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MODERN APPROACH TO BREAST CANCER SCREENING

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Annotation: *International Agency for Research on Cancer and WHO Cancer Division, proven in 7 prospective studies, – mammography (film or, better, digital) in all (regardless of risk groups) women included in the "targeted" cohort of 50-69 years*

Key words: *breast cancer, screening, diagnosis, treatment*

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From the perspective of the International Agency for Research on Cancer (IARC, Lyon) breast cancer (BC) is an "ideal" tumor for population – based screening. This is the most common tumor in women, especially over the age of 50. Of the 10 million new cases of malignant tumors of various organs detected in the world, 10% are in the mammary gland. If we estimate only the female population, the proportion of breast cancer increases to 22%. In industrialized countries, the proportion of BC is even higher – 27%. But breast cancer is also the most common cancer in developing countries. In 2020 Breast cancer identified from 471 million women in developing countries, i.e., most often cervical cancer (379 million), the leader in the preceding years [1, 2]. More than half of the cases of breast cancer (579 million) annually in North America, Western Europe, Australia and New Zealand, where breast cancer occurs in 6% of the female population lifetime (75 years). The same frequency of these tumors is found in Argentina and Uruguay. The lowest incidence of breast cancer is observed in sub-Saharan Africa, South Africa, and South Africa.-Inin eastern Asia and in Japan, where the probability of developing breast cancer is one-third compared to the West (2% of women live up to 75 years). The Russian Federation and the countries of Central and Eastern Europe occupy an intermediate position in terms of breast cancer frequency. In the Russian Federation, about 50 thousand new cases of breast cancer are detected annually . According to the latest WHO data published in 2018, deaths from Cancer dairy products glands in Uzbekistan they reached 1.449 or 0.92% of the total mortality rate. The age-adjusted mortality rate is 11.00 per 100,000 population, which takes **Uzbekistan** No. 144 in the world. [2, 3]. Until the 1990s, morbidity and mortality increased in both economically developed and developing countries. Further, as mammographic screening was introduced and the prognosis of breast cancer cases improved in economically developed Western countries, these indicators changed significantly, with a slowdown and then a decrease in mortality rates (IARC, 2006). In contrast, morbidity and mortality continued to increase in Eastern Europe and Latin America [7]. At present, secondary prevention, i.e. preventive treatment, plays a high role in the strategy to combat breast cancer. detection of breast tumors at the stage when they can be cured by existing methods of treatment. In the practice of healthcare in developed countries, the concept of "screening" is firmly established, which means a mass periodic

examination of a healthy population in order to detect a latent cancer, such as breast cancer [17, 19, 22, 26]. The ideology of screening is based on the fact that routine clinical examination and self-examination usually do not provide detection of curable forms of cancer. Therefore, it is necessary to use such instrumental diagnostic methods. drugs that would detect manifestations of significantly earlier forms of tumors that can be cured by existing surgical, chemohormonal, or radiation treatments. X-ray mammography was the most suitable method for this purpose. Screening involves the use of a method for detecting latent pathology in a large group of practically healthy individuals and therefore must meet the following requirements: High sensitivity of the applied method or test, which makes it possible to detect the majority of malignant tumors in the examined group with a minimum number of false negative conclusions.

High specificity of the method, which allows you to exclude the majority of healthy women who do not have breast cancer, and minimize the number of false positive conclusions. Acceptable average cost per detected cancer case. Minimal harm to the health of the subject. Easy operation and maintenance of equipment. Screening should not be confused with diagnostics. Mammography can only detect areas of the gland parenchyma that are suspicious of a tumor, the nature of changes in which needs to be clarified using additional diagnostic methods (stereotaxisbiopsy using the Mammotom complex mammotest or directed biopsy by ultrasound). The widespread use of mammographic screening in a number of countries has changed the ratio of removed benign and malignant breast tumors. In particular, the incidence of non-invasive breast cancer (in situ carcinoma) has dramatically increased, which causes a constant debate about the optimal treatment of such "initial" forms of cancer. While the ultimate goal of screening is to reduce breast cancer mortality, its immediate goal is to detect cancer before clinical manifestation. At the same time, the detection of cancer (or its consequences) occurs. pre-clinical presentation increases the risk of false positive diagnosis and overtreatment [31]. Breast cancer is a heterogeneous disease characterized by a different "natural history". The widespread opinion that epithelial breast tumors inevitably progress from atypia to carcinoma in situ, then to invasive cancer and subsequent metastasis is not supported by all researchers [6, 8]. Ductal and lobular epithelial proliferation, especially with atypia, undoubtedly increase the risk of breast cancer (RR=2-4). However, these diseases, most likely, only a part of the breast cancer incidence spectrum is determined. It is possible that this pathology is not the main basis for the development of all forms of breast cancer. Since screening mammography, in contrast to the clinical method (palpation), allows early detection of a variety of breast pathology, it becomes especially important to know more about the risk of progression of various types and forms of identified pathology. Understanding the threat and frequency of progression of this pathology is critical when conducting a screening program, including the choice of adequate treatment for the detected disease. Molecular and genetic features studies of DCIS (ductal carcinoma in situ) and atypical ductal hyperplasia using the "loss of heterozygosity" method showed similar genetic damage, indicating a clonal origin of these diseases [18]. In addition, it was shown that non-invasive (in situ) and invasive structures of breast cancer have identical molecular and genetic changes, i.e. they are steps of the same pathogenetic pathway. These findings coincide with observations on the similarity of the morphological characteristics of in situ and invasive components of cancer [3]. Data from the Swedish Screening Project they gave a basis for an alternative hypothesis. According to Tabar [28], the tumor progresses from a low to a high degree of malignancy, and the proportion of high-grade tumors increases with increasing tumor size. Ductal cancers, which make up the majority of breast

tumors, are characterized by time-dependent prognostic factors (tumor size, lymph node status) that indicate the possible effectiveness of screening (for example, with a minimal tumor size and the absence of regional metastases). Invasive breast cancer presents It is a malignant tumor, part or all of which sprouts the basement membrane of the epithelial lining of the duct or lobule. Breast cancer prognosis depends on two groups of parameters. The first of them are the mentioned time-dependent indicators that determine the stage of cancer: the size of the tumor, the presence of regional or distant metastases. The second group determines the" internal " biological features of the tumor: histological type, degree of malignancy, expression of hormone receptors, growth factors (NER2), and other molecular characteristics of the tumor. From the listed signs, the size of the tumor, histological the type, degree of malignancy, vascular invasion, and condition of regional lymph nodes are directly related to the outcome of the disease. Both clinicians and pathologists agreed that both screening evaluation and treatment planning should initially focus on the minimum set of signs reflected in the TNM system from stage 0 (in situ) to stage IV. Determining the size of the primary tumor is particularly important during screening. The term "minimal" breast cancer was originally proposed to identify forms of breast cancer characterized by a particularly favorable prognosis. Gallagher [13] referred to "minimal" breast cancer is all forms of cancer in situ (ductal and lobular) and invasive cancers no more than 5 mm in diameter. Subsequently, the term was revised to take into account the tasks of mammographic screening, and, in particular, the American College of Surgeons, and later radiologists, adopted a size of 10 mm or less as the standard defining a "minimum" breast cancer. Tumor size is an important criterion for evaluating the quality of screening and determining the ability of X-ray mammography to detect non-palpable tumors. Therefore, it is extremely important that pathologists measure the diameter of the tumor as accurately as possible. The smaller the primary size is the greater the probability of error in determining the size of a tumor [31]. Mammography remains the main component of screening. X-ray mammography as a screening test was comprehensively studied and evaluated in randomized trials in which women with previously diagnosed breast cancer were excluded from the list of participants. In almost all trials (seven out of eight), the effect of early detection of invasive cancer was shown to manifest itself 5 years after the start of screening. In other words, the reduction in breast cancer mortality is delayed even with well-organized and high-quality screening. The positive effect can also occur much later if the women participating in the screening are younger than 50 years of age [6, 22, 28], as was observed in the Swedish Screening. As population-based screening programs are implemented (nationwide or regionally), the techniques developed in randomized trials need to be adapted to the more complex situation of practical healthcare. In contrast to randomized trials, population-based screening programs will require a significantly longer interval (more than 7 years) to demonstrate a reduction in breast cancer mortality. In contrast from female volunteers in experimental screening studies, the general female population often hesitates whether to participate in the proposed program, and women with previously diagnosed and treated breast cancer are not easily excluded when calculating overall mortality rates. Accurate mortality rates can be established if there is a cancer registry and a well-established link to the screening program database. Therefore, predictive screening estimates based on short-term criteria are useful for determining the future expected reduction in breast cancer mortality. Short-term criteria These include such parameters as "sensitivity", "specificity", distribution by stages of breast cancer, frequency of "interval" inter-screening breast cancer. This method of determining the benefits of screening may be useful only in the initial stages of screening

programs, but it cannot replace the subsequent analysis of the overall survival of breast cancer patients and the determination of observed (actual) mortality. Almost all non-palpable forms of breast cancer were detected by chance during mammography or ultrasonography earlier (in the pre-screening period). There is always a question concerning the choice of an effective algorithm for diagnostic measures if focal formations or calcifications of unclear origin are detected on mammograms. Until recently, there were two ways to solve this problem: the first – performing an excisional biopsy, i.e., a sectoral resection with urgent morphological examination; the second-dynamic observation. The first approach did not always turn out to be optimal, since it is not always possible to make an accurate diagnosis with an urgent study, which ultimately can lead to an inadequate amount of surgical intervention (both over-economical and ultra-radical surgery). In addition, in more than 50% of cases an excisional biopsy is performed for a benign process and not always a tumor. The second way may result in delayed detection of a malignant tumor. In order to avoid these mistakes, recently they are trying to establish an accurate diagnosis already at the preoperative (outpatient) stage, for which a biopsy under the control of ultrasound or radiography of the breast is increasingly used – the so-called stethotactic biopsy. At the same time, the choice of the type of biopsy depends on the method in which the tumor is better visualized and there is convenient access for the procedure, which means that It depends on the size of the breast, the ratio of fat and glandular components, the location, size and nature of the pathological focus. All these parameters should be carefully evaluated before performing a targeted biopsy. Puncture under ultrasound control. Using ultrasound, you can perform both a fine-needle aspiration biopsy and a trepan biopsy. The procedure is performed in the following situations: with nodular formations (less often with microcalcinates), in the case of the location of the tumor in those areas of the breast that are not reflected on mammograms (submammary, subclavian and axillary area). Under the control of ultrasound, it is most convenient to perform a biopsy for relatively large nodular non-palpable formations, which are better fixed during the procedure than small ones (less than 0.5 cm). Despite the fact that some of these formations are clearly visible on mammography, an ultrasound-guided biopsy may be preferred as the simplest method in such cases. However, in situations where an ultrasound-guided biopsy cannot produce enough material for verification, patients need to perform a stereotactic biopsy. Stereotactic biopsy. Indications for breast trepaniopsy under X-ray control are X-ray signs that require verification: the presence of a formation with signs of malignancy, for example, high-density foci, grouped or diffuse microcalculates, local deformation of the breast structure, etc. The biopsy is performed using a stereotactic biopsy unit. The procedure is performed under local anesthesia using 11G or 14G trepaniopsy needles. During each biopsy, 6 to 20 samples are taken (an average of 10). The number of samples depends on the nature of the resulting tissue. If there is a predominance of adipose tissue (especially in diffuse microcalcification), it is necessary to increase the number of samples in order to ensure that the probability of obtaining tumor tissue remains high. To confirm the accuracy of the biopsy, a follow-up mammogram is always performed after each procedure, and if there is a buildup of microcalcifications

The only "natural" risk factor that significantly increases the incidence of breast cancer is age, especially from the age of 50. That is why in 20 of the 22 countries where nationwide (population-based) mammography screening is conducted, the lower age peak is defined at 50 years, and the upper age peak is 69 years. There is no reliable evidence, recognized by the WHO Cancer Division and IARC, of a positive effect of screening in women younger than 50 years and older than 70 years.

Constantly and carefully analyzing various methods and proposals for mass preventive examination For women, the International Agency for Research on Cancer (IARC, Lyon) and the WHO Cancer Division recommend only one test proven in 7 prospective studies – mammography (film or, better, digital) in all (regardless of risk groups) women included in the "targeted" cohort of 50-69 years. Based on 25 years of screening experience in Europe and North America, IARC guidelines are simple and clear: 1) a single screening test, mammography, is used; 2) the examination of women is repeated every 2 years and for many years; 3) all women are examined and invited for examination 50-69 years of age (regardless of belonging to risk groups); 4) all women invited to participate in screening should be informed that no other screening tests other than mammography (self-examination, physical examination, ultrasonography, etc.) lead to a decrease in breast cancer mortality; 5) in countries where general mammographic screening and standard treatment are not practiced, there is no decrease in breast cancer mortality [12].

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