

Progresses of Functional Magnetic Resonance Imaging Diagnosis in Breast Cancer

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Abstract

Breast cancer is the most common malignant tumor that threatens women's health. Breast magnetic resonance imaging (MRI) is a commonly used method recommended for the diagnosis of breast cancer. Diffusion weighted imaging (DWI) and dynamic enhanced magnetic resonance imaging (DCE-MRI) are now widely used. At present, with the continuous advancement of magnetic resonance technology, Magnetic resonance spectroscopy (MRS), Perfusion weighted imaging (PWI), Positron emission tomography-magnetic resonance imaging (PET-MRI) and so on are gradually being used in clinical practice. Mammography imaging and imaging genomics are hot topics. This article will briefly introduce several functional magnetic resonance techniques and their latest applications.

Keywords

Breast Cancer, Functional Magnetic Resonance Techniques, Diagnostic Imaging

1. Introduction

Breast cancer is the most common malignant tumor that threatens women's health. Early detection and accurate diagnosis are especially important. The American Academy of Radiology (ACR) recommended guidelines for the use of breast magnetic resonance [1], suggesting that magnetic resonance can be used not only for people with malignant lymph node metastasis and chest wall infiltration that cannot be accurately analyzed by other tests, but also for screening high-risk groups. Compared with other examinations, such as X-ray, CT and ultrasonography, in addition to clearly show the shape, location, size and signal characteristics of the lesion, breast MRI can also make a correct judgment of

breast lesions according to the hemodynamic characteristics of the lesion, which is beneficial for early diagnosis of breast cancer [2]. At present, especially the development of magnetic resonance spectroscopy (MRS), dynamic enhanced magnetic resonance imaging (DCE-MRI) and diffusion-weighted imaging (DWI) have enabled breast cancer to enter the field of morphological and functional diagnosis [3], this article will briefly introduce several functional magnetic resonance techniques and their latest applications.

2. Diffusion Weighted Imaging (DWI)

DWI is a non-invasive method for detecting the dispersion of water molecules in living tissue at the level of molecular motion. It has the advantages of no radiation, no contrast agent, no invasiveness and high sensitivity. Meta-analysis showed that the sensitivity and specificity of differential diagnosis of breast cancer by DWI were 86.0% and 75.6%, respectively [4] (as we can see in **Figure 1**). We usually use the apparent diffusion coefficient (ADC value) to reflect the dispersion characteristics. Studies [5] have shown that due to the rich blood supply, the ADC value of breast cancer is lower than that of benign lesions. The optimal threshold range for identifying the benign and malignant breast tumors ranged from $1.06 \times 10^{-3} \text{ mm}^2/\text{s}$ to $1.10 \times 10^{-3} \text{ mm}^2/\text{s}$ [6] [7]. Wang Shouhong *et al.* [8] analyzed 60 lymph node lesions in 40 patients with breast cancer, and finally found that the sensitivity, accuracy and specificity of DWI in evaluating lymph node metastasis of breast cancer reached 91.9%, 87.0% and 88.7%, respectively. This suggests that DWI is of great value in assessing lymph node metastasis in breast cancer. In addition, Luo Ningbin [9] and others also demonstrated that ADC values can also reflect the proliferative activity of breast cancer cells, and help to evaluate the efficacy of neoadjuvant chemotherapy. At the same time, the sensitivity coefficient (b value) can also describe the diffusion ability of water molecules. It is very important to select the appropriate b value. Generation

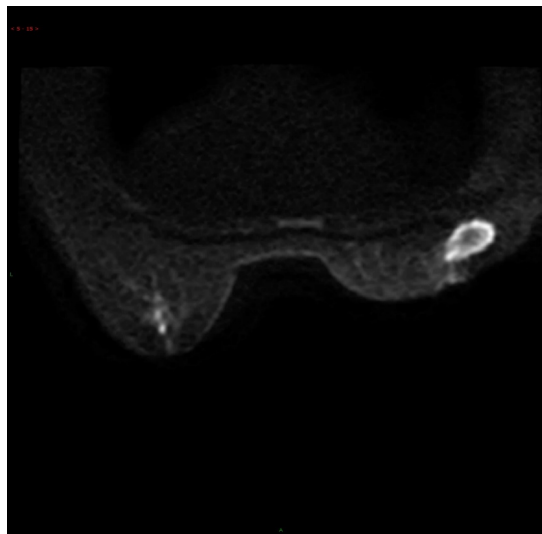


Figure 1. DWI image of breast cancer. The arrow refers to breast cancer lesions.

Ocean *et al.* [10] calculated the ADC values of breast tumors under different b-values, and found that when b value = 1000 s/mm², DWI has the highest sensitivity and specificity for the diagnosis of benign and malignant breast tumors. However, due to the poor signal-to-noise ratio of the DWI image, it is easy to be deformed, often causing missed diagnosis of small lesions. Therefore, it is necessary to combine other sequences in the diagnosis.

DWI includes a single exponential model, a double exponential model, and a tensile exponential model. The traditional DWI calculates the dispersion motion of water molecules in the interstitial space by a single exponential function. Intravoxel incoherent motion (IVIM) imaging is a double-exponential model, and IVIM is more specific for the diagnosis of breast cancer than DWI [11]. Another study [12] found that the specificity and accuracy of IVIM combined with DCE-MRI in the diagnosis of breast cancer were higher than DCE-MRI alone. The relevant parameters of the tensile index model include the diffusion coefficient (DDC) and the diffusion heterogeneity index (α). Compared with traditional DWI, DDC10% combined with α mean to diagnose breast cancer has higher sensitivity and specificity [13]. At present, with the deep research of various index models of DWI, more precise individualized treatment is provided for breast cancer patients with different molecular subtypes (Table 1).

3. Dynamic Enhanced Magnetic Resonance Imaging (DCE-MRI)

Dynamic enhanced magnetic resonance imaging is a non-invasive imaging technique for evaluating angiogenesis of breast tumors and is recognized as the most sensitive imaging method for diagnosing breast cancer. Pinker *et al.* [14] found that DCE-MRI is 100% sensitive to breast cancer diagnosis, and the accuracy and specificity are as high as 96.6%. And 90% (as we can see in Figure 2). In addition, compared with DCE-MRI or DWI, the two imaging methods combined with the diagnosis of breast cancer specificity (94%), sensitivity (98%) and accuracy (96%) were high [15]. In addition to its high imaging sensitivity, DCE-MRI clearly shows the location, shape, size, and blood flow of the breast mass, by plotting the TIC (practice-signal intensity) curve of the breast mass for breast tumors. The diagnosis of benign and malignant provides a reference value (as we can see in Figure 3). The TIC curve is actually a semi-quantitative analysis method, so many scholars try to apply the DCE-MRI image information more objectively and quantitatively, and thus apply it to the field of breast diseases. DCE-MRI quantitative examination can reflect the blood perfusion and blood

Table 1. Comparison of different models of DWI.

Different models of DWI	Sensitivity	Specificity
Single exponential model	86.0%	75.6% [4]
Double exponential model	90.5% - 93.1%	94.8% - 95.7% [11]
Tensile exponential model	90.2%	95.5% [13]

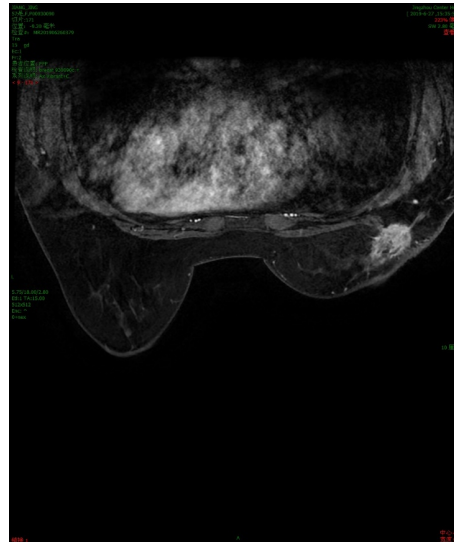


Figure 2. Dynamic enhanced magnetic resonance imaging of breast cancer, showing obvious enhancement of lesions.

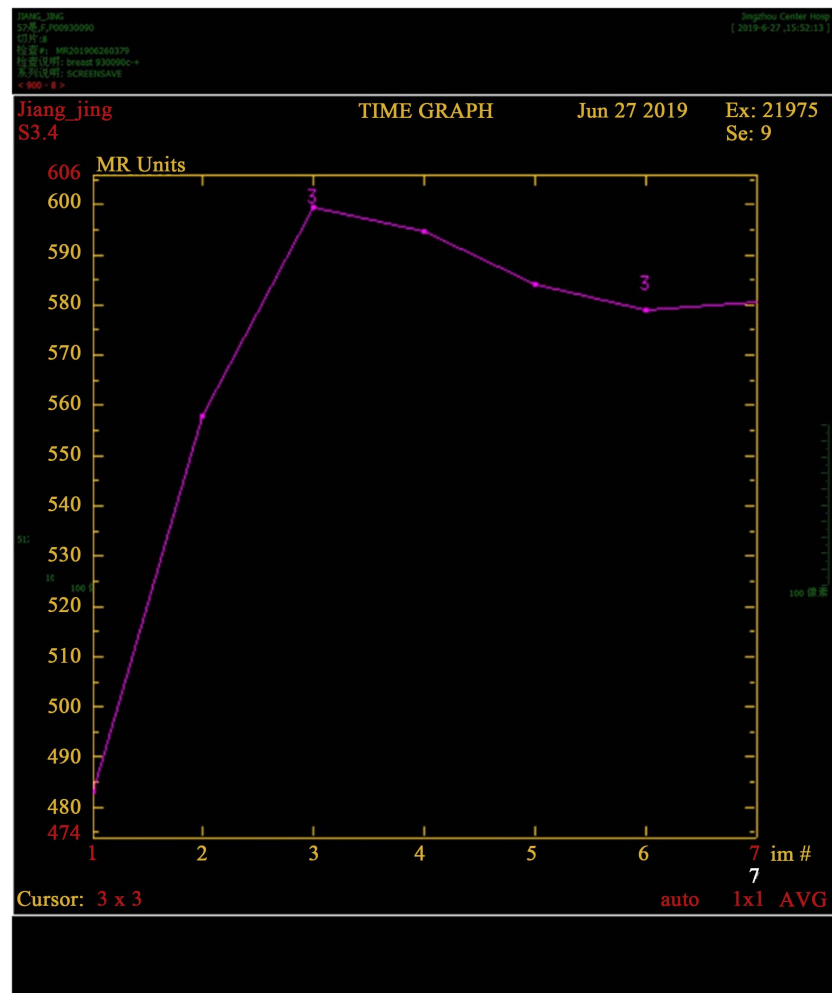


Figure 3. TIC curve of breast cancer lesions. This image curve represents the way in which breast cancer is strengthened.

vessel distribution of tumor tissues at the molecular level, and make quantitative judgment on the nature of breast tumors [16]. The study [17] showed that Ktrans and Kep are feasible for the diagnosis of benign and malignant breast diseases, and the complete quantification of parameters can show the difference of angiogenesis in benign and malignant tumors. The diagnosis of benign and malignant breast tumors is more intuitive and accurate.

In addition, DCE-MRI is also used in the histological grade, prognosis assessment and molecular typing of breast cancer. Hye Ryoung Koo *et al.* [18] have shown that tumors with relatively low Ktrans and Kep values have relatively few neovascularizations, tumor vascular maturation is higher, tumor malignancy is lower, and prognosis is better. Shin *et al.* [19] found that using Ktrans values combined with ADC values can help identify low-risk breast cancer and is instructive for treatment decisions. The results of the study [20] showed that the smaller the Ktrans and Kep values, the lower the Ki-67 degree, and the greater the possibility that the ER and PR were positive, indicating that the breast tumor is highly differentiated, low malignant, and the better the prognosis.

In conclusion, the quantitative parameters of DCE-MRI not only have predictive value for the prognosis of patients with different subtypes of breast cancer, but also help to select individualized treatment options.

4. Magnetic Resonance Spectroscopy (MRS)

Magnetic resonance spectroscopy (MRS) is a promising non-invasive diagnostic technique for studying breast cancer metabolism. MRS can analyze changes in the content of choline and its related metabolites in the body, thereby showing the metabolic and biochemical information of the lesions in the human body to diagnose the disease. We can identify breast tumors by observing changes in the choline concentration of the breast tissue. Yeung [21] found that the sensitivity of MRS in the diagnosis of breast cancer was 92%, the specificity was 83%, and the accuracy was 90%. At the same time, in addition to the analysis of choline peaks, Thakur *et al.* [22] found that quantitative assessment of lipid metabolism in vivo can help distinguish breast benign and malignant tumors, distinguish breast cancer molecular subtypes, and predict long-term survival outcomes, thus providing a possible Additional non-invasive imaging biomarkers to guide the decision to treat breast cancer. Galati [23] and other 132 patients with breast cancer confirmed by biopsy performed 3T breast MR imaging. Finally, it was found that there was a significant difference between the appearance of choline peak and the increase of tumor grade, Ki-67 value and lesion range. Correlation. This indicates that MRS is an effective means to further understand breast cancer biological information and predict tumor invasiveness.

In addition, according to the relevant study [24], the accuracy and specificity of MRS combined with DCE-MRI in the diagnosis of breast cancer were higher than that of MRS or DCE-MRI alone, indicating the combined use of MRS and DCE-MRI has better diagnostic performance in assessing suspected breast le-

sions. However, because MRS imaging technology is affected by many factors, such as longer imaging time and difficulty in standardizing choline concentration, the application of MRS needs further improvement.

5. Perfusion Weighted Imaging (PWI)

Magnetic resonance perfusion imaging is an imaging technique that reflects the microvascular distribution and blood perfusion of breast tissue. There are significant differences in the number of blood vessels and the permeability of blood vessels between healthy people and breast cancer patients, so there is a significant difference in signal intensity during perfusion imaging. Because of the large specific range of magnetic resonance dynamic enhancement diagnosis, it is recommended in the literature [25] to use T2 * WI to identify benign and malignant lesions of the breast. T2 * WI can better reflect the microvascular distribution of tumor tissue and the microcirculation of tumor tissue, especially the characteristics of microvascular permeability [26]. According to the study [27], the sensitivity of PWI for the diagnosis of breast cancer was 79% - 90.3%, the specificity was 83.8% - 93%, and the accuracy was 82.61% - 85.0%. Moreover, Li *et al.* [28] found that the sensitivity of T2 * WI in the identification of benign and metastatic lymph nodes was 94.6% and the specificity was 98.5% by studying the axillary lymph nodes of 35 breast cancer women. This suggests that T2 * WI in vivo can help distinguish between benign and metastatic axillary lymph nodes in breast cancer patients, thus providing a basis for subsequent surgery/chemotherapy. In addition, in terms of neoadjuvant chemotherapy, Wang Xiaohong *et al.* [29] found that T2 * WI can also evaluate and predict the efficacy of neoadjuvant chemotherapy.

There are many shortcomings in the application of MR perfusion weighting in the diagnosis of breast cancer, For example, the signal intensity-time curve of the selected region of interest does not represent the perfusion of the entire tumor, because the tumor is in vivo. There is heterogeneity in blood perfusion. Moreover, T2 * WI has a higher diagnostic specificity for breast cancer, but its sensitivity is lower. Therefore, the combination of T1 dynamic enhancement and perfusion imaging can fully improve the diagnostic specificity (Table 2).

6. PET/MRI

PET/MRI is a molecular level functional imaging and structure imaging system

Table 2. Comparison of different magnetic resonance scanning methods in diagnosis of breast cancer.

Imaging method	Sensitivity	Accuracy	Specificity
DCE-MRI	100%	96.6%	90.0% [14]
DCE-MRI combined with DWI	98.0%	96.0%	94.0% [15]
MRS	92.0%	90.0%	83.0% [21]
PWI	79.0% - 90.3%	82.61% - 85.0%	83.8% - 93.0% [27]

that combines PET (positron emission tomography) and MRI (magnetic resonance tomography) technology. The combination of the two can fully exert their respective advantages and have a higher accuracy in the diagnosis of breast diseases [30]. Some studies [31] found that the accuracy of PET/MRI combined with DCE-MRI in the diagnosis of breast cancer was 20% higher than that of DCE-MRI alone, and the specificity could be increased to 97%. Xu Yuanfan [32] and others retrospectively analyzed 59 patients with suspected breast tumors, and let them perform PET/CT and PET/MRI examinations on the same day. Finally, the sensitivity, specificity and accuracy of PET/MR were higher than PET/CT. However, because PET/MRI instruments are relatively expensive, there are fewer technicians and diagnosticians with expertise in processing and diagnosing images of PET/MRI, thereby limiting its use.

7. Mammography Imaging and Imaging Genomics

Image grouping was proposed by Gillies [33] and further refined by scholars Lambin *et al.* [34], which refers to the acquisition of a large number of characteristic image parameters from high-throughput medical image data, thereby uncovering image features and diseases. Association. Image grouping is divided into five parts, namely image acquisition, segmentation of lesions, feature extraction of lesion images, database establishment and data analysis [35]. Studies [36] have shown that mammography can effectively identify the benign and malignant breast diseases and improve the consistency of MRI diagnosis and pathological diagnosis. Whitney *et al.* [37] found that morphological features extracted from DCE-MRI images were helpful in distinguishing Luminal A breast and benign breast lesions. Breast magnetic resonance imaging has developed rapidly in recent years, which not only helps to identify the benign and malignant breast diseases, but also has a wide range of applications in molecular classification of breast cancer, evaluation of prognostic factors and risk of recurrence. For example, study [38] found that HR+ tumor cells have higher entropy values than HR-cells. In addition, Hui *et al.* [39] retrospectively analyzed 84 breast cancer patients and found that the enhanced scan texture analysis parameter values were inversely proportional to the risk of recurrence.

Image genomics refers to the study of the relationship between genomic features and imaging features of breast cancer, and then uses image features to reflect gene activity and ultimately guide the diagnosis and prevention of breast cancer [40]. Mammography genomics is developing rapidly. With the advent of the era of big data, mammography and imaging genomics are the future development trend (Table 3).

8. Summary and Outlook

In summary, with the continuous advancement of magnetic resonance technology, the magnetic resonance diagnosis method of the breast is also constantly developing. Currently, the role of diffusion-weighted imaging and dynamic

Table 3. Comparison of six magnetic resonance imaging methods. These six methods can be used to diagnose breast cancer, each with its own advantages and disadvantages. But the first two are the most widely used in clinical practice.

Method	Definition principle	Advantage	Disadvantage	Clinical application
DWI	Detection of diffusion of water molecules in living tissue	No contrast agent; High sensitivity; Easy to operate;	Low image resolution; Low specificity	Most basic and widely used
DCE-MRI	Evaluation of breast tumor angiogenesis	High sensitivity, accuracy and specificity; Quantitative judgment	Complex to operate;	Most basic and widely used
MRS	Study changes in tumor metabolite content	analyze metabolites; Quantitative assessment of lipid metabolism	Longer imaging time; Quantification of choline concentration is difficult to standardize	Frequently used
PWI	Reflecting microvascular distribution and blood perfusion status of breast tissue	Reflect microvascular distribution and blood perfusion status; Higher diagnostic specificity	Low sensitivity; Heterogeneity in blood perfusion;	Less used
PET/MRI	A system of functional imaging and structural imaging at the molecular level	Functional imaging at the molecular level; High sensitivity, accuracy and specificity;	Complex to operate; Less technicians and diagnosticians; Radioactivity expensive	Rarely used
Mammography imaging and imaging genomics	Studying the link between breast cancer genomic features and imaging features	Create a high-dimensional data set; Using image features to reflect gene activity	Too small sample size; Clinically practical is not strong	Used only for academic research

enhanced magnetic resonance imaging in the diagnosis of breast cancer has been recognized. Imaging techniques such as MRS, PWI, and PET-MRI are limited in their use. With the advancement of magnetic resonance technology, many new imaging technologies have been born, such as blood oxygen level-dependent functional magnetic resonance imaging, elastic imaging technology, and breast magnetic sensitive imaging.

Advanced and cost-effective magnetic resonance equipment should promote the research and clinical application of breast imaging worldwide. Here we have summarized the magnetic resonance equipment from home and abroad (**Table 4**). At present, China's magnetic resonance equipment is mainly from imports, and magnetic resonance equipment of domestic brands (Shanghai United Imaging Healthcare, Neusoft, Alltech) is also available in China and exported to developed countries. Since some models of domestic MRI equipment combined with the actual situation of China's domestic medical requirement, the overall experience of domestic equipment is significantly higher than that of imported brands [41]. Moreover, the investment recovery period of domestic magnetic resonance equipment only needs 2.5 years [42], which has a good diagnostic cost performance. However, due to the late start of domestic equipment, MRI practitioners have a higher level of understanding of the imported brands than domestic brands, and the application of domestic brand machines requires more

Table 4. Main domestic and imported magnetic resonance equipment and models.

Field strength	Brand	Main model
3T	Shanghai United Imaging Healthcare	uMR770 uMR780
	Siemens	MAGNETOM Verio
	Philips	Achieva Ingenia
	GE	HDxt
	Neusoft	NSM-S15P
	Alltech	Centauri Echo Star
1.5T	Shanghai United Imaging Healthcare	uMR 560 uMR570
	Siemens	MAGNETOM Avanto
	Philips	Achieva Ingenia
	GE	HDx

education of MRI practitioners [43]. Finally, I believe that with the advancement and development of medical technology, the future research and application progress of breast magnetic resonance can be expected.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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