HOW VACUUM-ASSISTED TOMOSYNTHESIS-GUIDED BIOPSY FACILITATES THE DIAGNOSIS OF BREAST CHANGES

KAKO VAKUUM-ASISTIRANA BIOPSIJA VOĐENA TOMOSINTEZOM OLAKŠAVA DIJAGNOSTIKU PROMENA NA DOJKAMA

Dijana NIĆIFOROVIĆ[1,2], Marijana BASTA NIKOLIĆ[1,2], Daniela DONAT[1], Danica DOJČINOV[2], Sonja LUKAČ[1] and Sanja STOJANOVIĆ[1,2]

Summary

Introduction. Breast cancer stands as the predominant form of cancer diagnosed in women worldwide. In the Republic of Serbia, breast cancer held the top position in 2020, accounting for 22.6% of all cancer cases. Early diagnosis of the disease can lead to favorable prognosis and high survival rates. National and opportunistic screening aim to conduct preventive mammography examinations in women aged 50-69, with vacuum-assisted biopsy guided by tomosynthesis being performed when necessary as a diagnostic procedure. **Material and Methods.** The vacuum-assisted tomosynthesis guided breast procedure typically takes half as the time of a stereotaxic biopsy. The procedure begins with planning the approach to the lesion, contingent up on its localization within the breast. **Results**. The first vacuum-assisted biopsy guided by tomosynthesis in Serbia was conducted at the Radiology Center of the Clinical Center of Vojvodina in December 2020, utilizing Selenia Hologic mammography unit. Between December 2020 and June 2023, a total of 161 tomosynthesis-guided VABs were performed in 160 patients, with one patient undergoing the procedure on both breasts. **Conclusion**. Most authors report using the vacuum sampling technique during the vacuum-assisted biopsy guided by tomosynthesis. Given the potential of complete removal of the lesion with this method, it is standard practice to place a marker at the biopsy site. The increasing incidence of breast cancer is observed globally, and it is attributed to advancements in standards of living and lifestyle changes.
Key words: Breast Neoplasms; Mammography; Biopsy, Needle; Image-Guided Biopsy; Imaging, Three-Dimensional; Early Diagnosis

Sažetak

Uvod. Karcinom dojke je vodeća lokalizacija svih karcinoma dijagnostikovanih kod žena širom sveta. U Republici Srbiji u 2020. godini, karcinom dojke je na prvom mestu sa učešćem od 22,6%. Rana dijagnoza bolesti može dovesti do dobre prognoze i visoke stope preživljavanja. Cilj nacionalnog i oportunog skrininga bio je obavljanje preventivnih mamografskih pregleda kod žena starosti 50−69 godina. Vakuum-asistirana biopsija vođena tomosintezom urađena je kod pacijentkinja kojima je ovakva dijagnostička procedura bila neophodna. **Materijal i metode.** Procedura biopsije dojke vođena tomosintezom traje približno upola kraće od one koja je potrebna za stereotaksičnu biopsiju. Postupak počinje planiranjem pristupa promeni i zavisi od njene lokalizacije u dojci. **Rezultati**. Prva vakuum-asistirana biopsija vođena tomosintezom u Srbiji obavljena je u Kliničkom centru Vojvodine, Centru za radiologiju decembra 2020. godine na mamografu *Selenia Hologic*. Od decembra 2020. do juna 2023. urađena je 161 vakuum-asistirana biopsija vođena tomosintezom kod 160 pacijentkinja, a kod jedne pacijentkinje operacija je obavljena na obe dojke. Postupak počinje planiranjem pristupa promeni i zavisi od njene lokalizacije u dojci. **Zaključak**. Većina autora navodi da su prilikom ove procedure dojke vođene tomosintezom, koristili tehniku vakuumskog uzorkovanja. S obzirom na verovatnoću potpunog uklanjanja promene ovom metodom, rutinska je praksa postavljanje markera na mesto biopsije. Porast incidencije raka dojke beleži se u svim razvijenim zemljama i zemljama u razvoju i pripisuje se porastu standarda i promeni načina života.
Ključne reči: karcinom dojke; mamografija; biopsija iglom; biopsija vođena slikom; trodimenzionalni imidžing; rana dijagnoza

Introduction

Breast cancer stands as the predominant form of cancer diagnosed in women worldwide, emerging as one of the leading public health concerns in recent decades. According to the World Health Organization (WHO) projections, the number of women affected with this disease is expected to double by 2030 [1]. In 2020, the International Fund for Cancer Research reported 2,261,419 newly diagnosed cases of breast cancer worldwide, with Belgium and the Netherlands ranking among the leading with standardized incidence rates of 113.2/100,000 and 100.9/100,000 respectively [2]. In the Republic of Serbia, breast cancer held the top position among cancer diagnoses in women in 2020, with preva-

Corresponding Author: Prof. dr Dijana Nićiforović, Medicinski fakultet Novi Sad, UKCV – Centar za radiologiju, 21000 Novi Sad, Hajduk Veljkova 1-7, E-mail: dijana.niciforovic@mf.uns.ac.rs

lence rate of 22.6%, surpassing lung cancer and bronchus (11.3%) and colon and rectal cancer (10.5%) [3].

In 2020, there were 4,368 new cases registered in Serbia and 1,246 in Vojvodina, accounting for approximately one quarter of all malignant diseases in women. Based on the data from the Cancer Registry in the Republic of Serbia, the standardized incidence rate of breast cancer in 2020 was 112.4/100,000 inhabitants for the Republic of Serbia and even higher at 121.6/100,000 inhabitants for Vojvodina [3]. The incidence of breast cancer is constantly increasing, which is partly attributed to demographic aging trends. Incidence and mortality rates are often linked to a country's level of development. Higher incidence rates are observed in highly developed countries, attributed to better and more advanced preventive healthcare measures. Conversely, higher mortality rates are prevalent in underdeveloped countries, indicating insufficiently developed preventive healthcare and limited access to healthcare services.

Breast cancer is one of the leading causes of premature death among women, ranking four in terms of years of lost life after ischemic cerebrovascular disease, ischemic heart disease and type 2 diabetes mellitus [4]. Globally, the average standardized mortality rate for breast cancer in 2020 was 13.6/100,000, with the highest number of deaths reported in Barbados and Fiji, at 42.2/100,000 and 41/100,000, respectively [2]. In the Republic of Serbia, based on data from the Cancer Registry, the standardized mortality rate for breast cancer in 2020 was 20.3/100,000, and 22.5/100,000 in Vojvodina. In the same year, 1,782 deaths were attributed to breast cancer in the Republic of Serbia, with 526 deaths reported in Vojvodina. Regarding mortality from various cancer types in women, breast cancer ranked highest in the Republic of Serbia in 2020, accounting for 19.5% of deaths, ahead of lung and bronchus cancer (17.5%) and colon and rectum cancer (10.4%) [3].

Early detection of breast cancer is paramount for improving outcomes and survival rates. In the Republic of Serbia, organized breast cancer screening has been underway since 2012 as a decentralized program. Defined by regulations on the content and scope of the right to health care from mandatory healthcare coverage and participation, the screening targets women aged 50-69, with a population coverage goal of at least 75% of women within the specified age group. However, it is recommended that all women within this age range participate in screening [5]. In Vojvodina, Novi Sad was included in this program in December 2012, followed by Subotica, Senta, Zrenjanin, Sremska Mitrovica, and Ruma, where opportunistic screening has been implemented in these healthcare centers.

Over the past two decades, research concerning breast cancer has shown remarkable advancements in early diagnosis and treatment, leading to prolonged survival and better quality of life post-therapy.

Breast cancer has the ability to metastasize, spreading to distant organs such as bones, liver, lungs, and brain, which largely accounts for its incurability. Early diagnosis of the disease can result in favorable prognoses and high survival rates [6,7].

Breast tumors typically originate from ductal hyperproliferation, progressing to benign tumors or metastatic cancers under the continuous stimulation of various carcinogenic factors. The tumor microenvironment, including stromal influences or macrophages, plays a vital role in the initiation and progression of breast cancer [8]. Several risk factors contribute to the likelihood of developing breast cancer, including gender, aging, estrogen exposure, family history, gene mutations, smoking, and an unhealthy lifestyle [9]. The majority of breast cancer cases occur in women, with incidence rates approximately 100 times higher in women compared to men [10].

Presentation of the situation
Breast cancer poses a global public health challenge, not only due to its epidemic proportions but also because its consequences affect virtually all sectors of society.

In Serbia, breast cancer ranks as the most common malignant tumor in terms of both morbidity and mortality among women. Over the past five years, an average of about 4,500 newly diagnosed cases have been registered annually, with an average of 1,723 deaths attributed to breast cancer during the same period.

According to estimates from the Global Breast Cancer Initiative of the WHO, women in Serbia face a medium risk of developing breast cancer and a high risk of mortality from this malignancy [11].

Imaging techniques such as mammography, mammography with tomosynthesis, ultrasound, magnetic resonance imaging, and contrast mammography play pivotal roles in breast cancer diagnosis.

Any suspicious findings should be subject to cytological or histological evaluation. Minimally invasive methods, including targeted cytological puncture, core needle biopsy, stereotaxic vacuum-assisted biopsy (SVAB), or vacuum-assisted biopsy (VAB) guided by tomosynthesis, are utilized for preoperative diagnosis. The first such biopsy was performed in June 2013 at the University of Pittsburgh Medical Center Magee-Womens Hospital in the United States of America.

The objective of the national and opportunistic screening was to conduct preventive mammography examinations for women aged 50-69. Any suspicious findings should be subject to cytological or histological evaluation. To ensure timely and definitive diagnosis, VAB guided by tomosynthesis was performed in cases where such diagnostic procedure was deemed necessary.

Material and Methods

The introduction of tomosynthesis into clinical practice enabled the detection of changes that may not be visible with two-dimensional (2D) mammography, thereby necessitating biopsies guided by tomosynthesis.

In biopsies guided by tomosynthesis, tomosynthesis images are utilized to identify the lesion without the need for additional imaging of the breast from different angles and triangulation, resulting in significantly shorter procedure durations. According to literature, the tomosynthesis-guided breast biopsy procedures last approximately half as long as stereotaxic biopsies [12].

The radiation dose during tomosynthesis is slightly higher compared to 2D mammography: CC: 2D =1,366 mGy, 3DT=1,858 mGy; p<0.0001; MLO: 2D=1,374 mGy, 3DT=1,877 mGy; p<0.0001 [13]. Due to fewer exposures (up to 1/4), the average radiation dose in tomosynthesis-guided biopsy is lower than that in stereotaxic biopsy [14].

According to the available literature, the success rate of sample retrieval under the guidance of tomosynthesis ranges from 99 to 100%, while the success rate of stereotaxic biopsy ranges from 87 to 98%. Inadequate visualization of the lesion on stereotaxic images is the primary cause of technical failure in the procedure [15].

Vacuum-assisted biopsy guided by tomosynthesis is a method that enables biopsying soft tissue changes not visualized on 2D mammograms but detectable on tomosynthesis, especially those devoid of microcalcifications. It is also allows biopsy of changes/suspicious microcalcifications located in hard-to-reach areas.

Results

The first VAB guided by tomosynthesis in Serbia was conducted at the University Clinical Centre of Vojvodina Radiology Center in December 2020, utilizing Selenia Hologic mammography unit. From December 2020 to June 2023, a total of 161 tomosynthesis-guided VABs were performed in 160 patients, with one patient undergoing the procedure on both breasts. Prior to each procedure, patients received explanations regarding the necessity to perform VAB with tomosynthesis. Anamnesis was obtained in regard to any antiplatelet or anticoagulant therapy, coagulopathies, and allergies, especially concerning administered anesthesia. Before the beginning of the biopsy, the patients signed their informed consent to the procedure.

Attempts were made to perform this type of biopsy in two additional patients. In the first patient, despite several efforts to approach the lesion from different projections and multiple adjustments in the patient's position due to the small thickness of the breast, the apparatus did not permit continuation of the procedure. In the second patient, the presence of microcalcifications detected on the mammography initially suggested their location within the breast parenchyma. However, upon attempting to biopsy them, the system did not allow the procedure to continue as anticipated. Only after repositioning the patient did it become apparent that the microcalcifications were actually situated in the skin itself rather than within the breast parenchyma.

The procedure begins with planning of the approach to the lesion and depends on its localization within the breast. For this purpose, a specially constructed attachment for biopsies is employed, which connects to the tomosynthesis device, effectively converting the diagnostic 3D mammography suite into a biopsy device. Depending on the localization of the suspicious lesion, the patient is positioned on the mammography chair, either in a sitting or in a side-lying position. The approach to the lesion was selected so that the needle passes the shortest way from the skin to the lesion.
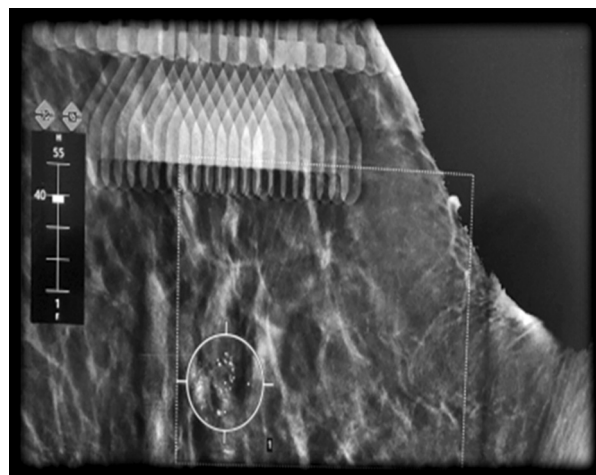

Figure 1. Target determination by tomosynthesis
***Slika 1.** Određivanje cilja tomosintezom*

After skin disinfection, local anesthesia is administered by injecting 10 ml of 2% Lidocaine subcutaneously and in depth along the expected trajectory of the biopsy needle. For VAB, with negative pressure, Eviva needles of 9 G are used, with lengths of 10 cm and 13 cm, and openings of 12 mm and 20 mm, enabling retrieval of 9 to 12 samples. The breast is immobilized to ensure that the area of interest aligns with the opening (5 x 5 cm) of the compression pad. An initial tomosynthesis is performed, allowing for the marking of the suspicious lesion on the layer of the image where it is most visible **(Figure 1).** The biopsy software then automatically determines all three coordinates as the depth of the layer is also the depth of the lesion **(Figure 2).** Following local anesthesia, the needle is automatically introduced until the previously calculated coordinates are reached. Using tomosynthesis, the position of the needle tip can be checked before and after sampling **(Figure 3).** During the sampling procedure, another 10 ml of anesthetic is dispensed automatically. The position of
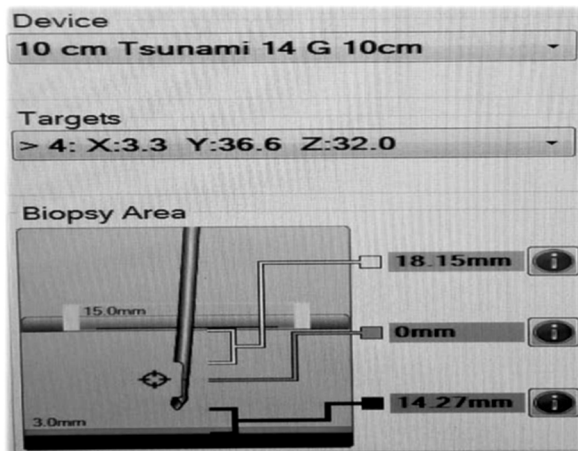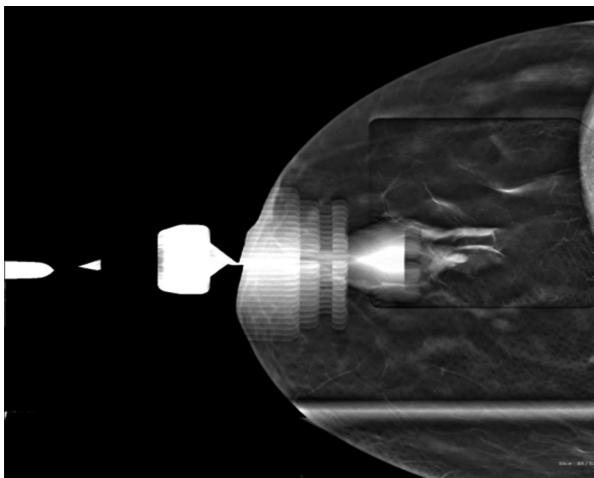
Figure 2. Automatic determination of coordinates
*Slika 2. Automatsko određivanje koordinata*
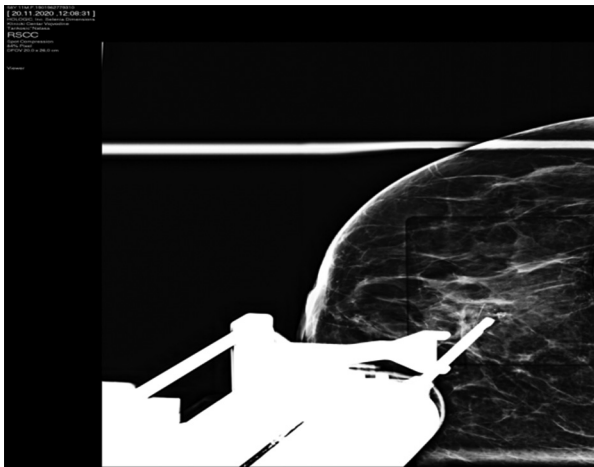
Figure 3. The position of the needle tip can be checked before and after sampling
*Slika 3. Položaj vrha igle se može proveriti pre i posle uzorkovanja*

Figure 4. Checking after sampling
Slika 4. Provera nakon uzorkovanja

the needle tip can be checked before and after sampling **(Figure 4).** A marker is then placed in the cavity created after the biopsy, for the purpose of applying a sparing surgical procedure or monitoring **(Figure 5).** Finally, the obtained tissue samples are re-
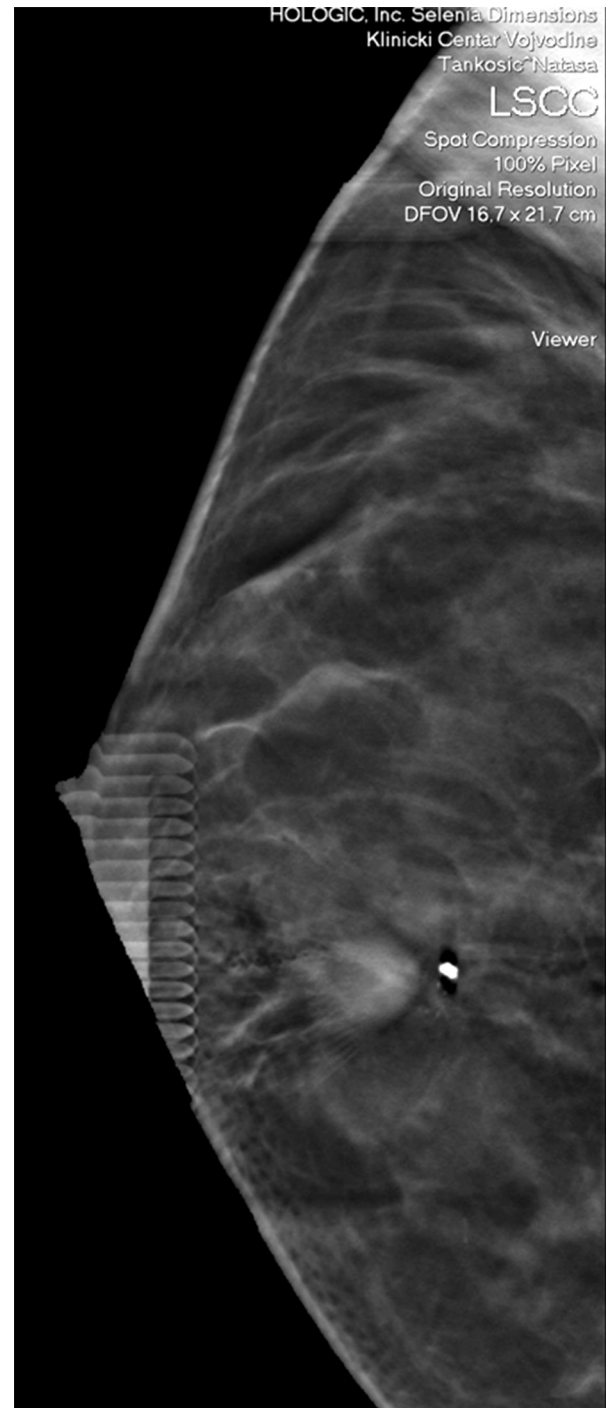
Figure 5. Marker is placed in the cavity created after the biopsy
Slika 5. Marker se postavlja u šupljinu nastalu nakon biopsije
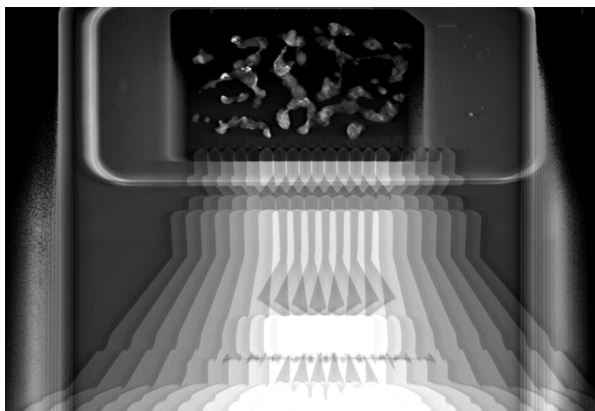
Figure 6. Obtained tissue samples are recorded, with those containing microcalcifications separated from those without
Slika 6. Dobijeni uzorci tkiva se snimaju, odvajaju se oni sa mikrokalcifikacijama i oni bez mikrokalcifikacija

corded, with those containing microcalcifications separated from those without **(Figure 6.)**

The most common approach to the lesion was craniocaudal, which was used in 146 cases or 90.6%, followed by lateromedial in 12 cases or 7.4%, and mediolateral in two cases (1.2%). No biopsies were performed caudocranially. The decision regarding the approach was based on selecting the shortest path from the skin to the lesion.

The youngest patient was 43, and the oldest 80 years old, the average age was 59.4 years. The vast majority of biopsied lesions consisted of grouped microcalcifications, comprising 97.5% (157/161), while tumor shadows accounted for only 4 cases or 2.4%. All 161 lesions were biopsied with patients in a sitting position.

Our research analyzed the data of 160 women who underwent 161 VABs, with one patient undergoing biopsy of both breasts as Ductal Carcinoma in situ (DCIS) was proven in one breast and Invasive Ductal Carcinoma (IDC) in the other.

The increase in the incidence of breast cancer is recorded in all developed and developing countries, and is attributed to various risk factors. In our research, the respondents completed a survey aimed at gathering information of particular importance to us, including family history of breast malignancy, use of oral contraceptives and smoking habits.

Discussion

Tomosynthesis-guided breast biopsy is a relatively recent addition to clinical practice, and comparative studies with stereotaxic biopsy, particularly on large samples, remain scarce. However, the published works indicate distinct advantages of this method over conventional stereotaxic biopsy. By utilizing tomosynthesis images for lesion identification, the need for additional imaging from different angles is eliminated, leading to shorter procedure durations and faster lesion identification [16].

The majority of authors advocate for the use of vacuum sampling technique during the VAB guided

by tomosynthesis breast biopsy procedures.. Considering the likelihood of complete lesion removal with this method, it has become routine practice to place a marker at the biopsy site [17].

In our research, the majority of biopsied changes, comprising 114 cases or 71%, were benign [18]. Histopathological analysis of biopsies confirmed 47 cases or 29% malignant breast changes, of which 33 were diagnosed as DCIS, ten as IDC, three as invasive lobular carcinomas, and one as mucinous invasive carcinoma. This distribution roughly aligns with the ratio reported by the Stony Brook Cancer Center in New York.

A 2017 research by Sun et al. from China identified risk factors for breast cancer, including gender, age, genetic factors, reproductive factors, exposure to estrogens and lifestyle choices. In addition to gender, age stands as one of the most significant risk factors, as the incidence of breast cancer increases with age [7].

According to a study conducted by Brewer et al. [19] in the United Kingdom in 2017, 15% of subjects diagnosed with breast cancer reported having a positive family history of the disease. In our study, among patients diagnosed with breast cancer, 11.8% reported having a positive family history of breast malignancy, a percentage that aligns with the findings of Brewer et al.

Previous use of oral contraceptives is not associated with an increased risk of breast cancer. However, current use of oral contraceptives is associated with a higher risk of breast cancer [20]. In our study, 41 respondents (25.6%) reported using oral contraceptives for a significant period during their lifetime. None of the subjects were using oral contraceptives at the time of breast cancer diagnosis or immediately prior to it. Therefore, there was no statistically significant difference between the number of subjects with a history of oral contraceptive use who did not have confirmed breast cancer by biopsy and those who did.

Smoking has been associated with a moderate but noticeable increase in the risk of breast cancer, especially among women who started smoking during adolescence or the perimenarchal period. The relative risk of breast cancer among women who smoke is notably higher if they also have a positive family history of the disease [21].

Conclusion

The rise in the incidence of breast cancer worldwide is attributed to improvements in standards of living and lifestyle changes. While primary prevention strategies for breast cancer are currently very limited, preventive activities are focused on early detection and reduction of mortality rates.

Organized programs for breast cancer prevention and early detection, coupled with timely treatment, have contributed to a significant drop in mortality rates in many developed countries over the past decade.

Given the importance of the problem, it is necessary to continue raising awareness among women

of all ages, particularly those over 40, about the importance of regular preventive examinations

through both national and opportunistic stereotaxic vacuum assisted biopsy screening.

References

1. World Health Organization. Breast cancer [Internet]. [cited 2023 Sep 22]. Available from: https://www.who.int/cancer/prevention/diagnosis-screening/breast-cancer/en/

2. World Cancer Research Fund International. Breast cancer statistics [Internet]. 2020 [cited 2023 Sep 22]. Available from: https://www.wcrf.org/cancer-trends/breast-cancer-statistics/

3. Serbian Cancer Registry. Malignant tumors in Republic of Serbia, 2020. Belgrade: Institute of Public Health of Serbia "Dr. Milan Jovanović Batut"; 2022.

4. IHME. GBD compare [Internet]. [cited 2023 Sep 25]. Available from: https://vizhub.healthdata.org/gbd-compare/#

5. Pravilnik o sadržaju i obimu prava na zdravstvenu zaštitu iz obaveznog zdravstvenog osiguranja i o participaciji za 2022. godinu. Službeni glasnik Republike Srbije. 2022;(24).

6. Pokrajinski sekretarijat za zdravstvo. Projekti: prva mamografija [Internet]. Novi Sad: Pokrajinski sekretarijat za zdravstvo; 2019 [cited 2024 Jan 12]. Available from: https://www.zdravstvo.vojvodina.gov.rs/projekti-projekti / %D0%BF%D1-%80%D0%B2%D0%B0-%D0%BC%D0%B0%D0%BC%D0%BE%D0%B3%D1%80%D0%B0%D1%84%D0%B8%D1%98%D0%B0/

7. Sun YS, Zhao Z, Yang ZN, Xu F, Lu HJ, Zhu ZY, et al. Risk factors and preventions of breast cancer. Int J Biol Sci. 2017;13(11):1387-97.

8. Sonnenschein C, Soto AM. Carcinogenesis explained within the context of a theory of organisms. Prog Biophys Mol Biol. 2016;122(1):70-6.

9. Majeed W, Aslam B, Javed I, Khaliq T, Muhammad F, Ali A, et al. Breast cancer: major risk factors and recent developments in treatment. Asian Pac J Cancer Prev. 2014;15(8):3353-8.

10. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin. 2017;67(1):7-30.

11. Epidemiološke karakteristike karcinoma dojke: svet [Internet]. [cited 2023 Sep 14]. Available from: https://www.batut.org.rs/download/aktuelno/Epid%20karakteristike%20karcinoma%20dojke%20svet%20Evropa%20Srbija%202023.pdf

12. Waldherr C, Berclaz G, Altermatt HJ, Cerny P, Keller P, Dietz U, et al. Tomosynthesis-guided vacuum-assisted breast biopsy: a feasibility study. Eur Radiol. 2016;26(6):1582-9.

13. Gennaro G, Bernardi D, Houssami N. Radiation dose with digital breast tomosynthesis compared to digital mammography: per-view analysis. Eur Radiol. 2018;28(2):573-81.

14. Grimm L. Clinical benefits of tomosynthesis guided breast biopsy [Internet]. 2018 [cited 2024 Jan 12]. Available from: https://www.hologic.com/sites/default/files/Clinical-Benefits-of-Tomosynthesis-Guided-Breast-Biopsy.pdf

15. Bahl M, Maunglay M, D'Alessandro HA, Lehman CD. Comparison of upright digital breast tomosynthesis-guided versus prone stereotactic vacuum-assisted breast biopsy. Radiology. 2019;290(2):298-304.

16. Lukač S, Stankov M, Nićiforović D, Pilipović-Grubor J, Donat D, Mrđanin T. Unusual presentation of dermal microcalcifications on mammography images: a case report. Med Pregl. 2022;75(9-10):305-7.

17. Ames V, Britton PD. Stereotactically guided breast biopsy: a review. Insights Imaging. 2011;2(2):171-6.

18. Different kinds of breast lumps [Internet]. 2022 [cited 2022 Feb 16]. Available from: https://cancer.stonybrookmedicine.edu/breast-cancer-team/patients/bse/breastlumps

19. Brewer HR, Jones ME, Schoemaker MJ, Ashworth A, Swerdlow AJ. Family history and risk of breast cancer: an analysis accounting for family structure. Breast Cancer Res Treat. 2017;165(1):193-200.

20. Hunter DJ, Colditz GA, Hankinson SE, Malspeis S, Spiegelman D, Chen W, et al. Oral contraceptive use and breast cancer: a prospective study of young women. Cancer Epidemiol Biomarkers Prev. 2010;19(10):2496-502.

21. Jones ME, Schoemaker MJ, Wright LB, Ashworth A, Swerdlow AJ. Smoking and risk of breast cancer in the Generations Study cohort. Breast Cancer Res. 2017;19(1):118.