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.

5183 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).

5184 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 June2007. 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 (range34−91). 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.

5185 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.

5186 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

to include racial information to help provide insight into the potential impact of race and ethnicity on treatment outcomes.

5187 POSTER

Multifactorial CNS relapse susceptibility in HER-2-positive breast cancer patients: first results from a population-based registry study

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Background: A series of retrospective studies have reported a higher incidence of central nervous system (CNS) metastases in HER-2-positive (HER-2+) metastatic breast cancer. Trastuzumab, which does not cross the blood-brain barrier, has been associated with this increased risk.
Materials and Methods: The aim of this study was to evaluate incidence, survival and risk factors of CNS metastases in the incident breast cancer population systematically collected by the Tumor Registry of Parma Province over the 4-year period, 2004–2007. Study endpoints were: any distant metastasis as first event; CNS metastasis as first event; CNS metastasis at any time. Associations between CNS metastases and HER-2 status in the entire population and between trastuzumab and CNS metastases in HER-2+ patients (pts) were estimated. A multivariate analysis was performed to test the effect of covariates.
Results: We evaluated the total resident population (n = 1500) of breast cancer pts diagnosed during the period 2004–2007 in Parma Province. Two-hundred and twenty-five pts (15%) were HER-2+ (IHC 3+/FISH amplified). Of these, 100 pts were treated with adjuvant trastuzumab-based therapy. At a median follow-up of 36 months from the diagnosis, the incidence of CNS relapse was 3% (1.3% as first recurrence). The median time to death from the diagnosis of CNS metastases was 25 months. Among the HER-2+ pts, there was a significant association between trastuzumab and subsequent CNS metastases ($P = 0.02$). However, in multivariate analysis, HER-2 status regardless of trastuzumab therapy was found to be the only independent predictive factor for CNS metastases (either as first or as subsequent recurrences; $P < 0.001$).
Conclusions: This is the first population-based registry study analyzing CNS metastases in breast cancer in relation to tumor biological features, systemic treatment, and clinical outcome. Based on our results, HER-2 status independently distinguishes pts with a higher risk of CNS metastases. It is however presumable that, in some cases, improvements in systemic control and overall survival associated with trastuzumab-based therapy lead to an “unmasking” of CNS relapse that would otherwise have remained clinically silent prior to a patient’s death.

5188 POSTER

A breast cancer fingerprint in peripheral blood – a novel method for early diagnosis

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Background: Existing technology for detecting breast cancer has its limitation, especially among women with dense breast tissue. To reduce mortality early detection is crucial in order to start treatment before the disease becomes metastatic. We here propose a novel method for early detection of breast cancer using blood as clinical sample. Blood samples are easily available, minimally invasive and can be sampled at low cost.
Material and Methods: A total of 130 blood samples were analyzed using high density oligonucleotide microarrays from Applied Biosystems. Blood samples were collected from women participating in the national mammography screening program that were called in for a second look after a first suspect mammogram. Further clinical examination revealed that 67 subjects had breast cancer, while 54 had no malignant findings. In addition 9 samples from healthy controls were included. Partial Least Square Regression (PLSR) in combination with a 20-fold double cross validation (CV) approach was used to identify differentially expressed genes between cases and controls, and to estimate their prediction efficiency.
Results: We have identified a gene signature consisting of 689 probes that predict cancer patients from controls with an accuracy of 81% ($\pm$7%). Functional enrichment analysis of the genes in the signature suggests that a defense response is provoked in breast cancer patients. Furthermore, genes involved in lipid- and steroid metabolism seem to be differentially expressed between cases and controls. A 96 probe TaqMan based diagnostic tool BCtect® is developed partly based on these results and will be launched in Europe in 2009.
Conclusion: Our results indicate that the blood transcriptome of breast cancer patients carries biological relevant information about breast tumor growth. The genes identified possibly reflect a crosstalk between the growing tumor and the immune system of the host. We believe that this tool can constitute a supplement to existing diagnostic technology, but also offer a breast cancer test in areas were mammography screening is insufficient.

5189 POSTER

M0 breast cancer patients exhibited a decreasing incidence of metastases but no improvement in prognosis after metastases since 1978 in Bayern: report from Munich Cancer Registry

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Background: The course of breast cancer may be changing over time, related to detection and treatment. We explored trends in metastasis in breast cancer patients without metastasis at diagnosis (M0).
Patients and Methods: Data of 28,687 M0 patients with primary breast cancer diagnosed between 1978 and 2003 in Bayern were obtained from the first (general) hospital-based, later population-based, Munich Cancer Registry, which uniquely documents metastases during follow up. Time to metastasis and survival following metastases were determined for the most common sites of metastases, and were assessed per time period (1978–1984 vs 1985–1994 vs 1995–2003) with follow-up until October 2008. Cox regression was performed to identify the following determinants associated with time to metastases and survival: period of diagnosis, age, pT, pN, differentiation grade, receptor status, histological grade, site of metastasis and time to metastasis.
Results: In the recent decade the incidence of metastases among M0 patients decreased markedly, however survival after metastases did not improve (HR 1.00 vs 1.18 vs 1.19, $p < 0.001$). Furthermore, within 5 years following diagnosis, the actuarial rate for time to metastases became shorter in the last decade (35% vs 43% vs 24%, $p < 0.001$). The proportion of bone metastases decreased whereas liver and CNS metastases occurred more often. Skin and lymph node metastases showed best prognosis until 10 years follow up. Time to and survival after metastases was worse for patients with ER or PR negative tumours.
Discussion and Conclusions: In recent decades, development of metastases in M0 breast cancer seems to have been increasingly prevented, probably due to both stage migration by screening and developments in systemic therapy. However, if metastases occur shortly after diagnosis of M0 patients, they appear sooner, which might be mainly determined by more aggressive tumours following initial treatment. Potential improvements in treatment of M0-patients who developed metastases seem to be nullified by a worse pattern of metastases, with the shift to liver and CZS.
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5190 POSTER

Importance of breast cancer screening in women aged between 35 and 49 years old

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Today 1 in every 8 women has breast cancer (ca) in the world. Its early detection and treatment are the most important factors affecting breast ca mortality. Therefore to detect the sucpicious lesions via imaging modalities before they become palpable and their pathological assesment have recently gained importance a lot. Imaging guided wire localization breast biopsy (IGWLBB) is one of the techniques used to get pathological diagnosis of these nonpalpable lesions. And with these study we aimed to show even in 35−49 year old women how important the mammography (MMG) is to detect breast ca at an earlier stage.
From August 2006 to June 2007, 233 patients underwent 242 IGWLBB to nonpalpable lesions. 9 patients had 2 simultaneous localizations: 4 to ipsilateral breast, 5 to contralateral breast. 191 localizations were guided sonographically (USG) and 51via MMG. Of 242 lesions, 237 were excised completely, 1 was excised partially and 4 was not excised at all (success rate: 97.9%).