

Research Article

Operational Mechanisms as a Reliable Tool for the Challenging Task of Differentiating Neoplasms

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Abstract

In recent years, breast cancer has emerged as one of the most critical challenges in modern medicine and remains the leading cause of cancer-related mortality among women, with invasive ductal carcinoma representing the predominant histological subtype responsible for death. Early detection and precise molecular subtyping are essential for the timely initiation of targeted therapies, which significantly improve prognosis and clinical outcomes. When ductal carcinoma is identified at the receptor expression stage, the therapeutic landscape becomes more favorable, often allowing for effective intervention with minimal risk of remission. In this context, we employed a diagnostic pathway beginning with ultrasonographic screening, followed by mammographic imaging and culminating in histopathological confirmation. This approach was applied to a patient presenting to our clinic in 2024 with severe systemic symptoms, including a 15 kg weight loss over one month and marked general fatigue. The study outlines a comprehensive diagnostic algorithm implemented at the Diagnostic Department of the National Oncology Center. It provides a detailed exploration of the synergistic roles of Doppler ultrasonography and mammography in the stepwise differential diagnosis of ductal carcinoma of mammary gland. The diagnostic accuracy was enhanced via high-precision Doppler system optimized for directional sound wave propagation. Special consideration was given to the constant velocity of acoustic wave transmission through biological tissues and the impact of the beam-to-tissue angle (conicity) on Doppler frequency shifts. Following surgical excision of the neoplasm, receptor-targeted adjuvant therapy was promptly initiated to mitigate the risk of recurrence. The article concludes with strategic recommendations for future research directions aimed at refining diagnostic methodologies and improving personalized treatment strategies in ductal breast carcinoma.

Keywords

Operational Mechanisms, Mammography, Doppler USG, USG Tru-cut Biopsy, Ductal Invasive Carcinoma

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1. Introduction

Cancer arises when genetic mutations lead to unchecked replication and uncontrolled cellular proliferation. Breast cancer is the second most prevalent malignancy among women, following lung cancer, and remains the most frequently diagnosed cancer type worldwide [1]. Over the past decade, routine screening has been widely recommended to facilitate early detection and improve clinical outcomes [2]. In confirmed cases, total or partial mastectomy is often performed as a means to reduce disease-associated mortality [3-5]. Breast cancer primarily originates in the glandular structures, specifically within either the lobules or the ducts, with invasive ductal carcinoma (IDC) accounting for approximately 80% of cases. As a major oncological concern, breast cancer not only poses a significant risk to patient survival but also contributes to physical and cosmetic morbidity [6].

Invasive breast carcinomas exhibit considerable heterogeneity in terms of morphology, biomarker expression, histopathological features, and disease progression. A substantial proportion of these malignancies remain unclassifiable based on histological parameters alone [7]. The molecular classification of breast cancer has led to the identification of distinct subtypes. The classification of breast cancer based on hormone receptor status and molecular profiling has provided critical insights into tumor behavior and therapeutic responsiveness. Estrogen receptor (ER) and progesterone receptor (PR) expression define the luminal subtype, which is further stratified into luminal A and luminal B subgroups based on proliferative indices and HER2 status. Conversely, ER/PR-negative breast cancers are characterized by distinct molecular subtypes, including basal-like, ErbB2-enriched, and normal-like classifications.

Basal-like tumors exhibit a transcriptional profile that closely resembles that of basal epithelial cells within the mammary gland. These tumors lack ER expression and are typically negative for PR and HER2 (triple-negative phenotype). Molecular analyses have demonstrated that basal-like breast cancers frequently overexpress markers associated with myoepithelial differentiation, including cytokeratins 5/6, EGFR, and P-cadherin, while exhibiting an aggressive clinical course and limited therapeutic options due to their resistance to endocrine and HER2-targeted therapies [8-10]. Despite advancements in predictive oncology, existing methodologies for prognostication and early detection remain suboptimal, lowering the survivability of patients [11, 12]. Notably, correlations between histological subtypes and molecular classifications have been established, underscoring their significance in guiding therapeutic strategies [13].

Metastatic potential varies among invasive breast carcinomas, and tumor localization serves as a critical factor in subclassification. Specific histopathological subtypes include adenoid cystic carcinoma, poorly differentiated adenosquamous carcinoma, medullary carcinoma, mucinous (colloid)

carcinoma, papillary carcinoma, and tubular carcinoma. Prognostic outcomes differ among these subtypes, with certain variants demonstrating relatively indolent behavior, whereas others, such as poorly differentiated adenosquamous carcinoma, fall under the category of metaplastic carcinoma, characterized by aggressive progression and limited treatment responsiveness.

Invasive ductal carcinoma, the most prevalent histological subtype, originates within the luminal epithelium of the mammary ducts. In contrast, invasive lobular carcinoma arises from the lobular structures of the breast. IDC is particularly notable for its high metastatic propensity, with malignant cells infiltrating the adjacent breast parenchyma and subsequently disseminating via both lymphatic and hematogenous routes. The transition from *in situ* ductal carcinoma to an invasive phenotype involves the breaching of the ductal basement membrane by atypical epithelial cells, marking the onset of systemic metastasis. Additional invasive subtypes, including metaplastic carcinoma, micropapillary carcinoma, and mixed carcinomas (comprising both invasive ductal and invasive lobular components), often exhibit prognostic outcomes comparable to or worse than those of IDC.

A major challenge in the clinical management of breast carcinoma is its potential for misdiagnosis, which can result in delayed therapeutic intervention and diminished treatment efficacy. While certain cases present with overt clinical manifestations — including breast asymmetry, localized pain, nipple discharge, areolar thickening, and increased tissue density — others remain asymptomatic until advanced stages. Consequently, radiological modalities such as mammography play a pivotal role in detecting occult malignancies. By employing an integrated diagnostic approach encompassing mammographic imaging, differential diagnostics, and ultrasonographic evaluation, we have successfully identified breast ductal carcinoma at an early receptor-secreting stage. This early detection has enabled the prompt initiation of adjuvant therapy, thereby improving patient prognosis and enhancing the likelihood of favorable clinical outcomes.

2. Materials and Methods of the Study

In June 2024, a 55-year-old female patient applied to the Diagnostic Department of the National Oncology Center with complaints of general weakness, fatigue, and weight loss of up to 15 kg in the last month. The diagnosis was confirmed based on the indicators of the "Mammomat inspirator prime" device. The histological analysis was conducted using Hematoxylin and Eosin (H&E) staining.

3. Results of the Study and Discussion

During general examination, an abnormal mass was pal-

pated in the left breast. During USG examination, a regional mass of approximately 35 x 33 mm in size with a solid consistency, spicular contour, bilateral acoustic shadow, consisting of several loci (Figure 1), and fed by intranodular active vessels was detected in color Doppler with a clock face in the direction corresponding to 2 o'clock.



Figure 1. Left mammary gland Doppler examination. Lesion 33 x 35 mm at the 2 o'clock position, exhibiting a clock-shaped appearance with spiculated margins and two loci.

In addition, a cystic structure with smooth edges (thought to be a simple cyst) measuring approximately 4.8 x 4 mm was observed at 1-2 o'clock. The left breast was evaluated as US BIRADS-5. When ultrasound propagated in the mammary gland, there was an irreversible transition of the sound wave energy into other types of energy, mainly into heat, i.e. the sound was absorbed by the mammary gland soft tissue. It was taken into account that the decrease in the amplitude of particle oscillations and ultrasound intensity due to absorption is exponential:

$$A = A_0 e^{-\alpha h} \text{ and } I = I_0 e^{-\alpha h},$$

where A , A_0 were the tissue particles amplitudes of oscillations at the surface of the neoplasm substance and at a depth "h"; and I , I_0 were the corresponding intensities of the ultrasound wave; α was the absorption coefficient, depending on the frequency of the ultrasound wave, temperature and properties of the measured tissue medium. To obtain an accurate diagnosis, it should be taken into account that the absorption coefficient is inversely proportional to the distance at which the amplitude of the sound wave decreases in "e", i.e. as a result, the higher the absorption coefficient, the more the tissue absorbs ultrasound, which means the denser, different from the normal, the neoplasm is. The efficiency of reflection from tumor tissue was determined not only by geometric relationships, but also by the reflection coefficient r , which depends on the ratio of the wave resistances of the malignant environment of the mammary gland x .

$$X = \frac{R_{min}}{R_{max}} \quad r = ((1 - x)/(1 + x))^2$$

When ultrasound waves passed through the boundaries of soft tissues, in norm the refraction is minimal due to the small differences in sound speed in them. The difference in sound speed affects the focusing of the beam in different tissues. The applied ultrasound diagnostics echolocation method allowed to register the boundaries of areas with different wave resistances inside the mammary gland. A linear probe was used for ultrasound examination of mammary gland superficial soft tissues. Using a vibrator built into the probe, a low-frequency sound mechanical wave was created, the propagation speed of which along the underlying tissues was estimated using ultrasound with a frequency of $v = 3.1$ MHz. The linear probe operated at a frequency of 5-10 MHz/42 mm. Using the formula

$$v = \sqrt{E/\rho}$$

for the longitudinal wave velocity, the E modulus (elasticity) of the breast tissue and tumor was calculated.

During mammographic examination, a hyperdense pathological mass of $d=36 \times 40$ mm in size causing asymmetric parenchymatous distortion was observed in the left breast at 11.30 o'clock radius, 28 mm from the nipple (Figure 2).

In the projection of this area, deformation and exaggeration of the skin were noted. No pathological lymph nodes were observed in the bilateral axillary regions. (Figure 3). In the right mammary gland, there were not detected any pathological changes upon examination.

To obtain additional information about the lesions detected during the examination, the color Doppler method was used. The Doppler contains two piezoelectric elements: an ultrasound emitter operating in continuous mode, and a receiver of reflected signals. By measuring the Doppler frequency shift of an ultrasound wave reflected from a moving object (in particular, from a tumor found in the breast), the speed of the reflecting object was determined, which was reflected using different shades of color. This Doppler effect visualized that the sound source and the reflector were moving towards each other, and the sound waves reached the receiver at a higher frequency (F_0) than the original radiation frequency (F_E). It should be taken into account that Doppler frequency shift intensity (ΔF) is proportional not only to the particle velocity (v) and sound wave initial frequency (F_0), but also to the speed of sound in lymph nodules (C) and the angle of the ultrasound beam relative to the longitudinal axis of the tissue (α). We measured this angle in order to obtain the most accurate information about the particle velocity. We also took into account that, since sound waves propagate through the human body at a relatively constant speed of about 1540 m/s, and other factors of the Doppler equation have already been determined, the frequency shift depends on the conicity of the angle between the beam and the tissue. Therefore, to obtain the most accurate measurement, the beam was directed at an angle of 90° towards the lymph nodules and the frequency shift was zero. When examining

the lymph nodes using Doppler ultrasonography, an active vascular network associated with the tumor was found in the lymph node (Figure 4).

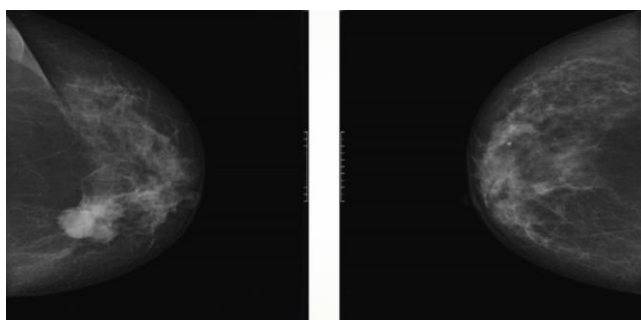


Figure 2. Mammography of left mammary gland in the CC-projection: ductal carcinoma has been found.

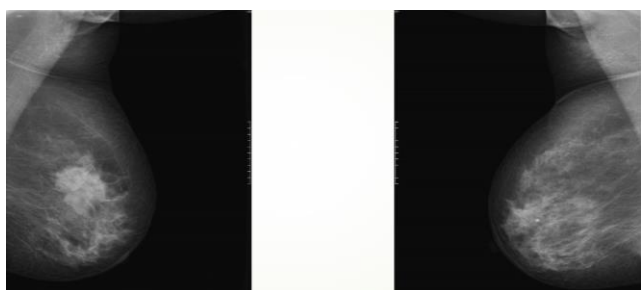


Figure 3. Mammography of left mammary gland in the MLO-projection: ductal carcinoma mammary gland.

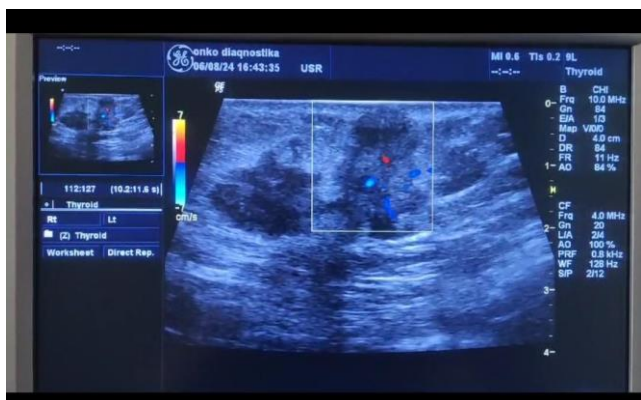


Figure 4. Color Doppler shows active tumor vasculature within the lymph node.

Carcinoma can be often confused with some diseases, as a result, incorrectly performed differential diagnosis in suspicious mammary lesions leads to the addition of biopsy to the list of diagnostic methods, when it is not necessary, which in turn creates additional physical and psychological trauma for

the patient. Therefore, we also conducted differential diagnostics of the disease in order to clarify the diagnosis before biopsy. Due to thickening and redness of the skin, carcinoma can sometimes be mistaken for other neoplasms, such as lymphoma (mammary gland lymphoma), breast metastases (e.g., neuroendocrine or extramedullary acute myeloid leukemia-like metastatic lesions originating from primary organs), inflammatory carcinoma, or mastitis. Given the differential diagnosis, we distinguished this case from other potential disease entities before proceeding with a biopsy of the left mammary gland. A tru-cut biopsy was performed on the lesion, with tissue samples obtained from both the left mammary gland and the left axillary region. Histopathological and immunohistochemical analyses confirmed the presence of invasive ductal carcinoma.

Surgical intervention was undertaken, during which a 3.7 cm tumor was excised from the left mammary gland at the intersection of the quadrants. The tumor was located 4 cm from the lateral surgical margin, 0.2 cm from the skin, 1.5 cm from the fascia, and 7 cm from the gland. A 17×17 cm skin ellipse was included in the resected specimen for macroscopic examination. The total surgical specimen measured 18×17×4 cm. No tumor involvement was observed at the resection margins, indicating a clear surgical excision. However, vascular invasion was identified within the tumor. Importantly, perineural invasion was absent, and the tumor did not infiltrate the underlying pectoral fascia, overlying skin, or lateral surgical boundary.

Histopathological assessment determined the carcinoma to be unifocal, with an intermediate histological differentiation grade, G2 (Figure 5).

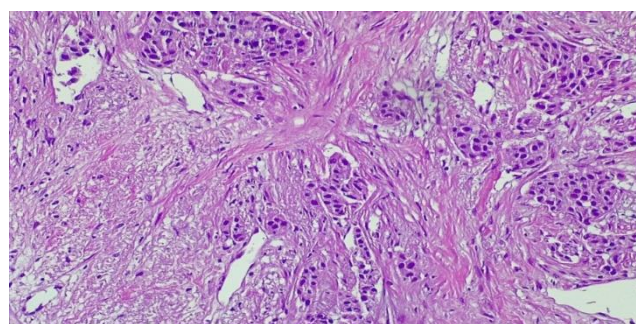


Figure 5. Histological identification of tumor. Biopsy hematoxylin-eosin staining revealed mammary gland ductal carcinoma.

The following algorithm outlines the essential procedures and appropriate equipment required to achieve an mammary glands ductal carcinoma accurate diagnosis (Figure 6).

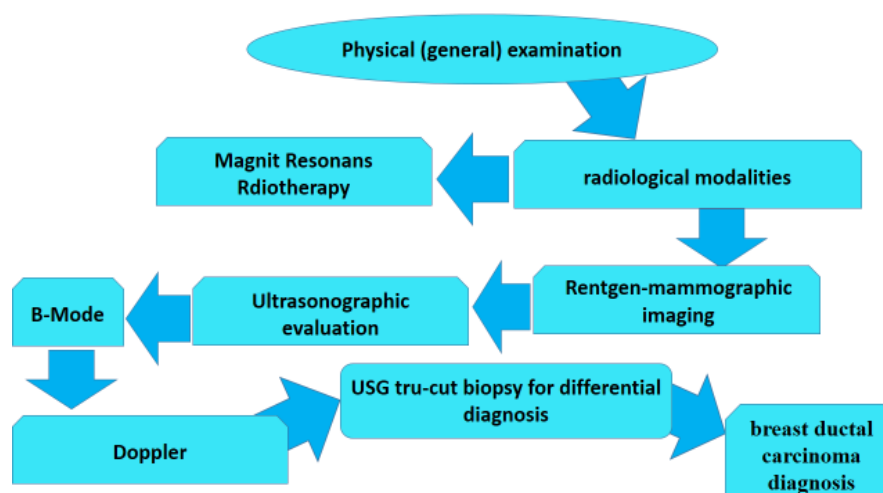


Figure 6. A sequence of procedures carried out to achieve an accurate diagnosis.

Regional lymph node analysis (pN) revealed metastatic involvement in a single lymph node, measuring 1.6 cm in diameter, indicative of disease progression to an advanced stage. Perinodal tumor extension was not observed, though reactive hyperplasia was present in five left axillary lymph nodes. The final pathological diagnosis was as follows:

1. Histopathological Type: Invasive Ductal Carcinoma
2. Tumor Size & Localization: 3.7 cm, unifocal, left mammary gland
3. Histological Grade: G2 (Moderate Differentiation)
4. Pathological Stage: pT2N1aMx
5. Lymphovascular Invasion: Present
6. Perineural Invasion: Absent
7. Surgical Margins: Negative for tumor involvement (clear resection margins)
8. Involvement of Adjacent Structures: No invasion of skin, fascia, or lateral surgical margin.
9. Lymph Node Status was revealed as follows:
10. Metastatic Lymph Nodes: 1 positive lymph node (1.6 cm)
11. Perinodal Spread: Not detected
12. Reactive Hyperplasia: Present in 5 left axillary lymph nodes

These findings confirm an invasive ductal carcinoma with regional lymph node metastasis, necessitating further oncological evaluation for appropriate adjuvant therapy.

Before starting the invasive ductal carcinoma treatment, it is necessary to clarify the molecular subtype of the neoplasm. During the immunohistochemical examination, the hormonal receptors located on the surface of tissue cells was shown to be available as follows: estrogen 90% +3, progesterone 90% +3, HER2 +1, which increased the patient's likelihood of recovering from carcinoma in the future. Based on the results obtained, the patient's therapy strategy was selected and chemotherapy was offered to the patient [14]. A neoadjuvant approach, which has proven successful over the past 5 years, was used for therapy [15].

4. Conclusion

Mammographic examination revealed a hyperdense pathological mass.

Doppler examination of the lymph nodes enabled the early detection of the neoplasm vasculature.

USG tru-cut biopsy confirmed the invasive ductal carcinoma diagnosis.

The early detection of breast ductal carcinoma at a stage characterized by high expression of estrogen (ER), progesterone (PR), and human epidermal growth factor receptor 2 (HER2) facilitates the implementation of neoadjuvant therapy. This targeted approach enhances the tumor's responsiveness to chemotherapy, potentially improving treatment outcomes and increasing overall patient survival rates.

To enhance ductal carcinoma early detection, we recommend a combined screening approach utilizing ultrasound and mammography, including its advanced modality, digital breast tomosynthesis. In cases where ultrasound does not reveal definitive neoplastic alterations, it is essential to promptly proceed to the diagnostic phase with mammographic imaging.

Abbreviations

USG	Ultrasonography
IDC	Invasive Ductal Carcinoma
ER	Estrogen Receptor
PR	Progesterone Receptor
EGFR	Epidermal Growth Factor Receptor
HER2	Human Epidermal Growth Factor Receptor 2 (Also Known as ErbB2 - Erythroblastic Leukemia Oncogene Homolog 2)

Conflicts of Interest

The authors declare no conflicts of interest.

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