

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.

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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  $\chi^2$ -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 received 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.

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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 hematoxylin-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.

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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%).

**Conclusion:** The breast cancer screening programme has been implemented in the majority of municipal districts in Yugra. Compared with a similar program in Moscow, the Yugra breast cancer detection rate was 1.5 times higher and amounted to 0.3% of the total number of screening women over 40 years (in Moscow – 0.2%).

However, it should be noted that at the moment, insufficient detailed information has been collected on the breast cancers detected within the BCSP, in particular the histological findings (size of primary tumor, involvement of lymph nodes in disease). We are going to improve the quality of data collection in order to give an accurate estimate of screening test and program sensitivity, standardized detection ratios and positive predictive value of recall for assessment. In addition, it is anticipated that these data will allow us to provide a tentative prediction of the likely future effect of the screening on breast cancer mortality. In addition, we will assess the feasibility, resource needs, and likely effects of incorporating routine blood marker studies into the Yugra screening program.

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POSTER

**Sequence variants in BRCA1 and BRCA2 genes detected by high-resolution melting analysis as a tool in molecular genetics analysis of inherited breast cancers**

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**Background:** Epidemiological data indicates that 5–10% of all breast cancers is hereditary, of which at least a third are associated with inherited mutations in the autosomal dominant tumor suppressor susceptibility genes BRCA1 and BRCA2. Carriers of BRCA1 and BRCA2 are at higher risk for developing of breast cancer by age 70 (between 45–85%) and of ovarian cancer (between 11–62%). Therefore, screening for variants in the BRCA1 and BRCA2 genes can contribute to prevention and early cancer detection in cases with familial predisposition.

**Materials and Methods:** Several screening methods are accepted by Eurogentest, and one of latest is based on high-resolution melting approach, that is efficient for rapid detection of sequence variants in cancer patients and their family members.

This approach is based on differences in melting curves caused by variations in nucleotide sequence, but detected variants have to be confirmed by direct sequencing.

Our lab established procedures for genetic analyses of those genes in families with high frequencies of breast/ovarian cancer in concordance with EMQN best practice guidelines for molecular genetic analysis in hereditary breast/ovarian cancer accepted at the EMQN workshop 2007.

**Results:** We found 21 different polymorphisms of BRCA1 and 36 of BRCA2 gene as normal variants in 200 BRCA1 and BRCA2 samples of healthy volunteers. We also tested the application of this approach using 25 coded samples with known mutations.

**Conclusions:** First screening was performed on elderly women with no personal or familial history of cancer, in order to identify benign high frequency variants of BRCA1 and BRCA2 in Croatian population. Intention of this pilot project was to introduce genetic testing into the national program of early detection of breast and ovarian cancer. In Croatian population of 4.5 million, an average of 2,200 new breast cancer and 400 ovarian cancer cases annually have been reported over the last ten years and 800 women die of breast cancer each year (data from Croatian National Institute of Public Health, 2006).

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POSTER

**Chest x-ray as a staging investigation in early operable breast cancer – is it necessary?**

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**Introduction:** Confusion exists about performing chest x-ray routinely, as a staging investigation, to detect metastasis, in patients with early operable breast cancer (T1, T2, N0, N1). The aim of this study was to find what proportion of chest x-rays detected metastasis in early operable breast cancer and if this investigation was necessary.

**Method:** Retrospective study of 200 consecutive breast cancer patients between September 2006 and June 2007. We excluded 78 patients who either had DCIS, neo-adjuvant chemotherapy, multiple tumours, bilateral tumours, inoperable tumours, recurrent tumours or toilet mastectomy. We studied 122 patients who had surgery for primary invasive breast cancer.

**Results:** 95% patients (n = 116) had preoperative chest x-ray. Mean age was 61 years (range 34–91). 53% of patients were below 60 years of age. Average size of tumour was 27.7 mm (range 1.5–120 mm). 78% (n = 91) had T1 or T2 tumour (diameter of 5 cms or less). Out of 116 chest x-ray, 113 (97.4%) showed no metastasis. Chest x-ray of 3 patients (2.6%)

showed suspicious abnormality. Subsequent CT scan of thorax showed no pulmonary metastasis in these 3 patients.

**Conclusion:** While there are issues with cost and radiation in performing routine chest x-ray for all operable breast cancer patients, it can also produce false positive results (as observed in 3 of our patients). This can be associated with immense patient anxiety. In our cohort none of the patients had lung metastasis. Therefore for asymptomatic, early, operable breast cancer patients, routine preoperative chest x-ray to detect metastasis is not necessary.

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POSTER

**Identification and localisation of sentinel lymph nodes using microbubble enhanced ultrasound in pre-operative breast cancer patients**

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**Background:** In patients with breast cancer, tumour staging is dependant upon surgical excision of ipsilateral axillary lymph nodes (LN). Sentinel lymph node (SLN) biopsy has been shown to be a safe and accurate first-line technique in patients with early invasive disease. In animal models, superficial lymphatics can be imaged using ultrasound and intradermal microbubbles. This study aimed to identify and localise SLN using microbubble enhanced ultrasound in pre-operative breast cancer patients.

**Materials and Methods:** Seventy consecutive consenting patients with primary breast cancer were recruited. Pre-operatively, patients received periareolar intra-dermal injection of microbubble contrast agent, breast lymphatics were visualised by ultrasound and followed to identify putative axillary SLN. Contrast-pulse sequencing and grey-scale ultrasound modalities were used to image LN. Sentinel LN were then localised with guide-wires. One day later, patients underwent standard tumour excision and SLN biopsy using blue dye and radio-isotope with subsequent histopathological analysis.

**Results:** Operative findings confirmed that guide-wires were successfully inserted into SLN of 61 patients. In 36 patients, SLN were visualised as areas of contrast accumulation within a defined LN structure seen clearly on grey-scale imaging. In 23 patients, SLN were identified as areas of contrast accumulation within ill-defined nodal structures. In 2 patients, SLN were identified only as areas of contrast accumulation. In 9 patients, the procedure failed. Contrast enhanced ultrasound correctly identified SLN in 61 of 70 patients (87%). Eleven patients were found to have LN metastasis. In all metastatic cases, SLN were correctly identified and localised with guide-wires pre-operatively.

**Conclusions:** By means of this novel technique, SLN may be readily identified and localised in the pre-operative period. Ultrasonic identification of SLN would enable targeted biopsy in the breast clinic and may reduce the numbers of patients requiring primary or secondary axillary surgery. This technique may also be applicable to other superficial malignancies.

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POSTER

**Breast cancer trials – is race an important factor?**

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**Objective:** Breast Cancer is a global disease. Much of the research is done in the western countries and these results are applied to women from different ethnic backgrounds. The objective of this study was to examine the demographics of all published Phase III non-surgical treatment randomized controlled trials (RCTs) in breast cancer, and to determine whether there is a discrepancy in the representation of different racial groups in these trials.

**Methods:** Phase III non-surgical therapeutic RCTs in breast cancer published from 1965 to present were identified using the Medline and Pubmed databases. Demographics including age and race were recorded. Comparisons were made between the proportion of Caucasians compared to non-Caucasians enrolled in the RCTs; and the proportion of RCTs published in developed Western countries in comparison to other countries.

**Results:** 325 RCTs were identified. The average mean and median age reported were 56.5 and 55 respectively. For the studies that reported age in categories, 65% of the participants were under the age of 60. Only 50 studies (15.4%) reported racial data. Within the 50 studies, 90% of the participants were Caucasians. Of the 325 trials, only 40 (12.3%) trials were done outside of North America or Western Europe.

**Conclusion:** Racial/ethnic information was provided in only a minority of trials. Also most of these trials were led, developed and conducted in the western world. This limits the generalizability of the data from current breast cancer research to the global level. With the growing incidence of breast cancer worldwide, it is important to perform these trials internationally and