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The Research Progress of Cone-Beam Breast Computed Tomography in Clinical Application

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Abstract

Cone-beam breast computed tomography (CBBCT) is a specialized imaging modality for breast examination that can generate high-resolution three-dimensional images with 3D isotropic resolution. This method has high sensitivity and better displays breast cancer lesions and microcalcifications, especially in the dense breast. When combined with CBBCT plain and enhanced scans, the efficiency of diagnosis and treatment can be further improved. Enhanced CT scans provide a better display of the morphological characteristics of tumor lesions, surrounding tissues, and blood vessels, thereby providing more comprehensive diagnostic information.

The imaging manifestations of breast cancer on CBBCT are closely related to the molecular subtypes and immunohistochemical receptor status of the tumor. By incorporating imaging characteristics, the molecular subtypes, and the status of immunohistochemical receptors of breast cancer, the diagnosis and evaluation of the disease can be predicted and assessed accurately.

In recent years, CBBCT has shown great potential in the diagnosis and evaluation of breast cancer. This article provides a review of the operational characteristics of cone beam breast CT and the recent research progress in the diagnosis and evaluation of breast diseases.

Keywords: breast cancer, CBBCT, mammography, MRI

1. Introduction

Breast cancer is the most commonly occurring malignant tumor among women worldwide, and its incidence and mortality rates have been on the rise. According to global cancer statistics, breast cancer surpassed lung cancer as the most prevalent cancer in women in 2020, and it remains the leading cause of death among women (SUNG H, FERLAY J, SIEGEL R L, et al., 2021). Current imaging methods for the diagnosis of breast diseases include ultrasound (US), mammography (MG), cone-beam breast computed tomography (CBBCT), and breast magnetic resonance imaging (MRI). CBBCT is a novel breast imaging method that avoids compressing the breast tissue and eliminates the overlapping imaging of tissue. It enables multi-angle and comprehensive observation of breast tissue and lesions, providing more diagnostic information on the morphological characteristics of the lesions and peripheral blood vessels with enhanced examination. Moreover, CBBCT allows for vacuum-assisted biopsy of breast lesions, and it has been shown to be faster than standard stereotactic vacuum-assisted biopsy (WIENBECK S, LOTZ J, FISCHER U., 2017). In recent years, CBBCT has been increasingly applied in clinical practice, and its clinical value in the diagnosis of breast diseases has been recognized. This paper provides a detailed introduction to the characteristics of CBBCT and the research progress in the diagnosis and evaluation of breast diseases.

2. Brief introduction to CBBCT

2.1 Workflow and Characteristics of CBBCT

CBBCT comprises a horizontal CT door frame examination table, a cone-beam X-ray tube, a plate detector, and other components. The X-ray tube and detector are installed on the CT frame, with the tube emitting rays and the plate detector collecting images. During a breast CT examination, the breast under examination is suspended in the imaging space using a platform with a diameter of 39 cm, with the maximum coverage of the examination being 28 x 28 x 16cm. The patient is positioned in a prone position on the examination bed, and one breast is fully examined while the other is kept outside the examination area. The images obtained from a 360° rotation around the breast with the X-ray tube and plate detector can be viewed in sagittal, axial, and coronal positions. The image thickness ranges from 0.27 to 10mm. Additionally, maximum density projection (MIP) and multiplanar reconstruction (MPR) can be achieved through image post-processing, while 3D volume reconstruction (VR) can be achieved using 3D virtual rendering technology. Table 1 provides details of the CBBCT system parameters.

Table 1. System Parameters for a CBBCT

Parameter	Value
Tube voltage	49kVp
Tube voltage	50-200mA
Tube pulse time	8ms
Focal spot size	0.3mm
Data acquisition rate	30 frames/s
Magnification	1.42
Number of projections	300
Acquisition time	10s
Coverage	16×28×28cm

2.2 Plain Scan and Enhanced Examination

The patient was positioned in a prone posture with their arms extended backward, and the breast was allowed to sag naturally, occupying the central position in the scanning field. Following a bilateral breast plain scan, intravenous administration of iodine contrast agent was carried out using a double-chamber high-pressure syringe. Currently, there is no standardized protocol for CBBCT enhanced scanning or intravenous contrast agent injection, and different research institutions have varying approaches (HE N, WU Y P, KONG Y, et al., 2016; WIENBECK S, FISCHER U, LUFTNER-NAGEL S, et al., 2018; AMINOLOLAMA-SHAKERI S, ABBEY C K, GAZI P, et al., 2016). Aminolama-Shakeri et al. used a total volume of 100 ml of iodinated contrast agent iohexol 320 (320 mg/ml), with a flow rate of 4 ml/s, and obtained enhanced images after 90 seconds of intravenous injection (AMINOLOLAMA-SHAKERI S, ABBEY C K, GAZI P, et al., 2016). Wienbeck et al. injected 90 ml of iodinated contrast agent iopromide 350 (350 mg/ml), with a flow rate of 3 ml/s, and obtained CE-CBBCT images after 120 seconds of intravenous injection, followed by 30 ml of normal saline (WIENBECK S, FISCHER U, LUFTNER-NAGEL S, et al., 2018). HE N et al (HE N, WU Y P, KONG Y, et al., 2016) used 0.1mmol/kg iodohexyl alcohol, administered at a flow rate of 2ml/s, with an image acquisition time of 50-80s, followed by 30ml of normal saline injection. Uhlig et al. (UHLIG J, FISCHER U, SUROV A, et al., 2018) found that a contrast injection time of 120s helped to differentiate between benign and malignant lesions. There is still no consensus on whether the contrast dose should be adjusted based on body weight or given as a standard dose irrespective of body weight. The administration of intravenous contrast agents can aid in the detection of diseased blood vessels in the breast, aid in distinguishing between benign and malignant lesions, and facilitate the identification of the histopathological and immunohistochemical subtypes of breast cancer (UHLIG J, FISCHER U, SUROV A, et al., 2018; UHLIG J, FISCHER U, VON FINTEL E, et al., 2017).

3. The Imaging Advantage of CBBCT

3.1 Imaging Advantages Compared to Mammography

Mammography is considered the primary screening test for breast diseases due to its high specificity. However, its detection rate for dense breast lesions is limited. Mammography requires the patient to stand and undergo multiple breast tissue compressions, often resulting in discomfort or pain. In contrast, CBBCT allows patients to lie in a prone position without any compression or twisting of the breast tissue, significantly improving patient comfort during examination. Additionally, CBBCT eliminates overlapping tissue images, thereby reducing the likelihood of false positives and unnecessary additional examinations.

CBBCT enables multi-planar and three-dimensional reconstruction, providing direct visualization of morphological features of breast masses, including the number and morphology of masses, secondary changes in boundary and surrounding structures. Studies have indicated that CBBCT exhibits a higher diagnostic classification accuracy for benign and malignant breast masses than mammography (ZHAO B, ZHANG X, CAI W, et al., 2015). Furthermore, the ROC curve analysis demonstrated that the AUC value of CBBCT was 0.911, which was significantly higher than that of mammography (0.827), $p<0.01$. At a critical value of BI-RADS4b, the sensitivity (86.6%) and specificity (87.5%) of CBBCT were superior to radiography (sensitivity 77.7% and specificity 72.5%).

Mammography's sensitivity and specificity significantly decrease in dense breast, and breast density is an independent risk factor for breast cancer (MELNIKOW J, FENTON J J, WHITLOCK E P, et al., 2016). However, CBBCT has been shown to be more sensitive than mammography for detecting dense breast cancer (O'CONNELL A M, MARINI T J, et al., 2021), potentially improving cancer survival by detecting cancer earlier.

3.2 Imaging Advantages Compared to Breast Ultrasound

Ultrasonography faces challenges in accurately diagnosing lesions located in the peripheral adipose tissue, heterogeneously positioned lesions under a complex background, deep breast lesions, and subareolar lesions, and its diagnostic accuracy is also influenced by the operator's technical expertise. Although ultrasonography is a real-time examination, it may not yield ideal results during a comparison review. Currently, ultrasound has limitations in evaluating breast lesions with calcification, as it may be difficult to detect lesions that present only as calcifications or microcalcifications. In comparison, the combined use of CBBCT plain and enhanced scans outperforms ultrasound in detecting and differentiating type c and d small breast lesions.

3.3 Imaging Advantages Compared to MRI

MRI has the advantage of multi-orientation and multi-sequence imaging, with high sensitivity in detecting breast lesions, especially in dense mammary glands where mammography often falls short. MRI can also detect multiple and hidden lesions while simultaneously imaging both mammary glands for comparison purposes. It surpasses other imaging methods in staging, preoperative evaluation, postoperative prognosis of breast cancer, as well as evaluating mammoplasty. Nonetheless, MRI examinations are time-consuming, expensive, and have numerous contraindications.

CBBCT, on the other hand, offers a rapid imaging speed, taking only 10 seconds to complete a single breast scan and roughly 10 minutes for plain scanning (including patient localization and image analysis) and 15 minutes for enhanced scanning (including patient localization, injection of contrast, and image analysis) per breast (WIENBECK S, LOTZ J, & FISCHER U., 2017). The isotropic imaging capability of CBBCT allows for consistent spatial resolution on the X, Y, and Z planes, with a standard imaging unit of 0.273mm. In comparison, the spatial resolution of magnetic resonance imaging using a 1.5T magnet is approximately 1mm, making CBBCT significantly superior. Furthermore, CBBCT boasts a spatial resolution of calcification reaching 0.122mm, making it more effective than MRI in detecting microcalcification, which is present in about 55% of unpalpable breast cancers (ALSHEH ALI M, CZENE K, HALL P, et al., 2019).

4. Detection and Evaluation of Breast Diseases of CBBCT

Cone-beam breast computed tomography (CBBCT) is capable of multi-plane and three-dimensional reconstruction, providing visual representation of morphological characteristics of breast lesions, making it an effective method for evaluating breast lesions under the BI-RADS standard. In a study by Zhao et al. (ZHAO B, ZHANG X, CAI W, et al., 2015), which included 85 breast lesions (45 malignant tumors and 40 benign lesions), CBBCT was found to be helpful in distinguishing breast tumors from breast lobular hyperplasia, fibrocystic, or cystic lesions. Additionally, CBBCT images can depict the main breast duct and its branches, which aids in the differential diagnosis of intraductal and intraductal breast lesions. CBBCT evaluated benign and malignant breast masses under the BI-RADS classification, resulting in greater agreement with pathological findings than mammography. He N et al. (HE N, WU Y P, KONG Y, et al., 2016) demonstrated that CBBCT plain scan had higher diagnostic accuracy for differentiating benign and malignant breast lesions than breast ultrasound and mammography. For dense breasts, the diagnostic accuracy of enhanced CBBCT was higher than plain scan.

CBBCT enhanced scan provides additional information, such as the mode of enhancement, degree of enhancement, and peritumoral vessels, facilitating a more comprehensive analysis of the lesion. Uhlig et al. (UHLIG J, FISCHER U, VON FINTEL E, et al., 2017) illustrated that the enhanced features of CBBCT can aid in distinguishing the molecular subtypes of breast cancer. Zhu et al. (ZHU Y, ZHANG Y, MA Y, et al., 2020) found that imaging features of contrast-enhanced digital breast tomosynthesis (CBBCT), including tumor maximum diameter, tumor shape, tumor margin, lobulation, calcifications, enhancement pattern, and degree, combined with clinical information can predict the Her-2 expression status in breast cancer. Pathological grade, maximum diameter, lobulation, enhancement degree, and calcification pattern are independent predictors of HER-2 overexpression (ZHU Y, ZHANG Y, MA Y, et al., 2020). Ma et al. (MA Y, LIU A, O'CONNELL A M, et al., 2021) found that the enhanced image features of CBBCT could predict the status of immunohistochemical receptors of breast cancer and distinguish the molecular subtypes of breast cancer. They also reported that the molecular subtypes of breast cancer were related to the number of lesions, lesion type, tumor size, lesion density, internal enhancement mode, lesion enhancement degree, mass morphology, burr, calcification, calcification distribution, and peripheral vascular increase.

In summary, CBBCT can decrease missed diagnoses of breast diseases and has good diagnostic efficacy in differentiating benign and malignant diseases. A detailed analysis of CBBCT images can supplement histopathological findings, thus contributing to individualized treatment decision-making and prognosis prediction.

5. Summary

CBBCT, as a specialized imaging modality for the breast, offers several advantages such as minimal tissue overlap, high resolution, fast imaging and improved patient comfort. Presently, CBBCT is also used as a guide for clinical puncture biopsy, which offers accurate localization, swift operation, high success rates, and reduced associated complications. In comparison to other existing imaging modalities, CBBCT has demonstrated good diagnostic efficacy in the diagnosis of breast diseases and can be combined with image omics characteristics to predict the status of molecular subtypes and immunohistochemical receptors in breast cancer. However, CBBCT does involve the use of ionizing radiation, and there is a lack of consensus regarding examination procedures and standardization of image feature analysis. Despite this, the enhanced diagnostic accuracy of CBBCT is comparable to published breast MRI meta-analysis, (KOMOLAFE T E, ZHANG C, OLAGBAJU O A, et al., 2022) and can be considered as the first-choice imaging modality for patients who are contraindicated for MRI. In conclusion, CBBCT has immense potential for clinical application, particularly in the neoadjuvant chemotherapy of breast cancer. It is anticipated that with the future clinical promotion of CBBCT, the diagnostic efficiency of breast diseases will be further improved, especially in the early detection of breast cancer.

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