



Diagnostic value of breast ultrasound in mammography BI-RADS 0 and clinically indeterminate or suspicious of malignancy breast lesions

Dijagnostička vrednost ultrazvučnog pregleda dojke kod žena sa mamografskom kategorijom BI-RADS 0 i lezijom koja je klinički nejasna ili sumnjiva na malignitet

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Abstract

Background/Aim. Not only that ultrasound makes the difference between cystic and solid changes in breast tissue, as it was the case at the beginning of its use, but it also makes the differential diagnosis in terms of benign-malignant. The aim of this study was to assess the role of sonography in the diagnosis of palpable breast masses according to the American College of Radiology Ultrasonographic Breast Imaging Reporting and Data System (BI-RADS) and to correlate the BI-RADS 4 and BI-RADS 5 category with pathohistological findings. **Methods.** A retrospective study was conducted with the breast sonograms of 30 women presented with palpable breast masses found to be mammography category BI-RADS 0 and ultrasonographic BI-RADS categories 4 and 5. The sonographic categories were correlated with pathohistological findings. **Results.** Surgical biopsy in 30 masses revealed: malignancy (56.7%), fibroadenoma (26.7%), fibrocystic dysplasia with/without atypia (10%), lipoma (3.3%) and intramammary lymph node (3.3%). Correlation between BI-RADS categories and pathohistological findings was found ($p < 0.05$). All BI-RADS 5 masses were malignant, while in BI-RADS 4A category fibroadenomas dominated. A total of 53.8% of all benign lesions were found in women 49 years of age or younger as compared with 35.3% of all malignancies in this group ($p < 0.05$). **Conclusion.** Ultrasonography BI-RADS improved classification of breast masses. The ultrasound BI-RADS 4 (A, B, C) and BI-RADS 5 lesions should be worked-up with biopsy.

Key words:

breast neoplasms; diagnosis, differential; mammography; ultrasonography, doppler, color; predictive value of tests; risk assessment.

Apstrakt

Uvod/Cilj. Ultrazvučnim pregledom može ne samo da se napravi razlika između cističnih i solidnih promena u tkivu dojke, kao što je bilo na početku njegove primene, već i da se napravi diferencijalna dijagnoza u smislu razlikovanja benignih od malignih promena. Cilj rada bio je procena uloge ultrazvuka u dijagnostici palpabilnih promena u dojci u skladu sa terminologijom *Breast Imaging Reporting and Data Systems* (BI-RADS) i korelacija kategorija BI-RADS 4 i BI-RADS 5 sa patohistološkim nalazom. **Metode.** Retrospektivna studija sprovedena je u grupi od 30 žena sa palpabilnim promenama u dojci, sa mamografskom kategorijom BI-RADS 0 i ultrazvučnim kategorijama BI-RADS 4 i 5. Sonografske kategorije su korelisane sa patohistološkim nalazom. **Rezultati.** Ekscizionna biopsija 30 promena je pokazala: malignitet (56,7%), fibroadenom (26,7%), fibrocističnu displaziju sa ili bez atipije (10%), lipom (3,3%) i intramamarni limfni nodus (3,3%). Korelacija između BI-RADS kategorija i patohistološkog nalaza je dokazana ($p < 0,05$). Sve BI-RADS 5 promene bile su maligne, dok je u BI-RADS 4A kategoriji dominirao fibroadenom. Ukupno 53,8% svih benignih promena pronađene su kod žena starosti 49 godina ili mlađih u poređenju sa 35,3% malignih promena u ovoj grupi ($p < 0,05$). **Zaključak.** Upotreba ultrazvučne BI-RADS nomenklature poboljšala je klasifikaciju promena u dojci. U slučaju ultrazvučnih kategorija BI-RADS 4 (A, B, C) i BI-RADS 5 trebalo bi raditi biopsiju.

Ključne reči:

dojka, neoplazme; dijagnoza, diferencijalna; mamografija; ultrasonografija, dopler, kolor; testovi, prognostička vrednost; rizik, procena.

Introduction

Breast cancer is a leading disease by mortality in Serbian women regardless age and it is a leading cause of early death in women between 25 and 44 years of age in Serbia¹. Mammography is still the “gold standard” for breast examination. Screening mammography has certain limitations as well. First of all, about 20% of cancers present during mammography examination may be overlooked. This happens more often in young women due to density of their breast parenchyma². Then, if we take into account the amount of radiation in a ten-year time period starting at the age of 40, cancer induced by radiation will be a cause of death at most in 8 women in 100,000 performed mammography examinations³. Ultrasonography is an additional diagnostic method. Not only that ultrasound can make the difference between cystic and solid changes, as it was a case at the beginning of its use, but it can also make the differential diagnosis in terms of benign-malignant. The main objection of ultrasonographic examination in early detection of cancer is inability to recognize microcalcifications. According to the latest papers, microcalcifications may be viewed in 70%, and in case of cancer itself in 90% of cases by new ultrasonographic devices. The Breast Imaging Reporting and Data System (BI-RADS) was developed by American College of Radiology (ACR) in 1993, in order to standardize mammography reports and to enable easier communication between clinical practitioners dealing with this issue. BI-RADS classification has been applied in mammography only, and it appeared for two breast imaging modalities in the fourth revision of BI-RADS atlas: breast ultrasonography and magnetic resonance imaging (MRI). BI-RADS system is aimed to assess the risk, whether a viewed change is malignant, *ie* the following could be advised: biopsy, frequent radiology follow-ups or regular preventive examinations. The essence of BI-RADS nomenclature is a final radiology report with a clearly numerically

indicated conclusion. A motive for this paper was the fact that ultrasonography BI-RADS lexicon has had short history and that there have been fewer data on its use as compared to mammography⁴.

Criteria for assessment of pathological changes in the breast, diagnosed by ultrasonography examination are as follows: shape (round, oval or irregular), orientation (horizontal or vertical), contours (very well-defined, poorly defined, angular, micro-lobular and spiculated), transition zone (well-defined or echogenic halo), echogenicity (non-echogenic, hyperechogenic, complex lesion, hypoechogenic and isoechogenic), posterior phenomena (without posterior phenomena, acoustic amplification, acoustic attenuation, alternating posterior phenomena), tissue around lesion (ductis, direction of Cooper’s ligaments, parenchymal edema, skin and impaired architectonic of tissue), calcifications, special examples (grouped cysts, complicated cysts), flow (without color signals, with color signals and with color signals around the change) (Table 1).

There are seven BI-RADS categories. BI-RADS 0 category implies need for further evaluation with the other available methods except for ultrasonography, *ie* definite ultrasonographic evaluation is not possible. BI-RADS 1 category implies negative finding. BI-RADS 2 category is a benign finding. BI-RADS 3 category implies possibly benign finding, and a follow-up in a short period is recommended. The probability of this lesion being malignant is < 2%. Some papers report that this kind of changes may be observed periodically not longer than 2 years, and after that time it can be considered as absolutely benign. BI-RADS 4 category is a finding suspect to a malignant change and biopsy is recommended. A risk that it is about a malignant change is between 3% and 94% of patients. BI-RADS 5 category is a highly suspicious finding with a high risk for malignant disease being more than 95%. BI-RADS 6 category is a pathohistologically proved malignant disease¹.

Table 1

Characteristics of tumor changes depending on BI-RADS category		
Characteristics	BI-RADS 4 (A, B, C)	BI-RADS 5
Tumor change		
shape	Lobular/oval	Irregular
orientation	Horizontal/vertical	Vertical
contours	Well-defined or poorly defined	Poorly defined
transition zone	Well-defined or echogenic halo	Echogenic halo
echogenicity of change	Hypoechogenic, isoechogenic, complex lesion	
posterior phenomena	Acoustic amplification, acoustic attenuation, alternating posterior phenomena, without posterior phenomena	Acoustic attenuation, alternating posterior phenomena
tumor change surroundings	Change of ductus direction and/or echogenic content, thickening and/or withdrawal of Cooper’s ligaments, parenchymal edema, altered breast echostructure	
Calcifications		
within tumor change or in surrounding tissue	Observed only in correlation with mammography, for targeted detection by ultrasonography, and for evaluation of nature of change, and which can be achieved only by mammography	
Flow (vascularization)		
within tumor change or in surrounding tissue	With no color signals, with color signals within a change, with color signals around it (marginally, diffusively)	With color signals around it (marginally, diffusively)

BI-RADS – the Breast Imaging Reporting and Data System.

BI-RADS classification in breast diseases defines whether a change detected in a breast carries a risk of malignancy and whether biopsy of that change is indicated. For BI-RADS 4 (A, B, C) and BI-RADS 5 categories of ultrasonographic finding, pathohistological (PH) verification is necessary, which yields an appropriate indicator of BI-RADS classification accuracy. Therefore, the aim of this study was to categorize breast ultrasonographic finding into BI-RADS 4 (A, B, C) and BI-RADS 5 categories and correlation between BI-RADS 4 (A, B, C) and BI-RADS 5 categories with PH finding of a breast change.

Methods

From the Registry of Cancer from the Institute for Oncology and Radiology of Serbia, and from radiological reports of ultrasonographic breast examinations performed in the Clinic for Radiotherapy and Radiology Diagnostics in the same institution, a group of 30 women was created, having clinical, mammographic and ultrasound breast examination followed by surgical biopsy with PH verification of a breast change in a period between November 1 2008 and March 31 2009. Criteria for patient selection were clinical, mammographic and ultrasonographic. Clinical criteria implied: premenopausal and postmenopausal patients; breast cancer diameter up to 3 cm or resistance with the third dimension regardless dimensions, but without engagement of the skin [T1 and T2 category as *per* tumor-nodus-metastasis (TNM) classification], status of regional lymph nodes N0, without distant metastasis (M0), mammographic criteria: a change scored as BI-RADS 0 based on standard mammography in two directions, *ie* a change that is not completely defined and which requires additional diagnostics; and ultrasonographic criteria: additional diagnostic procedures, additional ultrasonography examination, clinically and mammographically, detected a change scored as BI-RADS 4A (slightly suspicious of malignancy), BI-RADS 4B (moderately suspicious of malignancy), BI-RADS 4C (medium suspicious of malignancy) and BI-RADS 5 (highly suspicious of malignancy) according to BI-RADS classification. Ultrasonographic examination of breasts was performed with a 7.5 MHz probe (Sonoview, Acuson device). Before ultrasonographic examination of breasts, the oncologists clinically examined breasts of every patient, and mammography in two directions was performed and analyzed by the radiologist (analogue mammography Lorad M-4, Hologic and digital mammography Selenia, Hologic). Ultrasonographic examination of breasts was performed with the standard approach, with a patient being in supination and lateral decubitus position, with examination of regional lymph nodes and by using power Doppler color signalization. PH analysis implied *ex tempore* evaluation of preparations obtained by surgical biopsy, and than a standard analysis of preparations colored with hematoxylin eosin (HE). The results are presented in Tables and as graphs. Evaluation of normal distribution as *per* age of patients revealed that data are homogenous and that parameter methods (χ^2 -test, level of significance $p < 0.05$) can be used for further comparisons.

Results

Sonographic morphology of cancer in BI-RADS 5 category is of the stellate type: irregular tumor change, with hypoechoogenic, heteroechoogenic centre, hyperechoogenic border, acoustic posterior attenuation, interruption of ligaments and fascia, with removing hypoechoogenicity of subcutaneous fat tissue and thick skin (Figure 1).

Figures 1 and 2 depict ultrasound features of breast masses categorized as BI-RADS 5 and BI-RADS 4A, respectively.

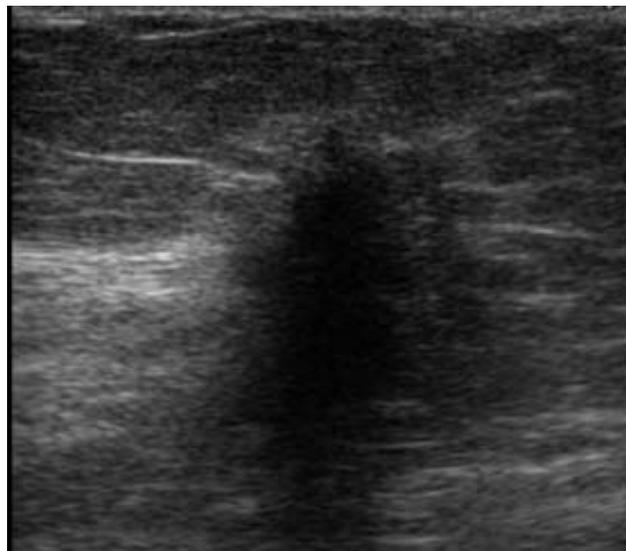


Fig. 1 – Ultrasound image of breast masses categorized as Breast Imaging Reporting and Data System (BI-RADS) 5.

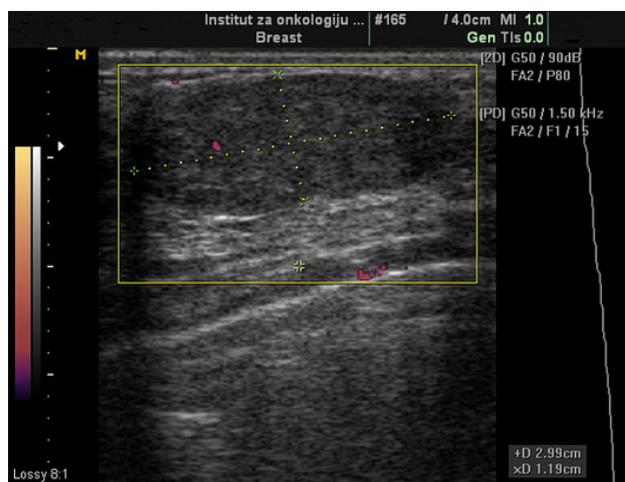


Fig. 2 – Ultrasound image of breast masses categorized as Breast Imaging Reporting and Data System (BI-RADS) 4A.

Analysis of a total number of BI-RADS categories in the group of 30 patients (Table 2) revealed a highly statistically significant difference ($\chi^2 = 18.174$; $df = 1$; $p < 0.01$), resulting from the much greater presence of BI-RADS 4 (86.7%) as compared to BI-RADS 5 (13.3%). Practically, the ratio was 6 : 1. The analysis of a total number of PH findings as compared to BI-RADS in the group of 30 patients (Table 2) also revealed a statistically significant difference ($F = 7.338$; $df = 8$; $p < 0.05$), resulting from the greater presence

Table 2
Pathohistological (PH) finding of tumors in relation to BI-RADS 4 and BI-RADS 5 categories

PH finding	BI-RADS 5 (n)	BI-RADS 4 (n)	Total (n)
Carcinoma			
<i>ductale invasivum</i>	1	6	7
<i>lobulare invasivum</i>	2	5	7
<i>tubulare</i>	0	1	1
<i>in situ</i>	1	1	2
Fibroadenoma	0	8	8
Lipoma	0	1	1
<i>Nodus lymphaticus intramammarius</i>	0	1	1
<i>Dysplasia atypica</i>	0	2	2
<i>Dysplasia fibrocystica</i>	0	1	1
Total	4	26	30

BI-RADS – Breast Imaging Reporting and Data System.

of fibroadenoma in BI-RADS 4 while each finding in patients with BI-RADS 5 was cancer.

Analysis of a total number of PH findings in the group of 30 patients (Table 3) also revealed a highly statistically significant difference ($F = 11.278$; $df = 5$; $p < 0.01$), resulting from the greater presence of cancer (56.7%) and fibroadenoma (26.7%) as compared to other types of findings, and particularly relatively rare lipomas, fibrocystic dysplasia and lymph nodes in breasts (by 3.3%).

In 6 patients with BI-RADS 4C category, PH findings were as follows: invasive ductal cancer in three patients, invasive lobular cancer in two, and intramammary lymph node hyperplasia in one patient.

In 9 patients with BI-RADS 4B category, PH findings were as follows: invasive lobular cancer in three patients, ductal cancer in two, tubular cancer (one patient), atypical lobular hyperplasia (one patient), fibroadenoma (one patient)

and fibrocystic dysplasia (one patient).

In 11 patients with BI-RADS 4A category, PH findings were as follows: fibroadenoma in seven patients, lipoma in one patient, invasive ductal cancer one patient, ductal cancer *in situ* in one patient, and ductal hyperplasia with atypia in one patient.

If PH findings assigned into two categories (benign and malignant) are compared with BI-RADS categories (Table 4) we get a statistically significant difference ($F = 6.188$; $df = 6$; $p < 0.05$), resulting from the fact that BI-RADS 4B and C (64.7%) prevail in malignant tumors, while BI-RADS 4A (69.2%) being a rather rare finding in malignant tumors (11.8%) prevails in benign tumors. It could be said that BI-RADS 4A finding is almost always related to benign changes, and all the other with malignant ones (sensitivity for BI-RADS 5 is 100.0%, for BI-RADS 4C 83.3%, and for BI-RADS 4B 67%).

Table 3
Pathohistological (PH) finding of tumors in relation to BI-RADS 4A, B, C and BI-RADS 5 categories

PH finding	BI-RADS 5 (n)	BI-RADS 4C (n)	BI-RADS 4B, (n)	BI-RADS 4A, (n)	Total n (%)
<i>Carcinoma mammae</i>	4	5	6	2	17 (56.8)
Fibroadenoma	0	0	1	7	8 (26.6)
Lipoma	0	0	0	1	1 (3.3)
<i>Nodus lymphaticus intramammarius</i>	0	1	0	0	1 (3.3)
<i>Dysplasia atypical</i>	0	0	1	1	2 (6.7)
<i>Dysplasia fibrocystica</i>	0	0	1	0	1 (3.3)
Total	4	6	9	11	30 (100)

BI-RADS – Breast Imaging Reporting and Data System.

Table 4
Benign and malignant changes in relation to BI-RADS 4A, B, C and BI-RADS 5

BI-RADS types	Pathological finding (n)		Total
	benign	malignant	
BI-RADS 4 (n = 26)			
A	9	2	11
B	3	6	9
C	1	5	6
BI-RADS 5 (n = 4)	0	4	4
Total	13	17	30

BI-RADS – Breast Imaging Reporting and Data System.

If PH findings are compared with BI-RADS findings assigned into only two gradations (Table 4) we get a highly statistically significant difference ($p = 0.002$; $p < 0.01$), resulting from fact that BI-RADS 5 (100.0%) prevails in patients with malignant tumors, while BI-RADS 4 is present in an equal number of benign and malignant tumors.

When we consider age of the patients in relation to BI-RADS findings assigned into only two gradations (Table 5) we get a highly statistically significant difference ($p = 0.002$; $p < 0.01$), resulting from the fact that patients from BI-RADS 5 group were older than 50 years of age, while only 50% of patients from BI-RADS 4 group were older than 50.

If age of the patients is compared with PH findings assigned into two gradations (benign/malignant) (Table 6) we get a highly statistically significant difference ($p = 0.032$; $p < 0.05$), resulting from the fact that 53.8% of patients from the group with benign tumors were younger than 50 years of age, while this part was only 35.3% of patients with malignant findings; accordingly they were much older.

Table 5

Age of the patients in relation to BI-RADS 4 and BI-RADS 5 categories

Age (years)	BI-RADS 5 (n)	BI-RADS 4 (n)	Total (n)
30–49	0	13	13
50–79	4	13	17
Total	4	26	30

BI-RADS – Breast Imaging Reporting and Data System.

Table 6

Age of the patients in relation to pathohistological (PH) finding of either benign or malignant changes

Age (years)	Benign (n)	Malignant (n)	Total (n)
30–49	7	6	13
50–79	6	11	17
Total	13	17	30

Discussion

Ultrasonographic evaluation of breast changes, as a method complemented to clinical examination and to either diagnostic (“symptomatic” breast) or screening mammography (“asymptomatic” breast) can identify malignancy in some cases, which would otherwise be unidentified, which particularly relates to the glandular structure of breasts because sensitivity of mammography reduces as density of glandular breast tissue becomes higher^{5,6}. When it is about ultrasound descriptors according to data in the literature, the highest objectivity and concordance in the assessment among various physicians performing examination, is for a criterion of tumor change orientation (horizontal, *ie* in parallel with skin, characteristic for benign changes, or vertical, typical for malignant changes). The least accordance is found in the assessment of change contour (very well-defined contours usually in benign changes, poorly defined usually in malignant changes) and its echogenicity (nonechogenic and hyperechogenic are benign changes, while hypoechogenic, isoechogenic changes and complex lesions can be seen in both types

of changes, but they are more suspicious of malignant nature) while shape, surrounding tissue and posterior phenomena are between these extremes⁷. According to pathohistological findings in our study, breast cancer was identified in 17 out of 30 women (56.6%), invasive ductal carcinoma in 7 women, invasive lobular carcinoma also in 7 women, tubular carcinoma in one woman and ductal carcinoma *in situ* in 2 women. Fibroadenoma was identified in 8 women (26.6%), dysplasia with atypia in two women (6.7%), while lipoma, intramammary lymph node or fibrocystic dysplasia was pathohistological finding in other patients (by 3.3%). If patients are assigned into two groups: the first one of 49-year-old patients and younger, and the second one of 50-year-old patients and older in relation to PH finding of benign/malignant change, we will get a statistically significant difference because 53.8% of patients from the group with benign changes are younger than 49 years, while only 35.3% of patients have malignant finding. This information is consistent with data in the literature stating that cancer rate suddenly increases after 40 years of age and with data for Central Serbia stating that in less than one fourth of the total number of women breast cancer was diagnosed before their 50 years of age⁸. BI-RADS 4 changes were six times more common reason for biopsy than BI-RADS 5 ($p < 0.01$) which is consistent with data from the literature. BI-RADS 4 category is a change with ultrasonographic characteristics having small (A), moderate (B) or medium (C) risk of malignancy. A supposed risk of cancer is 3–94% in this category. BI-RADS 5 is a change of ultrasonographic finding with high malignancy risk (risk of cancer is higher than 95%) and biopsy is required⁹.

Therefore, this paper proves the correlation between BI-RADS 4 and 5 categories and PH finding ($p < 0.05$). Every tumor in BI-RADS 5 category was cancer (4/4), while none of benign tumors belonged to BI-RADS 5 category. In BI-RADS 4 category, in malignant tumors, it was found that BI-RADS 4 B and C prevail (64.7%), while BI-RADS 4A prevail in benign tumors (69.2%), being a very rare finding in malignant tumors (11.8%). Therefore, it could be said that a BI-RADS 4A finding is almost always related to benign changes, primarily to fibroadenoma, and all other with malignant (specificity for BI-RADS 5 is 100.0%, for BI-RADS 4C 83.3%, and for BI-RADS 4B 67%).

A PH finding was invasive ductal cancer in one patient, then ductal cancer *in situ* in one, and invasive lobular cancer in two out of four patients with BI-RADS 5 category.

According to the literature, this is a typical ultrasonographic view of malignant tumors, with specificity for cancer up to 98%. Pathohistologically, it corresponds to cancers with pronounced desmoplastic reaction and it most often confirms invasive ductal, tubular or lobular cancer.

Ultrasonographic findings correspond to nodular tumor type: irregular, circular or oval tumor change, microlobular contours, hyperechogenic border, vertical orientation, with possible areas of microcystic degeneration (by the type of complex lesion – solid change with nonechogenic zones), without posterior phenomena or with posterior amplification of the acoustic beam. According to the literature, an ultra-

sonographic finding being nodular cancer type corresponds to dominant cellularity tumors and it is mostly found in invasive lobular cancer and invasive ductal cancer³.

Moreover, according to a new, molecular classification of breast cancers, triple-negative breast cancers [estrogen-receptor negative, progesterone-receptor negative and human epidermal receptor (HER)2 negative cancer], have mostly nodular type of expression in ultrasonographic finding with no necessary elements for a benign change¹⁰. Triple-negative breast cancer are aggressive tumors with poor prognosis, and their frequency is higher in women younger than 50 years of age¹¹.

Intramammary lymph node certainly belongs to a benign finding (BI-RADS 2). The basis of certainly benign change is visible fat tissue within lymph node hilus¹². However, in case of lymph node hyperplasia, when it crosses longitudinal diameter of 1 cm, then in atypical localization (inner quadrants) or unfavorable contrast in relation to basic structure of breasts, and accordingly its poor visualization, intramammary lymph node may simulate a malignant change^{13,14}.

The BI-RADS 4B group presents heterogeneity of pathohistological and sonomorphological characteristics by four types: nodular form (previously mentioned), well-bordered tumor with pseudocapsule, cystic tumor type and diffuse infiltrative growth tumors.

The pseudobeneign aspect of well-defined tumor with pseudocapsule implies: circular or oval shape, well-defined contours, non-homogeneous echotexture and pseudocapsule. According to the literature, this type is particularly characteristic for medullary carcinoma, when they look like cysts with thick content and acoustic amplification. The probability of malignancy in this sonomorphological type is 1–4% at more than 40 years of age³.

Structurally changed zone, without defined border, angular and dilated ductus, hypoechogenic zones with acoustic shadow are viewed in ultrasonographic finding of diffuse infiltrative growth tumor. This way of sonographic expression is most common in lobular cancer, confirmed in three patients in our group with BI-RADS 4B category. During tumor growth, three-dimensional tumor change does not develop initially, but most often focal nodularity or parenchymal asymmetry, like dysplastic changes, and therefore tumor is diagnosed in its late stage¹⁴.

Cystic cancer is cystic with intracystic proliferation (complex – semisolid, semicystic lesion) by type. According to the literature, it is a lesion with low frequency of occurrence (less than 1%)³. In our group, one patient had pathohistological finding *Dysplasia polycystica proliferativa mammae*. Four types of cystic lesions are listed in BI-RADS atlas: simple cyst, grouped microcysts, complicated cyst and complex lesion. Simple cyst belongs to BI-RADS 2 category. Grouped microcysts belong to BI-RADS 3 if they are nonpalpable, while palpable cysts are subjected to fine needle aspiration. Complicated cysts (not necessarily indicating inflamed cysts) refer to hypoechogenic lesion with other characteristics of a benign change. Nonpalpable cysts belong to BI-RADS 3 category, and palpable are subjected to fine nee-

dle aspiration. Complex lesion refers to the presence of solid and cystic component and it can belong to: intracystic papilloma, cancer, cystic degeneration of either malignant or benign tumors and it is classified into BI-RADS 4 category.

The aforementioned overlaps of sonomorphological types seen in this type of cancer with benign changes are the reason for biopsy and pathohistological evaluation, but false negative findings are possible, as well.

Sonomorphological pseudobeneign tumor type with capsule prevailed in the group with BI-RADS 4A category, while the most common PH finding was fibroadenoma.

Overlapping of clinical, mammographic and sonographic findings of fibroadenoma with malignant changes is possible. Therefore, a question remains on the algorithm of diagnostics in palpable change of clinically benign aspect, which is mammographically a type of circular, oval or lobular and well-defined shadow. In this case, ultrasonographic diagnostics is a necessary additional modality of examination, after clinical examination and mammography. If a change is of the solid type, not cystic, a finding is defined as solid tumor, with sonomorphologically benign characteristics, with low risk of malignancy (BI-RADS 4A category) and core needle biopsy of change is indicated (Figure 2). The probability of malignancy is excluded only if fibroadenoma is pathohistologically proved. Therefore, fibroadenoma is significantly present in BI-RADS 4A in this study. A common incidental sonographic finding of non-palpable solid tumors with benign aspect, with size less than 1 cm, has defined another algorithm over time, and it differs from the abovementioned algorithm so far as it is related to nonpalpable change. Namely, a retrospective analysis revealed that risk of malignancy for nonpalpable changes being sonographically a solid type and benign morphology is less than 1–2%. Therefore, the approach is sonographic monitoring in 2 years' time every 6 months, as BI-RADS 3 category, and in case of a stationary finding, it should be translated into BI-RADS 2 category (certainly benign change) after two years of monitoring, without indications for biopsy¹⁵.

Ductal carcinoma *in situ* is normally nonpalpable, subclinical change, detected by mammography during preventive examinations, primarily through microcalcifications typical for malignant changes. However, it was found in two patients with palpable change in our group of patients, as BI-RADS 5 and BI-RADS 4A ultrasound category. Ductal carcinoma *in situ* may sometimes clinically manifest as palpable resistance or nodularity. Non-specific cystic or solid lesion, not well bordered hypoechogenic change, microlobular tumor, ductus dilatation or calcifications, are present in the ultrasonographic finding. It is hard to differentiate ductal carcinoma *in situ* without typical radiologic suspicious calcifications on mammography from benign lesions only by ultrasonography, so further cytological or pathohistological evaluation is necessary¹⁶.

Conclusion

Changes poorly defined by mammography, belonging to either BI-RADS 5 or BI-RADS 4 (A, B, C) have the following characteristics according to our results: BI-RADS 4 category is

six times more common cause for biopsy than BI-RADS 5 category. BI-RADS 5 and BI-RADS 4 categories are the following pathohistological types of lesions: breast cancer (56.7%), fibroadenoma (26.7%), dysplasia with atypia (6.7%) and lipoma, intramammary lymph node or fibrocystic dysplasia by 3.3%. There is a correlation between BI-RADS 4 and 5 categories and pathohistological findings: BI-RADS 4A finding is almost always related to benign changes, primarily to fibroadenoma, and all other with malignant (specificity for BI-RADS 5 is 100.0%, for BI-RADS 4C 83.3%, and for BI-

RADS 4B 67%). BI-RADS 4 and 5 categories and age of women are related to pathohistological finding: benign changes are more present (53.8% of all benign changes) than malignant (35.3% of all malignant changes) in 49 year-old women and younger. Heterogeneity of pathohistological findings in BI-RADS 4 category with the domination of malignant changes in BI-RADS 4B and BI-RADS 4C groups, as well as only malignant changes in BI-RADS 5 category confirm necessity of pathohistological verification of lesions from these categories, particularly in women older than 50 years of age.

R E F E R E N C E S

1. Milošević Z. Newspapers mammography in the diagnosis of breast cancer. In: Nešković-Konstantinović Z, Borjović N, Vučković-Dekić Lj, editors. Newspapers in the diagnosis and treatment of breast cancer. Belgrade: Akademija medicinskih nauka Srpskog lekarskog društva, Institut za onkologiju i radiologiju Srbije; 2008. p. 41–52. (Serbian)
2. Crystal P, Strano SD, Shebarynski S, Koretz MJ. Using sonography to screen women with mammographically dense breasts. *AJR Am J Roentgenol* 2003; 181(1): 177–82.
3. Pichler E. Ultrasound breast atlas: differential diagnosis and intervention techniques. Zagreb: Školska knjiga; 2005. (Croatian)
4. Levy L, Suissa M, Chiche JF, Teman G, Martin B. BIRADS ultrasoundography. *Eur J Radiol* 2007; 61(2): 202–11.
5. Dobrosavljević A, Brković V, Vujković B, Milošević Z. Basic constitutional and reproductive parameters in optimalise application of mammography in the diagnosis of breast diseases. *Medicinski podmladak* 2004; 55: 61–3. (Serbian)
6. Milošević Z. Malignant tumors of the breast. In: Goldner B, Milošević Z, Jovanović T, editors. Mammography in the diagnosis of breast diseases. Belgrade: Velarta; 2001. p. 217–82. (Serbian)
7. Park CS, Lee JH, Yim HW, Kang BJ, Kim HS, Jung JI, et al. Observer Agreement Using the ACR Breast Imaging Reporting and Data System (BI-RADS)-Ultrasound, First Edition (2003). *Korean J Radiol* 2007; 8(5): 397–402.
8. Jovičević BA. Epidemiology and prevention of breast cancer. In: Nešković-Konstantinović Z, Borjović N, Vučković-Dekić Lj, editors. Newspapers in the diagnosis and treatment of breast cancer. 2nd ed. Belgrade: Akademija medicinskih nauka Srpskog lekarskog društva i Institut za onkologiju i radiologiju Srbije. 2008. p. 11–24. (Serbian)
9. American College of Radiology. ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas. 4th ed. Reston, VA: American College of Radiology; 2003.
10. Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. *Radiology* 1995; 196(1): 123–34.
11. Ko ES, Lee BH, Kim H, Nob W, Kim MS, Lee S. Triple-negative breast cancer: correlation between imaging and pathological findings. *Eur Radiol* 2009; 20(5): 1111–7.
12. Radisky ES, Radisky DC. Matrix metalloproteinase-induced epithelial-mesenchymal transition in breast cancer. *J Mammary Gland Biol Neoplasia* 2010; 15(2): 201–12.
13. Kinoshita T, Yashiro N, Yoshigi J, Ibara N, Fukuma E, Narita M. Inflammatory intramammary lymph node mimicking the malignant lesion in dynamic MRI: a case report. *Clin Imaging* 2002; 26(4): 258–62.
14. Tabár L, Duffy SW, Vitak B, Chen HH, Prevost TC. The natural history of breast carcinoma: what have we learned from screening. *Cancer* 1999; 86(3): 449–62.
15. Graf O, Helbich TH, Hopf G, Graf C, Sickles EA. Probably benign breast masses at US: is follow-up an acceptable alternative to biopsy. *Radiology* 2007; 244(1): 87–93.
16. Izumori A, Takebe K, Sato A. Ultrasound findings and histological features of ductal carcinoma in situ detected by ultrasound examination alone. *Breast Cancer* 2010; 17(2): 136–41.

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