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Complementary mamma diagnostics to characterize focal breast lesions: a case-based overview

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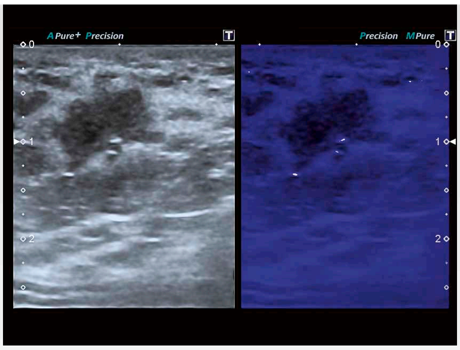
Introduction

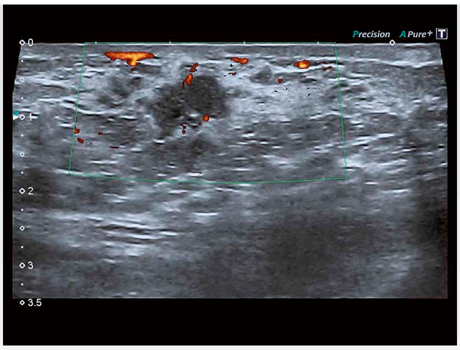
Contemporary breast cancer diagnosis is a team effort requiring multidisciplinary assessment of the patient and the application of multimodality diagnostic techniques to optimize detection and characterization of breast tumors. Ultrasound used in this context requires highly specialized systems with optimized presets enhancing B-mode image quality and providing functional tumor analysis such as tissue elasticity and microcalcification visualization. Focused "second look" sonography supports diagnostic work-up by correlating previously undetected lesions using MRI and ultrasound and requires ultrasound systems with exact presets and premium technology.

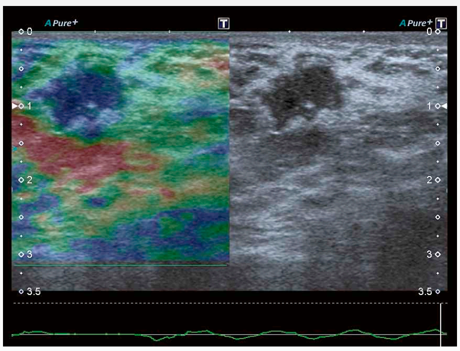
Elastography

Elasticity is an important feature of tissue which can change corresponding to age and pathophysiological processes. An established criterion in the assessment of breast lesions relates to the clinical evaluation of elasticity by palpation. Ultrasound elastography is an imaging procedure which can describe the stiffness of a suspect region. Problematic cases in breast cancer diagnosis relate to lesions in the BI-RADS score categories 3 and 4, and small lesions with lipomatous involution. If elastography as a supplementary procedure can provide information about the lesion stiffness it may allow a better, more unambiguous classification of lesions into BI-RADS categories 3 and 4. Several studies confirm this additional tissue elasticity information enhances the specificity of the ultrasound evaluation allowing differentiation of malignant breast lesions. Subsequently histological confirmation of such lesions may no longer be necessary, sparing the patient unnecessary biopsies.

Changes in elasticity can be described quantitatively. The elasticity parameter can be determined as a strain ratio between normal and suspect breast tissue, the so-called Fat-Lesion-Ratio (FLR), facilitating differentiation of lesions and further standardization of the method.







Microcalcifications

Microcalcifications are important incidental findings in asymptomatic patients with pre-cancerous pathologies or existing breast cancer. In approximately 40 % of the patients with a non-palpable tumor, microcalcifications are the first indication of malignancy detectable in mammography. Mammography remains the gold standard for detection, characterization and localization of microcalcifications in the breast and in breast biopsy samples. While the role of ultrasound in the detection of microcalcifications is still being debated, the combination of sonography and mammography to detect microcalcifications increases both the specificity and positive predictive value of mammography. This suggests that sonography should be used in a highly targeted manner to localize microcalcifications in combination with mammography, rather than as a screening tool in isolation.

Moreover, sonography is capable of detecting invasive components of a tumor in case of existing microcalcifications, which means that the transition from DCIS to invasive carcinoma can be diagnosed to avoid underestimation of subsequent biopsy findings. Additionally ultrasound-guided biopsies provide a clinically important tool to assess microcalcifications detected in sonography and mammography with the added advantages that they are comparatively inexpensive, do not involve radiation exposure and are more comfortable for the patient than the more complex and less well tolerated stereotactic biopsies.

Image quality

As early as 1988, Kasumi showed that sonography was capable of detecting microcalcifications of 110 µm. Ultrasound image quality has significantly advanced ever since. The introduction of high-resolution ultrasound performed with high frequency transducers, modern technologies to reduce noise such as Tissue Harmonic Imaging

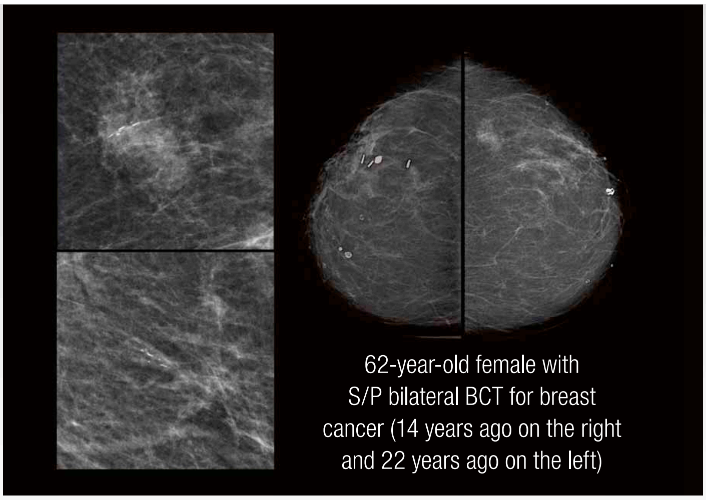


Fig. 1A: Digital mammography of 62-year-old patient with surgical clips and macrocalcifications after breast-conserving therapy. Enlargement shows a microcalcification cluster on the left rim.

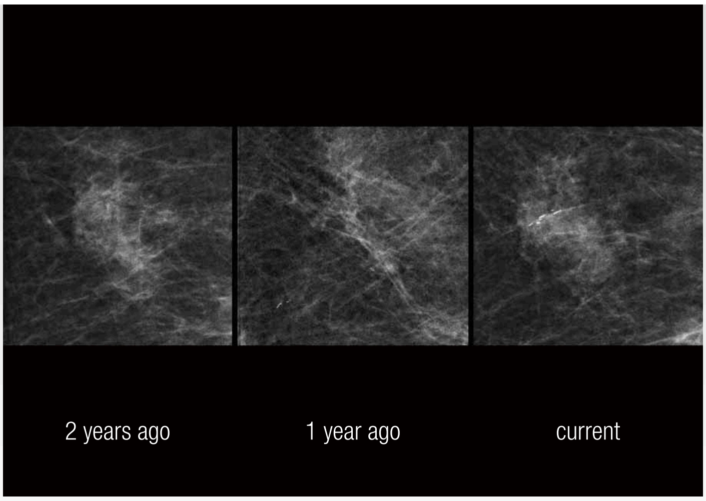


Fig. 1B: The cluster has clearly progressed within two years.

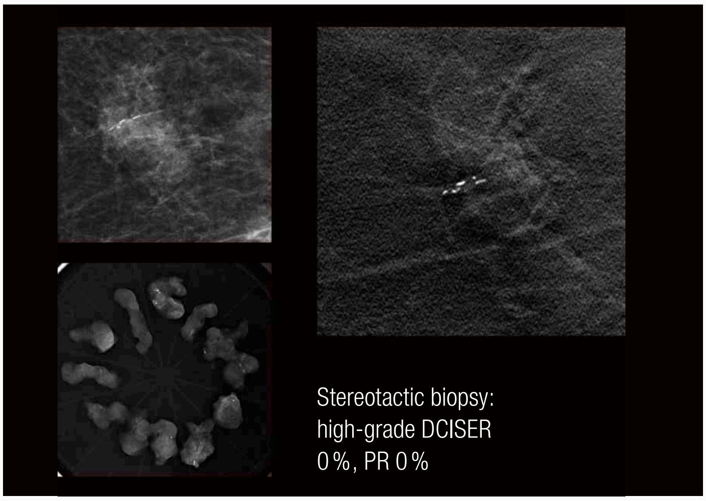


Fig. 1C: Tissue sample radiography after stereotactic biopsy and surgery planning with digital mammography

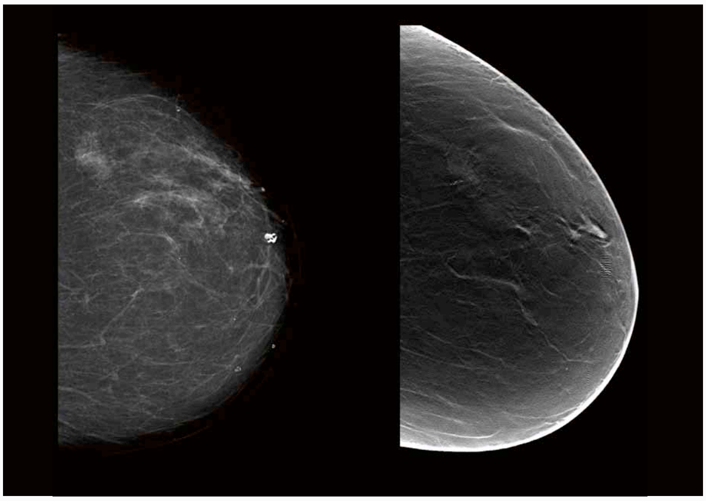


Fig. 1D: Mammography (left) and tomosynthesis; only tomosynthesis allows clear delineation of the finding (right, arrow).

(THI), spatial and frequency compounding and volume imaging of carcinoma in the frontal plane, have boasteddiagnostic performance significantly. Nevertheless, the detection of microcalcifications with ultrasound remains a challenge, particularly in hyperechoic, fibroglandular breast tissue with many hyperechoic areas. Visibility and detectability of hyperechoic microcalcifications are enhanced on a hypoechoic background. With this in mind, MicroPure was developed as a novel ultrasound technique to improve the visibility of microcalcifications. Combined with advanced signal processing options such as Precision Imaging, speckle noise can be greatly reduced and microcalcifications are highlighted, analogous to airplane radar systems.

Case study

A 62-year-old patient presented at a Breast Unit certified since 2003 by the German Cancer Society and the German Senology Society. The patient participated in a special senology program for intensified early detection and follow-up of high-risk patients with BRCA 2 mutation. Patient history revealed breast-conserving surgery 22 years ago (left) and 14 years ago (right) subsequent to the diagnosis of invasive ductal mamma carcinoma. Currently the patient reported left sided pain, however no lesion was palpable. Sonography and mammography were performed with neither detecting a tumor. Mammography however did show cluster-shaped microcalcifications (digital mammography in two planes, Fig. 1A) with serial studies confirming enlargement of the microcalcifications and hence their progress (Fig. 1B). Stereotactic vacuum aspiration biopsy confirmed high-grade DCIS (Fig. 1C).

Since this high-risk patient was participating in a program for intensified early detection she underwent additional MRI and tomosynthesis (Fig. 1D). Here both modalities showed a lesion of 5 mm

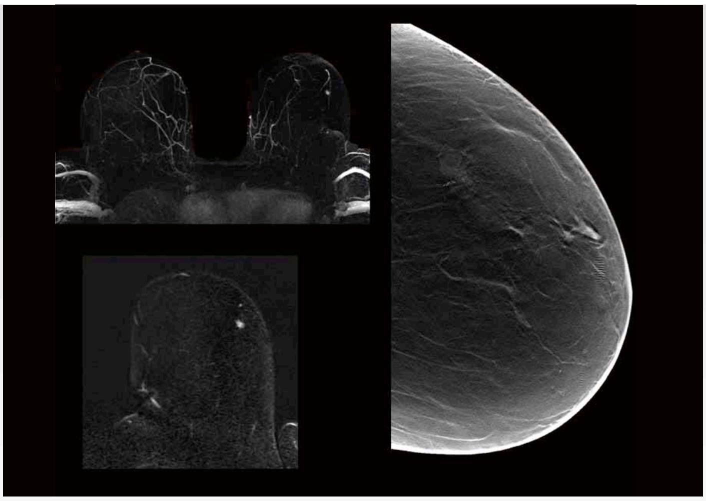


Fig. 2: MIP and subtraction after contrast agent application (left) show early and strong enhancement of the small lesion on the left side; in addition, the broad vessel in the surrounding tissue is visible in correlation to power Doppler (see Fig. 5); tomosynthesis shows the morphology of the lesion (right) particularly well.

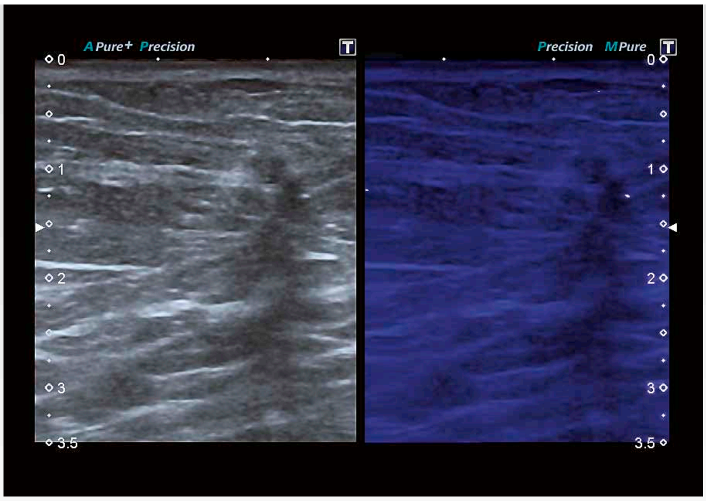


Fig. 3: 4 mm hypoechoic lesion (left) and microcalcifications in the rims (right).

Category	ACR BI-RADS	Tsukuba Score
0	Incomplete	
1	Negative	Strain in the entire area (lesion and surrounding area)
2	Benign finding(s)	Strain in the lesion
3	Probably benign	Strain only in the peripheral areas
4	Suspicious abnormality	No strain in the lesion
5	Highly suggestive of malignancy	No strain in the entire area (lesion and surrounding area)
6	Known biopsy-proven malignancy	

Tab. 1: Simultaneous image analysis with BI-RADS and Tsukuba score.

suspicious for malignancy. Following these MRI investigations and findings a “second-look” sonogram was scheduled (Fig. 2).

This targeted sonographic re-evaluation utilized a premium ultrasound system, the Aplio 500 and a linear broadband transducer PLT-805AT at 9 MHz (both Toshiba Medical Systems, Otawara, Japan). To best delineate the advanced lipomatous involution of the breast, parameters which optimize the B-mode image to enhance lateral and axial resolution and reduce speckle noise were integrated in the standardized preset (spatial and frequency compounding as well as Differential Tissue Harmonic Imaging). Targeted sonography revealed a hypoechoic architectural distortion of 4 mm x 3 mm with unilateral shadowing and a disrupted Cooper’s ligament. In addition, MicroPure was able to visualize an adjacent microcalcification (Fig. 3). Border delineation of the lesion was not clearly assessable.

Due to the small size of the lesion and its categorization as BI-RADS 4 Tissue Doppler Imaging (TDI) and elastography including FLR determination were performed. Despite its small size the lesion showed low elasticity (blue = stiff, non-elastic tissue) which corresponds to an elastography or Tsukuba score of 4 (Tab. 1). Vibro-elastography performed with TDI showed a color defect in the tumor. The FLR of the lesion compared to surrounding tissue was 3.17 and thus higher than the cut-off value of 2.2 (Fig. 4A-C).

In a final step vascularization of the lesion was documented using Power Doppler at low PRF and imaging the frontal plane using a 14 MHz high-resolution volume transducer (Fig. 5 and 6).

Imaging the lateral plane (Fig. 6) allows confirmation of major malignancy criteria (retraction and spiculation) even in small lesions. Vertical orientation, surroundings (disrupted Cooper´s ligaments) and

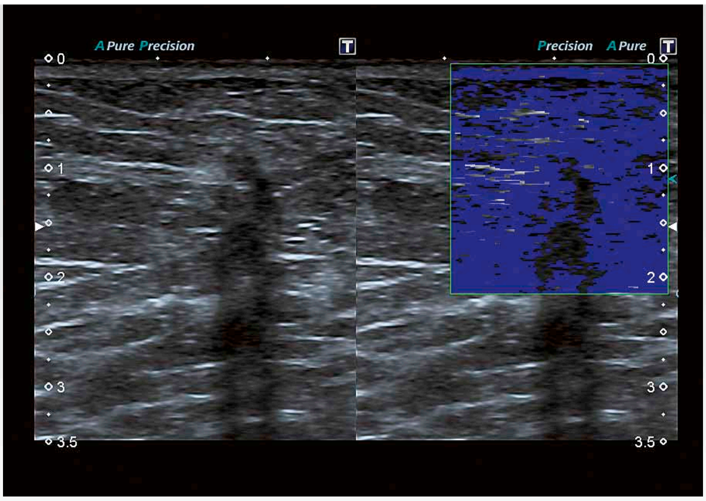


Fig. 4A: Tissue Doppler Imaging (TDI) with defect of the suspected tumor area, vibration elastography, a pressure-independent real-time procedure.

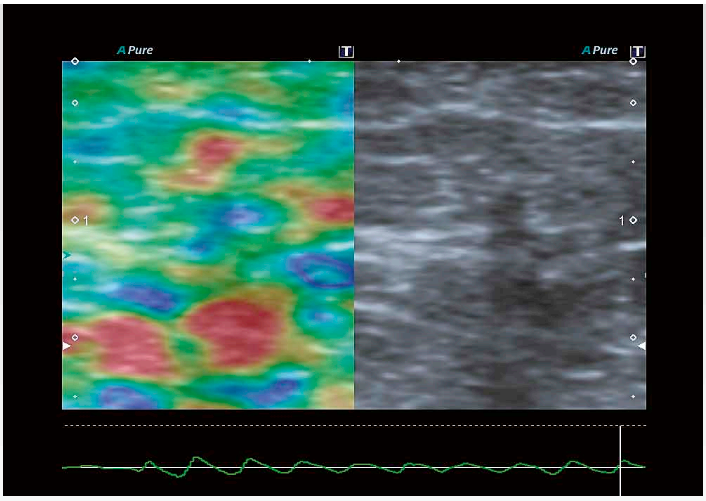


Fig. 4B: Elastography (left) and parallel B-mode image (right): low strain on the lesion.

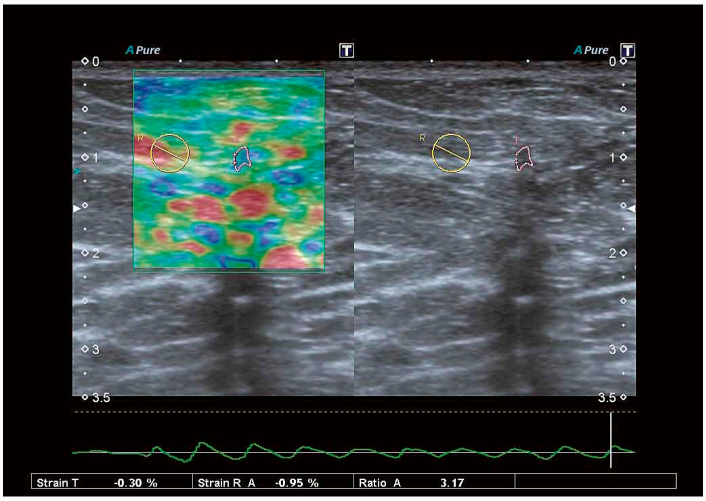


Fig. 4C: FLR of 3.17 is slightly above the cut-off value. In previous studies findings above a cut-off value of 2.2 were classified as malignant with high sensitivity and specificity.

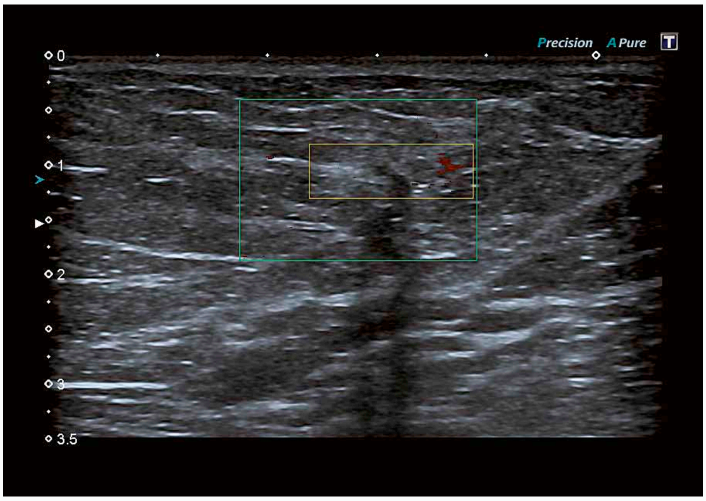


Fig. 5: Power Doppler shows strong vessels adjacent to the tumor, the vascularization index at 5.7 % of the entire area is rather low. Nevertheless the branching-off of the strong vessel is typical for a tumor feeder vessel.

strong acoustic shadowing are further criteria that allow categorization of small lesions with optimized ultrasound technology into BI-RADS category 5. The most important criteria are summarized in Table 2.

Histological assessment was performed with high-speed core biopsy (Bard MAGNUM Biopsy System, Bard, Tempe, USA), using a 14 g x 16 cm biopsy needle (Fig. 7). Two biopsies were performed and exact needle position was documented. In addition to standard HE staining immune histological investigations were performed and the hormone receptor status was linked (Fig. 8A and 8B). An invasive ductal mamma carcinoma was diagnosed (G2, ER 100 %, PR 0 %, HER 2 negative, MIB-1 10 %).

Discussion

Early elastography studies were difficult and complex making the technology unsuitable for routine clinical use. State of the art clinical systems now integrate high resolution imaging and elastography allowing easy application into routine patient care. Studies report increased diagnostic specificity when breast ultrasound combines elastography and B-mode image information. Comparison and correlation of the Tsukuba score for elastography, the BI-RADS criteria for mammography and B-mode image could potentially contribute to improved standardization of sonoelastography examinations, as evidenced by the present case study.

In this case standardized investigation in the context of second-look ultrasonography allowed definite categorization of the lesion as neoplastic with histological confirmation of the finding. Due to its small size the lesion had not been detected in either initial routine sonography or mammography. This example underlines the diagnostic value of MRI for early detection of breast cancer. However, in order to further evaluate and classify suspicious MRI findings a premium ultrasound system with state

Criteria	**2D imaging**		**3D imaging, frontal plane**	
	malignant	**benign**	**malignant**	**benign**
Shape	irregular	oval, round		
Orientation	vertical	parallel		
Echogenicity	hypoechoic towards fat	iso-, hyperechoicw		
Echo texture	complex	homogeneous		
Microcalcifications (white spots)	present	absent		
Margin	hyperechoic halo	thin capsule		
Shadowing	shadow	enhancement		
Surrounding tissue	architectural distortion	compression		
Margins	irregular, spiculated	even, lobulated (<5)	irregular, spiculated	even, lobulated (<5)
Delineation	poor	good	poor	good
Retraction			present	absent

Tab. 2: Especially criteria such as the presence of microcalcifications, surrounding tissue structure and tissue retractions (in bold) can be well visualized with modern sonography technology; retractions are specific to 3D ultrasound.

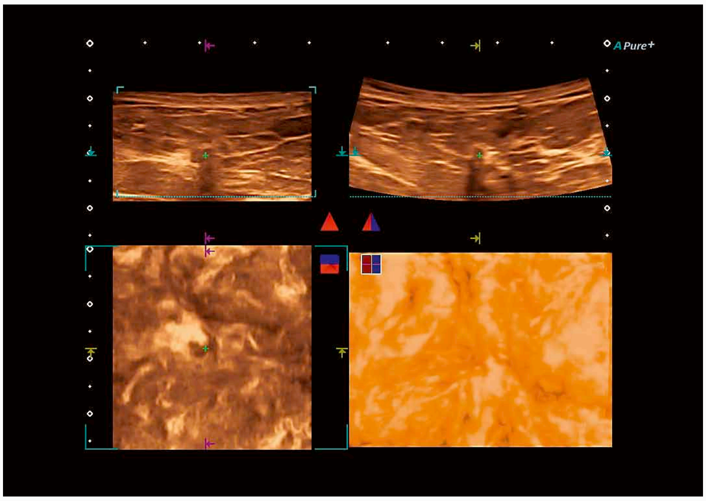


Fig. 6: Volume sonography and 3D visualization of the lesion. In the frontal plane note irregular delineation and retraction which are both malignancy criteria.

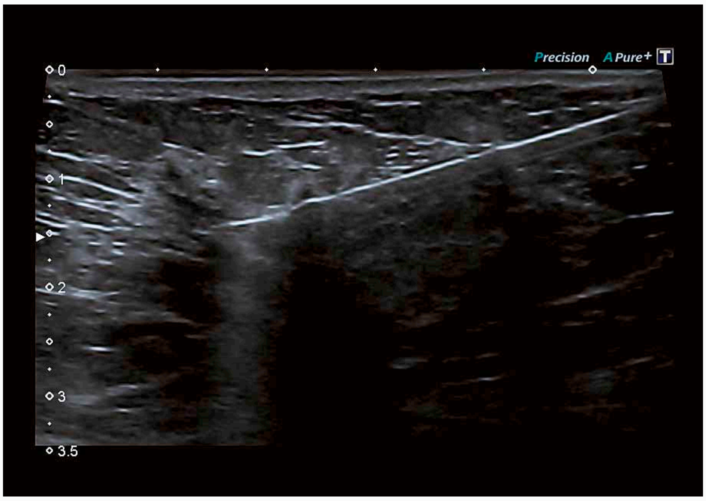


Fig. 7: Histological confirmation with US-guided core biopsy.

of the art applications for lesion characterization is required. In the present case, following extensive consultation and confirmation of DCIS and invasive carcinoma, the patient decided to undergo left-side mastectomy.

While the high-quality B-mode image was the foundation of the sonographic malignancy assessment in breast, several approaches to tumor characterization were applied: Tissue Doppler Imaging (TDI), elastography with FLR determination, visualization of microcalcifications with MicroPure and volume sonography (retractions visible in the C-plane). One of the most impressive results was the good correlation of ultrasound, tomosynthesis and dynamic MRI despite the fact that the lesion had not been clearly visible in the initial sonography and mammography. Microcalcifications on the other hand were clearly detected and confirmed in mammography.

Aware of the MRI results, final histological confirmation of the breast cancer was based on enhanced B-mode image technology and ultrasound-guided core biopsy.

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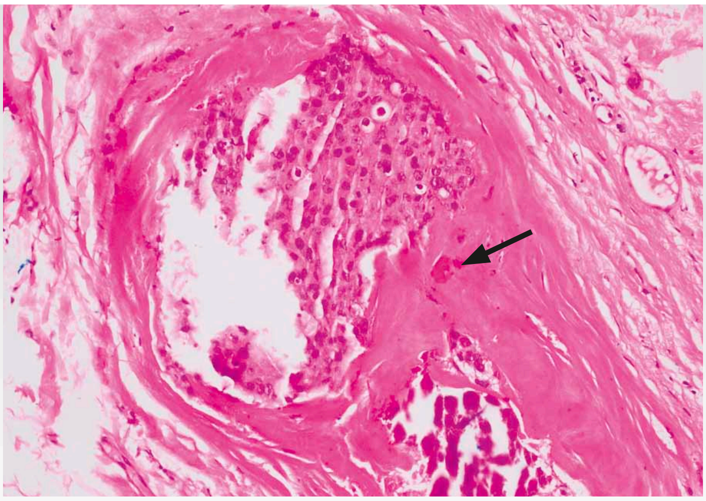

Fig. 8A: Result of the vacuum aspiration biopsy: DCIS with microcalcifications (arrow), HE stain, 20x

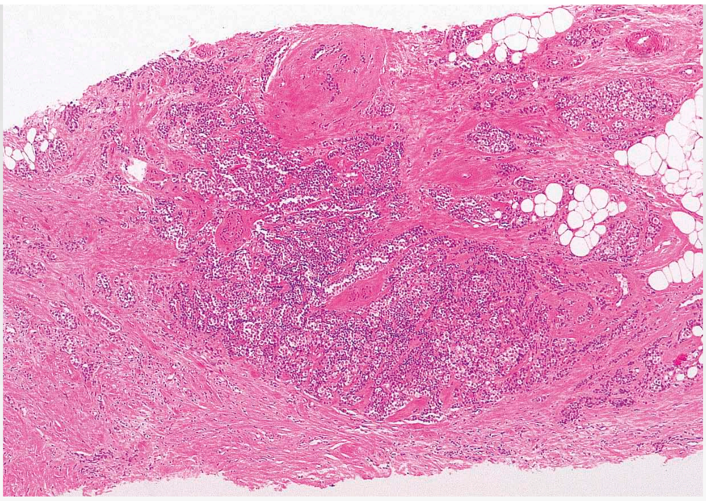

Fig. 8B: Result of the US-guided core biopsy: invasive ductal mamma carcinoma G2, ER 100 %, PR 0 %, HER 2 negative, MIB-1 10 %, HE stain, 10x

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