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## Breast cancer susceptibility gene (BRCA) analysis in Serbia

**KEYWORDS:** Genes, BRCA1; Genes, BRCA2; Mutation; Breast Neoplasms

**Background:** Breast cancer is the most common type of cancer and leading cause of death among women. Approximately 5-10% of all breast cancers are hereditary. Mutations in highly penetrant BRCA1/2 tumor suppressor genes, involved in maintenance of genome stability, are associated with hereditary form of breast and ovarian cancer. BRCA mutations are scattered throughout these large genes without clustering. Therefore, automatic sequencing of whole coding region of both genes is the gold standard in mutation detection. BRCA mutation carriers exhibit elevated lifetime risk for the development of breast cancer - while the lifetime risk for breast cancer in general population is 10%, their lifetime risk is about 5 to 8 fold higher. Lifetime risk for ovarian cancer in BRCA mutation carriers is also elevated - it is about 10 to 20 fold higher than in general population (lifetime risk is about 2%).

**Methods:** Genomic DNA bank has been formed in Laboratory of Molecular Genetics of the Institute for Oncology and Radiology of Serbia. So far, it is consisted of about 190 blood samples from the individuals who are, according to established criteria, potential carriers of BRCA mutations. DNA for BRCA gene analysis is isolated by phenol/chloroform extraction. Coding region of BRCA1 gene is further amplified by polymerase chain reaction (PCR) in the presence of specific primers. PCR products were purified, labeled with fluorescent 3'-dye labeled dideoxynucleotide triphosphates and precipitated by EDTA/ethanol precipitation method. These samples were then bi-directionally sequenced by automatic ABI PRISM 310 genetic analyzer.

**Results:** Complete (n=45) or partial analysis (n=7) of BRCA1 coding region has been performed. Mutations were detected in 5/45 samples. The presence of 4 known mutations, previously detected elsewhere, has been shown: 185delAG, 3447del4, C61G and 5382insC (detected twice). Also, genetic polymorphism of BRCA1 (2430T>C) was identified in one case. The majority of BRCA1 and BRCA2 gene analysis was performed within joint research program with National Center for Scientific Research *Demokritos* from Athens, Greece.

**Conclusion:** Our preliminary results have shown the presence of deleterious BRCA1 mutations that were previously reported. These mutations belong to the small group of recurrent BRCA1 mutations that are detected in almost all populations. So far, we have not identified any novel mutation that would be characteristic for Serbian population. In general, the goal of systematic BRCA analysis is the establishment of frequency and types of BRCA mutations in our population.

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## Possibilities of scintimammography in differentiation benign from malignant breast tumors in preoperative diagnostics

**KEYWORDS:** Mammography; Radionuclide Imaging; Breast Neoplasms; Diagnosis

**Background:** Breast cancer is the most frequent malignant tumor in female population, and is on the second place by mortality, after the lung cancer. Incidence increased over the last few years for 3 % per year, 1 of 9 women being affected by this disease. The question is whether scintimammography, as a functional, visual method, could help to increase specificity and sensitivity of diagnostic methods (mammography) in preoperative diagnostic of breast tumors. Aim: Differentiation between benign and malignant breast tumors.

**Methods:** Eighty-two female patients were included in our study with palpable breast tumor, to whom scintimammography was done and who underwent breast cancer surgery for histology confirmation. All patients were divided in 3 groups. Group I (n=69) included patients with palpable breast tumor suspected to be malignant. Group II (n=3) included patients who had been previously treated with surgery having been histological confirmed, and currently were presented with suspect tumor recurrence. In III (n=10) there were the patients with benign breast changes. Scintimammography was done with 99mTc-MIBI with an activity of 555MBq, 10 minutes after intravenous application in the cubital vein on the contralateral side where the breast changes were detected. Gamma camera Orbiter 45 Siemens and Siemens e. cam double-headed camera was used. The patient is in prone position. The images were obtained in lateral and anterior position of both breasts.

**Results:** In I group 54/69 patients, scintimammography was true positive (TP) (78%), true negative (TN) in 8/69 patients (12.9 %), false negative (FN) in 3/69 patients (4.3%), false positive (FP) in 4/69 patients (5.7 %). In II group 1/3 patients scintimammography was TN (33.3%), in 2/3 patients was TP (66.6%). In III group 8/10 patients scintimammography was TN (80%), in 2/10 patients was FP (20%). Sensitivity (SE) was 94%, specificity (SP) 73%, and accuracy (A) 89%, respectively.

**Conclusion:** Based on the achieved results, we proved the high sensitivity, specificity and accuracy of the method. We can conclude that the scintimammography findings can be very helpful as an accessory method in the differentiation between benign and malignant breast tumors and should have a place in preoperative evaluation of palpable breast tumors.



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## Noninvasive breast cancer

**KEYWORDS:** Breast Neoplasms; Carcinoma in Situ; Carcinoma, Intraductal, Noninfiltrating

**Background:** Noninvasive breast cancer (BC) includes - lobular carcinoma *in situ* (LCIS) and ductal carcinoma *in situ* (DCIS), as well, and Paget's disease of the nipple when there is no associated invasive cancer. More noninvasive BCs are being diagnosed due to the increasing use of screening mammography in developed countries. Optimal treatment of these malignancies is still controversial and continues to evolve as the results of clinical trials.

**Methods:** Hospital files of 1412 BC patients (pts) were reviewed (from July 1996 up to 2003), and it was found that only 18 pts (1.27%) were diagnosed as noninvasive (*in situ*) BC. Data for 17 pts were available.

**Results:** Median age of pts with noninvasive BC was 49 years (range 28-69 years), 53% of them were premenopausal and 47% postmenopausal. Pathologic reports described DCIS in 11 pts (3 of them with Paget's disease, without invasive cancer); 2 pts had LCIS, 4 reports were not specified (described only as BC *in situ*). Treatment options included surgery (conservative or radical mastectomy with or without axillary dissection), postoperative radiotherapy and treatment with tamoxifen for the prevention of secondary invasive BC. Conservative surgery performed in 70.5% pts; 58% of them were premenopausal. Radical mastectomy was done in 29.5% pts with or without axillary dissection. In 83% patients with conservative procedures, radiotherapy was applied, while in 17% pts with conservative surgery, radical mastectomy with or without axillary dissection was performed subsequently as the definitive treatment. After primary surgical treatment with or without radiotherapy, 18% of pts were treated with tamoxifen. Local recurrence was registered only in one patient (5.8%) after 6 years, being presented as ductal invasive breast carcinoma. No distant recurrences were observed.

**Conclusion:** Lower incidence of noninvasive BC in our population, compared with literature data, probably resulted from the lack of screening mammography and low level of patients' education. Optimal treatment of Stage 0 breast cancer is still debatable. However, our results are in line with the recommendation that multimodal treatment should be discussed for each patient individually.

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## Stereotactic breast biopsy procedures in detection of non-palpable lesions: Current status and further objectives

**KEYWORDS:** Breast Neoplasms; Stereotactic Techniques; Biopsy, Needle; Palpation

**Background:** Stereotactic breast biopsy (SBB) of non-palpable lesions is the key surgical tool in early breast cancer detection and therapy. Current methods using vacuum-assisted core needle biopsy and the excision biopsy system shows reliability when compared with open biopsy, suggesting further significant declining in unnecessary surgical procedures for benign breast lesion, as well as the increase in rate of tissue-sparing breast surgery for malignant lesions. The aim of this study was to analyze recent results of stereotactic wire-guided excision (WGE) performed in our Institution, which could dictate further objectives of this therapeutic procedure.

**Methods:** Briefly, WGE was performed using Mammomat with specimen radiography, frozen section and standard histopathological (HP) analysis.

**Results:** In 30 of 33 patients (90%), (median age 52), clustered microcalcifications were demonstrable and confirmed by specimen mammography and HP analysis. After wide excision, measurable tumor was present in 31 patients (average diameter 6.4 mm). Eleven of 33 patients (33.4%) had malignant tumor, 5 patients with *in situ* or pTmic carcinoma (15%), and 6 patients (18.2%) with invasive carcinoma. In 5 patients distance from resection margin was less than 5mm and further quadrantectomy was performed when invasive carcinoma was diagnosed on frozen section (3 patients) and margins were measurable, while in 2 patients with non-comedo DCIS with margins 3,5 and 4mm underwent quadrantectomy in the second act. All patients with diagnosed malignancy underwent axillary dissection. Four patients (12.0%) had lymph node metastases (2 patients with pN1a, one with 2 and one with more than 4 metastases). Obtained results did not differ much in comparison with results obtained in large series with accuracy in diagnosis of malignant lesions. Possible introduction of 11- or 14- gauge needle stereotactic biopsies, as well as refined radiographic and/or ultrasound guidance could result in further decrease of morbidity period. Low incidence of lymph node metastases implies introduction of possible axillary sparing surgery with previous sentinel lymph node labeling.

**Conclusion:** It is necessary to investigate WGE in diagnosis and treatment of breast cancer within internationally monitored trials, in order to confirm accuracy and disease control, as well as its role as the future end-tool in breast cancer screening.



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## Surgical management of non-palpable breast lesions

**KEYWORDS:** Breast Neoplasms; Surgery; Biopsy; Intraoperative Period; Diagnosis

**Background:** A wide spread use of mammography has resulted in an increased number of clinically non-palpable breast lesions. The surgical management of these occult lesions is challenging. Several localization techniques were developed none of those considered ideal. Every technique considers placing a needle at least 1cm to the lesion and than introducing a marker (wire-hook, blue dye or radio labeled albumin). The use of the latest is known as radioguided occult lesion localization (ROLL).

**Methods:** A total of 39 patients with impalpable breast lesions were treated at the department of surgery at the Institute of oncology in Sremska Kamenica. All patients underwent needle localization under stereotactic or ultrasound guidance before surgical biopsy. Wire-hook localization was used in 27 patients, blue dye in 3 and ROLL in 9. Surgical biopsies were taken under general anesthesia and the surgeons intended to remove the lesions aiming for tumor free surgical margins. Specimen radiographs were performed to confirm the removal of the occult lesion. Whenever surgical margins were tumor positive re-excision was performed or mastectomy if necessary. Biopsies with tumor free margins consisting of ductal carcinoma in situ (DCIS) up to 3cm require no additional surgery. In case invasive breast cancer was diagnosed, we performed a second surgical procedure, at least axillary dissection, except in ROLL group where sentinel node (SN) biopsy was performed.

**Results:** Out of 39 patients treated 30 occult lesions proved to be benign (77%) and 9 malignant (23%). Among the latter, we found DCIS in 3 cases (30%) and infiltrating carcinoma in other 6, all these patients underwent breast-conserving surgery, only one patient had positive SN and had axillary clearance. The average tumor diameter was 8mm the average weight of the excised specimen 45grams. Specimen radiographs proved that every lesion was successfully excised, margins reported to be free of tumor.

**Conclusion:** localization techniques are feasible and reliable in surgical management of occult breast lesions. Volume of the excised specimen can be smaller, resulting in better cosmesis.

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## Is there any change in the early detection of breast cancer in Montenegro since the Breast Cancer Consultation Board has been formed?

**KEYWORDS:** Breast Neoplasms; Epidemiology; Incidence; Mass Screening

**Background:** Nine years ago Multidisciplinary Breast Diseases Consultation Board was formed in the Clinic Center of Montenegro (CCOM) in intention to gather all medical subjects in the breast cancer (BC) diagnosis and therapy. The aim of this study is to show some facts on the BC epidemiology in Montenegro since 1996: incidence, structure and distribution of early diagnosed BC.

**Methods:** We retrospectively analyzed clinical and pathological data of 1412 new detected BC treated in CCOM in eight years period (1996-2003). Prognostic groups are defined by system of Barr and Baum: three groups of primary BC with minimal, low and high risk of relapse (PG 1-3), locally advanced disease (PG4) and metastatic disease (PG5).

**Results:** We showed distribution of initially diagnosed groups of patients for every year and compare rates of early breast cancer (PG 1-3) with advanced disease (PG 4-5). Early breast cancer was significantly ( $p < 0.01$ ,  $\chi^2$  test) more frequent in the period 2000-2003, when compared with first four years. Incidence of the BC showed increase in eight years period (125 new BCs in 1996 compared to 199 in 2003). For both analyzed periods, the frequency of new diagnosed *in situ* malignancies was unacceptably low (9 patients in each period, total 18-1.27%).

**Conclusion:** Increase of BC incidence in analyzed period does not show real increase in number of mammary carcinoma in Montenegro per year. It just shows that well organized work of oncology competent team finds its place and that it is well accepted in health system. Highly statistically significant difference between numbers of early cancers shows that social efforts in health education of women in well-organized health system made some relative initial success. But facts that we have just one percent of patients with *in situ* carcinoma shows that we are still far from the developed countries frequency of detecting noninvasive tumors. That is probably because we have not organized screening system with regular mammography of all women in Montenegro. This indicates possible future directions of social, medical and oncology activities in this field.



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## Our selection criteria for conservative vs. radical surgical treatment of breast cancer

## Breast cancer- clinical vs. histopathological status of axillary lymph nodes

**KEYWORDS:** Breast Neoplasms; Surgical Procedures, Operative; Mastectomy

**KEYWORDS:** Breast Neoplasms; Neoplasm Staging; Lymph Nodes; Prognosis

**Background:** Our goal is to evaluate the outcome of operations we performed at the Dept. of Breast Cancer Surgery at the Institute of Oncology and Radiology of Serbia in relation to the tumor size and the type of surgical procedure in breast cancer patients.

**Methods:** During the 2003 and 2004 we have performed 1310 modified radical mastectomies (Madden) and 356 quadrantectomies with axillary dissection. We analyzed 137 randomly chosen patients who had quadrantectomy with axillary dissection and 132 randomly chosen patients who had modified radical mastectomy. According to our protocol at the Institute of Oncology and Radiology of Serbia, indications for quadrantectomy with axillary dissection are tumors less than 30 mm in diameter with clinically negative axillary lymph nodes. The average age of our breast cancer patients was 55.9 years (rang: 40-80 years).

**Results:** Our analysis shows that 83.2% of the patients who underwent quadrantectomy with axillary dissection had tumor less than 20 mm, and 97.1% had tumor less than 30 mm in diameter. Out of 132 patients who had mastectomy, 45.4% had a tumor less than 20 mm, and 81.8% had tumor less than 30 mm in diameter, meaning that they were good candidates for quadrantectomy with axillary dissection.

**Conclusion:** The results obtained meet the international standards as far as indications for quadrantectomy with axillary dissection are concerned. We are still not satisfied with a large number of mastectomies performed at our Institute and we think that we should set up higher standards that must be followed more strictly during the decision-making process in setting up an indication for mastectomy.

**Background:** Our goal was to make an assessment of the value of clinical examination of breast cancer patients at the Institute of Oncology and Radiology of Serbia.

**Methods:** During the years 2003 and 2004 we performed 1310 modified radical mastectomies (Madden) and 356 quadrantectomies with axillary dissection at the Institute of Oncology and Radiology of Serbia. We analyzed 183 randomly chosen breast cancer patients who had axillary dissection. The average age of our patients was 55.9.

**Results:** Out of 183 patients, 104 were classified as N0 and 79 as N1. In the N0 subgroup, with no palpable axillary lymph nodes, we found that 42 patients (40.4%) had positive lymph nodes verified histopathologically (false negative). In N1 subgroup, with palpable axillary lymph nodes, we observed that 41 patients (51.9%) had negative (false positive) lymph nodes.

**Conclusion:** It was concluded that we cannot rely only on clinical exam in predicting histological involvement of axillary lymph nodes. Knowing this shortcoming of clinical exams is very important because histological confirmation of positive axillary lymph nodes highly correlates with prognosis.



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## T and N category in the prognosis and prediction of response to neoadjuvant chemotherapy in breast cancer patients

**KEYWORDS:** Breast Neoplasms; Neoplasm Staging; Prognosis; Neoadjuvant Therapy

**Background:** It is well known that tumor size (T) and nodal involvement (N) are most important factors in breast cancer prognosis. The increase in tumor size is commonly followed by the increase of probability of nodal involvement and the increase in number of involved nodes, but it is not known which of these two factors is more important. Cases of large tumors with no nodal involvement, or, on the contrary, those with small tumors and massive nodal involvements, are rare, and could serve to analyze the relative importance of each of these factors.

**Methods:** For this purpose, in the group of 215 patients with locally advanced breast cancer, we selected patients with extremely discordant T size and N status: of 35 patients, there were 28 with T3-4 N0-1, and 7 patients with T0-1 N2, respectively. Since the whole group of patients was treated with neoadjuvant FAC chemotherapy, clinical response to the primary treatment was correlated to the TN category, as well as the disease-free survival (DFS).

**Results:** There was no difference in age, histology tumor type and grade between two groups with discordant TN status. Clinical response was assessed as partial remission (PR) in 19/28 (68%) patients in T3-4 N0-1 group, and in 4/7 (57%) patients in T0-1 N2 group, while remaining pts had disease stabilization (SD). There were no either complete clinical responses, or progressions, while on neoadjuvant treatment. Concerning the DFS, it was longer than 12 months in 16/28 (57%) patients (pts) in group T3-4 N0-1, and in 3/7 (43%) pts in group T0-1 N2, while in remaining patients it was shorter than, or equal to 12 months.

**Conclusion:** Although these differences do not reach statistical significance, probably due to the small sample size, it seems that both the local tumor response, and the overall outcome are slightly better in patients with large tumors and low nodal involvement, compared to those with small tumor size, but massive nodal involvement. Our result suggest that relative predictive and prognostic importance of T/N category deserves further investigation in the larger group of breast cancer patients.

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## Early breast cancer patients' characteristics in Jablanica region for the period 1999-2004

**KEYWORDS:** Breast Neoplasms; Neoplasm Staging; Prognosis

**Background:** Breast cancer is the commonest malignancy between women in Jablanica region of Serbia. In 2002-2003, breast cancer presented 31% and in 2004, 23.5% of all newly diagnosed malignancy in women, most of the primary tumors (more than 80%) having been larger than 2 cm. Aim: To present the tumor and patients' characteristics in selected group of women, being diagnosed with primaries smaller than 2 cm, and to compare the data with the group diagnosed in higher tumor clinical stages.

**Methods:** Data were obtained from the patients' files in Oncology Department of Health Center Leskovac. During the period 1999-2004, there were 330 newly diagnosed women with breast cancer.

**Results:** In the whole group, 48 (15%) were presented with primary tumors smaller than 2 cm (pT1), while 282 (85%) patients had tumors classified as pT2-T4. In the group with pT1 tumors, slightly larger number of women lived on the villages (56.3%). Median age in pT1 group was 53.3, while in other group it was 61.6. Concerning menstrual status, pT1 stage was found in 52% cases in postmenopausal women, and in only 9.2% of perimenopausal ones perimenopausal. In the whole group, irrespective of the clinical stage, most common histology tumor type was ductal invasive cancer. In pT1 group, ductal invasive breast cancer was diagnosed in 76.7% patients, and in the group with larger tumors - in 70.5%. At diagnosis, 77% patients with pT1 tumors were node-negative (pN0), while there were only 45.7% node-negative patients in the larger tumors group. The steroid receptor status was positive in 85.7% and 65.1% of women in pT1 and pT2-T4 groups, respectively. However, SRs were not determined in all patients. Calculated mean disease-free interval of 49.8 and 27.9 months was registered for pT1 group and the group with larger tumors, respectively. No difference was found in the metastatic sites between two groups. Nearly identical frequency of bone and lung metastases, as well as local recurrences was found in both groups.

**Conclusion:** Although presented as the descriptive analysis, our results suggest that patients with pT1 tumors had better prognosis. The obtained data initiated the campaign for early detection of breast cancer in Jablanica region.



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## Complications of reconstructive procedures in early breast cancer

## Correlation between 99m Tc-DPD bone scan findings and Ca 15-3 values in early breast cancer patients follow-up

**KEYWORDS:** Breast Neoplasms; Reconstructive Surgical Procedures

**KEYWORDS:** Breast Neoplasms; Chemotherapy, Adjuvant; CA-15-3 Antigen

**Background:** Although without official confirmation, early breast cancer (EBC) includes forms of ductal and lobular *in situ* cancer, as well as invasive cancer sized up to 10mm with histology verification of negative axillary nodes. Reconstructive procedures in EBC have risk of complications - the early and the late ones. Infection can be considered an early complication. Late complications include prolapse of endoprosthesis, capsule contracture, iatrogenic damage of endoprosthesis, and local recurrence in case of inadequate subcutaneous mastectomy. Necrosis of a part of the skin, or of musculocutaneous lobe can be both early and late complication; it occurs as sequela of compromised vascularization, or influence of certain exogenous factors such as radiotherapy or infection.

**Methods:** During 2002-2004, 20 reconstructions in EBC patients were performed at Institute of Oncology and Radiology of Serbia (IORS). Primary reconstruction was performed in 16 cases, and secondary one in 4 cases. Endoprosthesis was positioned subcutaneously in 3 cases of the primary reconstruction, and subpectorally 13 times. On the occasion of the secondary reconstructions in EBC, implant was positioned submuscularly in all 4 cases, and in one case, latissimus dorsi musculo-cutaneous flap was used. Average age of these 20 women was 44.9 years (range: 29-62 years).

**Results:** A case of intrahospital infection, which later developed to necrosis of a part of a skin and prolapse of endoprosthesis positioned subcutaneously can be stated as early complication. The following cases can be considered as late and the most severe complications: prolapse of subcutaneously implanted endoprosthesis, the capsule contracture implanted subpectorally, and recurrence in the region of mamilla. Our sample also included one necrosis of a part of the skin in case of secondary subpectorally positioned endoprosthesis. Two cases of asymmetry can be reported as relative complications, one being completed by symmetrization, and the other by replacement of endoprosthesis.

**Conclusion:** In the period 2002-2004, twenty reconstructions of EBC were performed at IORS, 16 of which were primary reconstructions, and 4 were the secondary ones. An early complication was intrahospital infection with skin necrosis and prolapse of endoprosthesis, and the late one was one case of endoprosthesis prolapse, capsule contracture, local recurrence and necrosis of a part of the skin. The results depend on operational technique, method, extra oncology therapy, and the very subject, i.e. a patient as well.

**Background:** The aim of this study was to evaluate the correlation of CA 15-3, bone scan and complementary imaging methods (X-ray, CT and MRI) in follow-up of breast cancer patients, after neoadjuvant chemotherapy.

**Methods:** Sixty-three patients with histologically proven breast cancer were included (mean age 58, range 41- 82) and followed for having positive bone scan findings. Information was confirmed with other imaging methods: X-ray, CT, MRI. Ca 15-3 values were measured in the same time with the bone scan, using the same commercial test over the follow-up period. Bone scans were classified as negative (group 1), diffuse increased uptake in calvaria (group 2), solitary hot spot lesion (group 3), benign disorder (group 4), mixed benign and malignant patterns (group 5), multiple =3 metastatic focuses (group 6).

**Results:** Number of patients in groups 1 to 6 were: 13, 5, 18, 6, 4 and 17, respectively and had mean Ca 15-3 value U/ml: 17.6 (range 9.2 - 43.3); 12.7 (range 6.9-18.5); 74.26 (range 7.3-469.2); 92.9 (range 10.0-480.0); 52.8 (range 15.1-150.0); 404.8 range 8.9-3160.0). Five patients in group 6 had normal Ca 15-3- values. Metastatic involvement sites in group 3 were: lung, liver and skin, with frequencies 28%, 28% and 6% respectively, and in group 6: lung, liver, skin and brain with frequencies 12%; 35%; 6% 6%, respectively. The statistical difference in CA 15-3 level was not evident between groups 1 and 2+3+4+5, but was statistically significant between groups 6 and 2+3+4+5 (Mann-Whitney test,  $p < 0.01$ ). Multiple lesions bone scans were confirmed with radiology findings in 50% of cases (6 X-ray in 14 patients [pts], 2 CT in 2 pts); benign lesions in 100% (X-ray); 20% (X-ray) in calvaria; solitary hot spot lesions in 53 % (ribs 6 in 8; pelvis 2 in 3, vertebra 1 in 1 with X-ray and MRI 100% 2 in 2), and 8 of them solitary malignant lesions.

**Conclusion:** Normal Ca 15-3 value does not exclude bone metastasis, and cannot be helpful in confirming solitary lesions. Bone scan pathological findings require careful radiographic evaluation for early diagnosis of metastatic disease.



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## Early breast cancer in young premenopausal women

**KEYWORDS:** Breast Neoplasms; Age Factors; Prognosis; Premenopause

**Background:** It is well known that breast cancer (BC) prognosis is poor in very young patients. However, it is not yet clear whether this is the consequence of the higher frequency of unfavorable histological and biological characteristics, or the young age up to 35 is the intrinsic unfavorable prognostic factor. Since adjuvant chemotherapy lowers the risk of recurrence in very young early BC patients, it is suggested that only those young patients, who had not been treated with chemotherapy, would remain in the increased risk of recurrence.

**Methods:** Tumor characteristics in a group of very young premenopausal early BC patients were analyzed, and compared with the group of premenopausal patients older than 35. During the period 1995-2003, 46 very young EBC patients, aged 22-35, have been treated with radical surgery and adjuvant anthracycline chemotherapy, postoperative radiotherapy, if indicated, and endocrine therapy, if receptor-positive.

**Results:** In the group of very young EBC patients, 37% had tumor size less than 2 cm, 24% was node-negative, most common tumor types were ductal and lobular ones, while 91% had grade II tumors. ER and/or PR-positive status was found in 56.5% patients. Median follow-up was 35 months (range 5-121). In comparison with a group of 173 premenopausal patients older than 35, having been treated with the same chemotherapy, postoperative radiotherapy, and endocrine therapy, if indicated, no significant difference was found regarding the tumor size, grade and histological type, nodal status, ER status and DFS. However, significantly lower proportion of PR-positive tumors was found in younger, compared to older premenopausal patients: 35% vs. 55%,  $p=0.03$ .

**Conclusion:** Our results support the suggestion that the age does not seem to be a poor prognosticator *per se*, in very young premenopausal patients, having been treated with adjuvant chemotherapy.

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## Reconstructions in early breast cancer

**KEYWORDS:** Breast Neoplasms; Reconstructive Surgical Procedures

**Background:** Still, there is no official definition of early breast cancer (EBC), but valid criteria are that these are the forms of ductal and lobular in situ cancer, as well as invasive cancer of up to 10 mm size with HP verification of negative axillary nodes. Early breast cancer is the most commonly treated with conserving operation, not requiring extensive reconstructive procedures. However, there are cases when subcutaneous mastectomy is required (skin sparing mastectomy and reconstruction by implantation of endoprosthesis. The decision is mainly dependent on the patient's age, since breast cancer is very common in younger women, on multifocal cancer character, and also on cancer localization (medial and central quadrant). Very often, reason for this intervention can be patient's personal request.

**Methods:** In the period of 2002 to 2004, 278 reconstructions were performed at Institute of Oncology and Radiology of Serbia (IORS), out of which 235 were primary reconstructions and 43 secondary ones. Total number of reconstructions in EBC was 20. Average age of these twenty women was 44.9 years (range 29-62).

**Results:** Number of 20 cases of reconstructive procedures of EBC is 7.2% of total number of the reconstructions performed at IORS in the period of 2002-2004. Sixteen cases satisfied criteria for the primary reconstructions of EBC, and 4 cases met requirements for the secondary criteria with implantation of endoprosthesis. Endoprosthesis was positioned subcutaneously in 3 cases of the primary reconstructions, and subpectorally in 13 cases. Regarding the secondary reconstructions in EBC, implant was positioned submuscularly in all 4 cases, but in one case latissimus dorsi, musculo-cutaneous flap was used. There were no cases of reconstructions performed with the help of transverse abdominal musculo-cutaneous flap (TRAM). Three cases of multifocal cancer were recorded, while 11 cases had central or medial localization. Postoperative course lasted 7-11 days.

**Conclusion:** In the period of 2002-2004, twenty reconstructive procedures were performed at IORS due to EBC (7.2% of total number of the reconstructions). Indications for reconstructive surgery in EBC are limited and very dependent on individual assessment of the surgeon. Most commonly, the indications are patient's age, multifocal cancer character, and cancer localization as well. Patient's personal request can also be the reason.