Review

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# Future of Breast Radiology

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**ABSTRACT**

The landscape of breast imaging has transformed significantly since mammography's introduction in the 1960s, accelerated by ultrasound and image-guided biopsies in the 1990s. The emergence of magnetic resonance imaging (MRI) in the 2000s added a valuable dimension to advanced imaging. Multimodality and multiparametric imaging have firmly established breast radiology's pivotal role in managing breast disorders. A shift from conventional to digital radiology emerged in the late 20th and early 21st centuries, enabling advanced techniques like digital breast tomosynthesis, contrast-enhanced mammography, and artificial intelligence (AI) integration. AI's impending integration into breast radiology may enhance diagnostics and workflows. It involves computer-aided diagnosis (CAD) algorithms, workflow support algorithms, and data processing algorithms. CAD systems, developed since the 1980s, optimize cancer detection rates by addressing false positives and negatives. Radiologists' roles will evolve into specialized clinicians collaborating with AI for efficient patient care and utilizing advanced techniques with multiparametric imaging and radiomics. Wearable technologies, non-contrast MRI, and innovative modalities like photoacoustic imaging show potential to enhance diagnostics. Imaging-guided therapy, notably cryotherapy, and theranostics, gains traction. Theranostics, integrating therapy and diagnostics, holds potential for precise treatment. Advanced imaging, AI, and novel therapies will revolutionize breast radiology, offering refined diagnostics and personalized treatments. Personalized screening, AI's role, and imaging-guided therapies will shape the future of breast radiology.

**Keywords:** Artificial intelligence; breast imaging; diagnostic techniques; screening; theranostics; radiology; interventional

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**Key Points**

- Advancing integration of artificial intelligence (AI): AI is becoming integral to breast radiology, streamlining workflows, smart dataprocessing, aiding detection and diagnosis, and optimizing decision-making processes.
- Personalized screening and diagnosis: Evolving from mammography, automated breast ultrasound, magnetic resonance imaging (MRI), and contrast-enhanced mammography offer personalized screening options with AI-driven enhancements for accuracy.
- Innovative imaging and therapies: Multiparametric MRI, virtual biopsy, and photoacoustic imaging provide advanced diagnostic insights. Imaging-guided therapies and theranostics promise targeted precision treatment, transforming breast radiology's future.

Following the inception of mammography (MG) for screening purposes in the early 1960s, the field of breast imaging has undergone a transformative progression. This evolution gathered significant momentum by incorporating ultrasound (US) and advanced image-guided biopsies into routine clinical practice during the 1990s. Subsequently, in the early 2000s, magnetic resonance imaging (MRI) emerged as a discriminating option for advanced imaging modalities. Furthermore, the shift from conventional to digital radiology occurred between the late twentieth and early twenty-first centuries. Concerns mainly revolved around the reduced resolution of digital images compared to conventional MG, which raised worries about potentially missing lesions like microcalcifications and the challenge of detailed breast tissue visualization. Nevertheless, due to the broader dynamic range of digital MG compared to screen-film MG, it displayed greater tolerance to exposure errors. Additionally, the digital format of images offered a significant advantage, allowing for the integration of advanced techniques. This, in turn, facilitated the incorporation of digital breast tomosynthesis imaging, contrast-enhanced MG, and artificial intelligence (AI) applications. Subsequently, in the early 2000s, MRI emerged as a discerning option for advanced imaging modalities. Through the assessment of multimodality and multiparametric imaging, breast radiology has indisputably established itself as an indispensable and irreplaceable component in the management of breast disorders.

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The essence of AI lies in its ability to develop algorithms that emulate human intelligence, while learning from data and making informed decisions. Given the digital nature of radiology, AI's integration appears inevitable (1). However, the gradual integration of AI into breast radiology sparks curiosity and concern about the potential impact on the profession. AI will inevitably play a significant role in the future of breast radiology. The questions remain: what specific role will AI hold within breast radiology practice? Would AI replace radiologists, and could AI's findings be relied upon exclusively?

**The Integration of AI in Breast Radiology**

Radiology departments of the future will operate alongside AI, which will serve as a support mechanism, streamlining processes, aiding decision-making, and improving regulation. The role of AI in breast radiology will manifest in three key ways: Computer-aided diagnosis (CAD) algorithms, workflow support algorithms, and data processing algorithms.

AI as a support tool in breast radiology dates back to the 1980s when computer support was initiated for mammographic film evaluation (2, 3). Early systems flagged suspicious areas for the ultimate decision of the radiologist. Image perception errors, human factors like fatigue, and overlapping structures all contributed to erroneous diagnoses that could be reduced with such support algorithms (4). However, due to the emergence of convolutional neural networks and deep learning (DL), these CAD systems have transformed, transitioning from basic, user-defined algorithms to autonomous learning algorithms. This capability allows DL models to potentially uncover features that are unidentifiable or imperceptible to the human eye. Practical, AI driven new generation CAD applications, including detection, triage, and diagnosis, hold promise in breast imaging. These AI based applications address issues like false positives and negatives in screening mammograms, optimizing patient recall rates, and improving cancer detection rates (1). The prevalence of false positive outcomes in screening MG can be high as 30% (5, 6). On the other hand, retrospective analyses reveal that up to 60% of interval cancers exhibit affirmative findings within prior mammograms (6, 7). Research indicates that the introduction of AI systems in screening mammograms has the potential to decrease interval cancers and increase cancer detection rates in routine screening mammograms (8-10). AI algorithms will prioritize examinations, mark suspicious lesions, and facilitate decision-making, allowing radiologists to use their time more efficiently. This AI-assisted workflow will reshape the role of radiologists, transforming them into specialized clinicians engaging more in multidisciplinary collaborations (11-14). Pending examinations will be prioritized based on their significance, and comparative reports involving comparison with prior studies and meticulously AI-generated clinical information will be ready for review (15, 16). Naturally, as these advances unfold, radiologists' characteristics will also evolve. General radiologists, who constitute the majority, will gradually be succeeded by specialized radiologists who possess expertise in their specific domains and adopt a personalized clinical approach when engaging with patients (15, 16). Radiology clinic reading rooms will function as central "hubs", fostering multidisciplinary collaboration, shaping patient-centered diagnoses, and informing clinicians about treatment options. Leveraging AI alongside intranet and internet connectivity, patient data from hosting and external hospitals will be aggregated and showcased during multidisciplinary meetings. Thus, radiology will gain value as clinically based and patient oriented.

**From Volume Screening to Personalized Screening**

Screening in breast cancer, which began as a simple MG examination and has now evolved to a personalized screening approach. A better understanding of the significance of breast density has led to a change in screening strategies for women with dense fibroglandular tissue, driven by heightened awareness of its influence on false negatives and elevated breast cancer risk. Supplementary US screening is widely used for women with dense breast tissue. A recent large, randomized US screening study showed the impact of ultrasonography in detecting two additional cancers per 1000 women, in line with previous studies (17). However, US encounters significant limitations, including its real-time nature and user-dependent operation, leading to archiving and retrospective analysis challenges. Automated breast ultrasound system (ABUS) can be used for screening and diagnostically, providing a 3-dimensional volume view (18). Undoubtedly, AI algorithms to be developed in the future will enable better visualization of this 3D data, facilitate lesion detection with CAD solutions, and allow faster evaluation with decision support algorithms. Since ABUS can also help teleradiology, US scanning can be performed where radiologists are unavailable. Research continues on automated US imaging with a tomography mechanism by allowing the breast to sag with gravity in the prone position instead of the supine position (19). In this way, it will be possible to evaluate other parameters, such as speed of sound, which may show higher specificity in lesion differentiation (20).

Breast MRI is also valuable as a supplementary screening tool and is effective not only in high-risk women but also in women with average risk but increased breast density (21). Furthermore, a recent randomized controlled MRI screening study included women with extremely dense breast tissue from a national breast cancer screening program. These women were offered supplementary MRI screening every two years, resulting in a notable reduction in interval cancers and the detection of an additional 15 cancers per thousand screenings (22). However, breast MRI is expensive and hard to access as a large-volume screening method. Contrast-enhanced MG can be an excellent alternative to MRI and offers a cost-effective and convenient solution for screening high-risk women and those with dense breast tissue (23, 24). This approach has the potential to facilitate efficient and rapid large-scale female screening.

Wearable technologies, such as specialized bras equipped with US sensors, can potentially transform follow-up and screening approaches (25). Meanwhile, non-contrast MRI techniques are gaining traction, providing valuable information, particularly in screening without invasive contrast agents. Combining T2-weighted or STIR images with diffusion imaging can provide comparably high-sensitivity results to contrast-enhanced MR scanning (26, 27). Future advancements aim to enable rapid, non-contrast breast MRI scans, suitable even for women with contrast contraindications.

**Innovations in Diagnostic Imaging**

The cornerstone of breast MRI examination is dynamic contrast-enhanced imaging. MRI, highly sensitive in breast radiology, evaluates multiple parameters such as diffusion-weighted imaging, spectroscopy, and dynamic contrast enhancement (28-30). Through multiparametric MRI, neovascularization, tissue water diffusion, and molecular markers can be assessed enabling molecular-level imaging (31). Tumor characteristics like proliferation, angiogenesis, apoptosis, metabolism, and hypoxia can also be demonstrated (31). Dynamic contrast-enhanced MRI depicts contrast material kinetics, quantifying neovascularization via tumor perfusion. Excessive tumor cell proliferation narrows intercellular space and hinders fluid movement, detected through diffusion imaging and vectorial movement with diffusion tensor imaging. These methods allow contrast-free breast cancer screening with improving image quality. Furthermore, using these different parameters, radiomic information, which enhances diagnostic accuracy, is obtained. MR spectroscopy (MRS) examines various molecules; choline, used in cell membranes, enables molecular mapping for virtual biopsy. Hyperpolarized MRS imaging detects rare molecules. While current MRI visualizes hydrogen atoms, other rare particles like carbon (C) and phosphorous (P) can be facilitated, and different parametric MRI outcomes can be achieved (32).

Photoacoustic or optoacoustic imaging is a hybrid imaging modality combining optical illumination and US (33). Angiogenesis and hypoxia are some of the main features of cancer, and the capability of optical imaging to detect various hemoglobin forms enhances its sensitivity in imaging (33, 34). The oxygenation capacity of blood vessels and treatment-induced changes in the blood vessels can be demonstrated (34). The functional aspect of optoacoustic US has the potential to address certain challenges related to morphological similarities in distinguishing between benign and malignant masses (35-37). In recent studies, the incorporation of optoacoustic US (OA/US) showed an increase in breast mass assessment specificity of 14.9%, and high positive predictive values for malignancy (35, 38). Other studies show that utilizing OA/US may assist radiologists in more effectively distinguishing between various breast cancer molecular subtypes (39).

Virtual biopsy, notably through multiparametric MR examination, has emerged as a pivotal differential diagnostic tool. Imaging genomics (radiomics) plays a vital role here. Radiomics integration involves aligning the molecular attributes of diverse genetic subgroups of breast cancer with their multiparametric imaging features. This approach links disease imaging phenotypes with their genotype, representing their genetic expression - a vigorously researched subject (40). Leveraging AI-enhanced segmentation, lesion features identified by radiologists and computers can be matched with genotypes. This process enables classification and predictive model creation, addressing clinical and biological queries (40, 41).

Since MRI is a frequently used technique for screening, diagnosis, and staging in breast radiology, difficulties are often encountered in diagnosing lesions detected only by MR examination. MRI-guided biopsy is required for these lesions, but MRI-guided biopsy is a technically challenging, time-consuming, and expensive technique. MRI-guided biopsy can be performed in a few centers worldwide. Contrast-enhanced MG, an excellent alternative to MRI, also provides biopsy (42). In this way, the lesions detected only with contrast-enhanced MRI can be diagnosed with contrast-enhanced MG-guided stereotaxic vacuum biopsy. This method can be widely used as a more practical alternative to MRI-guided biopsy.

Conducting MRI scans with the patient in the prone position while performing surgical and biopsy procedures in the supine position presents challenges in accurately localizing lesions identified by MRI. This incongruity in patient positioning hinders precise pre-surgical planning, lesion evaluation, and procedures like biopsy or marking (43, 44). However, real-time US examinations can merge supine MRI images with US images, allowing for accurate lesion localization and guidance during interventional procedures (45, 46). Consequently, fusion US-guided biopsy is an alternative to MR-guided biopsy (46). With the advancement of fusion biopsy techniques and their integration with non-contrast MRI methods, this challenge will be more effectively addressed in the future. Transforming prone imaging to the supine position also holds significance in preoperative planning and locating tumors before and after neoadjuvant chemotherapy, providing crucial guidance for surgical interventions.



### Imaging Guided Therapy

Cryotherapy is a treatment method that can be applied with US guidance and has been recently researched to treat breast cancer. A pivotal study on this subject is the Ice3 study, in which 194 women over 60 were evaluated, and the tumor size ranged from 8-14.9 mm. In a mean follow-up of 3 years after treatment, ipsilateral tumor recurrence was 2.06% (47). Cryotherapy holds promise as a viable alternative treatment avenue, particularly for instances wherein surgical intervention is not feasible.

Theranostics is derived from therapy and diagnostics and can be defined as using diagnostic methods to provide targeted therapy. Modern breast cancer treatment is optimally individualized and targeted, and theranostics appears to be an excellent method to achieve this goal. In theranostics, the active therapeutic substance will be delivered to the target cell without affecting the surrounding healthy tissues, and the process will be monitored with imaging guidance. The basic procedure is to load the lethal dose to the contrast agent carriers, monitor the agent with imaging, and control the release of the therapeutic agent loaded to the contrast agent into the tumor with the help of imaging methods when it reaches the tumor tissue. For example, after loading the chemotherapeutic agent into microbubbles with US contrast, this contrast agent is injected into the patient, and the tumor is monitored under ultrasonography (48). After tracking the contrast material reaching the tumor, these carrier microbubbles are deflated with the help of US waves, and the drug is released within the tumor without damaging the surrounding tissue (48). Particles or nanoparticles suitable for imaging modality are used as therapeutic agent carriers. One of the most used particles for MRI are superparamagnetic iron oxide nanoparticles (49, 50). Carbon nanotubes are important carriers for MRI, and targeted molecules such as drugs, contrast agents, antibodies, cell membrane penetrants, and iron oxide nanoparticles can be loaded onto these nanotubes (50). Theranostics will play an important role in targeted precision therapy in the future.

## Conclusion

In the future, breast radiology will be able to offer more patient-focused diagnosis and treatment approaches, thanks to the developing technological applications and AI's support to radiologists in every field, from workflow to image formation and CAD systems. Integrating imaging genomics will aid differential diagnosis, aligning genetics with multiparametric features via AI-enhanced solutions. Novel image-guided therapeutic solutions will provide alternative treatment approaches. The future holds enhanced integration of imaging, AI, and innovative therapies in breast radiology. From personalized screening to innovative theranostics, the trajectory of breast imaging is laden with promise, transforming the landscape of breast radiology, and ultimately improving patient outcomes. The future of breast radiology is not one of replacement, but of transformation as technology and human expertise converge to advance patient care to new heights.

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