

Automated Breast Ultrasound

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Abstract

Due to the growing number of breast cancer patients, an early diagnosis is important in order to reduce the mortality rate of those affected. Methods such as mammography, DBT, MRI, HHUS or ABUS are used in the detection of breast cancer. The aim of this article is to review the literature showing the basic principle of ABUS and to point out its advantages and disadvantages in relation to conventional methods of breast imaging. ABUS is a relatively new ultrasound method that performs well on patients with dense breast tissue. It reduces operator dependence and provides valuable diagnostic information with multiplanar reconstructions. Using evidence from reliable researches, studies have demonstrated that ABUS has a higher diagnostic accuracy compared to mammography, which remains the primary modality for early diagnosis of breast cancer. Applying ABUS as an adjunct to mammography during the screening test has proven effective and further confirmed the importance of their application in clinical practice. The disadvantage of the combination of ABUS and mammography was that in a large number of studies the specificity was lower compared to mammography itself. Compared to DBT, ABUS has demonstrated to have a higher diagnostic performance, with the exception that it lacks the ability to effectively detect calcifications. Although MRI seem to outperform ABUS, ABUS devices offer a cost-effective and easy to use imaging system, making it the best alternative. The HHUS technique, on the other hand, was perceived by many studies as less painful, with a shorter operative time compared to ABUS. However, the sensitivity and specificity of this screening method continues to remain inferior to ABUS. The use of artificial intelligence is becoming widely used today. As a result, the CAD software has been developed to be applied in conjunction with ABUS in order to improve the detection rate of breast cancer as well as its accuracy. The use of CAD significantly reduced image reading time and improved the overall diagnostic accuracy of ABUS. According to all the presented data, the use of ABUS medical devices in clinical practice continues to grow in importance and with the further development of technology and medicine, its full integration into healthcare systems around the world is expected.

Keywords: ABUS; breast cancer; CAD; mammography; screening

Abbreviations and acronyms: ABUS (Automated breast ultrasound), AUC (Area under the curve), BI-RADS (Breast imaging reporting and database system score), BRCA (Breast cancer gene), CAD (Computer aided detection), DBT (Digital breast tomosynthesis), FFDM (Full-field digital mammography), HHUS (Hand-held ultrasound), MRI (Magnetic resonance imaging), RT (Reading time), TMI (Testing morbidities index)

Introduction

The number of cases of breast cancer is on the rise. According to the World Health Organization, in 2020, around 2.3 million are diagnosed each year, with 685 000 deaths globally [1]. In Croatia, in 2020 alone, 2894 women were affected with breast cancer, and an estimated 832 did not manage to survive [2]. Risk factors for the development of breast cancer included: age, high breast density, early menarche, family history of breast cancer, late menopause, unhealthy lifestyles and exposure to carcinogens. Women with BRCA1 and BRCA2 gene mutations also have an increased risk of developing breast cancer [3].

If breast cancer is detected at an early stage (up to 1 cm), there is a relatively high chance of survival (98%) [4]. For this reason, screening is carried out on a yearly basis in order to detect the disease in asymptomatic patients within its early stages of development. Death rates from breast cancer can be reduced significantly through a series of preventive examinations. As a result, the Croatian government introduced the 'National Breast Cancer Early Detection Program', a program dedicated towards providing early detection testing for women aged 50 to 69. Once every two years, women are invited to undergo a mammographic examination of the breasts, with the objective of reducing the mortality rate by 25% to 30% [5].

There are different radiological methods available to detect breast cancer, some of these consist of the hand-held breast ultrasound (HHUS), the automated breast ultrasound (ABUS), the full-field digital mammography (FFDM), the digital breast tomosynthesis (DBT) and the magnetic resonance imaging (MRI). Following mammography screening, ultrasound is the most common method for breast imaging. Women under the age of 40, especially women with a family history of breast cancer, should undergo a preventive breast ultrasound examination. The examination should be repeated yearly or **biyearly** [6].

The automated breast ultrasound

The ABUS is a cancer screening technology, developed with the aim of standardizing breast ultrasonography screening. With all advantages, the ABUS has the potential to act as a supplemental screening tool in patients with dense breasts, given that mammography screening offers a low sensitivity [7]. Women with dense breasts have an increased risk of developing breast cancer (6-8 times higher) compared to women with more adipose tissue [8]. This method was approved in 2012 by the Food and Drug Administration (FDA) [9].

During an ABUS examination, the imaging is performed by a radiologic technologist, which is then followed by a reading of the findings from a radiologist [8]. This method, like the HHUS, uses high-frequency sound waves that pass through and reflect off the breast tissue, while simultaneously providing a 3D volumetric image of the entire breast. The ultrasound probe automatically scans the breast, reducing the level of operator dependence compared to the HHUS [10]. The ABUS increases reproducibility, decreases operator dependency, and shortens

the physician's time due to its reliable imaging method and valuable diagnostic information with multiplanar reconstructions. There are, however, certain limitations, such as the exclusion of the axillary regions from the field of view and the absence of tools to assess vascularity and tissue elasticity [11].

The device is composed of three different probes, with measurements usually amounting to 15 cm x 17 cm, distinguishing it between other classic ultrasound devices (Figure 1). The high-frequency ultrasound probe provides excellent image quality. The probe is shaped to match the anatomy of the breast and thus enables complete coverage of the breast tissue (Figure 2). Equal pressure distribution provides additional comfort for patients during examination [12].

The scan is performed while the patient is lying on her back, which flattens the breast and improves contact with the probe. Once the breast is exposed, the patient raises her hand on the side that is about to be examined and the technologist applies an appropriate amount of gel to the entire surface area of the breast. An additional amount of gel is applied to the nipple-areolar complex area to ensure proper scanning and to avoid any scan artifacts. The probe is then placed on the breast with slight pressure to avoid movement artifacts. The scan is performed in three standard planes (coronal, sagittal and transverse) to allow adequate coverage of the entire breast tissue. Using the nipple as the center point, the anteroposterior position is first assumed. The lateral position is taken by tilting the probe from the axilla towards the sternum, and for the medial position the probe is at an angle from the sternum towards the axilla (Figure 3) [13].

The images are at first examined on the monitor to ensure the quality of the recordings and the obtained volumetric data are automatically transferred to the



Figure 1. A visual of the ABUS device
Source: <https://ge-ultrasound.eu/wp-content/uploads/2020/06/abus-2-0-pro-2.jpg> 17



Figure 2. The ABUS probe
Source: <http://www.medgadget.com/wp-content/uploads/2011/11/sese3224re.jpg>

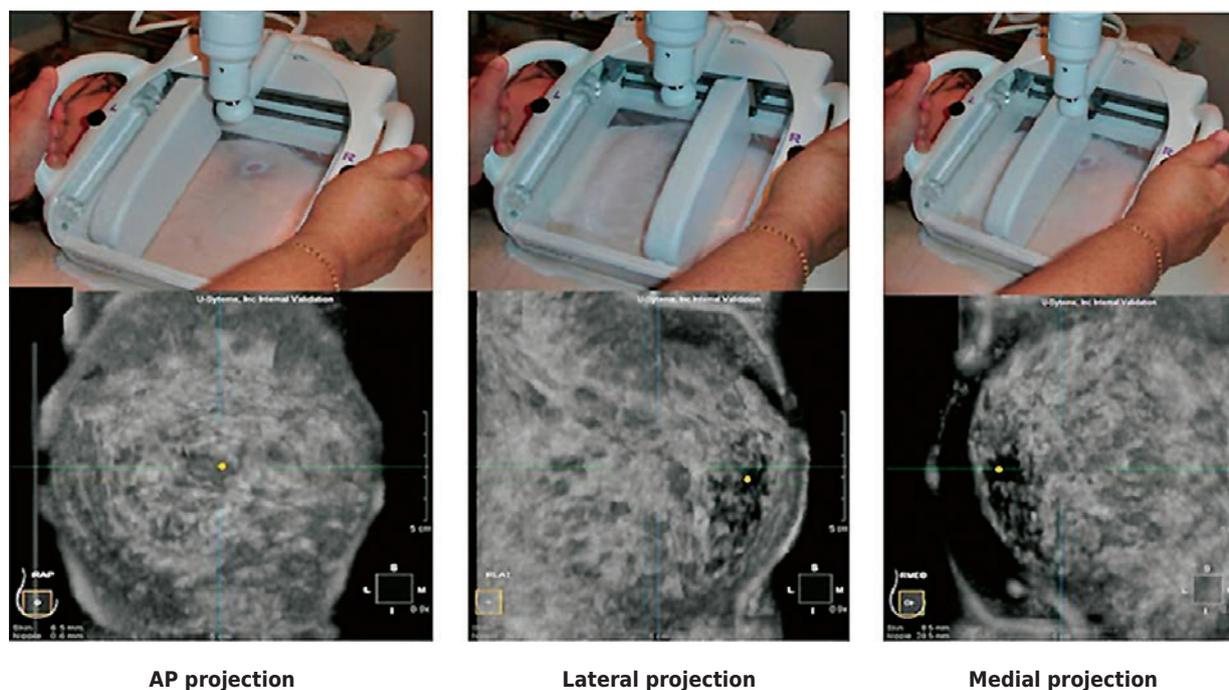


Figure 3. Three basic breast imaging projections

Source: <https://d3i71xaburhd42.cloudfront.net/6147351abf0f19beabdf31125d9972147523c9bf/3-Figure1-1.png>

workstation for post-processing, including the transverse, coronal and sagittal reformatting and analysis. The examination takes about 15 minutes for both breasts [13].

The aim of the article

The aim of this article is to describe the ABUS device, its screening technique and its application in clinical practice. By reviewing numerous studies published in the last ten years, its advantages and disadvantages compared to other conventional breast imaging methods are determined.

Discussion

Comparison of mammography and ABUS

Mammography screening is considered to be one of the most effective methods with regards to breast cancer screening, where it is also widely used. However, one of the main drawbacks of this screening method is that its sensitivity is affected by the density of the breast tissue [14]. The research of Xin et al. demonstrated that the ABUS is a significantly more sensitive method in women with dense breasts compared to the mammogram (92.54% vs. 83.77%) [15]. However, it is equally as sensitive as the mammogram considering women with a low breast density [15]. Exposure to radiation is one of the main disadvantages of mammography screening, with 43% of women refusing to undergo the procedure due to fear of radiation exposure [14]. In order to overcome such shortcomings, a new imaging technique, such as ABUS, was developed. The ABUS examination takes less time than a mammogram and it makes it possible to image the entire breast

without emitting radiation. A study conducted by Elkhalek et al., compared the application of these two methods on 25 patients [14]. According to the results, the sensitivity of the mammogram amounted to 85%, with a specificity of 100%. The ABUS, on the other hand, demonstrated a sensitivity of 100% and a specificity of 62.5% [14].

In a systematic review and meta-analysis, Hadadi et al. compared the performance of the mammogram versus the combination of mammography screening with the ABUS [16]. The average sensitivity of the mammogram was 72%, with an increased sensitivity amounting to 99.8% when combined with ABUS, whereas the combination of these two methods had a significantly higher recall rate than with the mammography screening alone. There was an increased number of detected breast tumors ($n=200$) than when solely relying on the mammogram ($n=138$) [16].

Giger et al. demonstrated that mammography screening, together with the ABUS, significantly increase the detection rate of breast cancer. Relying solely on the mammogram, the sensitivity amounted to 57.5% [17]. However, a combination of both the mammogram and the ABUS increased the sensitivity to 74.1%. The specificity was slightly higher when using the mammogram, with 78.1% for the mammogram and 76.1% for combined methods [17]. In a study conducted by Wilczek et al. the detection rate of the mammogram was 4.2/1000, whereas a combination of both methods resulted in an increased detection rate of 6.6/1000 [18]. Sensitivity increased significantly using both methods compared to applying solely a mammogram (63.6% vs. 100%) and specificity slightly decreased (99% vs. 98.4%) [18]. According to Gatta et al. combining both methods are more accurate in the detection of breast cancer [19]. According to the results, 4 breast cancers were detected by the mammogram, whereas 8 were detected by applying a combination of both the

Table 1. Characteristics of studies comparing the diagnostic performance of mammography, ABUS and combination of methods [14, 16-19]

Research	Sensitivity			Specificity			Cancer detection rate		
	MG	ABUS	MG + ABUS	MG	ABUS	MG + ABUS	MG	ABUS	MG + ABUS
Elkhalek et al.	85%	100%	—	100%	62,5%	—	25	25	—
Hadadi et al.	72%	—	99,8%	86,7%	—	74,6%	138	—	200
Giger et al.	57,5%	—	74,1%	78,1%	—	76,1%	—	—	—
Wilczek et al.	63,6%	—	100%	99%	—	98,4%	7	—	11
Gatta et al.	58,8%	—	93,5%	94%	—	87%	4	—	8

mammogram and the ABUS. The sensitivity of the mammogram was 58.8% and the combination of these two methods was 87%. The specificity of the mammography was 94% and the combination of these two methods was 87%. The combination of these two methods provides a sensitivity level that is comparable to the MRI [19]. Nevertheless, it is important to point out that there are certain disadvantages when it comes to mammography screening, one of which relates to the level of pain that patients are required to endure. On a scale of 1 to 10 (1 being the lowest and 10 being the highest), patients experienced a level of pain that amounted to an average score of 6.41 with the mammogram and 1.86 with the ABUS [20].

From all the aforementioned studies, it is evident that the sensitivity of the ABUS is slightly higher compared to the mammogram. The sensitivity and detection rate of breast cancer are the highest when both methods of screening are combined. The specificity, on the other hand, is slightly lower when the two methods are applied separately (Table 1). With joint application, a better and more precise diagnosis is obtained. Therefore, it is more beneficial to use both methods of screening rather than apply them individually. More studies and further research are needed to assess the advantage of each method, as well as their efficiency in terms of cost and benefit [18].

Comparison of DBT and ABUS

Research by Hashem et al. was conducted on 32 female patients with the aim of comparing the DBT and the ABUS [21]. Patients underwent both examinations and the images were analyzed by two experienced radiologists. The sensitivity in the detection of breast masses was 100% with the application of both methods, while the specificity with the ABUS was 75% and with the DBT 81.25%. The DBT showed significantly better results in the detection of calcifications, where 16 were detected. The ABUS method, on the other hand, only detected 2. In breast cancer screening, both mentioned methods showed very good results. However, the ABUS method of screening can be regarded as more effective given that it functions better on women with dense breasts and it exposes patients to less radiation compared to the DBT [21].

The Egyptian National Breast Cancer Screening conducted a study on 242 women with a high breast density and a positive mammogram, to compare the effectiveness between DBT and ABUS screening methods [22]. The study determined that each of these two screening tools detected a certain number of false positives. ABUS had 4 false positive findings and the DBT had 15. According to the presented data, the ABUS showed a higher accuracy rate in comparison to the DBT (Table 2) [22].

Table 2. Comparison of DBT and ABUS parameters in women with dense breasts [22]

Measure	Tomosynthesis	ABUS
Sensitivity	92%	92%
Specificity	92%	98%
Positive predictive value	76%	92%
Negative predictive value	98%	98%
Accuracy	92%	97%

Schäfigen et al., on the other hand, evaluated the performance of the FUSION-X-US-II prototype, which was developed to combine ABUS and DBT screening methods in a single device [23]. In 18 out of 101 scans (17.8%), the image quality was described as being relatively similar to the HHUS, with the exception that no scans were ranked on a level of 5 (equal or higher quality than HHUS). Overall, the combined performance of the tomosynthesis and the ABUS resulted in a sensitivity rate of 97.1% and a specificity of 59.7% [23]. Image quality varied greatly depending on the individual breast shape. Small breasts were more difficult to place under the device and in some cases, it was difficult to achieve adequate contact with the ultrasound probe. In this study, the combined use of the ABUS and the tomosynthesis showed a clear advantage over using the tomosynthesis method alone. Combination of those two methods decreases the time of the screening procedure and the results can be clinically applied [23].

Comparison of breast MRI and ABUS

An MRI examination of the breast is considered to be the most sensitive method for detecting breast cancer [24]. However, it is currently too expensive to use in breast cancer screening. Against this background, current standard MRI protocols include the use of an intravenous injection of a gadolinium contrast agent, which is also considered a limitation of MRI [24]. MRI screening has demonstrated to be highly sensitive when detecting breast cancers in women with BRCA1 and BRCA2 gene mutations, with sensitivity amounting to 93.6% [25]. This was further confirmed by Obdeijn et al., a study which concluded that the diagnostic contribution in high-risk women using MRI screening was much higher than using a mammogram [26].

According to Giuliano et al., similar morphologic features were observed in both benign and malignant lesions when the ABUS was compared with the MRI [27]. The ABUS offered the same multiplanar imaging capabilities as the MRI. It was also accepted by patients and easily integrated into the breast imaging practice. Ease of use and low cost make the ABUS an attractive alternative compared to MRI screening, especially for women with dense breasts, a family history of breast cancer or other risk factors. The ABUS is better accepted by patients than the mammogram due to the less amount of pressure that is required to be placed on the breast and there is less exposure to radiation. Despite these benefits, one of the disadvantages of this screening method is that it requires the cooperation of the patient, especially coordination in stopping breathing. The lack of patient's cooperation can directly deteriorate image quality [27].

Research by Schmachtenberg et al. aimed to compare the diagnostic value of the ABUS breast examination together with the use of breast MRI scans [28]. The MRI revealed 72 lesions and the ABUS 59 lesions. The size of the lesion using the ABUS method compared to the size of the lesion detected by the MRI was estimated accurately (± 3 mm) in 80% of cases [28]. Girometti et al. have confirmed that the size of lesions detected in MRI screening provides more accuracy with regards to the size than with the ABUS method [29].

Comparison of HHUS and ABUS

In order to overcome the limitations of operator dependence and the lack of image reproducibility that occurs with the HHUS, the ABUS was developed. Additional ABUS examination during the screening process increases the detection rate of breast cancer by 1.9-7.7% per 1000 women [30]. Poor reproducibility and dependence on the physician's experience are viewed as disadvantages of the HHUS, whereas the lack of blood flow affected the effectiveness of the ABUS [31].

In a study conducted by Yun et al. a total of 135 patients who underwent the ABUS and the HHUS were retrospectively examined. Among all discrepancies, there were 22 cases (78.6%) where a lower BI-RADS assessment category was assigned using the ABUS than with the HHUS [32]. Between the ABUS and the HHUS, the detection of the BI-RADS category was 86.63%, as confirmed by Chen et al. [33]. Similar results were obtained by Jeh et al., where the ABUS detected all malignant lesions that were

detected by the HHUS, with the exception that it failed to detect smaller benign lesions [34].

A comparison between the HHUS and the ABUS screening methods is shown by Wang HY et al., demonstrating that the HHUS functions similar to the ABUS in terms of sensitivity (90.6% vs. 95.3%) and specificity (82.5% vs 80.5%) [35]. Wang ZL et al. have also concluded that the ABUS is somewhat more sensitive (96.1% vs 93.2%) and more specific (91.9% vs. 88.7%) compared to the HHUS (Table 3) [35].

Table 3. Studies comparing the sensitivity and specificity of ABUS and HHUS in clinical practice [35]

Study	Sensitivity		Specificity	
	ABUS	HHUS	ABUS	HHUS
Wang HY et al.	95.3	90.6	80.5	82.5
Wang ZL et al.	96.1	93.2	91.9	88.7
Chen et al.	92.5	88.1	86.2	87.5
Jeh et al.	88	95.7	76.2	49.4

Tutar et al. conducted a study consisting of 340 female patients [36]. They concluded that the HHUS produced more negative results, whereas the ABUS had more false positives. The duration of the examination was significantly shorter with the HHUS (12.5 min) than with the ABUS (22.5 min). When using the ABUS, 10.6% of women stated that they experienced severe pain. 59.7% of women stated that they would choose the HHUS as a future form of examination, if provided with the opportunity, given that its shorter, offers more comfort and provides results immediately [36]. In addition, Brunetti et al. showed that the HHUS has a significantly shorter screening duration (average 5.2 minutes) compared to the ABUS (average 16.7 minutes) [37].

Mussetto et al. conducted their research on 79 patients who underwent a breast screening procedure with the HHUS and then with the ABUS on the same day [38]. The experience of the patients was assessed by the TMI (*Testing morbidities index*) questionnaire, and nine factors taken into consideration for assessing the effectiveness of both techniques. The ABUS technique received a higher score for each of the factors focused on during the examination, with the exception that 'fear or anxiety immediately before the test' was significantly higher for the HHUS. Regarding the question relating to 'pain or discomfort during the test', it was significantly higher for the ABUS (Table 4). When patients were asked which was their preferred method of screening, 32 out of 79 (40.5%) patients stated that they preferred the HHUS, whereas the ABUS was favored among 24 out of the 79 (30.4%) patients and the rest remain unbiased [38]. The ABUS screening method was less favorable given the pain and discomfort that patients had to endure during their examination, which is expected since additional pressure on the breast is necessary to obtain a high-quality image. Although the HHUS has a higher tolerance level compared to the ABUS, it can be concluded that patients can tolerate both methods and

that they could potentially be integrated as supplementary screening tools to mammography [38].

Table 4. Mean values and interquartile range for evaluated items [38]

Attributes	Median		Interquartile range		p value
	ABUS	HHUS	ABUS	HHUS	
Pain or discomfort before the test	1	1	1-2	1-1	p = 0.020
Pain or discomfort during the test	3	1	2-3	1-2	p < 0.001
Pain or discomfort after the test	1	1	1-1	1-1	p = 0.131
Fear or anxiety before the test	1	1	1-1	1-2	p = 0.001
Fear or anxiety during the test	1	1	1-1	1-1	p = 0.437
Physical function after testing	1	1	1-1	1-1	p = 0.107
Mental function after testing	1	1	1-1	1-1	p = 0.564
Embarrassment during the test	1	1	1-1	1-1	p = 0.577
Overall satisfaction	1	1	1-2	1-2	p = 0.060

Fusion of artificial intelligence and ABUS

Due to the subjectivity of ultrasound imaging and diagnosis, high rates of interobserver variation may occur. In addition, the large amount of data that needs to be analyzed when using the ABUS leaves significant room for errors. Therefore, the computer-aided detection (CAD) software is a desirable tool to assist radiologists in the detection and classification of breast cancer. The main objective is to improve the level of accuracy when distinguishing between malignant and benign lesions on 2D and 3D ultrasound images [39]. Research by Tan et al. showed that the use of the CAD software can improve the differentiation of malignant from benign breast lesions on 3D ultrasound images [40].

Van Zelst et al. attempted to determine the effect of the CAD software on the reading time (RT), and performance in breast cancer screening [41]. In their study, eight radiologists read the current findings, one with the application of both the CAD and the ABUS and one

without the CAD software (only the ABUS). The RT, sensitivity, specificity and area under the curve, AUC, were compared. It concluded that the RT was significantly lower using the CAD-ABUS method (133.4 s/case) compared to the ABUS (158.3 s/case). For both methods, sensitivity was 84%, with specificity being 67% for the ABUS and 71% for the combined CAD-ABUS method. The AUC together with the ABUS and the CAD software functioned on the same manner as the ABUS alone (0.82 vs. 0.83). In conclusion, the CAD software together with the ABUS can shorten the diagnosis time [41]. This is confirmed by Jiang et al., whose study of the RT decreased by 67% using the CAD system [42]. These studies have shown that the diagnostic accuracy and reading speed are improved with the application of CAD systems.

Conclusion

Breast cancer cases are gradually increasing per year. Therefore, early detection is necessary to increase the chances of survival. In the detection of breast cancer, new methods such as the ABUS are introduced, in order to overcome the shortcomings of previous screening methods. Mammography screening methods, for example, emit a certain level of radiation and the HHUS requires more operation dependence, whereas MRI scanning machines are not as cost-efficient. In this paper, by reviewing numerous studies, the advantages and disadvantages of the ABUS in clinical practice were analyzed. According to recent research, the ABUS has shown excellent results in women with dense breasts, which is particularly important given that such women have a 6-8 times higher risk of breast cancer. It is a cost-effective method of screening that is relatively easy to manage. However, despite these benefits, it does require patient cooperation, as breathing can cause artifacts and deteriorate the image quality. The ABUS offered the same multiplanar imaging capabilities as the MRI. Patients tolerated the ABUS examination better than the mammogram due to less pressure which is administered on the breast. Although, it was less favored among patients when compared to the HHUS as a result of the higher level of pain that patients had to endure during the screening procedure. The literature review demonstrated that screening procedures last longer with the ABUS than with the HHUS. The reading time of images produced by the ABUS is reduced with the application of the CAD software, with the exception that there is a high false-negative rate. In this regard, the efficiency in accurate diagnostic performance is not further improved by the ABUS. Against this background, both the ABUS and the CAD software still require additional development. The previous studies, on the other hand, demonstrated the excellent characteristics of ABUS and the importance of its integration into clinical practice for breast imaging. ■

Automatizirani pregled dojke ultrazvukom

Sažetak

Zbog sve većeg broja oboljelih od raka dojke, a kako bi se smanjila smrtnost, vrlo je važna rana dijagnostika. U dijagnostici raka dojke koriste se metode kao što su mamografija, DBT, MRI, HHUS ili ABUS. Cilj ovoga rada je bio pregledom literature prikazati princip rada ABUS-a te ukazati na njegove prednosti i nedostatke u odnosu na konvencionalne metode snimanja dojki. ABUS je relativno nova ultrazvučna metoda koja je pokazala izvrsne rezultate kod žena s gustim grudima. Korištenje ABUS-a smanjuje ovisnost o operateru, a omogućuje vrijedne dijagnostičke informacije s multiplanarnim rekonstrukcijama. Pregledom brojnih istraživanja u ovom radu, ABUS se pokazao kao značajno osjetljivija metoda sa boljom stopom otkrivanja raka dojke u odnosu na zlatni standard, mamografiju. Korištenje ovih dviju metoda zajedno u probiru pokazalo je izvrsne rezultate koji potvrđuju važnost implementacije u kliničku praksu. Nedostatak kombinacije ABUS-a i mamografije je bio taj što je u velikom broju studija specifičnost bila niža u odnosu na samu mamografiju. U odnosu na DBT, ABUS je pokazao superiornije rezultate, osim u detekciji kalcifikacija. Iako je ABUS pokazao nešto lošije rezultate u usporedbi s MRI-om, jednostavnost uporabe i niska cijena čine ga alternativom MRI-u. Što se pak HHUS-a tiče, kao njegovu prednost u odnosu na ABUS pacijentice su navele manje bolan pregled i kraće trajanje, iako se on pokazao manje osjetljivijim i specifičnijim u odnosu na ABUS. Korištenje umjetne inteligencije danas postaje svakodnevica, pa su tako razvijeni i posebni CAD softveri za ABUS kojima je svrha poboljšati stopu otkrivanja raka dojke i točnost radiologa. Korištenje CAD-a značajno je smanjilo vrijeme očitavanja slika te poboljšalo dijagnostičku točnost ABUS-a. Prema svim iznesenim podatcima, važnost ABUS uređaja u kliničkoj praksi je iznimno velika, a daljnim razvojem tehnologije i medicine, očekuje se njegova potpuna integracija u zdravstvene sustave diljem svijeta.

Ključne riječi: ABUS; CAD; mamografija; probir; rak dojke

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