

Comparative Characteristics of Radiological Imaging and Morphological Features in Breast Cancer (Review of the Literature)

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Abstract: The diagnosis of breast cancer was made using radiological images. The type of target for the patient's biopsy, pathological data, surgical excision samples, breast density, if any, and the results of subsequent imaging are compared with radiological images. The degree of discrepancy between the objectives of the biopsy and X-ray and pathological studies was compared between the two biopsy groups. Generalized mixed modeling was used to study the results before and after biopsy under the control of digital mammography.

Keywords: mammography, controlled biopsy, breast tomosynthesis, radiological imaging, morphological features.

Relevance. Non-palpable mammary gland formations are the most difficult to diagnose mammary gland formations. According to published works, non-palpable formations turn out to be malignant in 9-24% of cases [1, 8]. As mentioned above, the detection of early forms of cancer improves the prognosis of the disease. In a study by Tinnemans J.G. et al. An inverse relationship between the size of the primary tumor and non-aggressive and overall survival is proved [17]. Moreover, the size of the tumor affects the presence of regional metastases. Thus, in tumors no larger than 5mm, lymph node metastases were found in 7.7%, in tumors 6-10 mm in size – in 12.5%, in tumors larger than 10mm - in 29.5%. The same study showed the relationship between the presence of metastatic lesion of regional lymph nodes and 10-year overall survival: 96.4% for stage N0 and 78.8% for stage N1-3. Parameters of the classification of breast cancer. The main elements of the breast are lobules with glands that produce breast milk, as well as ducts that deliver it to the nipple. The tissues are permeated with blood and lymphatic vessels responsible for supplying the mammary gland (MF) with nutrients and excreting decomposition products. The disease begins when the normal cells of a woman's body begin to divide uncontrollably, while the process of their death is disrupted. Types of breast cancer are classified according to different criteria. According to the localization of the primary node, oncological pathologies are divided into neoplasms: nipple; areola; armpit area. Depending on the quadrant of the location, malignant nodes are: upper-inner; upper-outer; lower-inner; lower-outer. Up to 50% of primary neoplasms in women are formed in the upper upper quadrant of the breast, about 20% — in the area of the areola or the central part of the breast. In separate groups, specialists distinguish breast cancer of unspecified location, and beyond the boundaries of individual areas [13,37]. Tumor primary nodes can be ductal or lobular, based on which tissue element of the organ structure has begun to degenerate. In addition to location, the classification of the disease according to such parameters as: histological structure; stage of development; form; molecular taxonomy. Malignant neoplasms are also differentiated by the degree of aggressiveness of exposure, propagation speeds. Metastasis. Regardless of the location of the primary node, cancer can be: noninvasive — the tumor grows, but does not leave the boundaries of the affected part of the organ; invasive — a malignant neoplasm grows beyond the boundaries of the lobule (or milk duct), its metastases first "capture" healthy parts of the breast, then other organs and systems. Malignant cells "spread" through the body from the gland in two ways: lymphogenic — through lymphatic vessels; hematogenic — with blood flow [19, 21,27]. First, metastases affect regional lymph nodes under the shoulder blades, armpits, sternum or collarbones. Then they appear in remote areas of the lymphatic system, grow into the skin, soft and bone tissues. In the terminal stage, malignant cells are found in almost all internal organs of the human body. When the development of breast cancer ends with abnormal tissues separating from the "maternal" node and

being transferred to other parts of the woman's body, the disease is called metastatic. If the primary pathogenic node is formed again after treatment in the second breast, in the same place, closely located tissues or organs, we are talking about a recurrent type of cancer. Both forms of pathology belong to late-stage diseases, metastases may appear months or even years after the end of treatment. Relapse occurs in about 30% of women who have undergone therapy in the early stages of the disease. The average time of local "return" of oncology is five years. The risk of recurrence of the neoplasm is especially high — the first 24 months. Noninvasive breast cancer may acquire an invasive form as the size of the neoplasm increases. It is very important to monitor the intensity of its growth, to be able to start treatment on time, and to stop metastasis[11,29]. Experts identify three degrees of doubling the size of carcinomas in women: high – abnormal primary node grows twice in three months or less; medium – doubles over a period of 3 to 12 months; low – doubling lasts more than a year. Tumor cells undergo a separate differentiation. In medical documents, the parameter is indicated by the Latin letter "G". Doctors distinguish three degrees of danger of breast cancer: highly differentiated (G1) — malignant cells are similar to natural ones, divide slowly, have a low potential for metastasis; moderately differentiated (G2) — pathologically altered structures retain signs of normal, multiply at an average rate, are more prone to spread than the previous group; low—differentiated (G3) - cells are practically devoid of signs of healthy, divide rapidly, they have a high potential for the formation of metastases. They are a sign of an oncological disease with an aggressive, rapid, life-threatening course. Determining the type of malignant cells and the localization of the primary neoplasm helps to predict the possible spread of metastases. Histotypes of breast cancer. The histological form of the disease is determined by the place of its formation and the nature of its spread. Most often, women develop carcinomas — formations from malignant epithelial tissues of organs. Oncologists distinguish several main types of breast carcinomas by histotype: intracurrent carcinoma is the initial stage of cancer, it grows from epithelial cells, because of its small size it is not palpable, it happens to be an accidental finding during a medical examination. It is additionally designated by the Latin term *in situ* (translated, it means "in its place"). The form is successfully treatable, but the probability of recurrence in the first 10 years is about 30%.

Lobular carcinoma *in situ* – is formed from glandular tissue, remains within the boundaries of one lobule. Just like the previous view, it has a small size, it is palpable only with a subcutaneous location;

➤ infiltrating intracurrent carcinoma is the most common type of breast cancer in women. It accounts for about 80% of the total number of detected cases of organ cancer. The lesion originates in the milk duct, grows beyond its boundaries, affects the surrounding tissues, then the lymph nodes. It develops more often in ladies over 55 years old, but may appear in a young girl;

➤ infiltrating lobular carcinoma — originates from the lobule, attacks the chest, then the skin, muscles, bone tissue. It is diagnosed in 20% of women with breast cancer;• medullary carcinoma is a voluminous, soft neoplasm with clearly defined boundaries, belongs to the ductal group of oncological diseases. It is rare (it accounts for 3-5% of cases). The forecast is very favorable. The tumor grows slowly, almost never passes to the lymph nodes, and is treatable; Inflammatory carcinoma is a rare type of disease. It occupies 2% of the total structure of breast cancer, usually develops in young women. The name is due to the peculiarities of the course, similar to the inflammatory process. Infiltration is accompanied by pain, fever, swelling, redness of the skin. The tumor is extremely aggressive, spreads at lightning speed, and requires immediate surgical intervention; secreting carcinoma (or juvenile cancer) develops in children or adolescents. It looks like a knot with clear borders, reaches a size of 3 cm in diameter. It rarely spreads metastases; papillary carcinoma is another rare form (1-2% of cases), typical for women during post-menopause. The formation is soft, forms near the nipple, grows into the lumen of the milk duct, almost never metastases; apocrine carcinoma (1% of breast cancer cases). It develops slowly, but often affects regional lymph nodes. In addition to carcinomas, sarcomas can form in women. Tumors of this type are not formed from epithelial tissues. They are much less common than carcinomas, characterized by rapid growth, high levels of malignancy and mortality[5,11,23]. Taking into account these data, the identification of early forms of breast cancer leads to the appointment of less aggressive treatment with organ-preserving operations

and the rejection of extensive lymph dissections towards sentinel lymph node biopsy, as well as the exclusion of chemotherapy from the treatment algorithm. The combined work of a surgeon, radiologist and pathologist is important in the correct management of a patient, which helps to achieve optimal results and reduce mortality from breast cancer [28]. However, the identification of non-palpable mammary gland formations can be difficult. Firstly, they do not cause complaints, and a woman may not be aware of the presence of a tumor node for a long time. Secondly, due to their small size, especially with high density of breast tissue, non-palpable formations may be missed during examination. This is not a complete list of types of breast cancer in women. Each of them is divided into subtypes, and there are also mixed forms. Breast cancer (BC) can have various histomorphological characteristics [7]. There are more than ten different histological forms of this pathology, combined by one clinical diagnosis. Accordingly, the etiological factors of the development of each of these forms may be more or less specific. The genetic factor is considered one of the leading factors in terms of the development of breast cancer. Several candidate genes have been identified, mutations and polymorphisms of which are associated with the risk of its development [21, 25]. The genes from the BRCA group, as well as other regulatory genes (TP53, MSH2, MLH1, MSH6, PMS2, etc.) are most often considered among these [17,18]. Usually, the genetically determined component of the incidence of breast cancer is associated with familial forms, as well as with national and population peculiarities of gene distribution [20,22]. However, the impact of adverse environmental conditions can serve as one of the factors for increasing the frequency of mutations of any of the genes in the corresponding population [13,15]. The most dangerous in genetic terms is the radiation factor [16,19]. The various histological forms of breast cancer are far from ambiguous in terms of clinic, prognosis, and required treatment [6]. In most cases, infiltrating ductal cancer is the most common, and modern treatment approaches are accordingly the most adequate for its cure [4]. Changes in the structure of histological forms associated with the features of the etiology of the disease, including the genetic factor, if any, could be identified, serve as the basis for special attention to aspects of conservative treatment and follow-up of patients [3,14]. The territory of the radiological disadvantage of the Semipalatinsk nuclear test site is characterized by the residence of a large number of directly irradiated women and their descendants who are at the age of breast cancer development [9]. In many cases, they have a family history [2]. Therefore, the possibility of a relationship between the radiation factor, family radioecological and tumor history and the histological structure of malignant neoplasms of the breast is of great interest. Papillary cancer was observed in 10 cases and its distribution did not significantly depend on the presence of mutations. The only case of this cancer with a combination of mutations corresponded to 9.1% of the frequency, but there was no statistical significance of the differences. In a smaller number of cases, infiltrating lobular, secretory, squamous, adenocystic and tubular cancers were observed. It should be noted that the high incidence of squamous cell carcinoma in the subgroup with combined mutations is 4 times higher than that observed with isolated BRCA1 mutations and 3 times higher than TP53. There were no other significant differences in the structure of individual histological forms of cancer. At the same time, when analyzing the frequency ratios of infiltrating ductal cancer and other histological forms (Figure 1), the presence of statistically significant differences between all subgroups identified depending on the identified mutations was recorded. The differences in the overall frequency of IPR in the group with the absence of identified mutations with the group with the presence of the mutant BRCA1 genotype were $RR=1.18$ ($p=0.05$), with the mutant TP53 genotype $RR=1.55$ ($p=0.02$) and with a combination of BRCA1 and TP53 mutations $RR=1.82$ ($p=0.03$). If the frequency of the most common histological form of breast cancer was significantly lower, and, accordingly, the totality of less common forms was higher in the presence of identified mutations. Next, we identified a group of patients with familial breast cancer and carried out an appropriate distribution (Table 2). Of the 60 examined, the absolute majority were individuals with identified mutations, including 38.3% with the mutant BRCA1 genotype. In the subgroup with the absence of certain mutations, infiltrating ductal cancer was most common (81.0%), the same was noted in the presence of BRCA1 mutations (60.9%). On the contrary, when detecting the mutant TP53 genotype and a combination of BRCA1 and TP53 mutations, this histological type was detected in less than half of the cases (27.3% and 20.0%, respectively). The history of breast disease imaging began in

1913 with the work of Albert Salomon, a German physicist who experimentally studied the effect of X-rays on breast tissue, for which mastectomy samples were used. Salomon was the first to describe the characteristics of tumor nodes, their difference from benign formations, a multicentric variant of tumor growth, as well as microcalcifications in the malignant process. The method of X-ray mammography was not used until the 30s of the twentieth century due to the poor development of the equipment, poor image quality and high dose load [69, 145]. The revealed changes in the totality of their characteristics belong to one of the categories of the BI-RADS system from 0 to 6. Category 0 is set for screening examinations and requires additional diagnostic methods. Categories 1 and 2 correspond to normal or benign changes, do not require additional interventions, and a routine examination is prescribed. Category 3 speaks in favor of good quality, requires the appointment of dynamic monitoring after 3 or 6 months. Categories 4 and 5 require mandatory interventional intervention for morphological confirmation of the diagnosis. Category 6 means histologically confirmed breast cancer, the patient is subsequently referred to an oncologist to determine treatment tactics. This classification promotes continuity between radiologists of various diagnostic centers and hospitals, unifying the algorithm of examination and further management of patients with changes in the mammary glands. Despite the relatively high efficiency of the method, digital X-ray mammography has a number of disadvantages, such as radiation exposure, low sensitivity in dense breast tissues, and a high proportion of false positive and false negative responses. False results occur in different age groups, but are more common in young women with a dense background. This is due to the fact that with a dense ambient background, small formations and areas of restructuring of structures may be invisible. It is believed that about 20-30% of breast malignancies remain undetected according to traditional mammography [78]. The situation may develop in the opposite way, when compacted areas of tissue are mistaken for false formations, which occurs in 11-22% of cases and is the reason for the appointment of unjustified repeated studies, invasive interventions, and, as a result, leads to severe psychological trauma to the patient, after which the woman may not come to the next study [32]. Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are radionuclide research methods based on the assessment of the accumulation of radiopharmaceuticals in certain areas of interest. In combination with X-ray computed tomography, it is possible in one study to assess metabolic (according to SPECT and PET) and structural (according to CT) changes in certain organs and tissues. These hybrid technologies appeared in the early 2000s and are actively developing at the present time, becoming increasingly used in oncological practice. However, due to the high radiation doses and high cost, the use of these techniques in mammology remains limited. Works dedicated to the SPECT/CT scans of the mammary glands are few in number, however, according to some authors, the technique shows a fairly high sensitivity in the diagnosis of locally advanced breast cancer [125] and edematous infiltrative form of the disease [27]. Sensitivity of the SPECT/CT in the detection of breast cancer on average reaches 98.3%, specificity – 85.7%. The indicators decrease in small tumors (up to 1.5 cm) [4]. Ultrasound is an integral method of diagnosing breast diseases, playing a leading role in young women with high breast density, as well as during pregnancy and lactation. In the older age group, ultrasound of the mammary glands is an additional research method to X-ray mammography, which allows for a clarifying diagnosis of nodular formation, differentiating liquid formation from solid formation with great specificity, and evaluating their vascularization and density [11, 13]. According to various authors, the sensitivity of the ultrasound method at high density of mammary gland tissues ranges from 73-93%, specificity - 62-88% [54, 99, 119, 131]. The use of ultrasound in combination with X-ray mammography increases the sensitivity and specificity of both research methods to 92.9% and 87%, respectively [11]. Ultrasound examination of the mammary glands has a number of advantages: speed, lack of radiation exposure, high sensitivity with a dense background of mammary glands. An important advantage of the ultrasound method of mammary gland examination is the ability to assess the condition of regional lymph nodes, significantly surpassing the data of palpation and X-ray mammography in determining the nature and volume of lesion of regional lymph nodes, which, according to world literature, in 55% of cases of metastatic lesion are not palpated and are not displayed in an X-ray [25].

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