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POSSIBILITIES OF DUAL-ENERGY CONTRAST SPECTRAL MAMMOGRAPHY IN COMPLEX RADIATION DIAGNOSIS OF BREAST CANCER: A LITERATURE REVIEW

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ABSTRACT

Relevance: *Contrast spectral mammography (CSM) is an innovative technology that combines the principles of traditional digital mammography with intravenous administration of an iodine-containing contrast agent. This makes it possible to obtain images reflecting angiogenesis and vascularization of pathological foci, which potentially increases the sensitivity and specificity of breast cancer (BC) diagnosis. BC occupies the first place in the structure of cancer morbidity and mortality from cancer among the female population worldwide and remains an urgent problem today. Despite promising research results, many aspects of the clinical application of CSM require further study. In particular, it is relevant to compare the diagnostic value of CSM with other radiation imaging meth-ods such as digital mammography (DM) and magnetic resonance imaging (MRI) of the mammary glands.*

The study aimed to *explore the diagnostic capacity of contrast spectral mammography in breast cancer detection compared to other radiation methods.*

Methods: *A search and selection of articles in the databases PubMed, Web of Science, Scopus, and Google Scholar from 2015 to 2025, devoted to the diagnosis of breast cancer. To write this review, 107 literary sources were found for all resources, of which 30 were included in the presented review.*

Results: *The results showed that CSM is easily performed and well tolerated by patients. The meth-od is superior to DM because it provides information about the presence of pathological neoangiogenesis of the tumor. Compared to MRI, CSM is similar in sensitivity and specificity. Therefore, CSM can be used as an alternative method of breast imaging due to its higher accessibility and usability in patients with contraindications for MRI.*

Conclusion: *CSM exceeds the capacity of conventional DM, regardless of breast density. As a result, this method can reduce the number of false positive results and limit the number of unwanted invasive interventions. Early detection of BC significantly increases the chances of successful treat-ment, reduces the risk of metastasis, and improves overall and disease-free survival.*

Keywords: *contrast spectral mammography (CSM), digital mammography (DM), magnetic resonance imaging (MRI), breast cancer.*

Introduction: Breast cancer (BC) is a malignant tumor that originates from the epithelial cells of the ducts and lobules of the mammary gland. BC is characterized by aggressive growth and variability of the clinical course, with invasion into the ducts and lobules. The main risk factors are stress, immunosuppression, heredity, late menopause, hormonal factors, obesity, smoking, and alcoholism [1]. Globally, BC leads both in the number of detected cases and the mortality rate among women and remains a pressing problem today. According to GLOBOCAN (2022), more than 2.3 million new cases of BC are registered worldwide among both sexes, taking the lives of 670,000 women per year. The disease ranks first among the causes of cancer both in countries with mature and transitional economies. In Kazakhstan, about 5,500 new cases and 1,600 deaths from BC are registered annually [2]. With such high morbidity and mortality rates, timely and early diagnosis is of particular importance, requiring the improvement of existing visualization methods [3].

The study aimed to explore the diagnostic capacity of contrast spectral mammography in breast cancer detection compared to other radiation methods.

Materials and Methods: This review included the search and analysis of literature sources from PubMed, Web of Science, Scopus, and Google Scholar databases that were published from 2015 to 2025. The main objective was to study the effectiveness and accuracy of various methods for diagnosing breast cancer. The search keywords included: contrast spectral mammography (CSM), digital mammography (DM), magnetic resonance imaging (MRI), and breast cancer.

The literature analysis was conducted taking into account formal criteria: type of publication, level of evidence (according to the GRADE scale), quality of methodology, and indexation of the source in international databases. The following criteria were applied:

Inclusion criteria: open access, full text, period, article type: clinical trial, systematic reviews, original articles, and meta-analyses.

Exclusion criteria: Articles without a description of the methodology or with incomplete data on the group of patients and the diagnostic methods used. Publications without access to the full text and duplicate publications. Literature in languages other than Russian and English.

During the search, 107 literature sources were identified from all sources; of them, 30 were included in the final review. The main steps of the search were performed according to the PRISMA guidelines, as shown in Figure 1.

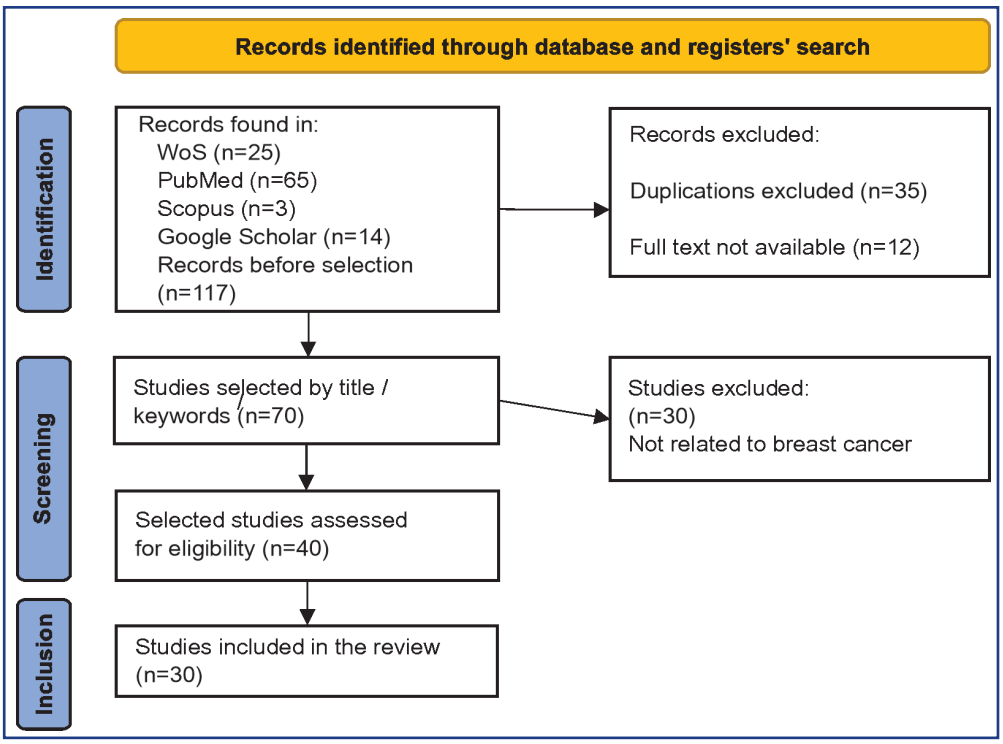

Figure 1 – PRISMA flow diagram

The quality of included publications was assessed using the Newcastle-Ottawa Scale (NOS), covering three domains: selection of participants, comparability of groups, and completeness of outcome reporting. The maximum score was 9 points. The GRADE approach was used to assess the certainty of evidence for key diagnostic indicators, taking into account study design, risk of bias, consistency, and precision of results [4].

In 2022, the Joint Commission for Quality Control of Medical Care of the Ministry of Health of the Republic of Kazakhstan approved clinical protocols for the diagnosis and treatment of breast cancer (Minutes No. 174) [5].

Digital mammography is a non-invasive radiological breast imaging method, considered the standard for breast cancer screening and diagnostics. The national screening program involves testing women aged 40 to 70 every two years. This approach has reduced mortality rates by 15-25% [3, 6]. However, this method's capacity is limited when visualizing mammary glands with high tissue density (dense breasts), which reduces the diagnostic sensitivity of digital mammography. The ratio of adipose and fibroglandular tissue determines the structure of the mammary gland. Dense breasts are assessed according to the classification of the American College of Radiology (ACR) [7]. BI-RADS system, in its latest edition (5th) applied since 2013, distinguishes the following categories: ACR A – predominantly adipose tissue (<25% fibroglandular); ACR B – moderately dense (25-50%); ACR C – heterogeneously dense (5-75%); ACR D – extremely dense (>75%). Digital mammography sensitivity is lower in detecting breast cancer in ACR C & D types' mammary glands.

CSM, as an innovative method of breast imaging, combines standard digital mammography with low (26-32 keV) and high (40-49 keV) energy modes with intravenous administration of iodine-containing contrast medium (ICCM). This makes it possible to visualize pathological changes accompanied by neovascularization, even with dense breasts [8]. CSM is gaining popularity since its introduction in 2003 [9]. Still, along with the benefits, it carries potential risks, including allergic reactions (0.2-0.7%) and nephrotoxicity, as described in the studies of K. Coffey et al.(2022) [10]. According to a meta-analysis, the frequency of side effects is comparable to CT – about 0.8%. In addition, the total radiation dose during CSM is 1.5-1.8 times higher than during digital mammography [11]. CSM technique involves bolus administration of ICCM at a dose of 1.5 ml/kg at a rate of 2.5 ml/s. Two minutes after the injection, a series of images of both mammary glands is taken in standard projections (CC and MLO). The use of low- and high-energy X-rays allows for constructing post-contrast maps reflecting zones of increased ICCM accumulation. MLO projection of the side of interest is performed last to estimate

the rate of contrast washout. If necessary, additional projections (lateral, enlarged) are possible [12]. L. Nicosia et al. demonstrated a higher sensitivity and specificity of CSM in diagnosing breast cancer, especially in women with dense breasts [13]. A systematic review by T. Tagliafico et al., covering retrospective and prospective studies, confirmed high diagnostic efficiency of the method: CSM sensitivity reaches 98% [14].

In addition to the above diagnostic methods, magnetic resonance imaging (MRI) is used for accurate diagnostics. The examination requires MRI machines with a power of 1.5 Tesla and higher, which provide higher spatial and temporal resolution. This increases diagnostic reliability in identifying pathological foci. MRI using gadolinium-enhanced ICCM can detect more aggressive and invasive types of breast cancer. MRI has a high sensitivity in detecting cancer compared to traditional diagnostic methods. Its high sensitivity is due to the fact that no cancerous tumor can grow larger than 2 mm without forming blood vessels, which provide large amounts of nutrients for tumor growth. Gadolinium-enhanced ICCMs have relatively large molecules that easily pass out of the vessels and quickly accumulate in the tumor stroma [15]. A standard MRI protocol includes T1 and T2 modes with signal suppression from fat tissue, dynamic contrast enhancement, diffusion-weighted images, and the construction of maps of the measured apparent diffusion coefficient [16]. High vascular permeability in cancer allows for rapid accumulation of ICCM in the tumor and leads to rapid leaching of ICCM from the lesion, which helps to better visualize pathological areas of enhancement and differentiate malignant and benign tumors [17]. According to the European Society of Breast Imaging (EUSOBI) recommendation [18], MRI is used when the results of standard imaging are inconclusive and it is necessary to exclude a malignant tumor, to determine preoperative staging, and to determine the exact tumor size. The tumor size of invasive carcinoma on MRI corresponds to the actual tumor size in the postoperative material. Besides, 25% of tumors are multifocal (one or more foci are located in one quadrant of the breast) and 20% are multicentric (one or more invasive foci are located at a distance of more than 4 cm from the primary tumor). Incorrect size assessment and failure to detect additional foci of spread may result in positive resection margins after surgery or early recurrence. Another MRI advantage is the detection of synchronous breast lesions, which occur in approximately 3% of all patients with breast cancer [19]. Digital mammography does not detect synchronous contralateral lesions, and they remain undetected in approximately 75% of cases. Main disadvantages of MRI include its high cost, the presence of contraindications in patients with metal implants in the body, pacemakers, allergy to gadolinium-enhanced ICCM, and claustrophobia, which limits the widespread use of MRI in breast imaging.

Results: CSM has a high sensitivity (90-95%) and specificity (85-90%), especially when cancer is detected in dense breasts. M. Mori et al. have compared CSM and digital mammography diagnostic effectiveness in dense breasts. In their study, CSM had a sensitivity of 86.2%, a specificity of 94.2%, and a diagnostic accuracy of 90.9%, while digital mammography had a low sensitivity of 53.4%, a specificity of 85.9%, and a diagnostic accuracy of 72.7% [20]. M. Helal et al. demonstrated the added benefit of CSM: their study showed that the method allows for effective differentiation of breast cancer recurrences after surgical intervention. The sensitivity of CSM in detecting breast cancer recurrence in the postoperative scar area was 91.2%, and the positive predictive value was 77.5%. Of all those examined, 48.6% had a postoperative relapse [21]. CSM allows detecting qualitative characteristics of breast cancer, such as the degree of ICCM accumulation (absent, weak, moderate, and pronounced). A type of accumulation in the pathological focus (lacunar, cloud-like, diffuse-spherical, point, mesh, cotton-like, ring-shaped, heterogeneous-ring-shaped) allows for differential diagnostics between benign and malignant neoplasms in the mammary gland [22].

S. Weigel et al. performed a systematic review of prospective studies to compare CSM and digital mammography in women with a varied degree of breast density. In their study, digital mammography sensitivity decreased with increasing breast density, from 100% with ACR A to 50% with ACR D. The sensitivity of digital mammography for the overall sample was 79.9%. The study included 438 patients, of whom 154 were confirmed to have malignant tumors, and 284 were confirmed to have benign tumors. Comparing the diagnostic characteristics of women with high-density breasts (ACR C & D), CSM demonstrated better results, with a sensitivity of 96.8%, specificity of 93.3%, and accuracy of 94.5%, compared to digital mammography, where the corresponding figures were 85.7%, 87.3%, and 86.8% [23].

Contrast-enhanced magnetic resonance imaging (MRI) can detect tumor formations inaccessible for visualization with digital mammography. A pilot study by M. Jochelson et al. (2023) assessed CSM and MRI diagnostic capacity under screening conditions in 307 women with moderate and high risk of developing breast cancer. All participants underwent both CSM and MRI and were monitored for two years. The first stage of screening revealed three cases of malignancies: two invasive cancers were detected by both CSM and MRI, while one duct carcinoma in situ was detected only by MRI. Neither of those cases was visible on low-energy CSM mammograms; also, no palpable interval tumors were found. Notably, the specificity indicators of CSM and MRI were comparable – 94.7% and 94.1%, respectively [24, 25]. Gadolinium-enhanced MRI allows differentiation between benign and malignant processes, assessment of

the anatomical localization and extent of tumor spread, and visualization of lymph nodes with signs of metastatic lesions. The method demonstrates high efficiency in detecting relapses of the disease after surgical intervention and remains a reliable diagnostic tool even in the presence of silicone implants. MRI is widely used to plan the volume of surgical treatment and monitor the treatment efficacy [26].

To improve the reliability and objectivity of the analysis of the observational and diagnostic studies included in the review, a quality assessment was performed using the NOS scale, which covers three domains: participant selection, group comparability, and outcome completeness. Most studies scored 7-9 points out of 9 possible, indicating their high methodological level.

In addition, the GRADE approach was used to assess the certainty of evidence for key diagnostic characteristics (sensitivity, specificity, accuracy), taking into account study design, risk of bias, indirect evidence, consistency, and precision. Thus, in the study by S. Weigel et al., the sensitivity of the CSM for dense tissue was 96.8% (for ACR density types C-D). This level of evidence is assessed as high, since the study was prospective, with a low risk of systematic errors and high consistency of indicators [23].

Table 1 presents the quality assessment of the included observational and diagnostic studies using the NOS scale.

Table 1 – Assessment of the quality of included studies using the NOS scale

Research / Year	Type of study	Selection (up to 4+)	Comparability (up to 2+)	Outcomes (up to 3+)	Σ NOS	Quality
Mori et al. (2016) [20]	Prospective study	++++	++	+++	9/9	High
Helal et al. (2019) [21]	Retrospective study	+++	++	++	7/9	Moderate - High
Weigel et al. (2022) [23]	Prospective study	+++	++	++	7/9	Moderate
Jochelson et al. (2023) [24]	Pilot cohort study	+++	++	++	7/9	Moderate
Hobbs et al. (2015) [29]	Small qualitative study	++	++	+	4/9	Low

CSM has become increasingly important in recent years not only as a diagnostic method, but as a tool for dynamic monitoring of patients with breast cancer under systemic therapy, including neoadjuvant chemotherapy (NACT). Studies show that CSM can detect changes in tumor vascularization, which can serve as an early marker of therapeutic response before the appearance of morphological signs of regression [27]. Comparative prospective studies demonstrated comparable performance of CSM and MRI in assessing residual tumor after NAC. At that, CSM advantages include lower cost, availability, and better tolerability of the procedure by patients [28]. CSM is also better perceived by patients. In a study by M. Hobbs et al., including 49 women, CSM was perceived as more comfortable than MRI. The patients reported lower anxiety, less noise, quicker examination, and better overall tolerability of the procedure. This makes the method particularly attractive for screening and repeat examinations, as well as for patients with contraindications to MRI [29]. Thus, CSM can be considered as an alternative to MRI in dynamic monitoring of treatment effectiveness in patients receiving NACT, especially in limited access or contraindications to MRI.

Discussion: Since its introduction into clinical practice, CSM has been actively spreading in some countries in Europe, Asia, and North America. CSM is most often used in France, Italy, Germany, Great Britain, the USA, China, and South Korea, where it serves as an addition or an alternative to MRI in breast cancer diagnosis and monitoring. In the UK, according to a 2017 study, CSM demonstrated comparable performance in screening women with dense breast tissue compared to MRI, with significantly lower cost of the examination [30]. Despite the high diagnostic efficacy of CSM, several factors limit its universal use and require critical thinking when interpreting results. Firstly, the method remains dependent on the quality of the examination and the experience of the radiologist. Interpretation of contrast enhancement may vary, especially in the presence of postoperative cicatricial changes, fibrosis, or benign proliferative processes, creating a risk of false positive results and overdiagnosis. CSM is a promising and clinically relevant imaging method, capable of increasing the accuracy of breast cancer diagnostics and improving the optimization of patient routing. Table 2 presents a comparison of modern visualization methods in the diagnosis of breast cancer.

Conclusion: The conducted analysis of domestic and foreign sources confirms that CSM has high diagnostic value and can serve as an effective addition to traditional methods of radiographic imaging in breast cancer. This method provides a simultaneous assessment of the morphological and functional characteristics of the tumor, including visualization of pathological neoangiogenesis, thus significantly expanding diagnostic capabilities, especially in women with dense breasts and a higher risk of developing breast cancer. A good tolerability, lower cost, and ease of implementation make CSM a practically significant tool for routine use in clinical practice. The use of CSM helps to increase oncological alertness, reduce the number of false positive results, and improve the effectiveness of treatment and diagnostic decisions.

Table 2 – Comparative characteristics of breast cancer imaging methods

Criterion	Digital mammography	Contrast-enhanced spectral mammography (CSM)	Magnetic resonance imaging (MRI)
Availability	Widely available, included in screening	Limited availability, being introduced into clinics	Limited, requires equipment ≥1.5 T
Sensitivity	53-80%, decreases with ACR C and D	86-98%, especially with highly dense breasts	90-100%, high even with thick fabric
Specificity	85-90%	85-95%	85-95%
The impact of breast density	The method's sensitivity and effec-tiveness are reduced	Less significant, works well with ACR C-D	Independent of tissue density
Invasiveness	Non-invasive	Invasive (ICCM administration)	Invasive (ICCM administration)
Radiation	Ionizing	Increased radiation exposure	No ionizing radiation
Contrast agent	Not required	Iodine containing	Gadolinium
Contraindications	Pregnancy	Allergy to iodine, renal failure	Metal implants, claustro-phobia, and allergy to ICCM
Detection of multifocality	Limited	Reliably identifies multifo-cal/ multicentric forms	Reliably identifies multifocal/ multicentric forms
Evaluation of recurrence after surgery	Low information content	High sensitivity	High sensitivity
Patient comfort	Good tolerance	Faster and more comforta-ble than MRI	Discomfort and anxiety may occur.
Cost	Relatively low	Average	High

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АҢДАТПА

СҮТ БЕЗІ ҚАТЕРЛІ ІСІГІНІҢ КЕШЕНДІ СӘУЛЕЛІК ДИАГНОСТИКАСЫНДАҒЫ ЕКІ ЭНЕРГИЯЛЫ КОНТРАСТТЫ СПЕКТРЛЬДЫ МАММОГРАФИЯНЫҢ МҮМКІНДІКТЕРІ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Контрасты спектральды маммография (КСМ) – бұл дәстүрлі маммография принциптерін йодты контрасты затты енгізумен біріктіретін инновациялық технология. Бұл патологиялық ошақтардың ангиогенезін және васкуляризациясын көрсететін суреттерді алуға мүмкіндік береді, бұл сүт безі қатерлі ісігін (СБҚІ) диагностикалаудың сезімталдығы мен спецификалығын потенциалды түрде арттырады. СБҚІ әлемдегі әйелдер арасында онкологиялық аурулар мен қатерлі ісіктер бойынша бірінші орында тұр және бүгінгі күнге дейін өзекті мәселе болып қала береді. Зерттеулердің көптеген нәтижелеріне қарамастан, КСМ клиникалық қолданысының аспектілері одан әрі зерттеуді қажет етеді. Атап айтқанда, цифрлық маммография (ЦМ) және сүт бездерінің магнитті-резонанстық томографиясы (МРТ) сияқты басқа да сәулелік әдістерімен салыстырғанда КСМ-ның диагностикалық құндылығын салыстырмалы бағалау өзекті болып табылады.*

Зерттеу мақсаты *– басқа сәулелік әдістермен салыстырғанда сүт безінің қатерлі ісігін диагностикалаудағы контрастты спектрльды маммографияның мүмкіндіктерін зерттеу.*

Әдістері: *СБҚІ диагностикасына арналған мақалаларды Pubmed, Web of Science, Scopus, Google scholar дерекқорларында 2015 жылдан 2025 жылға дейін іздеу және іріктеу жүргізілді. Осы шолуды жазу үшін барлық ресурстар бойынша 107 әдеби дереккөз табылды, оның 30-ы ұсынылған шолуға енгізілді.*

Нәтижелері: *Көптеген зерттеулердің нәтижелері бойынша КСМ-ның орындалуы оңай және пациенттер жақсы көтереді. Бұл әдіс ЦМ-дан артық, себебі ісіктің патологиялық неоангиогенезінің болуы туралы ақпарат береді. МРТ-мен салыстырғанда, КСМ сезімталдығы мен спецификалығы бойынша ұқсас. Демек, КСМ сүт бездерін визуализациялаудың балама әдісі ретінде қолданылуы мүмкін, бұл ретте КСМ қолжетімдірек және МРТ қарсы көрсеткіштері бар пациенттерге жасалуы мүмкін.*

Қорытынды: *КСМ әдісінің сезімталдығы, спецификалығы және дәлдігі сүт безінің тығыздығының түріне және пациенттердің жасына қарамастан, ЦМ көрсеткіштерінен асып түседі. Осының арқасында бұл әдіс жалған оң нәтижелердің санын азайтуға және қажетсіз инвазивті әдістердің санын шектеуге мүмкіндік береді. Қатерлі ісіктерді уақтылы анықтау сәтті емдеу мүмкіндігін едәуір арттырады және метастаздану қаупін төмендетеді.*

Түйінді сөздер: *контрасты спектральды маммография (КСМ), цифрлық маммография (ЦМ), магнитті-резонансты томография (МРТ), сүт безінің қатерлі ісігі (СБҚІ).*

АННОТАЦИЯ

ВОЗМОЖНОСТИ ДВУХЭНЕРГЕТИЧЕСКОЙ КОНТРАСТНОЙ СПЕКТРАЛЬНОЙ МАММОГРАФИИ ПРИ КОМПЛЕКСНОЙ ЛУЧЕВОЙ ДИАГНОСТИКЕ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Контрастная спектральная маммография (КСМ) представляет собой современную методику визуализации, сочетающую цифровую маммографию с внутривенным контрастированием на основе йода. Метод позволяет получать изображения, отражающие ангиогенез и васкуляризацию патологических очагов, тем самым потенциально повышая диагностическую точность при раке молочной железы (РМЖ). Заболеваемость и смертность от РМЖ среди женщин остаются на высоком уровне по всему миру, что определяет его актуальность. Несмотря на многообещающие результаты исследований, многие аспекты клинического применения КСМ требуют дальнейшего изучения. В частности, актуальным является сравнительная оценка диагностической ценности КСМ с другими лучевыми методами визуализации, как цифровой маммографии (ЦМ) и магнитно-резонансной томографии (МРТ).*

Цель исследования *– проанализировать диагностические возможности контрастной спектральной маммографии в сравнении с другими методами лучевой диагностики при раке молочной железы.*

Методы: *Произведен поиск и отбор статей, посвященных диагностике РМЖ, в базах данных PubMed, Web of Science, Scopus, Google Scholar за период с 2015 по 2025 года. Для написания данного обзора по всем ресурсам было найдено 107 литературных источника, из которых 30 были включены в представленный обзор.*

Результаты: *Исследования показывают, что КСМ является технически выполнимой процедурой и хорошо переносится пациентками. Метод позволяет визуализировать неоангиогенез опухоли, что делает его более информативным по сравнению с ЦМ. По чувствительности и специфичности КСМ сопоставима с МРТ, однако отличается большей доступностью и может применяться при наличии противопоказаний к МРТ.*

Заключение: *КСМ демонстрирует более высокую информативность по сравнению с традиционной ЦМ, особенно в случае высокой плотности тканей молочной железы. Благодаря которым, метод позволит уменьшить количество ложноположительных результатов и ограничить количество нежелательных инвазивных вмешательств. Своевременное выявление РМЖ на ранних стадиях существенно повышает шансы на успешное лечение, снизить риск метастазирования и улучшить показатели общей и безрецидивной выживаемости.*

Ключевые слова: *контрастная спектральная маммография (КСМ), цифровая маммография (ЦМ), магнитно-резонансная томография (МРТ), рак молочной железы (РМЖ).*

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