wjpmr, 2018,4(2), 31-47

SJIF Impact Factor: 4.103

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

THE FULL BREAST ULTRASONOGRAPHY USEFULNESS IN THE DIFFERENTIAL DIAGNOSIS OF THE BREAST TUMORS

***Dr. Aristida Colan-Georges, MD, PhD**

Prima Medical MedLife Craiova, Pan Med Laboratories Craiova.

***Corresponding Author: Dr. Aristida Colan-Georges, MD, PhD**

Prima Medical MedLife Craiova, Pan Med Laboratories Craiova.

Article Received on 10/12/2017 **Article Revised on 31/12/2017** **Article Accepted on 21/01/2018**

ABSTRACT

Objectives: To promote and illustrate a new hierarchy of the Ultrasound descriptors in addition to the US BI-RADS recommendations, for improving the differential diagnosis of the breast tumors. **Methods:** We made retrospective analysis of 1076 examinations by Full Breast Ultrasonography (FBU), an anatomical radial scanning that illustrates the main lactiferous structures (ducts and lobules) inside the mammary lobes, completed by Doppler and Sonoelastography (SE). **Results:** The positive diagnosis of the malignant breast masses included the triad: a salient ductal connection, an incident angle of the plunging arteries, and a scoring 4 or 5 Ueno for the SE, with a sensitivity, specificity and accuracy of 88.23%, 99.62% and respectively 99.26%. The lobar and the inflammatory breast cancer (BC) demonstrated salient new-formation vasculature associated with a raised strain. The benign lesions whatever the shape, orientation, posterior effects etc., illustrated an absent/reduced vasculature with an acute plunging angle, and a score BGR, 1, 2 or 3 Ueno. **Conclusions:** FBU represents an improved Ultrasound technique for screening / diagnosis allowing a whole breast mapping, for all patients, using the US BI-RADS lexicon but related to the lobar anatomy centered by the ductal-lobular tree. The integrative concept eliminates the limits of Doppler and SE as independent tools.

KEYWORDS: Breast anatomy, breast tumors, breast Ultrasonography, differential diagnosis, radial scanning, Sonoelastography.

INTRODUCTION

The differential diagnosis in the Radiological and Imaging diagnosis of the breast diseases presented in the literature is still not very well developed and it has less significance, thus the breast biopsy remains the final tool of diagnosis. That is due to the less specific descriptors of the breast findings, by one hand, and to the non-anatomical scanning and interpreting of the breast, neglecting the normal radial lobar architecture, by the other hand. Indeed, the distinct mammary lobes are well known since 1840, when Sir Astley Paston Cooper injected with different colored waxes the main galactophorous ducts and demonstrated the overlapped discrete lobar trees. Many anatomists since nowadays emphasized in vain the breast anatomy,[1] but the Mammography and consequently its complementary methods represented by the US and MRI are still using terms such as *"fibro-glandular tissue", "asymmetry"* and *"distorted architecture"*. None individual ultrasonographic descriptor, such as shape, orientation, borders, internal structure and posterior effects, included in the US BI-RADS assessment, can accurately predict a benign or malignant lesion; that is the reason the studies of the results of the recent *US Computed Aided Diagnosis (CAD)* were unsatisfactory.[2,3] Mammography is considered the first-intention examination, but it cannot differentiate the solid from the fluid lesions, and the microcalcifications used as indirect sign for the positive and the differential diagnosis of BC have low specificity, while their absence cannot completely exclude a breast malignancy. Digital mammography seems to improve the detection of the BC with 27 % in woman under 50 year-old, comparing with the analogue technique, according to the American College of Radiology Imaging Network (ACRIN) and other authors; [4; 5] however, all screening methods are intended in the diagnosis of a BC as early as possible, neglecting the benign or the premalignant lesions. In the meantime, there are not equivalent assessments to the screening BI-RADS for the symptomatic patients, which are examined without standardized protocols, with some complementary imaging techniques used before the mandatory final biopsy, determined by the lack of differential diagnosis.

The development of the *Automatic Breast Volume Scanning (ABVS)* was intended to be used as screening test because it is exploring the whole breast, with more objective acquisitions and with possibilities of CAD. However, the orthogonal planes remain non-anatomical related to the lobar architecture, the normal breast

parenchyma represented by ducts and lobules is neglected, and the coronal plane (plane C) has not a proved relationship with the nipple; nevertheless, some malignancies could not be differentiated from the benign masses only in the gray scale offered by the ABVS, the multifocal cancers could not be differentiated from the multifocal type, etc.

MRI has a sensibility superior to any classical method in use, especially in detecting the multiple BC, but without possibility to differentiate the multifocal from the multicentric lesions, too. Because of lack of specific descriptors useful in the differential diagnosis, the specificity of the breast MRI is low, even using the contrast enhancing curves, which are operator-dependent regarding the selection of suspect areas, thus the number of biopsies is still raised. The protocols of breast MRI are not standardized because of different manufacturers' solutions of acquisitions, and the resolution is not performing for the most first 5mm breast cancers. The prone position distorts the breast shape (Figure 1) and it is not useful in the precise location of the lesion, to be compared with the US detection or with the intraoperative supine lying. Consequently, some authors recommend a repeated breast MRI in the supine position before the surgical treatment, difficult to perform with all machines. The paramagnetic contrast agents in use have controversial side-effects; there were proved the remnants of the paramagnetic contrast agents in some areas of the brain long-time after injection, even in normal brain with intact blood-brain barrier, in a proportional quantity with the injected dose, thus the repeated examinations by breast MRI should be restricted.[6]

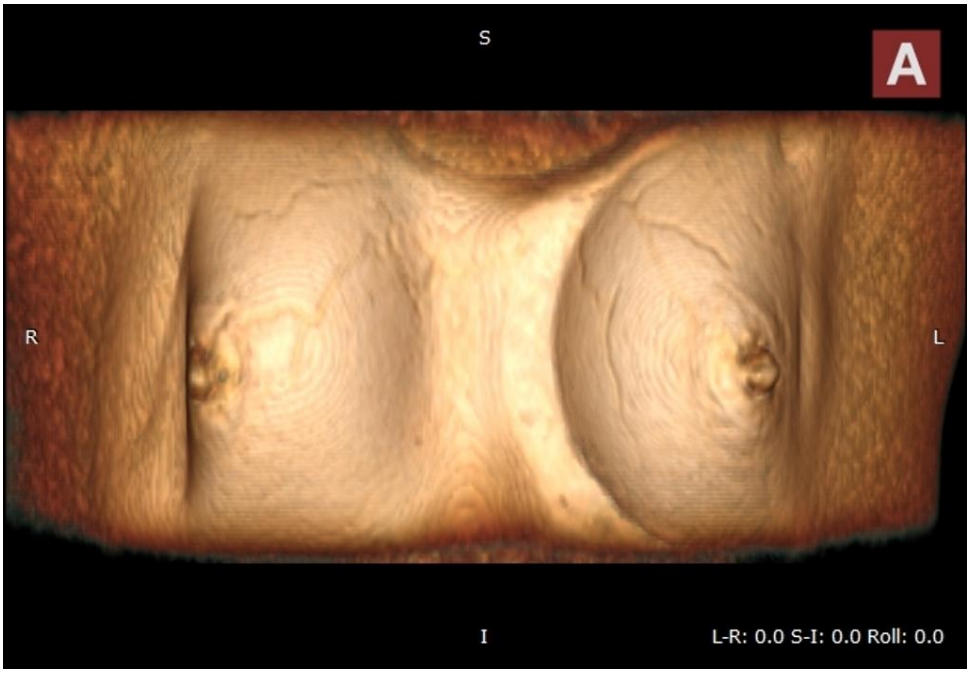

Fig. 1: MRI 3D reconstruction demonstrates breasts distortion due to the prone position and to the compression by the breast antenna, even if small volume of tissues.

AIMS OF THIS PRESENTATION

The anatomical US based on the radial scanning with lobar interpreting, upon the Ductal Echography (DE) technique of Teboul,[7] completed by Doppler and Sonoelastography (SE) realizes the comprehensive concept of the Full Breast Ultrasonography (FBU), which is proposed to reduce the false-positive and the false-negative diagnosis.[8,9] This paper describes and illustrates this new concept of US and promotes a new hierarchy of the US descriptors in addition to the US BI-RADS recommendations, to be used in the differential diagnosis of the breast tumors.

MATERIALS AND METHODS

We have made a retrospective analysis of 1076 FBU performed between February 2015 and April 2017, used as screening or diagnostic examinations, involving 720 patients of both sexes, aged 5 – 79 year-old. In our country, similar to many others, there is not any national screening for BC, but many centers promote a private screening. In this study, 106 patients had two or more FBU as follow-up examinations (high risk patients, or after treatment of breast conditions either benign or malignant), and their final diagnosis was based on the comparison of their results. In this subgroup, a significant number of 70 FBU examinations were performed as oncological follow-up during or after BC complex treatment. The majority of patients who had a unique examination (614/720 patients) were included in the study based either on a reliable normal/benign aspect in FBU (assessed with US BI-RADS 1, respectively US BI-RADS 2), or on a benign-type pathological report.

We used a basic US platform from Hitachi EUB 8500, and alternatively a GE Voluson E8 machine; we used a

long linear probe for the radial breast scanning with a water-bag device completed by a usual short linear probe with higher frequency (Hitachi) or a multi-frequency long transducer with virtual convex acquisitions and possibility of panoramic views (GE Voluson); both machines allowed scans of high resolution, with sensitive Doppler for the small parts dedicated to the breast and a qualitative Real-Time SE (strain SE) upon the Ueno (Tsukuba) scoring.[10,11] In addition, the Hitachi machine allowed a quantitative SE represented by the strain ratio calculated as a fat-to-lesion ratio (FLR), with a cut-off value established in previous studies as 4.70.[8]

We considered, in addition to the classical descriptors upon Stavros [12,13] and recommended by the 2003 and 2013 BI-RADS, [14,15] a triad of descriptors for the positive and the differential diagnosis of the BC:

a. **The relationship of the anatomical findings with the ductal-lobular tree,** mandatory for the inclusion in the breast glandular lesions set;
b. **The salient general (diffuse) or local (peripheral or intralesional) vasculature demonstrated by Doppler techniques,** with an incident angle of the plunging artery for the malignancies (the artery runs directly towards the core of the lesion) and an acute angle for the benign masses (the known arcuate course, significant for a slow development);
c. **And the strain of the region of interest evaluated by the real-time qualitative +/- quantitative SE,** with a scoring BGR, 1, 2, or 3 Ueno for a benign assessment and a 4 or 5 score Ueno for the diagnosis of the malignant lesions.

Because the DE depicts and describes the breast architecture using the anatomical elements of tinny size, ranged over 0.4mm, it is able to analyze the thickness of the lactiferous ductal walls or the lobular changes. Being accepted in the literature the ductal carcinoma represents approximately 80% of cases of BC, and the lobular carcinomas about 15% cases, we thought logical to include the *relationship of the anatomical findings with the ductal-lobular tree (present or absent)* as the first descriptor of any breast finding. This is easy to demonstrate in the dense breast because of the salient thicker ducts, while the dense breast is difficult to examine by Mammography; moreover, the ductal connection is essential to be demonstrated in the fatty breast, because the BC usually is hypoechoic similar to the fatty lobes delimited by the Cooper ligaments, and this ductal connection makes the differential diagnosis. In addition, the detailed anatomical radial scanning allows the precise localization of a lesion in *the terminal-ductal-lobular specific unit (TDLUs),* the site mentioned by the most pathologists as the starting point development of the BC and of many benign findings.[16,17,18] Its location is easy to demonstrate by the DE at the intersection of the main radial ductal axes with the Cooper's ligaments, according to Teboul.[7]

The Doppler assessment was reconsidered in the Fifths Edition of Breast US BI-RADS,[15] but still with a limited recommendation and an under evaluated interpretation and valorization. We searched for *the salient vasculature* in all cases, depicting the underlying vasculature and the focal abnormal increased Doppler signal that was characterized by: the number of vessels in relationship with the lesion's size, the orientation (peripheral or centripetal with an acute angle of the plunging artery for the benign lesions and with an incident angle for malignant masses upon Kujiraoka, Ueno et al. [19]); the enlargement of the vessel's diameter with tortuous course and eventually associated aliasing due to the turbulent flows were suggestive for malignancies.

Due to the multiplicity of simultaneous lesions, benign with/without malignant aspects associated in the same breast in the most cases, we used routinely *the SE for the differential diagnosis* both for the breast findings and for the satellite lymph nodes; the SE was applied always as a complementary technique of diagnosis, and we related its results with the Doppler findings (Figure 2).

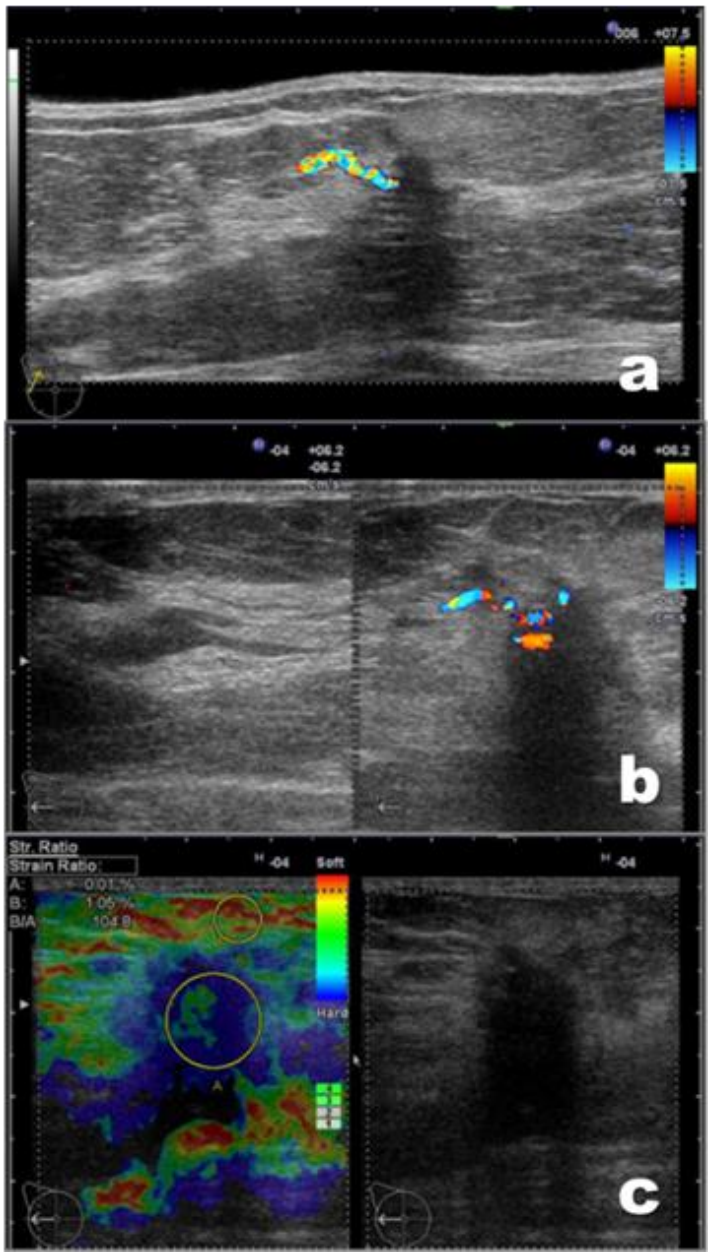

Fig. 2: Radial ductal US, with the nipple in the left-upper corner of the screen illustrates in R: 9:00 a typically malignant breast mass upon the US BI-RADS with demonstration of the three descriptors added by the FBU: the ductal connection, the incident angle of the plunging artery (a, b) and a score 5 Ueno with a raised strain ratio (c).

When there were discordances in the characterizations benign/malignant between Doppler and SE, the final FBU assessment was based on the Doppler aspect as the most specific descriptor for the breast masses, while the SE allowed the differential diagnosis in the diffuse, extended breast changes: lobar cancers, DCIS, breast edema and in the atypical lesions.[20]

The final US results were classified upon the US BI-RADS assessment, adding these three descriptors mentioned above, and the accuracy of the diagnosis was verified by the cytological-pathological reports, the microbiological tests and antibiograms of the fine-needle aspiration, of the nipple discharge (spontaneous or squeezed), and by the clinical-imaging follow-up examinations.

It was not the aim of this study to analyze a comparative diagnosis by different techniques of examination such as Mammography or MRI, but some cases were selected for illustration as additional diagnostic tools.

RESULTS

The distribution of cases upon the age and the US BI-RADS assessment are illustrated in the Chart 1.

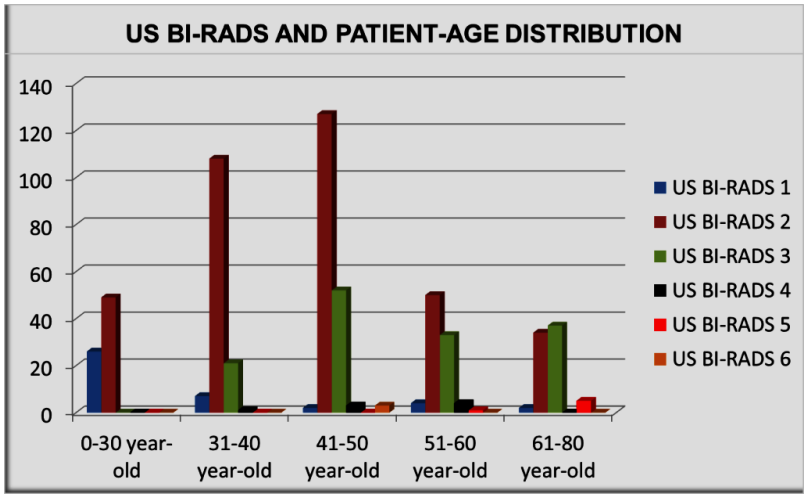

Chart 1: US BI-RADS categories and patient-age distribution.

The certain benign cases with US BI-RADS 1 and 2 categories represented 5.6% (60/1076) and respectively 68.0% (732/1076), almost ¾ of cases, usually clinically symptomatic, mostly presenting some secretory-type findings including different stages of chronic secreting galactophoritis and various types of fibro-cystic changes, from small, rare lesions to nodular fibro-micro-cystic dysplasia (FMCD) and from huge (50-80ml), few cysts to the Reclus disease. The duct hyperplasia and adenosis were rarely found, but when present in postmenopausal patients represented an alarm signal for an increased probability of an associated BC. The fibroadenoma, as typical benign finding (Figure 3), was differentiated from the inspissated cysts, from the FMCD that were more frequent and from the atypical BC that was very rare. Indeed, BC was usually found associated with various aspects of breast dysplasia that could obscure the malignancy in the usual radiological-imaging exams.

The 3rd category US BI-RADS represented 246 FBU (22.9%) and was found in all age-groups after 31 year-old, with a maximum incidence in the interval 41-50 year-old; we included the 70 follow-up examinations after BC treatment that did not present any suspicious findings, but their history raised the risk of recurrences (recidivate, metastasis, metachronous BC).[21]

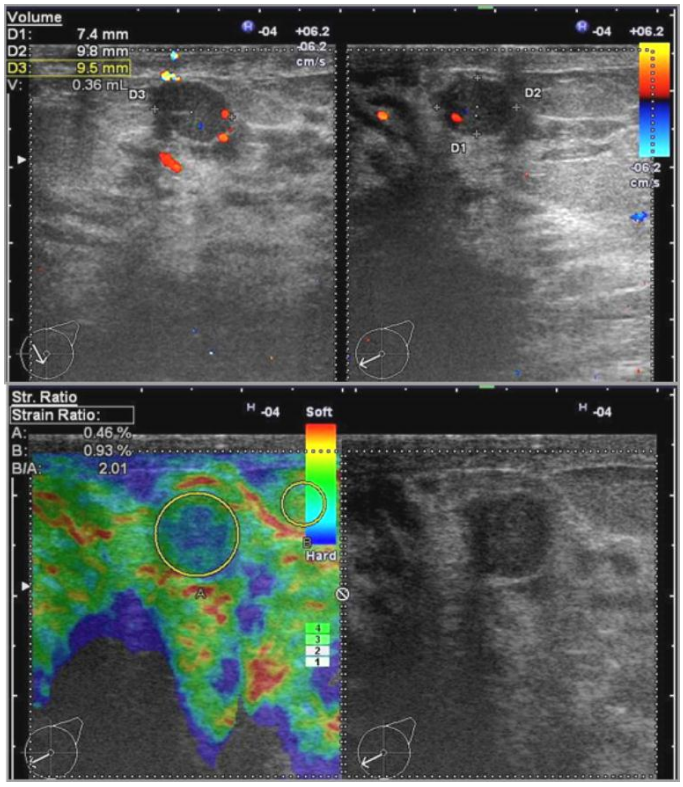

Fig. 3: Radial and antiradial high resolution US illustrates at L: 8:00 a typically benign infracentimetrical mass upon the US BI-RADS and with the three descriptors highlighted by the FBU: the ductal connection, the thin peripheral new-formation vasculature (upper) and a score 3 Ueno with low strain ratio (behind).

The 4th US BI-RADS category (16 examinations/1.5%) had a maximum distribution between 41 and 60 years, while the 5th category (12 FBU/1.1 %) was mostly diagnosed after 60 year-old. That means the doubtful cases (BI-RADS 4a and 4b) were found in the premenopausal and perimenopausal women, with dense breasts by one hand, and usually with an initial stage of development of BC by the other hand, represented by small tumors less 10mm that do not illustrate the most malignant descriptors upon the US BI-RADS assessment (less tall, less/ absent acoustic shadowing, more round with homogeneous texture, etc.); in these cases the FBU précised the salient incident angle of the plunging artery, whatever the SE with a score 2, 3 or 4 Ueno (Figure 4).

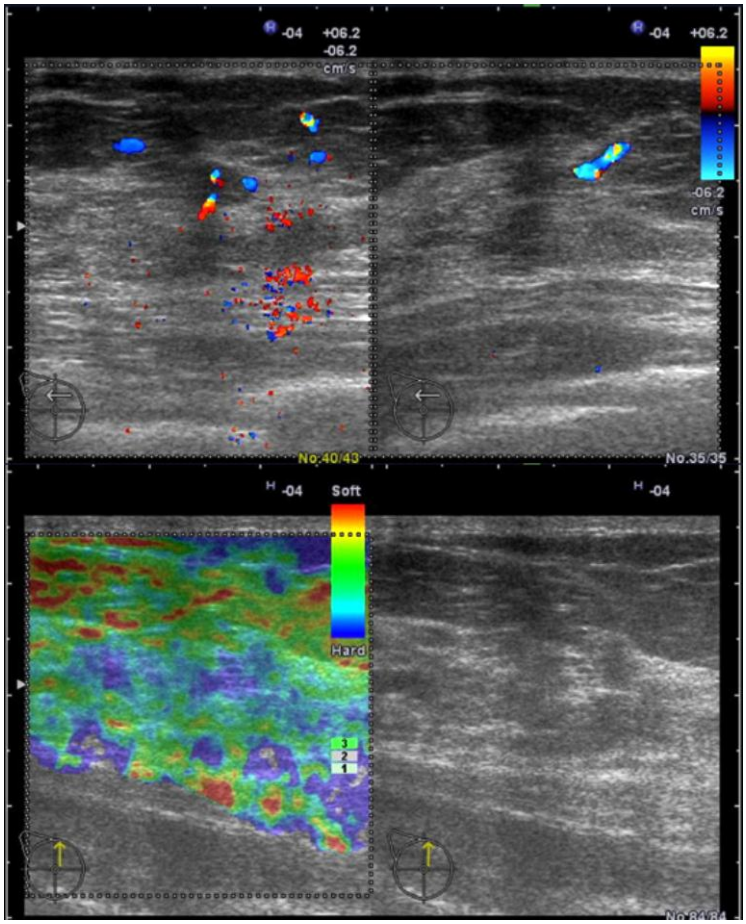

Fig. 4: FBU in a less 5mm BC demonstrates the triad: ductal connection, incident angle and increased stiffness.

From all 1076 examinations, we had assessed 34 positive for malignancies (3.16%), including the US BI-RADS categories 4, 5 and 6; from them 4 cases were false-negative, with a sensitivity of 88.23%, and 4 cases of false-positive, with a specificity of 99.62% and an overall accuracy of 99.26%. The false-positive diagnoses were related to the over assessment of the chronic breast infections associated with complex dysplasia including the nodular FMCD (3 patients), or to other inflammatory processes associated to a recent biopsy (1 case). Indeed, the FMCD represents the greatest mimicker for all techniques of diagnosis, Mammography, MRI, SE (Figure 5 and Figure 6).

The false-positive cases presented some features of malignant-type upon the US BI-RADS assessment, an increased strain or multipolar new-formation vasculature, without a categorical incident angle of the plunging artery, and were initially assessed BI-RADS 4b or 5 categories; from them three patients refused any interventional procedure and received conservatory treatment followed by a short-term repeated examination after 3 and 6 month interval, with a final assessment of BI-RADS 3 category, confirmed by breast MRI, while a single patient had conservatory surgery because of progressive evolution and the pathological report described FMCD associated with simple hyperplasia, metaplasia and lymphocytic stromal infiltration.

The 4 false-negative diagnoses were initially wrongly included in the US BI-RADS 3 category, and the short-interval follow-up examination demonstrated in 3 cases in the same quadrant and at the same radius a progressive increasing of the strain and a definitely new-formation vasculature with an incident angle, thus their assessment was changed in the 4c or 5 US BI-RADS.

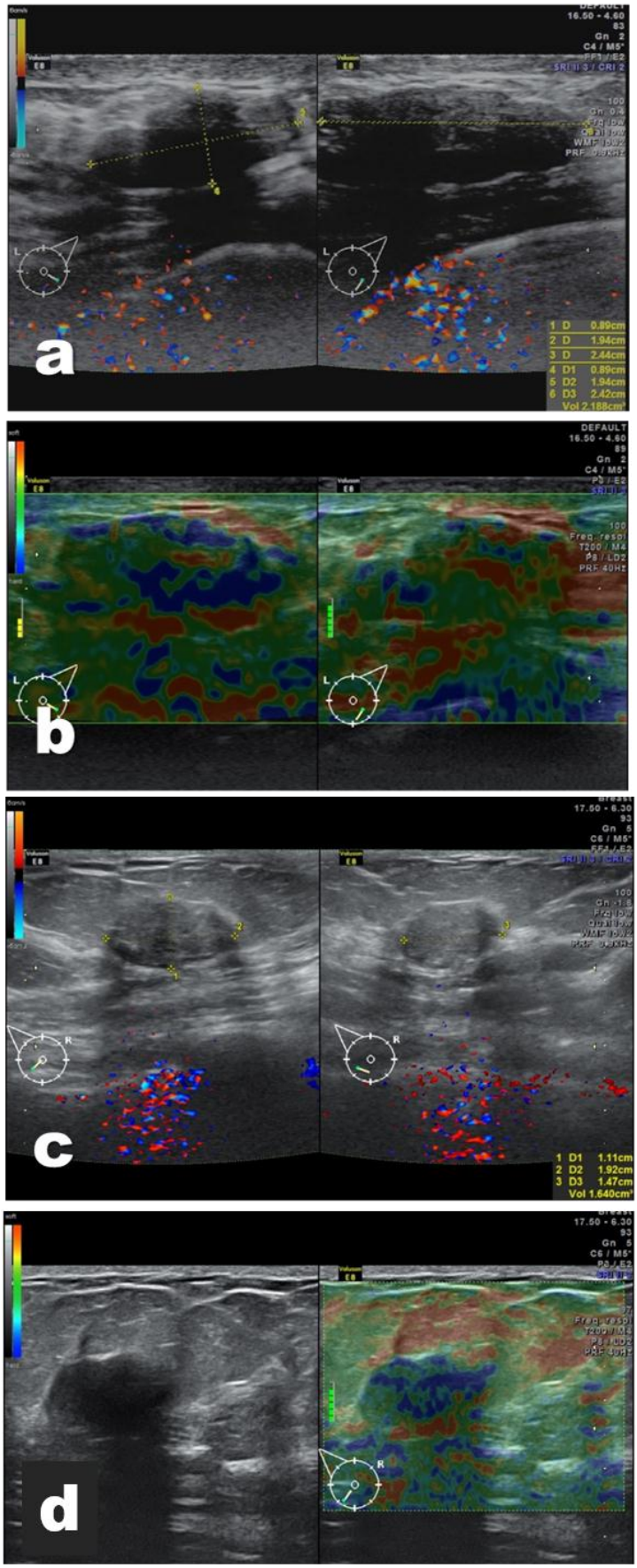

Fig. 5: Multicentric breast masses exemplified in L: 4:00 (a, b) and R: 7:00 (c, d) with benign or borderline aspect in the classical US, in a patient of 44-year old: the BGR- summation scoring and the unapparent new formation vasculature were the criteria for positive diagnosis of nodular FMCD.

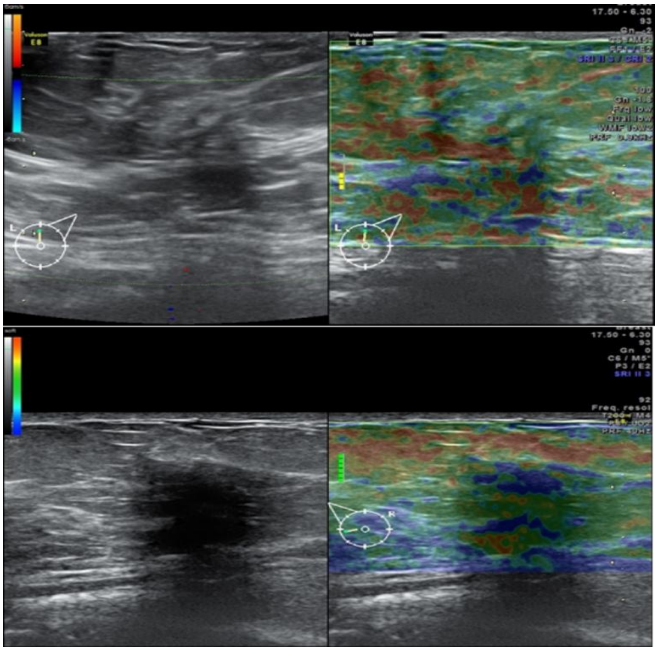

Fig. 6: Differential diagnosis of malignant-type aspect of multicentric breast masses in the classical US, in a patient of 62-year old: the BGR-summation scoring and the unapparent (reduced) new formation vasculature confirm the nodular FMCD, "the great mimicker".

From all, 3 cases performed biopsy and conservatory surgical treatment, confirming ductal carcinoma in situ (DCIS) associated with invasive ductal carcinoma (IDC) (two patients) and the third an atypical BC type medullary carcinoma with rapid evolution that presented a sentinel node at 6 months interval follow-up (Figure 7); the patients' age was not correlated with the diagnosis, perhaps due to the small number of cases. The forth case false-negative represented a follow-up examination of the BC with conservatory surgery 17 years previously, followed by complex treatment, with annual follow-up examination, which developed BC metastases in skin, bone and pleura in 4 months interval after the last FBU; despite the absence of any recurrence in the breasts, we considered the case as false-negative because of a sternochondral joint metastasis of the second homolateral rib that should be included in the volume to be explored by US and was lately detected. Despite unusual protocol, we recommend to explore by US all the anatomical structures, including the pleura and the subpleural lung in the area of interest.

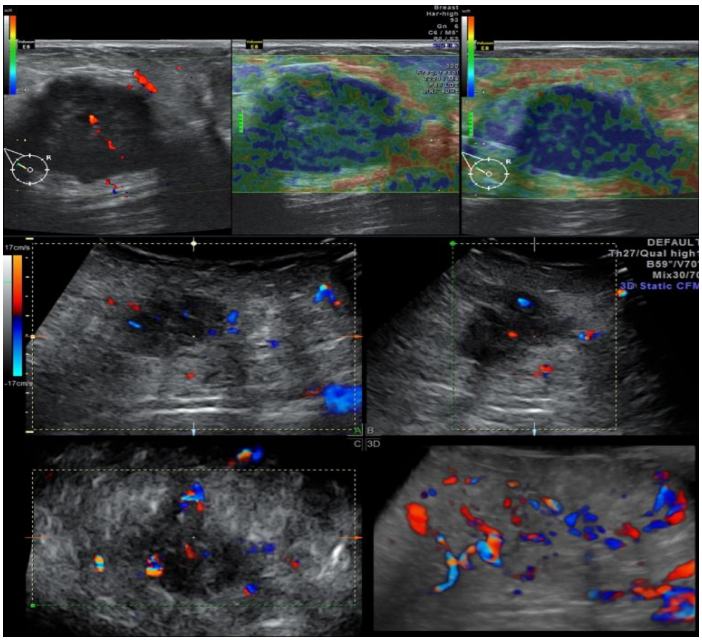

Fig. 7: FBU in a pseudo benign mass in a patient of 38-year old upon the BI-RADS criteria, except the angular borders; the SE of score 4 Ueno is suspect, an incident angle of the plunging artery is salient, but the 3D color Doppler acquisitions better demonstrate the multipolar nourishing vessels, suggestive for the malignancy.

In the subgroup of 30 FBU of true positive, we diagnosed 2 cases of DCIS from which a patient after incomplete surgical treatment by quadrantectomy, 3 cases of lobar-type diffuse BC from which one patient with false-negative diagnosis on Mammography, classical US and suspect breast MRI (Figure 8; Figure 9), 1 case of a malignant tumor in a 4 months pregnancy, with an accelerated development and a cancer in a breast-feeding woman, 6 months after delivery (Figure 10).

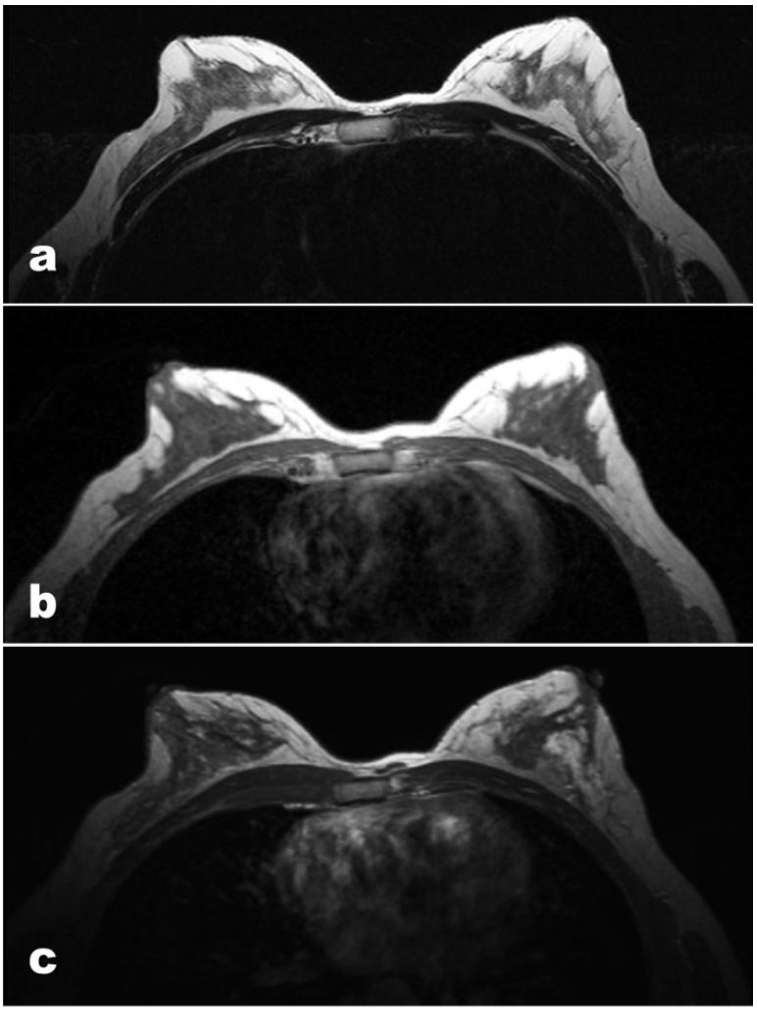

Fig. 8: Breast MRI in a patient of 40-year old: the axial scans in T2 weighted imaging (a), T1 native (b) and T1 Fat-Sat with contrast (c) demonstrate unspecific enhancement with lobar shape in the left upper-outer quadrant, with inconclusive analytic curves (not shown).

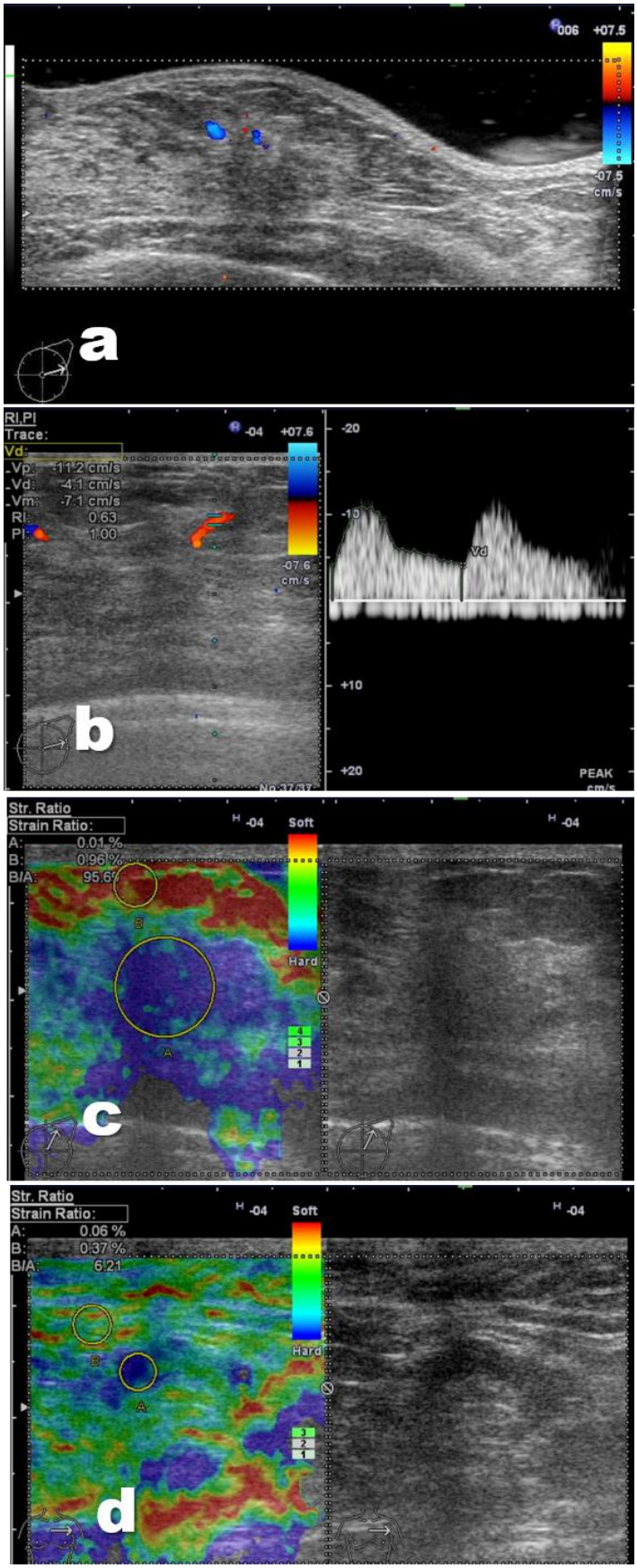

Fig. 9: The same case: FBU demonstrates in L 1:00-2:00 an unspecific isoechoic mass, with moderate acoustic shadowing, diffuse borders, but presenting the triad of ductal connection, incident angle and a sore 5 Ueno, conclusive for infiltrative BC (a, b, c). The partial involvement of the axillary sentinel node is demonstrated by the SE (d).

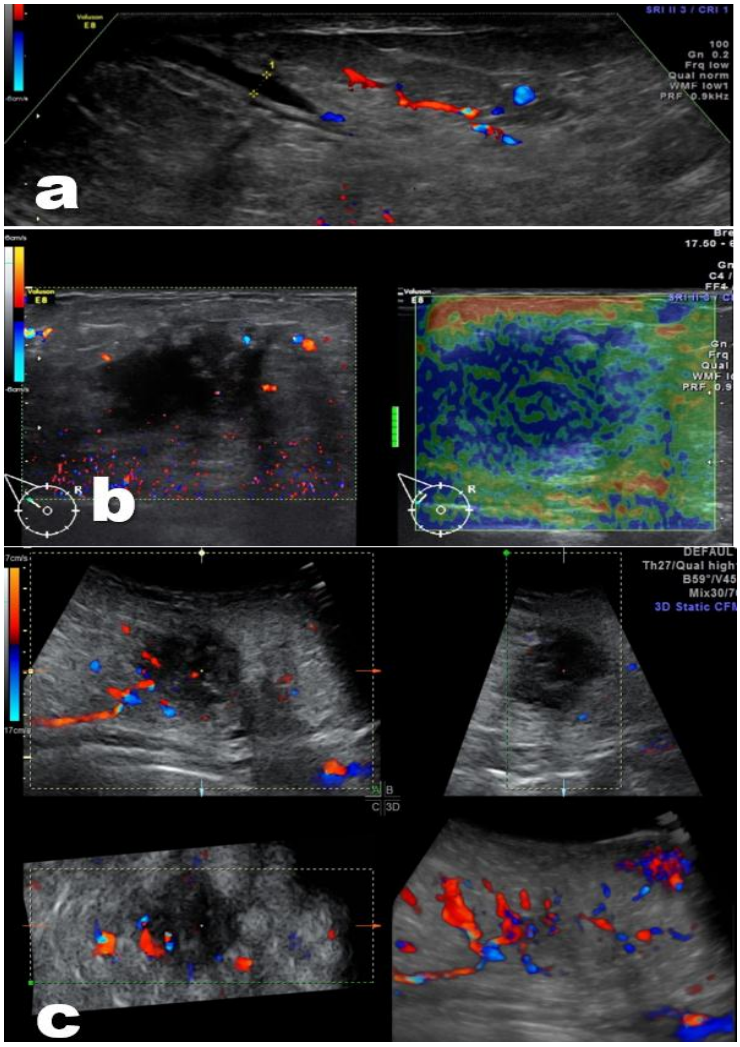

Fig. 10: FBU with 3D Doppler aspect of an atypical BC without acoustic shadowing in a lactating breast of a 46-year old patient with assisted fertilization: milky duct (a), the suspect mass at R: 10:00 with scoring 5Ueno (b) and the 3D Doppler demonstrating the incident angle of the plunging arteries (c).

DISCUSSIONS

As novelty, the 2013 US BI-RADS assessment stated a better role of the techniques of Doppler and SE, but with simplified characterization: absent, in rim, internal. [15] Doppler assessment is used for the evaluation of the new formation vessels in solid tumors, allowing the differentiation of the benign from the malignant masses. The prior 2003 US BI-RADS added the diffusely increased vascularity in the surrounding tissue. [14] For the benign lesions they were assumed less than 3 vascular poles, peripheral vessels with arched course, "in basket orientation", with few, thin internal branches or without salient Doppler signal; for the malignant masses were demonstrated more vascular poles, concordant with the tumor size, enlargement of the vessel diameter compared with those in the adjacent normal breast area, and the intratumoral arteriovenous shunts that give rise to flow detected as high-velocity signals, with aliasing similar to other cancers (thyroid, primary hepatocellular and renal cancer). [15] The intratumoral micro vessel density is considered an important prognostic marker of survival in BC. The use of contrast-enhanced US (CEUS) may increase the sensitivity and specificity to 100% in the differential diagnosis benign/ malignant of primary breast lesions according to some authors, which found breast CEUS significantly more accurate for the assessment within 2 mm of pathologic tumor size than other techniques.[22,23]

In our experience, all these vascular descriptors were useful in FBU in the differential diagnosis of the benign from the malignant breast lesions, but they are somewhere subjective; in addition, the anatomical scanning of the DE used the vascular assessment especially in demonstrating the multifocal ductal carcinoma with intralobar distribution by intraductal spreading following the lowest intraluminal pressure as it is already presented in the literature.[24] We found the number of the salient vessels and their size and velocity proportional with the main tumoral size, and decreased according to the size of the secondary (the nearest) or tertiary (distant) malignant foci, while the complementary SE proved the "hardened" connection between the disseminated lesions (Figure 11).

Our results confirmed one of the most important descriptors, objective and with pathognomonic role in the differentiation of benign from the malignant breast lesions: *the incident angle of the plunging artery* described by the above mentioned Japanese authors. Indeed, no cancer type focal, multifocal or multicentric was found without at least one vascular pole with incident angle of the plunging artery, thus the scanning in the radial and antiradial plane is mandatory; as exception, the lobar and the diffuse cancer demonstrated diffuse increased vasculature that highlighted the pathological findings.

In the cases with an unspecific diffuse increased vasculature the differential diagnosis with hyperprolactinemia, breast feeding, acute mastitis or the cardiac failure is reinforced by the SE in addition to the clinical data.

The incident angle was present in up to 99% cases of malignant masses, but absent in all benign findings. For comparison, power Doppler and spectral analysis have no contribution to US BI-RADS according to most studies, because of a significant decrease in specificity (around 52.7%-72%), positive predictive value (around 60%) and diagnostic accuracy (74.4%) and an increase in biopsy rate.[25,26]

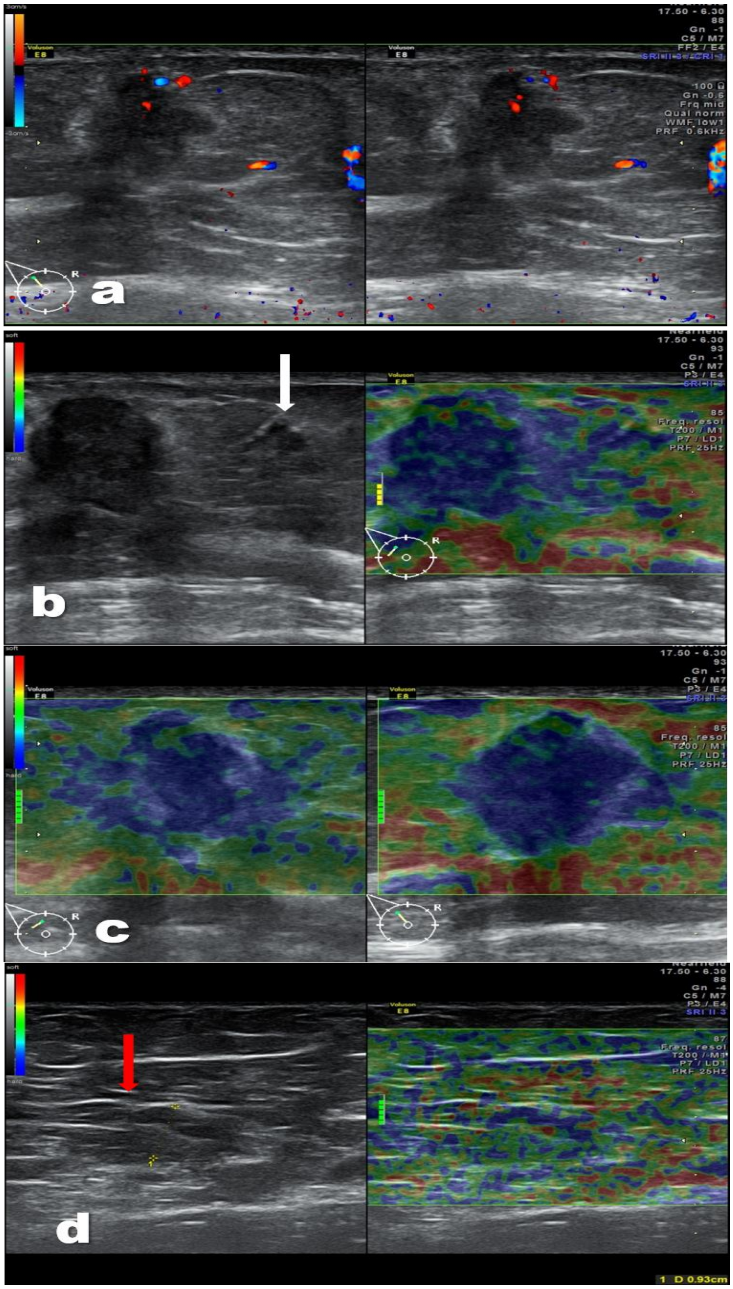

Fig. 11: FBU in multifocal BC in a menopausal woman of 56-year old with fatty breasts (a): the SE demonstrates the malignancy of the secondary millimetric lesion (white arrow) and its connection via the ductal way with the main tumor (b, c), and helps in detection of the axillary sentinel node (d – red arrow).

The machine performances, gain and the dedicated application selected from the menu are very important in quantifying the Doppler signal (Figure 12).

The Breast SE, despite the EFSRUMB guidelines, [27, 28] is still unstandardized because of different manufacturers and of various scoring systems; this is the reason two consecutive follow-up SE performed with different systems may be impossible to compare for any benign or malignant evolution of a breast lesion.

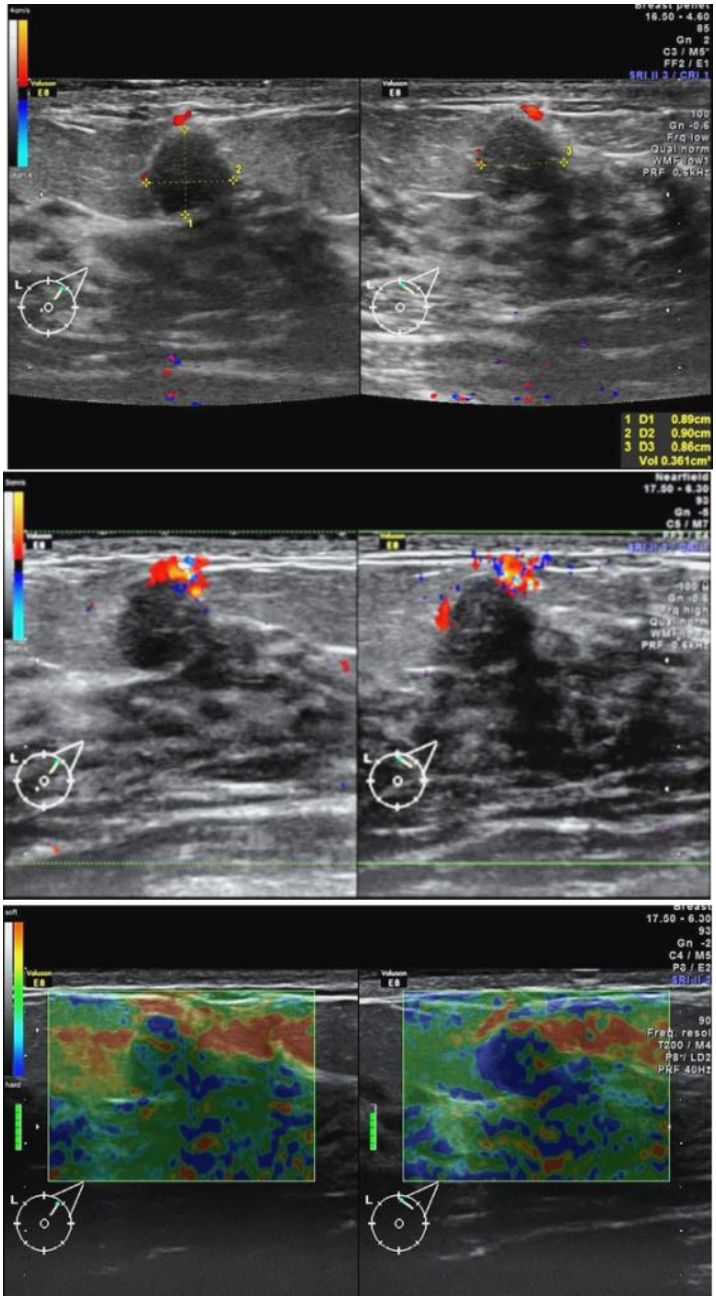

Fig. 12: Doppler sensitivity: for this lesion, with the same transducer, the sensitivity for "Breast" menu is inferior to the "Nearfield", but both demonstrate a benign mass, according to the BGR-summation score (final US BI-RADS 3 assessment).

Based on the breast anatomy includes the superficial fatty layer and the subjacent glandular structures inside the mammary lobes, and on the sonoelastographic comparison of the strain of different structures, it is logically to compare the lowest strain of the fat with the normal or abnormal mammary glandular structures; we thought the reliable way to compare them is using the strain SE, which we chose because it is applied parallel with the axe of the ultrasound waves, on the vertical axe, with simultaneous evaluation of the breast layers; as opposite, the Share Wave Elastography (SWE) that is useful in comparing the stiffness of a lesion with the surrounding tissues inside an organ, more homogeneous, such as liver, is based on the waves that are propagated

horizontally, incident to the direction of the ultrasound waves, and the comparison between the fatty layer and the breast glandular structures (the mammary lobes) is compromised. Thus, the results of the SE published in the literature are discordant, but the two techniques are not equivalent. SWE evaluates the stiffness of the surrounding tissues of the tumor, based on the changes in the speed of the shared waves; thus, the core of a breast malignant lesion appears softer than the periphery, representing the differences between the malignant tissue and the surrounding stromal reaction. In those cases of breast cancer without stromal reaction or in benign large scars the SWE has lower accuracy than the strain SE because of the neglecting of the fatty stiffness comparison (FLR). The SWE in combination with US BI-RADS has very good sensitivity of 100%, and a negative predictive value of 100%, but a low specificity 61% and positive predictive value 82%, which prove the unsatisfactory differential diagnosis implying the mandatory final biopsy.[29] However, the strain SE upon the Ueno (Tsukuba) scoring in our experience was performing as an objective technique, with comparable results on different machines with different operators; thus, it could be used in the follow-up examinations with good assessment of the evolution. The Real-time SE is admitted to be correlated with the US BI-RADS assessment, but surprisingly, the 2013 US BI-RADS recommends SE "with prudency, only if positive results".[15]

The sensibility of the SE was quite high in our practice for signaling: infracentimetric cancers that do not demonstrate the malignant descriptors upon Stavros and BI-RADS, sentinel satellite lymph nodes, local recidivism and malignant scars. SE in malignant less vascularized lesions is more sensitive than breast contrast MRI; it could halve the number of unnecessary biopsies,[30] and the characterization of the satellite lymph nodes combined to their Doppler evaluation is superior to any other non-invasive techniques and reinforces the diagnosis of malignancy in less specific cases (Figure 13). However, the diagnostic value of the SE alone must not be overestimated, because of the low specificity for the scoring 4 and 5 Ueno, found in malignant lesions as well as in benign ones such as scars, sclerosing adenosis, suture granulomas, etc., which demonstrate benign-type vasculature.

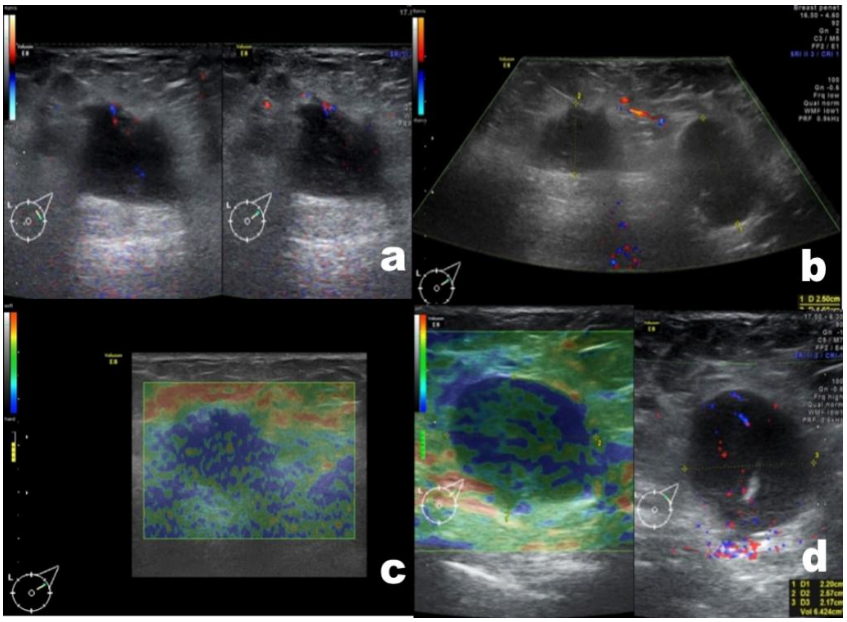

Fig. 13: Atypical BC in a 69-year old woman, with a lesion similar to the nodular FMCD at L: 2:00, but with a discreet sign of the incident angle of the plunging artery (a, b), a score 4 Ueno (c) and a satellite intra-mammary lymphadenopathy that demonstrates a new vascularization in the thickened, stiffened node cortex (b, d).

Table 1: The differential diagnosis according to the new triad of descriptors used by FBU added to the US BI-RADS, compared with the standard approach.

BREAST MASSES / DESCRIPTORS	TYPICAL MALIGNANT	TYPICAL BENIGN	PSEUDO-BENIGN (Atypical BC; less 5mm cancer)	PSEUDO-MALIGNANT (FMCD, scars, sclerosing adenosis)	NON-PARENCHYMAL breast lesions (Phyllodes, lipomas, neurinomas, lymphoma, metastases...)
Ductal connection	Present	Present	Present	Present	Absent
Incident angle of the plunging artery + **Increased new-formation vasculature**	Present	Absent	Present	Absent	Absent/Present
Sonoelastography scoring	4, 5, 6	1, 2, 3 and BGR	2, 3, 4, 5, 6	3,4,5 and Summation-type BGR	Any score 4, 5 in malignancies
Classical US BI-RADS descriptors (shape, orientation, internal structure, posterior effects, calcifications, asymmetry, etc.)	Some malignant-type descriptors	Some benign-type descriptors	Some benign-type descriptors	Some malignant-type descriptors	Any descriptors

FBU improves the differential diagnosis of the BC because of integration of *the ductal anatomical connection* with *the vascular findings* and *the SE scoring* (Table 1). This integration of the SE used as an adjunct to the standard gray-scale morphologic US and to the color Doppler was already recommended by some users of the classical US, for increasing the accuracy; but in the standard US approach the connection of the galactophorous duct with the lesion is not demonstrated and remains misunderstood.

For the solid findings such as a non vascularized fibroadenoma with hypoechoic aspect the SE may have a score 2 or 3 Ueno, while an atypical carcinoma type mucinous, medullary or papillary cancer illustrates benign 2D US features, usually with increased new formation vasculature of malignant-type of the plunging artery and a score 4 Ueno. The overall accuracy of the FBU was in our experience around 99.26%, while the false-results of the biopsies may represent up to 25%.[31]

CONCLUSIONS

In the worldwide practice, the absence of a pathognomonic descriptor or of an association of descriptors with high accuracy for the positive and the differential diagnosis of BC required the use of multiple complementariness techniques, with unsatisfactory results, including CAD diagnosis, followed by routine biopsies. FBU realizes a whole breast mapping, of all patients, for screening or symptomatic indication, using the well-known lexicon US BI-RADS, but related to the lobar anatomy centered by the ductal-lobular tree. The differential diagnosis of the abnormal findings is more accurate than any other techniques reported in the literature, avoiding unnecessary irradiation and biopsies or other more expansive additional techniques of examinations, and it is based on the radial scanning with a triad of descriptors: *the ductal connection* (present or absent), the *angle of the plunging artery* (*incident angle for malignancies, acute angle for benign structures)* and *the strain evaluation* by SE. This concept could be applied with the ultrasound platforms in use, but requires more training of the operators with respect to the breast anatomy. Some multicentric studies with a larger cohort are suitable in the future.

ACKNOWLEDGEMENT

The author is grateful to the study community and to the Imaging Centers' authorities and workers for their support during study implementation. We are also thankful to Dr. Manda Anamaria and to Dr. Andrei Ernestina, senior radiologists, who verified using the FBU as independent operators some cases with particular sonographic aspects.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-forprofit sectors.

REFERENCES

1. Going JJ. *In* Breast Cancer: A Lobar Disease, Tot T (Ed), Springer-Verlag London, XII, 2011; ISBN: 978-1-84996-313-8, http://www.springer.com/978-1-84996-313-8, doi: 10.1007/978-1-84996-314-5.
2. Choi J, Kang B, Kim E, Kim S. Usefulness of computer-aided diagnosis conjunction to breast ultrasound depending on experience of breast

imaging. ECR Viena, B-0080, 2017. http://ecronline.myesr.org/ecr2017.
3. Attard M, Ammary S, Pottier E, Mihoubi F, Dunant A, Balleyguier CS. Evaluation of a computer-aided-diagnosis system in breast ultrasound (S-Detect): intrinsic value and effect on junior radiologist's performance. ECR Viena, B-0081, 2017. http://ecronline.myesr.org/ecr2017.
4. Bloomquist AK, Yaffe MJ, Pisano ED, Hendrick RE, Mawdsley GE, Bright S, et al. Quality control for digital mammography in the ACRIN DMIST trial: part I**.** Med Phys, 2011; 33: 719–36. [PubMed].
5. Pisano ED, Hendrick RE, Yaffe MJ, et al. for the Digital Mammographic Imaging Screening Trial (DMIST) Investigators Group. Diagnostic accuracy of digital versus film mammography: exploratory analysis of selected population subgroups in DMIST. Radiology, 2008; 246(2): 376-83.
6. Olchowy C, Cebulski K, Łasecki M, Chaber R, Olchowy A, Kałwak K, et al. The presence of the gadolinium-based contrast agent depositions in the brain and symptoms of gadolinium neurotoxicity - A systematic review. PLoS ONE, 2017; 12(2): e0171704. doi:10.1371/journal.pone.0171704.
7. Teboul M. Practical Ductal Echography: Guide to Intelligent and Intelligible Ultrasound Imaging of the Breast. Saned Editors, Madrid, 2003.
8. Georgescu AC, Enachescu V, Bondari S. The Full Breast Ultrasonography: an Anatomical Standardized Imaging Approach of the Benign and Malignant Breast Lesions. ECR Vienna, 2010. DOI: 10.1594/ecr2010/C-0434.
9. Colan-Georges A. Sonoelastography in Addition to Doppler Ductal Echography: Full Breast Ultrasonography. *In* Atlas of Full Breast Ultrasonography, Springer Int. Publishing Switzerland, 2016; 53-66, DOI: 10.1007/978-3-319-31418-1.
10. Shiina T, Ueno E. In vivo breast examination by real-time freehand elasticity imaging system. 13th International Congress on the Ultrasonic Examination of the Breast. International Breast Ultrasound School. The 10th Meeting of Japan Association of Breast and Thyroid Sonology, 2003; *in* Research and Development in breast Ultrasound, Springer-Verlag Tokyo Ed, 2005; 7-15.
11. Itoh A, Ueno E, Tohno E, et al. Breast Disease: Clinical Application of US Elastography for Diagnosis. Radiology, 2006; 239: 341-350.
12. 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: 123-134.
13. Stavros AT, Rapp LC, Parker HS. Breast ultrasound. Lippincott Williams & Wilkins Ed, 2004.
14. American College of Radiology. Illustrated breast imaging reporting and data system (BI-RADS): ultrasound. American College of Radiology, Reston: 2003. http://www.acr.org/deparments/stand_accred/birads/us_assess.pdf.
15. Mendelson EB, Böhm-Vélez M, Berg WA, et al. ACR BI-RADS® Ultrasound. *In*: ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. Reston, VA, American College of Radiology, 2013.
16. Teboul M. Advantages of Ductal Echography (DE) over Conventional Breast Investigation in the diagnosis of breast malignancies. Med Ultrason, 2010; 12(1): 32-42.
17. Figueroa JD, Pfeiffer RM, Patel DA et al. Terminal duct lobular unit involution of the normal breast: implications for breast cancer etiology. J Natl Cancer Inst, 2014; Oct 1; 106(10). pii: dju286. doi: 10.1093/jnci/dju286.
18. Yang XR, Figueroa JD, Falk RT, et al. Analysis of Terminal Duct Lobular Unit (TDLU) Involution in Luminal A and Basal Breast Cancers. Breast Cancer, 2012; Res.; 14(2): R64. [PMC free article] [PubMed].
19. Kujiraoka Y, Ueno E, Yohno E, Morishima I, Tsunoda-Shimizu H. Incident angle of the plunging artery of breast tumors. *In* Research and development in breast ultrasound. Springer, Tokyo, 2005; 72–75.
20. Colan-Georges A. Unilateral Breast Edema: New Aspects of Diagnosis Using the Full Breast Ultrasonography ECR Viena, Epos ™, Voice of EPOS, 2017. doi I: 10.1594/ecr2017/C-0380.
21. Colan-Georges A. Full Breast Ultrasonography as Follow-up Examination after a Complex Treatment of Breast Cancer. *In* Atlas of Full Breast Ultrasonography, Springer International Publishing Switzerland, 2016; 289-332, doi: 10.1007/978-3-319-31418-1.
22. Ricci P, Cantisani V, Ballesio L et al. Benign and Malignant Breast Lesions: Efficacy of Real Time Contrast-Enhanced Ultrasound vs. Magnetic Resonance Imaging. Ultraschall in Med, 2006; 27: 57-62.
23. Xiaoyun Xiao, Bing Ou, Haiyun Yang, Huan Wu, Baoming Luo. Breast Contrast-Enhanced Ultrasound: Is a Scoring System Feasible? ----A Preliminary Study in China. PLoS One, 2014; 9(8): e105517. Published online 2014 Aug 18. doi: 10.1371/journal.pone.0105517, PMCID: PMC4136879.
24. Ohtake T, Abe R, Kimijima I, Fukushima T, Tsuchiya A, Hoshi K, Wakasa H. Intraductal extension of primary invasive breast carcinoma treated by breast-conservative surgery. Computer graphic three-dimensional reconstruction of the mammary duct-lobular systems. Cancer, 1995; 76: 32–45.
25. Gokalp G, Topal U, Kizilkaya E. Power Doppler sonography: anything to add to BI-RADS US in solid breast masses? Eur J Radiol, 2009; Apr; 70(1): 77-85. DOI: 10.1016/j.ejrad.2007.12.007. Epub 2008 Feb 19.

26. Tozaki M, Fukuma E. Does power Doppler ultrasonography improve the BI-RADS category assessment and diagnostic accuracy of solid breast lesions? Acta Radiol, 2011; Sep 1; 52(7): 706-10. DOI: 10.1258/ar.2011.110039. Epub, 2011; May 19.
27. *** The EFSUMB Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography. Part 1: Basic Principles and Technology. ePub, 2012; Nov, Ultraschall in der Medizin/EJU 2013 Issue 2.
28. *** The EFSUMB Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography. Part 2: Clinical Applications. Ultraschall in der Medizin, 2012 /EJU 2013 Issue 3.
29. Evans A, Whelehan P, Thomson K, et al. Differentiating benign from malignant solid breast masses: value of shear wave elastography according to lesion stiffness combined with greyscale ultrasound according to BI-RADS classification. Br J Cancer, 2012; Jul 10; 107(2): 224-9. DOI: 10.1038/bjc.2012.253. Epub 2012 Jun 12.
30. Svensson WE, Amiras DG, Shousha S, et al. Elasticity Imaging on 234 Breast Lesions Shows That it Could Halve Biopsy Rates of Benign Lesions. European Radiology, 2006; 16 supp 1: 213-4.
31. Jackman RJ, Nowels KW, Rodriguez-Soto J, et al. Stereo-Tactic, Automated, Large Core Needle Biopsy of Nonpalpable Breast Lesions: False-Negative and Histologic Underestimation Rates After Long-Term Follow-up. Radiology, 1999; 210: 799-805.