UDC: 618.19-006

N.M. TULEMISOV[1]

[1]Regional Oncology Center, the city of Uralsk, West Kazakhstan Oblast, the Republic of Kazakhstan

Invasive methods of breast neoplasm malignancy verification: analysis of efficiency, safety, and possibilities of implementation in the general healthcare network

The article contains the analysis of the current situation in the diagnostics of breast cancer. The implementation of preventive screening has increased the number of cases of suspected oncology which require timely diagnostics. Today, refining diagnostic is primarily available in oncological dispensaries. Such principle of organization can reduce the availability of this medical service, increase the queues and duration of the survey. Therefore, it is necessary to consider the possibility to provide refining diagnostics directly at the place of residence of the patients. The successful implementation requires choosing the most effective and safe method of invasive diagnostics. This research evaluates the efficiency of different biopsy techniques and the frequency of possible complications. The research results provide the evidence for decision-making on the choice of methods of diagnostics, training and monitoring of pre-trained professionals.

Keywords: *breast biopsy, general medical network, training of specialists.*

Introduction. Improving the methods of diagnosis and treatment of breast tumours is one of the most urgent problems of clinical medicine because their prevalence is wide and tends to grow in most of the countries including the Republic of Kazakhstan [1]. WHO reports lately that more than 1 million of women die from breast cancer (BC) each year [2, 3]. The Republic of Kazakhstan had more than 4 397 new cases of primary breast tumours in 2015, with the mortality of 7.9 per 100 000 (absolute number of deaths – 1 386) [2].

In West Kazakhstan, in 2011 BC amounted to 11.3% of all malignant tumours and 7.8% of cancer mortality. BC remains an actual problem of the time. High mortality from BC is specially due to its late detection and a high share of advanced cases which is a major criterion of the quality of diagnostics.

Progress in BC diagnostic is manly associated with an intensive use of modern diagnostic tools and methods of biopsy. Biopsy is an essential component of a comprehensive BC diagnostics and is mandatory in case of any suspicion for a malignant tumour [3, 4]. It allows not only to confirm the diagnosis but also provides information on the main biological characteristics of the tumour (histological type, degree of differentiation or malignancy, expression of receptors for steroid hormones and other biological markers) [5].

Today, the palpable and non-palpable mammary gland neoplasms are mainly diagnosed in outpatient departments of regional oncological dispensaries. The most popular methods include: fine-needle aspiration biopsy (FNAB), and trepanobiopsy under ultrasound or stereotactic control [6]. These two types of study were widely introduced in the course of implementation of the oncology service development program [7] and the expansion of the list of screening activities at the stage of refining diagnostics [8].

Until recently, the main method for breast neoplasm verification was the sectoral resection on the operating table. However, surgical biopsy is often accompanied with a significant risk of cosmetic defects and is not mandatory for the diagnostics of benign breast tumours.

The palpable and non-palpable mammary neoplasms are manifested by several main symptoms revealed during a complex X-ray-sonographic study.

Information capacity of biopsy depends on its adequate use and is mainly determined by mammographic and ultrasound parameters of the neoplasms. However, the optimal use of various methods of biopsy is still unspecified. At that, the introduction in our country of screening mammography that involves a multi-level examination has resulted in an increased number of patients with palpable and non-palpable neoplasms which required a morphological confirmation [9].

The growth in 2015-2016 of the number of people subject to examination has raised the questions of timely provision of diagnostic services, as well as the reduction of time from the moment of suspected oncology to its verification, in particular, for people living in remote places. The conducted study has shown that the existing methods of biopsy include a technique suitable for both general medical network and specialized centres. This method is not widely used today. Its introduction into the general medical network could reduce the workload on oncological dispensaries, increase the accessibility and reduce the time of examination before verification of the diagnosis.

Materials and methods. The following devices were used for the verification of processes of anatomical and structural changes in breast gland: ultrasound apparatus «ToshibaAplo 400» (Japan, 2015) «PhilipsHD 11» (USA, 2010), stereotaxic installation «SenographeEssential» (France, 2014). The studies were performed using conventional 10-20 ml thin needle syringes and biopsy needles for Bard Magnum 16 d x 13 cm [10].

The study included 1 807 women aged 25 to 78 years (average age – 55) with palpable and non-palpable mammary neoplasms detected during random, preventive (screening) mammography or ultrasonography during

2015-2016. All patients with neoplasms 2.0 to 7.5 cm underwent FNAB; neoplasms .5 to 1.5 cm in diameter were diagnosed under ultrasound control; neoplasms less than 0.5 cm - using encephalometer.

Biopsy under X-ray control was carried out in two stages:

1) digital mammography with image enlargement;

2) stereotactic biopsy.

Before digital mammography and stereotaxic biopsy, the pathological focus was mapped onto the mammogram in cranio-caudal projection: the distance from pathological formation to areola and to the medial or lateral margin of the mammary gland [11]. Measurements were recorded on the patient's breast in the projection of the expected location of the formation.

Localization of the suspected area. The patient was lying pronate on the table of the stereotactic X-ray mammographic unit with a hole for mammary gland that was fixed in the hole with a compression plate with a window 5x5 cm with the area marked on the skin located as close as possible to the centre of the window. Design of the apparatus mad it possible to locate the gland in different planes and to puncture the pathological sites located in nearly all parts of the mammary gland including such hard-to-reach places as the axillary area, the retromammary space, and the submammary fold [12].

Finally, all the patients underwent a mammographic and ultrasound study. Then, an optimal variant of a targeted biopsy was determined for each patient based on the clinical data and the data from radiation diagnostics.

In addition, the safety of methods was assessed by the risk of complications. Complications after biopsy are quite rare and most often associated with a contamination. Post-procedural monitoring included the following possible symptoms:

- oedema, bruises and extensive reddening of tissues;
- fever and heat;

bleeding at the puncture site;

- changing shape of the breast.

810 women were examined using FNAB method. The neoplasms were mostly 2 cm and more in diameter (2.0 to 7.5 cm). Malignant tumours detected during monitoring amounted to 62.8% (n=227). Registered complications: 0.6% in 2015, 0.2% in 2016 (see Table 1).

Table 1 – Comparative data of examinations made in 2015-2016 using main methods of biopsy

№	Name of the method	2015 г.				2016 г.			
		No. of examined women	No. of identified pathologies	Of them, cancer	Complications*	No. of examined women	No. of identified pathologies	Of them, cancer	Complications*
1	Fine needle aspiration biopsy (FNAB)	348	126	118	2	462	235	109	1
2	Ultrasound biopsy**	528	466	33	7	308	272	27	5
3	Encephalometer – controlled trepanobiopsy under control of stereoscopy **	115	43	10	5	167	86	22	5
	Total	929	635	161	14	878	593	123	11

** complications obtained at the entrance of the breast biopsy - 1.4% (25 of 1807) of the examined women;*
*** also based on the results of screenings*

Clinical detection of tumours larger than 1 cm usually presents no problems due to the presence of quite reliable clinical signs implying BC. However, the diagnosis of asymptomatic «minimal» (non-palpable) tumours and carcinoma in situ is complicated. In the countries and centres conducting screening, these forms account for 60-80% of all newly diagnosed cases of BC [12].

Ultrasonography (US) has revealed malignant tumours in 836 patients. In most cases, that was hypoechoic (less often, hyperechoic) formations of about 1 cm in diameter (0.5 to 1.5 cm). Ultrasound biopsy was mostly convenient in case of large nodal non-palpable formations which were better revealed during such procedure than the small ones (less than 0.5 cm). Though some of these formations were clearly visible during mammography, Ultrasound biopsy is an easier and preferred method in such cases. The malignant tumours detected during Ultrasound biopsy amounted to 8.1% (n=60) of the revealed pathologies. Registered complications: 1.3% in 2015, 1.6% in 2016 (see Table 1).

However, in the cases when Ultrasound biopsy could not provide enough material for verification, the patients underwent a stereotactic biopsy.

Mammographic studies for stereotactic biopsy have revealed suspected tumours in 201 patients with varied symptoms and radiographic manifestations. Non-palpable forms of BC were mostly manifested in mammograms by high density nodes (58%, 19 women), calcifications of various forms and densities (26%, 9 women), or a combination of those features (16%, 6 women). Calcifications can be single or multiple, grouped or scattered in the mammary gland tissue, have different densities, shapes and sizes. The foci of high density varied in size from 1 mm to 15 mm or more. The malignant tumours detected during stereotactic biopsy amounted to 25.6% (n=33). Registered complications: 4.4% in 2015, 3.0% in 2016.

The diagnosis was confirmed by post-surgery morphological study in all cases. No serious complications were registered after Ultrasound biopsy.

Small hematomas that required no special treatment were registered in 1.3-1.5% of cases. The patients with be-

nign tumours continue follow-up monitoring. No signs of malignant growth were detected in those patients till the date of the paper.

Conclusion. The opinions on the capacities of morphological methods of pre-surgery verification of diagnosis still vary. According to some authors, FNAP is the most affordable and efficient method of confirmation of breast diseases.

FNAB method provides the highest level of detection at a low level of complications, is simple and safe. It is the most accessible informative method for detecting malignant breast pathology in the general medical network.

Along with this, some changes are required into the existing legal acts, and a methodology of certification training of city and district oncologists on the topic: «Use of FNAB for early detection of breast cancer» shall be developed. During the implementation of the methodology, the training and methodological centres shall develop an algorithm for online tracking of its implementation results in medical organizations (with a monthly registration in the Training and Demonstration Centres of the patients' names and the obtained results) for at least 6 months upon completion of training.

Today, there is no clear algorithm for pre-surgery examination of patients with non-palpable mammary gland neoplasms using different methods of biopsy depending on sonographic and x-ray characteristics. However, the use of these ultrasound and stereotaxic biopsy techniques in the regional centres is a prerequisite for detection of neoplasms less than 1 cm in diameter. These technologies shall remain at the level of regional oncological dispensaries taking into account the frequency of complications vs. FNAB, the requirements towards medical equipment, certain knowledge, experience and skills of medical personnel.

The conducted studies resulted in the following conclusions that require the following decisions to be made:

1. FNAB is the main method of sampling for morphological study due to its simplicity and accessibility.

2. FNAB is the most suitable and safe method for diagnosing palpable tumours in the general medical network.

3. The introduction of FNAB in oncologists' offices will shorten the examination time by 1-2 days which are now spent by the patient for biopsy and waiting for its results.

4. FNAB is not suitable for verification of non-palpable mammary gland neoplasms as it returns an uninformative and false data.

5. Stereotaxic biopsy is a method of choice for the verification of areas with changed structure and microcalcification in mammary gland determined only by mammography.

6. The recommended algorithm for examining patients with non-palpable neoplasms of mammary gland shall include: complex X-ray sonography, Ultrasound biopsy (in case of clear visualization of the neoplasm during ultrasound computed tomography). In case of a failure, stereotaxic biopsy shall be recommended.

7. In more than half cases (55%), modern biopsy techniques allow avoiding sectoral resections of mammary glands with intra-surgery histological examination which conducted in the cases that require conservative treatment or dynamic follow-up.

8. Complications during FNAB do not exceed 0.6% what is 1.5-2 times less than during ultrasound biopsy (up to 1.6% of cases) or stereotactic biopsy (up to 4.4% of cases).

References

1. Kaidarova D.R., Ayezova E.T., Chingisova J.K., Seisenbaeva G.T. i dr. Pokazateli onkologicheskoi sluzhby Respubliki Kazahstan za 2015g. [Indicators of oncological service of the Republic of Kazakhstan for 2015]. – Almaty, 2016.

2. Cancer. WHO Newsletter. February 2017. http://www.who.int/mediacentre/factsheets/fs297/ru/ 12.05.2017.

3. Semiglazov V.F. Profilaktika opyholei molochnoi jelezi [Prevention of breast tumors]. – SPb: Znanie, 1993. – P. 5.

4. Gancev Sh.X. Onkologiya. [Oncology, 2nd edition, revised and enlarged]. – M.: Medicinskoe informacionnoe agentstvo. [Medical News Agency]. -2006. – P. 242-243.

5. Putyrski L.A. Rak molochnoy zhelezy: uchebnoe posobie. [Breast Cancer: Tutorial]. – Minsk: Visshaya shkola, [Minsk: Higher School]. -1998. – P. 84.

6. Klinicheskie rekomendacii po diagnostike i lecheniu bolnih rakom molochnoi jelezi. [Clinical recommendations for the diagnosis and treatment of patients with breast cancer]. Obsherossiiskii Souz Obshestvennih Obedinenii «Associaciya Onkologov Rossii». [All-Russian Union of Public Associations «Association of Russian Oncologists»] – M., 2014. – P. 3.

7. Decree of the Government of the Republic of Kazakhstan No. 378 of 06.04.2011 «On Extraordinary Changes and Amendments to the Administration of the Government of the Republic of Kazakhstan dated January 29, 2011 No. 41 «On Approval of the Action Plan for the Implementation of the State Program for Health Development of the Republic of Kazakhstan «Salamatty Kazakhstan» for 2011-2015».

8. Order of the Minister of Health of the Republic of Kazakhstan of December 29, 2014 No. 361 "On Amendment of the Order of the acting Minister of Health of the Republic of Kazakhstan of November 10, 2009, No. 685 «On the Approval of the Rules for Conducting Preventive Medical Examinations of Target Populations»"

9. Ilkevich A. G. Mammografiya v kompleksnoi diagnostike raka molochnoi jelezi. [Mammography in the complex diagnosis of breast cancer] // Novosti lychevoi diagnostiki. [News of radiodiagnosis]. – 2001. – № 12. – P. 29-31.

10. A. Bart Ducktales. Carcinomas in situ. In: A. Barto, R. Kochli, p. J., Brenner. Schweitz. Honey. Wochenschr. – 1995. – Br. 125, No. 4. – P. 103-112.

11. Rojkova N.I. Rentgendiagnostika zabolevanii molochnoi jelezi. [X-ray diagnosis of breast diseases]. – M.:Medicina. [M.: Medicine]. - 1993.– P. 35.

12. Levshin V.F., Fedichkina T.P., Drojjachih V.G. i dr. Issledovanie vozmojnostei vnedreniya i effektivnosti razlichnih vidov mammograficheskogo skrininga. [Research into the feasibility and effectiveness of different types of mammographic screening]. // Mammologiya. [Mammology]. – 1997. – № 4. – P.25-31.