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Introduction: Nowadays most developed countries in the world, including Russia, experience the increase of breast cancer rate. There has been a steady growth of breast cancer cases from 2002 to 2006 year both in Ugra and in Russia overall (cancer-register materials analysis of Khanty-Mansyisk State Clinical Hospital). At the present time, since February, 7th, 2007, there has been a Screening Program (SP) implemented on the territory of the region that is aimed at early breast cancer diagnostics. SP includes 3 consecutive stages. First stage particularity is based on northern regional aspects – town remoteness from each other and from big cities, absence of oncologists in each town. Gynecologists or medical assistants make a physical breast examination and order instrumental diagnostic. Second stage includes instrumental diagnostics measures. Third stage determines treatment-diagnostics measures performed by oncologists when second stage finds breast pathology.
Goal: Define SP first results with diagnostics equipment performance evaluation in region municipal districts.
Results: The reports have been provided by 21 municipal districts from March till October 2007. 38360 women have been inspected with use of mammography and ultrasound for the period of 8 month, including 18123 within screening program. This number represents around 7% of female population of over-20-years age group. 20575 women, age group over 40 years, have been inspected using mammography, including 11630 within the SP – 56.5% of the total inspections. Ultrasound inspection has been performed on 17785 women, including 6493 within the SP – 36.5% of the total inspections.
Conclusions: Reports analysis in the region has demonstrated SP active implementation in majority of municipal districts. However, it has shown that some districts do not perform sufficient screening inspections even though there is all required equipment in place. Also it indicated 6 districts with no mammography set up or functioning for various reasons. The following measures are required to resolve the above problems: appointment of those responsible for SP implementation in each district; educational courses for medical specialists involved in first stage of SP; sufficient employment of specialists to maintain mammography equipment operations in all municipal districts; telemedicine use in the region for histologist and cytologist consultations when performing verification of breast biopsy results.

P15
Genetic counseling in breast cancer. The National Cancer Institute of Naples experience

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Genetic factors appear to contribute to at least a fraction of 5–10% of the women with breast cancer. Today the recent molecular biology acquisitions lead us to consider different clinical approaches in the treatment of women with higher risk to develop breast carcinoma. In 1994 our Institute started a perspective program (named "Family Project") for genetic counselling on families with higher incidence of breast cancer. 245 women distributed in 93 families have been entered into this study. The only criterion for admission was the presence of breast cancer in at least 3 components of the family. This group was followed by a clinical-diagnostic protocol including anamnesis, genealogical tree reconstruction and clinical and instrumental examinations (ecography, mammography and FNAC where necessary). Peripheral blood samples were taken from each woman and genomic DNA was extracted to further evaluate putative genetic alterations after obtaining informed consent. This approach has permitted discovering pre-clinical lesions in 10 women enrolled belonging to family groups under study. From the first breast cancers analysis we found an hereditary component in 13% of all cases studied and these cases have peculiar characteristics: early age of diagnosis, frequent bilateral tumours, and the association with other tumours in the same person or in the same family group. The follow-up uses a protocol, which foresees the psychological approach, between the clinical team and the women in study, as a fundamental part of it.

P16
The patterns of BRCA1 and BRCA2 mutations in hereditary breast cancer in Ukrainian population

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Breast cancer (BC) is the most common malignancy in developed countries with lifetime risk about 70–90%. It is known, that specific inherited mutation in BRCA1 and BRCA2 (5–10% of overall BC incidence) associated with an extremely high risk of BC development. The most thoroughly studied manifestations of the founder effects are among Ashkenazi Jewish population where three common mutations in BRCA1 and BRCA2 are reported (185delAG, 5382insC in BRCA1 and 6174delT in BRCA2). The aim of the study: To estimate the patterns BRCA1 and BRCA2 mutations of Ukrainian population.
Material and Methods: We analyzed DNA samples of 20 patients with hereditary BC to determine the patterns of founder mutations and other mutations in BRCA1 and BRCA2 genes. We screened the genes BRCA1, BRCA2, and CHEK2 from 20 paraffin samples of Ukrainian patients with BC using gel electrophoresis and direct sequencing.
Results: 517delTG BRCA1 mutation has been found in 5 patients, T300G – in 3 patients, 5385insC – in 3 patients, 6174delT and 5909insA BRCA2 mutations has been found in 1 and 1 patient accordingly. IVS2+1G>A and I157T mutation CHEK2 where found in 4 patients and 3 patients accordingly. So the most frequent BRCA1 gene defects were detected 517delTG and 5382insC (founder mutations) in 5 and 3 patients accordingly. 617delT founder mutations in BRCA2 was identified in only one case.
Conclusion: Founder mutations in Ukrainian populations in our study make up only 15% for BRCA1 and 5% for BRCA2.

P17
The BRCA1 and BRCA2 mutation in Chinese breast cancer patients – a multi-center study of 489 cases

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To study the BRCA1 and BRCA2 mutations in Chinese patients with early onset breast cancer and affected relatives, 489 high-risk breast cancer patients from five breast clinical centers in China, were analyzed by using PCR-DHPLC or SSCP-DNA sequencing analysis. Allelotype analysis was done at five short tandem repeat (STR) markers in or adjacent to BRCA1 on the recurrent mutation carriers. In the 489 patients, 447 patients received mutation detection in both genes and 41 cases were analyzed only in BRCA1 gene. Twenty-three BRCA1 mutations and 21 BRCA2 ones were detected in our study. Two recurrent mutations in BRCA1, 1100delAT and 5589del8, were identified. The recurrent mutations account for 34.8% BRCA1 mutations in our series. Furthermore, 2 cases of BRCA1 5589del8 (0.5%) and one case of BRCA1 1100delAT (0.2%) was detected in 426 sporadic breast cancer patients and 564 healthy controls, respectively. Similar allelotypes were detected in most STR status for those harboring the same mutations. The frequency of BRCA1 and BRCA2 mutation in our study was both 4.7%. For those analyzed both genes, 8.7% of early-onset breast cancer cases and 12.9% of familial breast cancer cases had a BRCA1 or BRCA2 mutation, as compared with the 26.1% of cases with both early-onset breast cancer and affected relatives. When we stratified with number of breast cancer patients in family, the frequency had no statistical significance. However, the average age of disease onset in the families carrying BRCA1/2 mutations was significantly younger than the families without mutations ($P = 0.003$), and more the younger patients in family, higher the mutation frequency was. For those reporting malignancy family history other than breast/ovarian cancer, the prevalence of BRCA1/2 mutation is about 20.5%, and it was significantly higher than the patients only with family history of breast/ovarian cancer ($P = 0.02$). The family history of ovarian cancer (26.7% vs. 11.9%) and stomach cancer (23.8% vs. 11.8%) doubled the incidence of BRCA1/2, but the difference did not reach the statistical significance. We recommended the BRCA1 and BRCA2 genetic analysis could be done for high-risk breast cancer patient in Chinese population, especially for those with both early-onset breast cancer and affected relatives.

P18

Toremifene as a reference drug in the treatment of breast cancer

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Tamoxifen has opened the era of oestrogen receptor blockers. However, Tamoxifen has turned out to be a genotoxic and teratogenic drug as it has been reported by numerous authors and mentioned in the Statements of St. Gallen Consensus Conference.

During the past 15 years, we have been administering Tamoxifen instead of Toremifene. One thousand five hundred seventy one cases of administration of the drug in postmenopausal patients with breast cancer of above 50 years of age have been analysed. No cases of cancer of the liver or endometrium have been detected. Endometrium hyperplasia eliminated by a temporal cancellation of the administration of the drug was reported in 23 % of cases.

A study of the hormonal homeostasis has shown that administration of Toremifene makes it possible to achieve a fourfold reduction of follicle-stimulating hormone levels (reduction by 1/3 is observed on administration of Tamoxifen), which is important from an etiopathogenetic point of view. Moreover, Toremifene acts in both oestrogen-receptor-positive and oestrogen-receptor-negative patients (5 year survival is similar in both subpopulations).

Toremifene is advantageous as compared with Tamoxifen in the combined therapy of patients with advanced breast cancer: full remission has been achieved in 8.7 % of patients taking Toremifene and in 3.4 % of those taking Tamoxifen and time to progress is 5.1 months in patients on Toremifene and 3.9 months in patients on Tamoxifen.

The above data suggest that Toremifene should be a reference drug for the treatment of breast cancer.

P19

Multivariate discrimination functions composed with amino acid profiles (Amino Index®) as a novel diagnostic marker for breast and colon cancer

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Introduction: Amino acids balance is changed in patients of various diseases due to metabolic transition while it is maintained in healthy human. For example, Fisher ratio (ratio of branched amino acids to aromatic amino acids) is used as a primary index of hepatic failure. It is also known that the metabolism cancer cells are totally altered. Therefore, it is expected that the detection of metabolic transition using amino acid profiles is promising biomarker of various cancers. In this study, significant changes of plasma amino acid profiles of breast cancer and colon cancer patients were detected by discriminants (Amino Index®) by conducting with multivariate analysis.

Material and Methods: Blood samples were collected and cooled down from 50 colon cancer patients, 30 breast cancer patients, and age-gender adjusted healthy controls. Then, plasma samples were collected by centrifuge (3000rpm, 15min) and amino acid concentration was measured using LC/MS. The most appropriate discrimination functions for each cancer were estimated. The discrimination ability of discriminants was estimated as the area under the receiver-operator curve (ROC_AUC) of function values. The performances of the discriminants were also estimated using the test data randomly divided in advance. All the statistical and multivariate analysis was performed with MATLAB and GraphPad Prism.

Results: For discrimination of colon cancer, discriminant-1 composed with six amino acids (phenylalanine, threonine, alanine, glutamine, alpha-aminobutyric acid, and citrulline) was obtained. For breast cancer, discriminant-2 composed with composed with six amino acids (glutamine, arginine, isoleucine, alanine, ornithine, and histidine) was obtained. Both of them showed high performance for discrimination; 0.849 of ROC_AUC for discriminant-1 and 0.882 for discriminant-2, respectively. Then, the validation of performances of them using test data resulted 0.943 of ROC_AUC for discriminant-1 and 0.897 for discriminant-2, respectively, suggesting the reliability of these discriminants. Furthermore, the possibility of classification between these three groups was investigated. By conducting with discrimination analysis, it was suggested that the three statuses were