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Use of novel techniques combined with AI in mammography for breast cancer

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Abstract: *Breast cancer is the malignant tumour that accounts for the first place in the morbidity and mortality of women in China. Early detection and treatment can not only reduce the mortality rate of breast cancer patients, but also improve their five-year survival rate and quality of life. Mammography(MG) is currently the only screening method proven to reduce the mortality rate of breast cancer patients. Its derivatives, such as digital breast tomosynthesis (DBT),contrast-enhanced digital mammography (CEDM) and contrast-enhanced digital breast tomosynthesis (CEDBT) have shown unique advantages. As one of the core technologies in today's scientific and technological development, artificial intelligence has also made great progress in the field of breast imaging. This article analyses and reviews the current development and application of AI combined with mammography and its new techniques in breast cancer diagnosis.*

Keywords: *mammography, artificial intelligence, digital breast tomosynthesis, contrast-enhanced mammography, contrast-enhanced digital breast tomosynthesis*

1. Introduction

The latest data released by the International Agency for Research on Cancer (IARC) of the World Health Organization show that in 2020, breast cancer has surpassed lung cancer to become the most common malignant tumour in the world, and it is also the malignant tumour with the highest morbidity and mortality rate among women in the world. In 2020, the number of new cases of breast cancer in China reached 420,000, which is the highest incidence rate of female malignant tumours in China, and the trend is increasing year by year [1]. Although some studies have shown that factors such as delayed growth, high age at first birth, short breastfeeding time, oral contraceptive pills and family heredity increase the risk of breast cancer, the exact causes of breast cancer is still unclear [2], so the prevention and treatment of breast cancer is based on early screening and active treatment. The use of scientific and effective breast cancer detection methods for breast cancer screening of women of the appropriate age can effectively reduce the incidence and mortality of breast cancer, prolong the survival of breast cancer patients, and protect the health and safety of women's lives. Relevant studies have shown that the intervention treatment for patients with early breast cancer can make the 5-year survival rate of patients reach 87% [3]. In this paper, the value of existing X-ray imaging diagnostic methods and new artificial intelligence assisted diagnostic system for breast cancer is elaborated, aiming to provide reference for effectively assisting radiologist in detecting early breast cancer, and to provide ideas for further exploration of the related new assisted diagnostic system.

2. Mammography

MG is the only method that has been shown to reduce mortality in breast cancer patients, and it is also the preferred screening method recommended by the China Anti-Cancer Society's Breast Cancer Guidelines [4][5]. It uses X-ray to irradiate the breast and produces overlapping images of the tissue by receiving the residual rays that penetrate the breast. Based on the radiographic information from different areas, normal tissue and abnormal lesions such as masses, calcification, asymmetric densities, structural distortions and enlarged axillary lymph nodes can be identified in that area of the breast. Screening and evaluation of breast disease is generally performed using the Breast Imaging Reporting and Data System (BI-RADS) as an standard [6]. Even though the use of full-field digital mammography (FFDM) has further improved the clarity and contrast of images, the occlusion of non-calcified lesions by overlapping

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fibroglandular tissue still has a major impact on the diagnosis of suspicious lesions. Novel mammography techniques and artificial intelligence-assisted diagnostic systems based on radiomics are expected to improve the diagnostic and treatment strategies for breast diseases. Computer-Aided Diagnosis (CAD) systems that can be used for breast cancer imaging have been available since the 1960s [7]. Nowadays, with the rapid development of smart healthcare, the effectiveness of various AI assisted diagnosis systems in lesion detection, segmentation, benign and malignant classification, and BI-RADS grading has been demonstrated in clinical trials. Mao et al [8] demonstrated that the application of radiomics models in mammography could predict the risk of breast cancer in a multicentre study with an AUC of 0.92 using four machine learning algorithms in 2021. An international study conducted by Kim et al [9] that included the results of 170,230 mammograms validated that AI models developed based on large-scale data showed better diagnostic performance in mass detection, asymmetric density, distorted structure identification, and also led to a significant improvement in the performance of radiologists. Lauritzen et al [10] used artificial intelligence to score the images involved in the study on a scale of 0-10, representing the risk of malignancy. Normal mammograms (score <5) would be excluded from the radiologist's reading and suspicious mammograms (score > recall threshold) would be recalled. This resulted in a 62.6 percent reduction in the workload of radiologists.

3. Digital Breast Tomosynthesis

DBT was approved by the U.S. Food and Drug Administration in 2011 and is commonly used in conjunction with DM for the screening and diagnosis of breast disease. DBT is a three-dimensional scanning process in which a X-ray tube is rotated at a limited arc angle, and a series of high-resolution tomosynthesis images are reconstructed by computer post-processing. The reconstructed thin-layered images can be displayed in separate or consecutive forms. DBT can significantly minimize or even eliminate the influence due to overlapping glandular tissues, and thus has higher sensitivity and specificity than FFDM for the detection of non-calcified lesions such as masses, structural distortions, and asymmetric densities in the breast [11][12][13]. The current consensus on DBT focuses on the fact that the technique significantly improves the detection of early-stage, minimally invasive breast cancer in asymptomatic populations [14][15][16] and reduces the false-positive and recall rates of mammography results [17]. Although DBT may improve cancer detection rates, some studies have shown that the majority of cancers detected by DBT are not highly malignant, causing concerns about the issue of overdiagnosis [18]. Data which is currently available [19] shows no marked reduction in interstitial cancers in women screened with DBT compared with FFDM. Whereas, a recent study [20] demonstrated that DBT detected more invasive cancers with a poor prognosis at both first and secondary screening process than conventional FFDM. Even with increasing clinical data and widespread appliance, it remains uncertain whether DBT can also improve the prognosis of breast cancer patients compared to FFDM.

Due to the increased radiation dose associated with simultaneous DBT and FFDM is not acceptable for screening asymptomatic women, researchers have developed synthesized two-dimensional mammograms (SM) based on DBT.The SM algorithm is set to enhance the display of lesions such as calcifications, spiculations at the margins of the mass, and structural distortions [11]. Since SM is reconstructed from DBT, the radiation dose of SM combined with DBT equals to the radiation dose of DBT, and no additional image acquisition time is required. A two-centre retrospective study [21] showed that the screening efficacy for breast cancer remained within the baseline after DBT+SM replaced DBT+FFDM. A recent study [22] involved an diagnostic system that generated CAD-enhanced synthetic mammograms based on the degree of suspicion of soft tissue density as a means of avoiding the need for the reader to flip back and forth between DBT images. This application reduced reading time by 23% without compromising sensitivity, specificity, or recall rate.

Continued advances in DBT algorithms, such as deep learning-based post-processing, will provide high spatial resolution (synthetic) images with less image noise and fewer artefacts. A research [23] showed that using AI-enhanced synthetic with a 6 mm layer thickness instead of a 1mm layer thickness reconstruction scheme can significantly reduce DBT interpretation time without compromising interpretation accuracy. DBT contains more than 100 times more images than DM, and malignant features are usually only visible in a few layers. This combination of large data volume and small, subtle findings leads to a more complex process of segmentation, feature extraction and modelling of regions of interest (ROI) during deep learning model design. Therefore breaking down the technical barriers and optimising the performance of DBT is the way to popularize the use of DBT in clinical applications.

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4. Contrast-enhanced mammography

CEDM adds functional information to the anatomical and morphological information provided by FFDM and DBT. The clinical importance of tumour angiogenesis implied in the diagnosis of primary breast cancer is known to all. Study [24] have shown that intratumour microangiogenesis is an independent prognostic indicator that correlates with a higher incidence of metastasis of breast cancer. CDEM utilises the rapid proliferation of breast tumour cells and secretion of various tumour vascular growth factors to stimulate neovascularisation of the lesion, and peritumour enrichment of the contrast agent, which realistically reflects the distribution of the vascular network of the breast lesion and its haemodynamic characteristics, to improve the detection rate of the lesions of breast diseases and the diagnostic accuracy [25]. CEDM examination requires intravenous iodinated contrast agent on the basis of dual-energy mammography to obtain standard cephalocaudal and oblique lateral mammographic images. Each set of images consists of a "low-energy" image similar to FFDM and a "high-energy" image obtained by augmenting the contrast agent signal with kiloelectronvolts above the k-edge of iodine. Low-energy images are equivalent to FFDM for the detection of density and calcification and replace conventional mammography [26]. Post-processing of low- and high-energy images removes background signals, and the recombined iodine-only images help to identify enhancing lesions, with unique advantages in dense glands and occult lesions [27].

Although CEDM combines the disadvantages of FFDM (X-ray dose and compression of the breast) and breast MRI (requiring intravenous contrast agent), it overcomes the effects of tissue overlap in FFDM and is capable of detecting information on tumour neovascular phase function similar to that of MRI, while maintaining the high image resolution of FFDM [28].Sorin et al [29] showed that in 611 women at intermediate risk of breast cancer with dense glands, there was a 13.1 percent increase in cancer detection with CEDM compared to FFDM. Sung et al [30] reported the detection of six cancers that were not detected by FFDM in 904 patients examined with CEDM, with a complementary detection rate of 6.6 percent. Even though the clinical application of CEDM is not yet widely available, researchers have begun to develop related AI systems. A domestic study [31] showed the relationship between morphological features of lesions and different molecular subtypes to determine the biological behaviours and prognosis of breast tumours, providing clinical reference for precise treatment and indirect preoperative assessment of prognosis. Marino et al [32] identified invasiveness, hormone receptor status, and tumour staging of breast cancers by applying imaging histology to CEDM images, with an accuracy rate ranging from 78.4% to 100%.The results of Petrillo et al [33] confirmed that imaging histology texture features extracted from CEDM images can provide highly relevant information about the nature and grading of the tumour as well as the molecular subtypes of the tumour. This also proves that the combination of artificial intelligence algorithms with the concepts of radiomic analysis can be successful in creating tools to support radiologists in their diagnostic decisions for breast cancer.

5. Contrast-Enhanced Breast Tomosynthesis

CEDBT combines the features of DBT 3D imaging with the enhanced display of lesions by CEDM to provide contrast-enhanced images in three dimensions. Compared with CEDM, CEDBT can provide more accurate lesion details such as lesion morphology, size and location. A study by Huang et al [34] pointed out several potential clinical applications of CEDBT: (i) the 3D display of lesion features may be beneficial for evaluating the response to treatment after neoadjuvant chemotherapy, (ii) the contrast enhancement of the 3D and the anatomical information of the lesion provide better guidance for biopsy, (iii) compared with CEDM +DBT has a reduced radiometric measure compared to CEDBT, and (iv) similar to SM, synthetic CEDM can be extracted from CEDBT data and provides similar lesion contrast enhancement information as CEDM. A study carried out by Chou et al evaluated the AUC of CEDM, CEDBT, and DCE-MRI and showed that by adding CEDBT to CEDM, the diagnostic accuracy was not statistically significantly improved. This also raises the question of whether CEDBT can rationalise its extra radiation dose by providing better lesion characteristics and avoiding unnecessary biopsies. Further studies among domestic and worldwide on the diagnostic performance of CEDBT and related artificial intelligence are required.

6. Conclusion

Imaging diagnosis is an important means of secondary prevention of breast cancer. The new technology of mammography has a broad development prospect in the judgement of benignity and

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malignancy of breast cancer, preoperative staging, evaluation of the effect of neoadjuvant chemotherapy and prediction of recurrence and metastasis risk. The advantages of artificial intelligence technology in the era of big data cannot be ignored. Although there is a lot of controversy about the validity of the current new technologies and the reliability of artificial intelligence technology, it has to be believed that with the progress of technology, the combination of doctors and machine is the inevitable development trend in the field of diagnostic imaging.

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