Best Practice Guidelines – DEGUM Recommendations on Breast Ultrasound

Part III/2 – Special Clinical Indications

Best Practice Guideline – Empfehlungen der DEGUM zur Durchführung und Beurteilung der Mammasonografie

Teil III/2 – Spezielle Indikationsbereiche

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ABSTRACT

Breast ultrasound has been established for many years as an important method in addition to mammography for clarifying breast findings. The goal of the Best Practice Guidelines Part III of the DEGUM breast ultrasound working group is to provide colleagues working in senology with information regarding the specific medical indications for breast ultrasound in addition to the current ultrasound criteria and assessment categories published in part I and the additional and optional sonographic diagnostic methods described in part II. The value of breast ultrasound for specific indications including follow-up, evaluation of breast implants, diagnostic workup of dense breast tissue, diagnostic workup during pregnancy and lactation, and the diagnostic workup of breast findings in men is discussed. Each section after the general information section contains a description of specific pathologies, followed by a short summary and DEGUM recommendations for the particular indications. The latest S3 guidelines and AGO guidelines were taken into consideration.

ZUSAMMENFASSUNG

Die Mammasonografie hat sich seit vielen Jahren neben der Mammografie als wichtige Methode zur Abklärung von Brustbefunden etabliert.
Der Arbeitskreis Mammasonografie der DEGUM beabsichtigt mit der Best Practice Guideline Teil III, den senologisch tätigen Kolleginnen und Kollegen – neben dem in Teil I publizierten aktuellen Dignitätskriterien- und Befundungskatalog und den in Teil II beschriebenen additiven und fakultativen sonografischen diagnostischen Methoden – im vorliegenden Teil III die speziellen medizinischen Indikationsbereiche der Mammasonografie zu erläutern. Es wird der Stellenwert der Mammasonografie in Indikationsbereichen wie in der Nachsorge, bei der Beurteilung von Brustimplantaten, der Diagnostik bei dichtem Drüsenparenchym, Diagnostik in der Schwangerschaft und während der Stillzeit sowie in der Diagnostik von Brustbefunden beim Mann behandelt. Nach allgemeinen Informationen beinhaltet jedes Kapitel einen Teil mit Beschreibung spezieller Pathologien und zum Abschluss in gewohnter Manier eine kurze Zusammenfassung sowie die DEGUM-Empfehlungen zum jeweiligen Indikationsbereich. Dabei wurden die neuesten S3-LL und AGO-Guidelines berücksichtigt.

4 Breast ultrasound during pregnancy and lactation

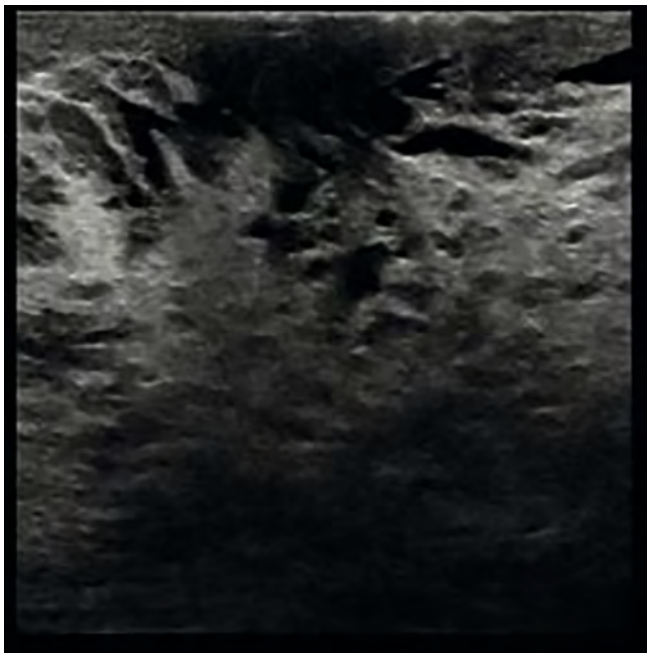
4.1 General information

Endocrine factors result in complex changes in breast tissue over an entire lifetime [1]. During pregnancy, physiological adaptations in preparation for subsequent lactation begin as early as the first trimester due to the increase in HCG (human choriongonadotropin). The proliferation of terminal ductulo-lobular units (TDLUs) represents a central mechanism. The glandular tissue subsequently increases compared to the lipomatous and mesenchymal portions of the breast (▶ **Fig. 1**) [2]. An increase in secretion can be detected beginning in the third trimester at the latest so that the lobules and milk ducts fill with colostrum (▶ **Fig. 2**) [3]. These changes affect the appearance of normal tissue and pathological changes on diagnostic imaging [4].

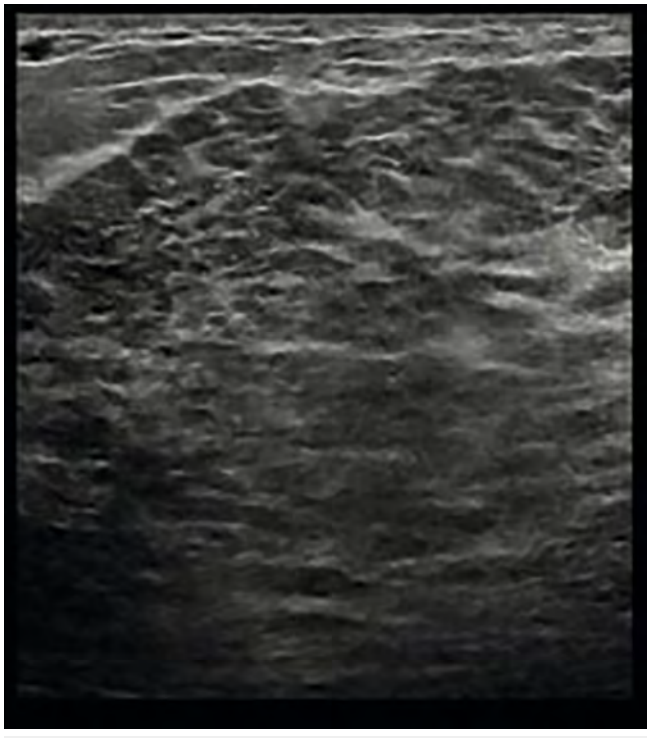
As a result of the increase in the parenchyma during pregnancy and lactation, increased breast density is seen on B-mode ultrasound analogous to DEGUM parenchyma categories c and d. At the same time, ductal and lobular hyperplasia occurs. This development begins focally in the first trimester so that hyperplastic areas alternate with unchanged parenchyma on the ultrasound image. During the lactation phase, the lactating parenchyma is at its maximum size and has a slightly hyperechoic, homogeneous aspect since the numerous lobules are directly adjacent to one another (▶ **Fig. 3–5**). The central milk ducts are visibly dilated on ultrasound and filled with fluid (▶ **Fig. 6**). A general increase in vascularization can be visualized on Doppler ultrasound (▶ **Fig. 7**).

4.2 Specific pathologies

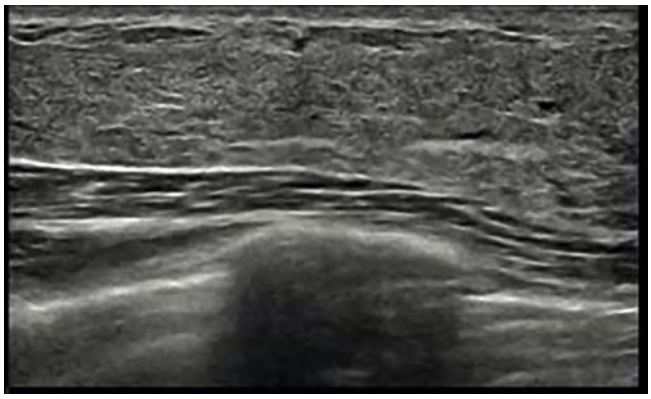
Lactating adenomas, fibroadenomas, cysts, lobular hyperplasia, galactoceles, abscesses, fibrolipomas, lipomas, and hamartomas are the most common benign focal findings that occur over the course of a pregnancy and lactation (▶ **Fig. 8–13**).



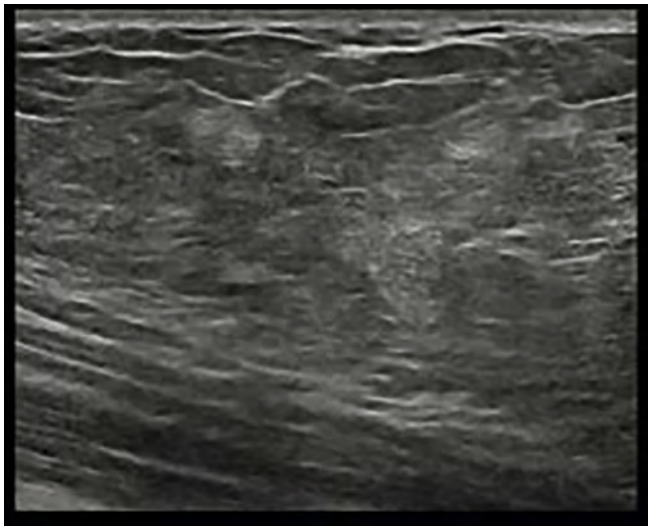
▶ **Fig. 2** Physiological changes in the central mammary gland during a pregnancy – 31st gestational week, the central milk ducts and lactiferous sinuses are dilated and increasingly filled with colostrum.



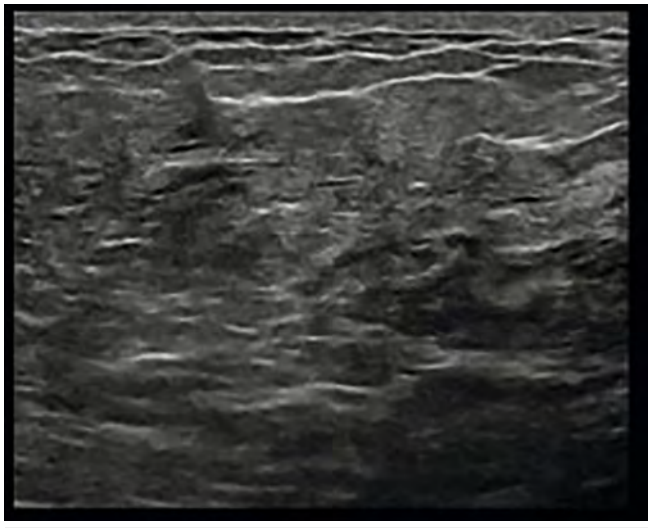
▶ **Fig. 1** Physiological changes in breast tissue over the course of a pregnancy: Increase in the size and density of the parenchyma, numerous hypoechoic lobulated areas merging into one another correspond to hyperplastic lobules and ducts.



▶ **Fig. 3** Physiological appearance of breast tissue in the lactation period.

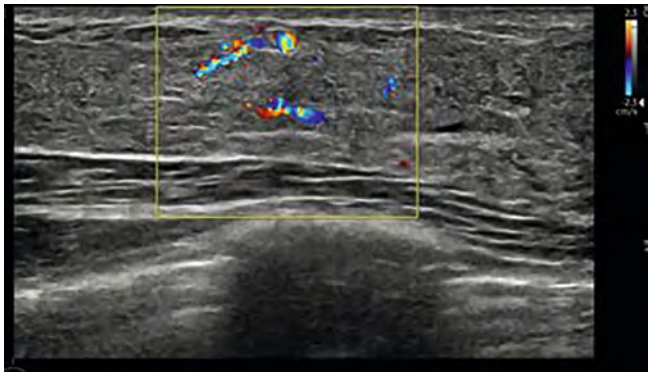


▶ **Fig. 4** Physiological appearance of breast tissue in the lactation period.

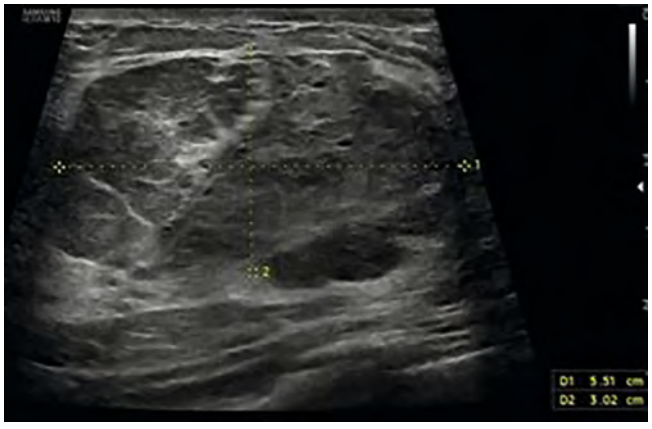


▶ **Fig. 5** Physiological appearance of breast tissue in the lactation period.

▶ **Fig. 6** Physiological dilation of the central milk ducts in the lactation period.



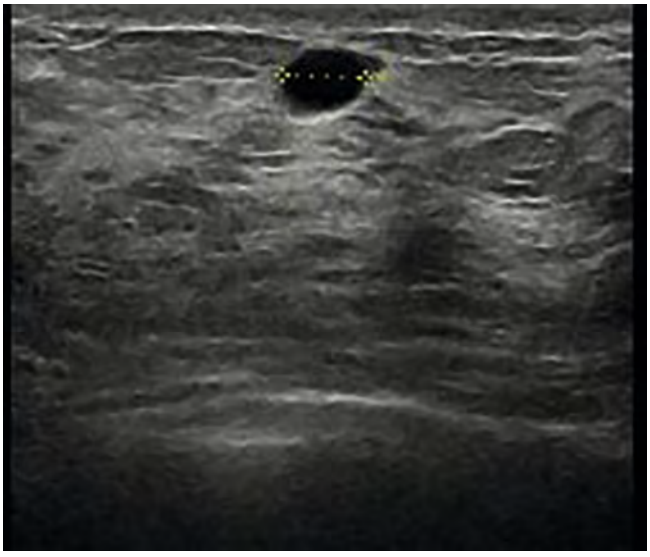
▶ **Fig. 7** Physiological hypervascularization of breast tissue in the lactation period.



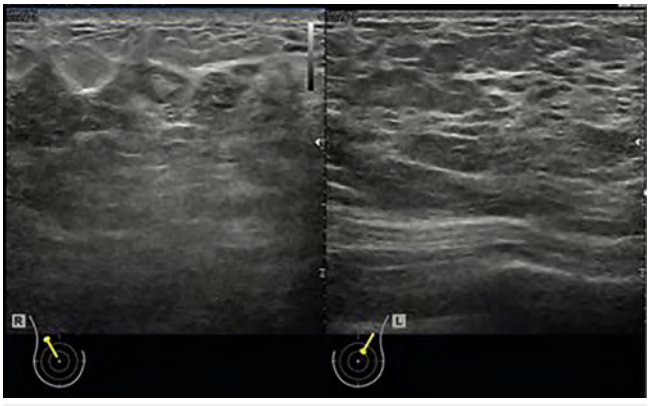
▶ **Fig. 8** Lactating adenoma in the lactation period.

Breast cancers that arise over the course of a pregnancy, over the course of the year following delivery, or during the lactation period are defined as pregnancy-associated breast cancer (PABC). Approximately 0.1 % of all pregnancies are associated with a cancer during this time period [5, 6]. PABC is a serious disease and has an incidence of 10 to 35 cases per 100 000 pregnancies [7, 8].

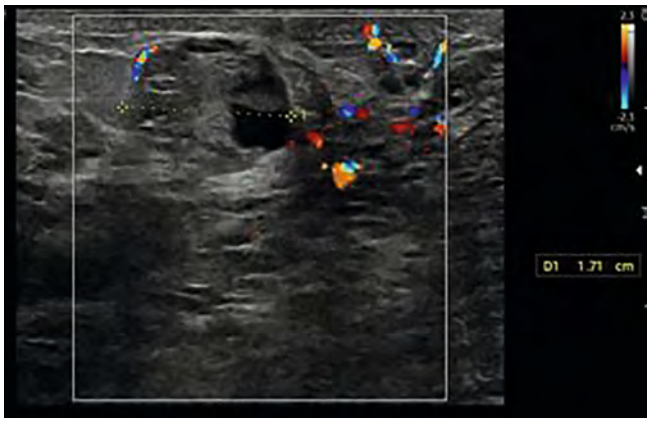
▶ **Fig. 9** Fibroadenoma during pregnancy.



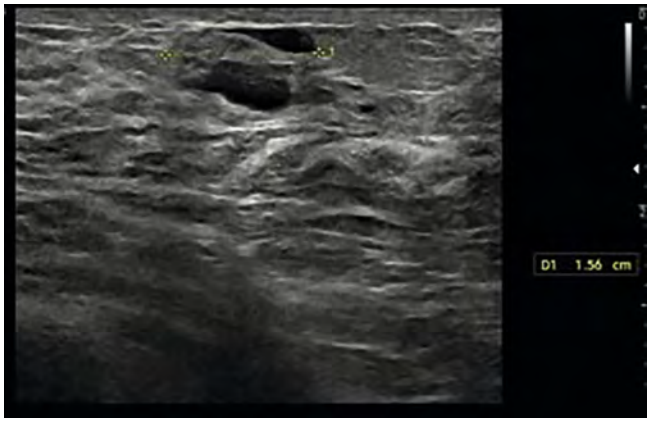
▶ **Fig. 10** Cyst during pregnancy.



▶ **Fig. 11** Granulomatous mastitis on the right side during pregnancy. Physiological changes on the left side.



▶ **Fig. 12** Galactocele in the lactation period. Hypervascularization in the periphery of the lesion and in the surrounding tissue. Mirroring due to thickening and sedimentation of the breast milk.



▶ **Fig. 13** Same patient as in ▶ **Fig. 12**. Regression over the course of 3 months.

The prognosis of pregnancy-associated breast cancer depends largely on early diagnosis. Delayed detection and a subsequent delay in the start of treatment can affect the outcome for the affected patient [9].

Pregnancy-associated changes in breast tissue result in an increase in breast density and subsequently in reduced mammography sensitivity of 62–80 % [8]. As a result, evaluation of the breast tissue is also limited on breast ultrasound but a sensitivity of approx. 93 % has been described in studies [10]. Therefore, breast ultrasound has primary importance for the diagnosis of breast diseases in this phase of life.

Breast cancer usually presents with the known typical sonographic malignancy criteria during pregnancy and lactation. However, it must be taken into consideration that the sonomorphology of PABC can imitate benign findings due to the younger age of these patients, the tumor biology, and the changes in the surrounding tissue [4, 10, 11]. Thus, dorsal acoustic enhancement instead of attenuation or acoustic shadowing can be seen more frequently in PABC compared to non-PABC (63.2 % versus 12.0–15.4 %) (▶ **Fig. 14**) [12].

▶ **Fig. 14** Pregnancy-associated breast carcinoma in dense breast parenchyma (31st gestational weeks).

4.3 Invasive diagnostic workup of the breast during pregnancy and lactation

Accelerated core needle biopsy (ACNB) can be performed during pregnancy and lactation [8]. Weaning prior to the procedure is not necessary. In lactating women, the breast should be emptied before the intervention (breastfeeding/breast pump) and the patient should be informed of the increased risk of milk fistulas, bleeding, and hematomas. In the second and third trimesters and in the lactation phase, the use of established local anesthesias like bupivacaine and ropivacaine is allowed [13]. During lactation, it must be taken into consideration that injection of a local anesthesia into the parenchyma and the milk ducts is to be avoided and infiltration is to be limited to the greatest extent possible to the skin in accordance with the label of the Rote Liste Service GmbH [14]. In this way, direct absorption of the local anesthesia into the mother's milk can be largely avoided. Ultrasound gel and disinfectant residue on the skin must be completely removed after the intervention and prior to the next feeding.

4.4 Conclusion and DEGUM recommendations

- The diagnostic accuracy of breast ultrasound is limited during pregnancy and lactation but is superior to that of mammography.
- It is safe to use breast ultrasound during pregnancy and lactation.
- During pregnancy and lactation, breast ultrasound should be used as the primary diagnostic method in the case of mammary gland changes.
- The sonomorphology of PABC can deviate from the usual malignancy criteria.
- Suspicious and unclear changes on ultrasound must be clarified according to the typical procedure used outside the pregnancy and lactation period.
- An automated cutting needle biopsy (ACNB) should be performed in the case of a corresponding indication during pregnancy and lactation in compliance with the precautionary measures mentioned above.

5 Breast ultrasound in men

5.1 General information

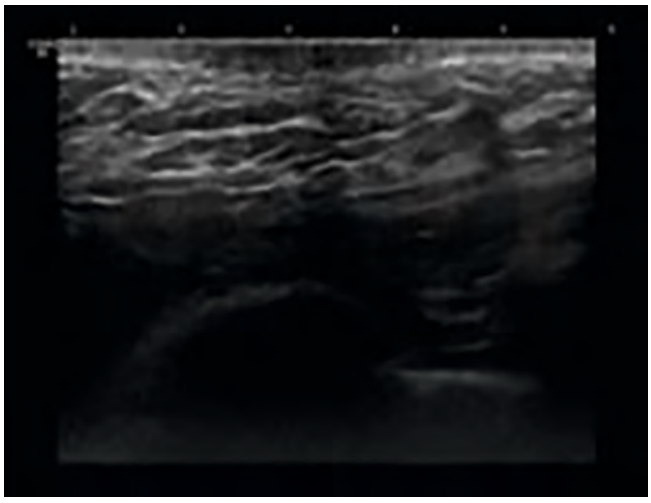
The most common reasons for a man to present for a diagnostic workup of the breast are unilateral or bilateral enlargement of the breast, a palpation finding, mastodynia, or cutaneous abnormalities [15]. Most changes are benign. Unilateral or bilateral gynecomastia is the most common change. Breast cancer in men is rare and comprises less than 1 % of all breast cancer cases [16]. Since the diagnosis is often first made at an advanced stage, suspicious axillary lymph nodes (approx. 50 %) are often the first indication. Therefore, the prognosis can be worse than in a woman.

Breast tissue in men is comprised almost exclusively of fat tissue with a few atrophic milk ducts and stromal tissue. Men do not have any Cooper's ligaments. Most of the breast tissue is retroareolar and can be more or less pronounced. The location and size of the male breast is greatly affected by the major and minor pectoral muscles (▶ **Fig. 15**).

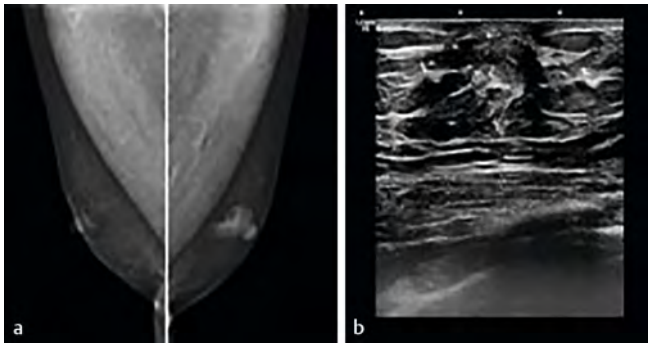
The diagnostic workup of the male breast includes inspection, palpation, breast ultrasound, and mammography when necessary. Contrast-enhanced methods can be used for certain medical questions.

In the case of men under the age of 40 with a palpation finding in the breast, breast ultrasound should be performed as the primary diagnostic method [17].

The practical implementation of breast ultrasound in men is the same as in women and includes the examination of both breasts and the axillae [22, 23].



▶ **Fig. 15** Unremarkable ultrasound scan of a male patient. Hypoechoic appearance of the areola at the level of the normal skin. Subcutaneous fat and connective tissue, almost no glandular tissue.



▶ **Fig. 16** **a** Nodular gynecomastia on the left side. Bilateral mammography, MLO. **b** Left retromamillary, hypoechoic, inhomogeneous structures.

Mammography is almost always technically feasible in men.

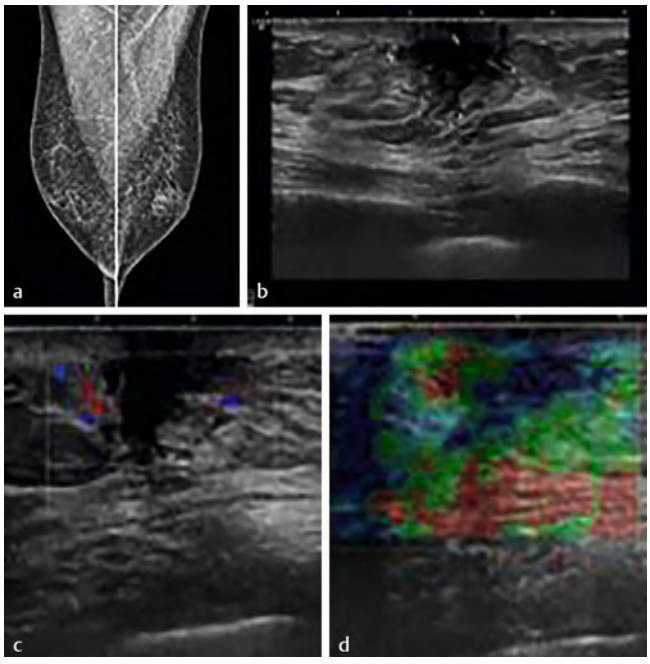
In the case of findings that are suspicious on ultrasound and/or mammography, an interventional diagnostic workup for histological confirmation is indicated.

5.2 Specific pathologies

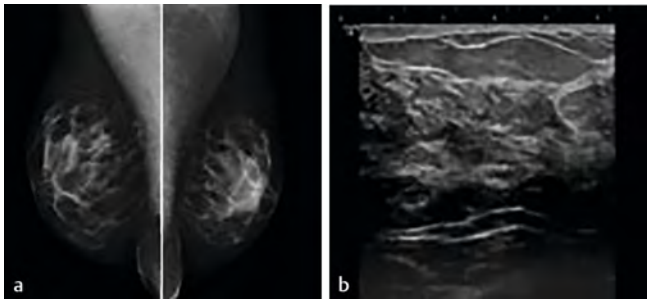
5.2.1 Benign sonographic findings in men

Gynecomastia and pseudogynecomastia

In contrast to pseudogynecomastia (lipomastia) with only a collection of fat tissue in the breast region, gynecomastia involves hypertrophy of the breast tissue.



▶ **Fig. 17** **a** Dendritic gynecomastia on the left side. Bilateral mammography, MLO. **b** Retroareolar hypoechoic structure with unclear borders and focal dendritic strands extending into the surrounding tissue. **c** Increased vascularization in the surrounding tissue. **d** Region with unclear borders appears hard on elastography.

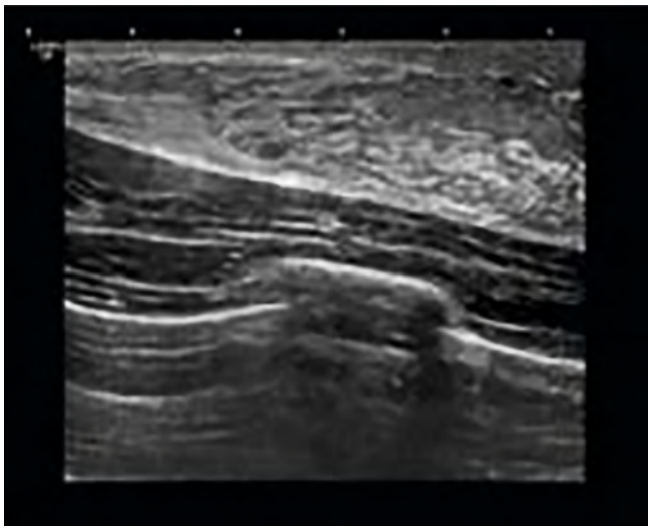


▶ **Fig. 18** **a** Diffuse, medication-induced gynecomastia that is more pronounced on the left. Bilateral mammography, MLO. Significantly enlarged breasts on both sides. **b** Breast ultrasound on the left side shows increased glandular tissue.

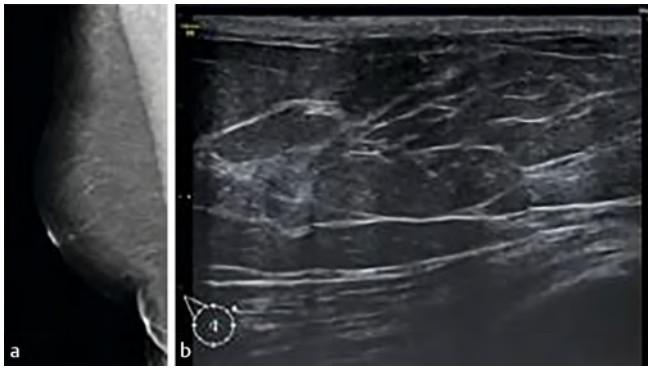
Gynecomastia is the result of a disruption of the estrogen-androgen balance and can be clinically symptomatic or asymptomatic [17]. In certain life phases, gynecomastia can be physiological (e. g. in newborns, during puberty, and in old age). The pathological types have different causes that result in an imbalance in hormone levels [17]. Mechanical causes are also discussed [18].

The most common clinical symptoms of gynecomastia are breast pain, breast enlargement, and/or a palpation finding. Symptoms can be unilateral or bilateral.

A differentiation between nodular, dendritic, and diffuse forms of gynecomastia is made.



▶ **Fig. 19** Pronounced proliferative gynecomastia under hormone substitution in the case of transidentity.



▶ **Fig. 20** **a** Pseudogynecomastia. Enlarged lipomatous right breast on mammography. **b** Enlarged fat tissue layer between the cutis and pectoral muscle on ultrasound.

Nodular gynecomastia indicates the early florid phase of ductal and stromal proliferation (less than 1 year). Disk-shaped or fan-shaped hypoechoic tissue is seen in the subareolar region on ultrasound (▶ **Fig. 16**).

The term **dendritic** gynecomastia is used to refer to a fibrotic latent phase and is seen in patients with a symptomatic increase in breast tissue for more than 1 year. The subareolar areas of increased density stretch in the shape of fingers or flames into the tissue (▶ **Fig. 17**).

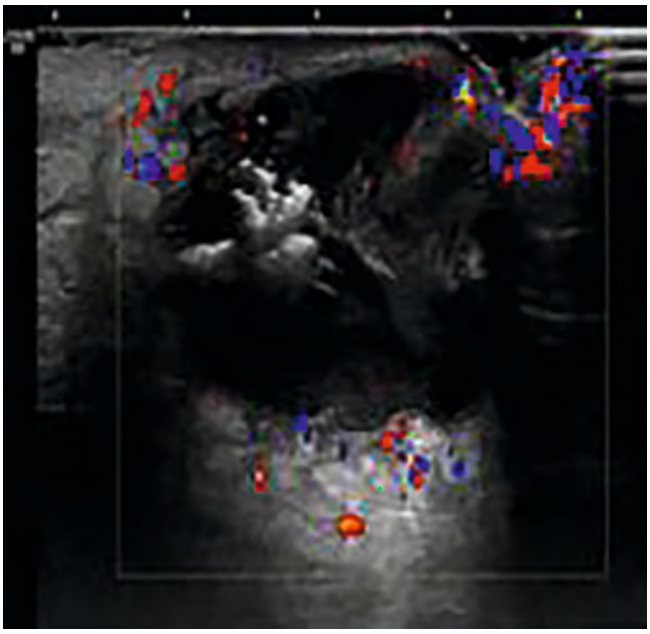
Diffuse gynecomastia is similar to heterogeneously dense female breast tissue (▶ **Fig. 18, 19**).

Pseudogynecomastia or lipomastia is more common in overweight men. It is characterized by the collection of fat tissue in the breast region with an increase in the volume of the breast. Fat tissue and connective tissue septa are seen on ultrasound (▶ **Fig. 20**).

Abscess

Brest abscesses are rare in men [19]. The etiology is usually unclear. Predisposing factors include trauma (e.g., nipple piercing), obesity, smoking, diabetes, and infectious diseases that lower the immune response (including HIV, tuberculosis, brucellosis). Clinically, an abscess appears with swelling that is tender when palpated and is often accompanied by erythema. Abscesses usually occur in a retromamillary or perimamillary location. An antibiogram should be created for targeted therapy.

On ultrasound, an abscess appears as an irregular usually complex cystic-solid lesion with unclear borders (anechoic/hypoechoic focal findings with hyperechoic regions). The findings usually have good perfusion. The overlying cutis is typically thickened and the ipsilateral axillary lymph nodes have reactive changes with an enlarged cortical structure (▶ **Fig. 21**).



▶ **Fig. 21** Periareolar abscess of the right breast with significant peritumoral vascularization. The cutis is thickened.

Epidermoid cyst

Epidermoid cysts are benign changes located in the dermis or adjacent thereto corresponding to a cystic mass lined with squamous epithelium and filled with keratin lamellae.

In the ultrasound examination, these cysts appear as round/oval, circumscribed lesions with homogeneous or heterogeneous echogenicity. These cysts can also have dorsal acoustic enhancement and internal echogenic foci. A sometimes visible stalk between the dermal origin and the dorsally displaced epidermoid cyst is indicative of this entity (▶ **Fig. 22**). A punch biopsy with rupture of the cyst can result in local inflammation with an abscess. Symptomatic epidermoid cysts should be completely removed surgically.

▶ **Fig. 22** Epidermoid cyst. Hypoechoic focal finding adjacent to the cutis and with distinct borders and dorsal acoustic enhancement on ultrasound.

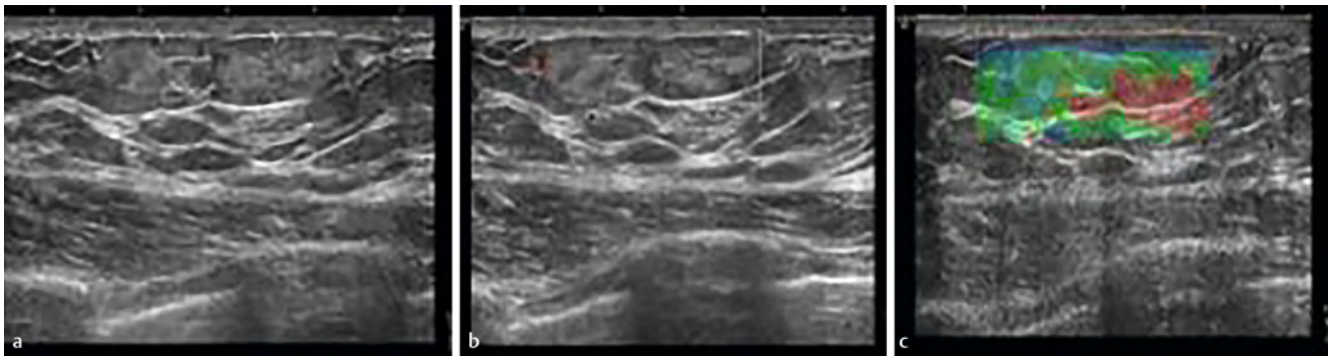
Lipoma/Fibrolipoma

A lipoma is a circumscribed mass comprised of mature fat tissue that is usually located in subcutaneous fat tissue and is typically asymptomatic. When palpated, it feels like a soft, mobile, fluctuating finding under the skin. The etiology is unclear. Obesity is not a risk factor.

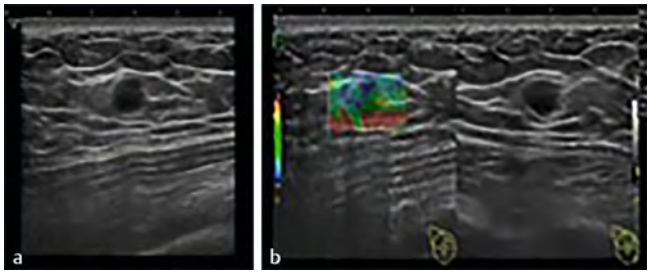
On ultrasound, lipomas appear as hyperechoic or isoechoic circumscribed oval focal findings parallel to the skin and bordered by a thin capsule of connective tissue (▶ **Fig. 23**).

Myofibroblastoma

Myofibroblastoma of the breast is a rare benign mesenchymal tumor. On imaging, myofibroblastomas tend to have benign characteristics, have smooth borders, be hypoechoic, and have an appearance similar to fibroadenomas (▶ **Fig. 24**).



▶ **Fig. 23** **a** Fibrolipomas. Two oval subcutaneous focal findings that are isoechoic and hyperechoic and have distinct borders on ultrasound. **b** No evidence of flow on Doppler ultrasound. **c** Soft to medium hard presentation on elastography.



▶ **Fig. 24** **a** Myofibroblastoma. Hypoechoic focal finding without increased perfusion on ultrasound. **b** Hard representation on elastography.

5.2.2 Malignant sonographic findings in men

Primary malignancy

Breast cancer

Breast cancer in men comprises less than 1 % of all cases of breast cancer.

80 % of carcinomas are ductal invasive carcinomas (NST). The second most common histology (approx. 5 %) is the papillary carcinoma, which presents as complex cystic-solid focal findings [20].

In the case of breast cancer in men, genetic testing is recommended since mutation of the BRCA 1/2 genes was able to be detected in 11 % of cases without a positive family history [21]. A positive breast cancer history of a first degree relative, hyperestrogenism, Klinefelter syndrome, advanced age, and irradiation of the chest wall in the past are considered further risk factors.

Typical clinical changes include a painless palpation finding, nipple inversion, possible secretion, skin thickening, and abnormal axillary lymph nodes.

The sonographic appearance and evaluation criteria are identical to those of breast cancer in women. The diagnostic workup and treatment largely correspond to that of breast cancer in women with a few exceptions (▶ **Fig. 25, 26**).

Secondary malignancies

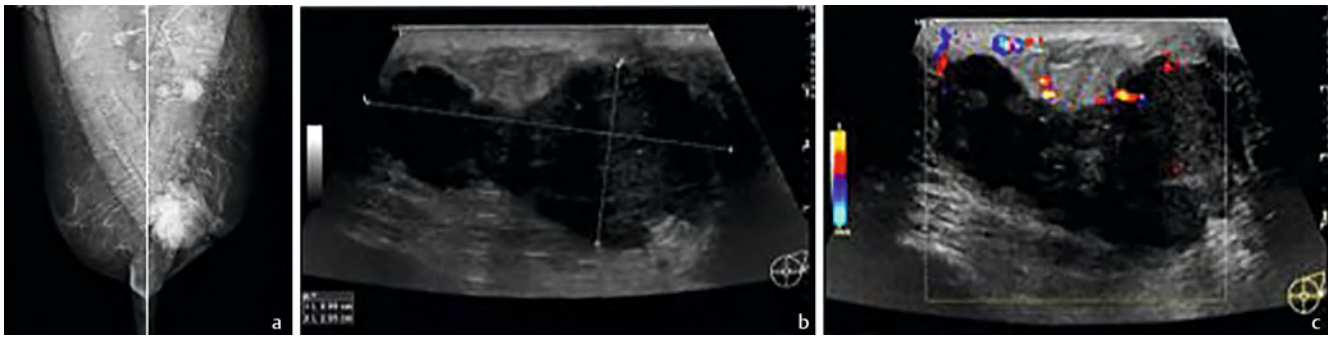
Metastases

Apart from primary breast cancers, only 0.5–3 % of metastases are in the breast regardless of sex, with 5 % of cases occurring in men. The most common primary malignancies that cause metastases in the breast are melanoma followed by non-Hodgkin lymphoma, pulmonary cancer, sarcoma, and gastric, renal, and prostate cancers.

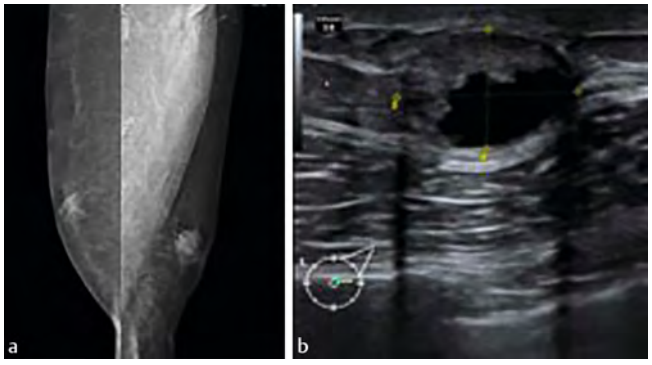
Since lymph node metastases on levels I–III can occur after various primary tumors, no direct conclusion about the primary tumor can be made. Therefore, histological confirmation is necessary (▶ **Fig. 27**).

5.3 Conclusion and DEGUM recommendations

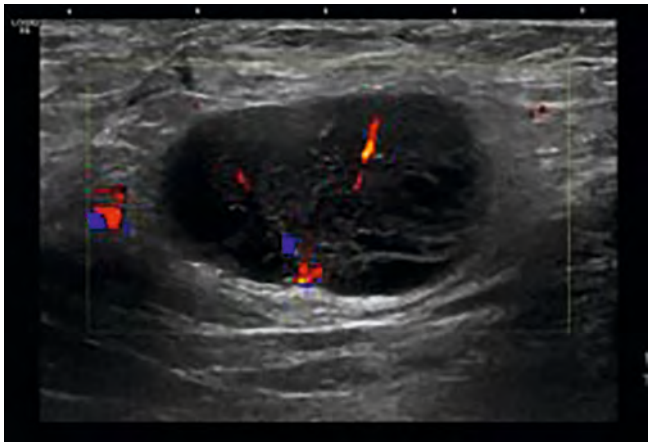
- The examination techniques and the DEGUM malignancy criteria, parenchyma categories, and finding categories are to be applied uniformly for ultrasound in both men and women. These are described in the DEGUM Best Practice Guidelines for Breast Ultrasound Part I.
- Gynecomastia is the most common change in the male breast. A differentiation is made between nodular, dendritic, and diffuse types.
- Pseudogynecomastia (lipomastia) typically occurs in overweight patients and should be differentiated from true gynecomastia.
- The same methods and treatment regimens used for women are available for the diagnostic workup and treatment of breast cancer in men. A delayed diagnosis and the consequently worse prognosis should be avoided.
- Genetic counselling should be offered to all men with breast cancer even in the case of a negative family history [S3 guidelines].



▶ **Fig. 25** **a** Breast cancer on the left side, NST G2. Irregular, hyperdense focal finding on the left side on mammography, retromamillary, nipple retraction. **b** Complex cystic-solid lesion on ultrasound. **c** Increased vascularization in the lesion, on the periphery and peritumoral.



▶ **Fig. 26** **a** Intracystic papillary carcinoma on the left side, G2. Focal finding on the left side with unclear borders on mammography. **b** Complex cystic-solid lesion on ultrasound.



▶ **Fig. 27** Lymph node on level I on the right side in a patient after melanoma.

Conflict of Interest

The authors declare that they have no conflict of interest.

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