 2 patients histopathological examination revealed a microscopic focus of viable tumor cells at the margin of the tumor and in 1 lesion viable cells were found lining the needle tract. Furthermore, in 2 cases the target lesion was completely destroyed, but viable DCIS was found just outside the ablated area.

Conclusions: Ultrasound-guided radiofrequency ablation can result in complete cell death in small invasive breast cancer, but a high level of accuracy is required in proper positioning of the needle electrode. Furthermore, our results have led to the decision to perform a "hot retraction" to burn the needle tract in our ensuing in vivo study.

5182   POSTER

Breast cancer screening program in Khanty-Mansiysk autonomous Okrug – Yugra

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Introduction: It is now widely accepted that early diagnosis of breast cancer reduces breast cancer specific mortality. Mammographic screening programmes are widespread in Europe and North America. In Russia, the most extensive program of screening for the early detection of breast cancer is currently being conducted in Moscow. Since February, 7th, 2007, there has been a breast cancer screening program (BCSP) implemented in Yugra.

Goal: Define the two-year results of Breast Cancer Screening Program in Khanty-Mansiysk Autonomous Okrug – Yugra.

Results: The reports have been provided by 21 municipal districts from March 2007 to December 2008.

149 478 women have been examined by mammography or ultrasound over this two year period, including 81 169 within the BCSP. Overall, 83 412 women from age group over 40 years have been examined using mammography, 46 254 within the BCSP. Total breast ultrasound examination has been performed on 66 066 women (34 915 within the BCSP – 55% of the total examinations).

In 2008 in the territory of Yugra 29562 women have been examined with mammography within the BCSP and 94 cases of breast cancer detected (a detection rate of 0.3%). Also detected were: 1546 cases of local pathology (fibroadenoma, local fibrocystic disease or adenosis) (5.2%), 9460 cases of fibrocystic disease of the breast (32%), 17 643 women had normal mammography (62.5%).