

Positron emission tomography/computed tomography using 2-deoxy-2-fluoro-18-fluoro-D-glucose peri-tumoral halo uptake layer method outperforms magnetic resonance imaging and ultrasound methods in tumor size measurement of breast cancer

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Abstract. As a non-invasive method, positron emission tomography (PET)/computed tomography (CT) using 2-deoxy-2-fluoro-18-fluoro-D-glucose (18F-FDG) is applied as a useful modality in the diagnosis of breast cancer. By evaluating glucose metabolism, this method can also be used in staging, restaging and post-therapeutic response evaluation. To evaluate the reliability of the ¹⁸F-FDG PET/CT-based peri-tumoral halo uptake layer (PHL) method for assessing tumor size, a total of 79 female patients with breast cancer who underwent ¹⁸F-FDG PET/CT, breast ultrasound and magnetic resonance imaging (MRI) evaluations were included in the present study. Upon examination by two independent nuclear medicine radiologists, tumor sizes were estimated by ¹⁸F-FDG PET/CT using margins defined as the inner line of the PHL. Pathological tumor sizes were evaluated on the direction of largest diameter indicated by previous imaging examination, which were also utilized as final standards. Statistical analysis of the results suggested that ¹⁸F-FDG PET/CT had a more linear correlation with pathology compared with breast ultrasound ($r^2=0.89$ vs. 0.73) and MRI ($r^2=0.89$ vs. 0.69) in terms of tumor size estimation, including a significantly lower bias in size difference relative to pathology. ¹⁸F-FDG PET/CT also exhibited improved performance compared with breast ultrasound and MRI in T stage assessment. These results indicated

that the ¹⁸F-FDG PET/CT-based PHL method was superior to breast ultrasound and MRI, and that it provides sufficient reliability and high accuracy for measuring tumor size in patients with breast cancer.

Introduction

Breast cancer is the most commonly diagnosed cancer in women, with 1,671,149 newly cases in 2012, accounting for 25.1% of all types of cancer, as well as its significant cancer-associated mortality in developed and developing countries (1,2). Estimating the condition of patients, including the size and stage of the tumor, and establishing scientific therapy are key to obtaining satisfactory therapeutic effects (3). A careful and complete examination prior to surgery is important for selection of the suitable operation method and for surgical planning (4). One of the most important pieces of information required from preoperative examination is the size and area of extension of the tumor, which is important for surgical treatment and chemo-radiotherapy (5). Thus, assessing tumor size and estimating the tumor stage is imperative in clinical practice. Although a variety of imaging modalities have been used to diagnose breast cancer, mammography remains the traditional standard method for diagnosing breast cancer (6), with a reported sensitivity of 85%, decreasing to 68% in women with dense breasts (7). However, this method does not estimate tumor size well, and it exhibits certain limitations regarding the qualitative diagnosis of breast tumors (8). It is best suited for breast examination and cancer screening (9). Additionally, the question of whether mammography should be recommended or not to women between the ages of 40 and 50 years depends upon the publication of relevant clinical trial data due to test sensitivity, disease prevalence, cost of screening and consequences of a false-positive result (10,11).

Although magnetic resonance imaging (MRI) has been widely used in clinical practice for years, the appropriate use of MRI in elderly patients with breast cancer remains unclear. It has been reported that MRI has the greatest benefit in women presenting with an occult primary cancer and minimal additional benefit in elderly patients with breast

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Abbreviations: ¹⁸F-FDG PET/CT, positron emission tomography/computed tomography using 2-deoxy-2-fluoro-18-fluoro-D-glucose; PHL, peri-tumoral halo uptake layer; MRI, magnetic resonance imaging; ICC, intraclass correlation coefficient

Key words: magnetic resonance imaging, ultrasound, tumor size, breast cancer, 18F-FDG PET/CT

cancer undergoing MRI for extent of disease evaluation or in post-treatment surveillance (12). MRI exhibits a high resolution and has been reported to accurately estimate tumor size (13,14). However, MRI has also been reported to overestimate tumor size, particularly in patients with tumor (T)2 or T3 stage (15,16). Although, MRI displays high sensitivity and specificity in breast cancer detection, the above limitation cannot be ignored. Sonography is more widely used in clinical practice, albeit as a method of cancer screening rather than tumor size estimation (17). Positron emission tomography (PET)/computed tomography (CT) using 2-deoxy-2-fluoro-18-fluoro-D-glucose (^{18}F -FDG) is a useful modality in the diagnosis of patients with breast cancer (18). By evaluating glucose metabolism, it can also be used in staging, restaging and post-therapeutic response evaluation (16,19). In a previous study, ^{18}F -FDG PET/CT was considered inappropriate for evaluation of tumor size and not recommended as a priority option in clinical practice due to its poor spatial resolution, which limits clear delineation of the tumor boundary (20). However, other studies have demonstrated the advantage of ^{18}F -FDG PET/CT in tumor size estimation (21). To the best of our knowledge, few studies have compared the sensitivity and accuracy of ^{18}F -FDG PET/CT with other traditional imaging modalities such as sonography and MRI. Besides, Jun *et al* (22) found a distinct layer between the tumor and background activity using a 10-step color scale with specific window level settings and named the distinct layer the peritumoral halo layer (PHL). Based on ^{18}F -FDG, Jun *et al*, proposed a volume measurement method using PHL (22). However, although the newly developed PHL method appears promising for accurate estimation of tumor size, it has not yet been fully validated.

This study aimed to evaluate the concordance between the ^{18}F -FDG PET/CT based peritumoral halo uptake layer (PHL) method and the pathologic size of breast cancer. By comparing the reliability and correlation of ^{18}F -FDG PET/CT, sonography and MRI in pathological tumor size assessment, experimental evidences were provided for the selection of imaging modalities in breast cancer diagnosis. In order to examine the factors associated with discordance size, the accuracy of ^{18}F -FDG PET/CT, sonography and MRI was also compared in different tumor sizes (T1-T3), histologic subgroups and intrinsic subtypes.

Materials and methods

Patients. A total of 79 female patients with breast cancer selected from the database of Changxing People's Hospital (Huzhou, China) were included in this retrospective study. The staging of breast cancer was performed according to the 6th Edition of the American Joint Committee on Cancer Staging Manual (23). The inclusion criteria included: i) Patients who had undergone ^{18}F -FDG PET/CT, preoperative sonography and MRI examinations prior to initial treatment between May 2015 and June 2018; ii) patients who underwent the aforementioned mentioned imaging modalities within 10 days of diagnosis prior to surgery, and iii) patients with complete medical history and stored paraffin sample of the tumor obtained from surgery. The average time point when patients finished imaging using different modalities was 3 days before surgery. The exclusion

criteria included: i) Patients with a history of neo-adjuvant treatment; ii) patients who had undergone preoperative mammotomy; iii) patients with non-avid tumor and clustered tumors, and iv) patients with incomplete data or insufficient results (such as MRI without contrast enhancement and pathology results without exact tumor size). The present study was supported by the Ethics Committee of Changxing People's Hospital (Huzhou, China; approval no. CPH 201505). All the patients signed informed consent forms.

Diagnostic imaging examination. A high-resolution 5-12 MHz linear array transducer, VOLUSON 530 and 730D (Kretztechnik AG) was used with a width of 50 mm to perform sonography imaging and the results were recorded according to the estimation of two independent examiners based on a widely accepted standard described in a previous study (24). The echo-poor center of the lesion and the echogenic halo were considered for the measurement of tumor size. Sonography was carried out by 2 independent experienced, board-certified breast radiologists.

A MAGNETOM Verio 3.0T (Siemens AG) was used to perform MRI. All patients were imaged in the prone position with both breasts placed into a dedicated 16-channel breast coil. The MRI protocols included the following: i) Bilateral axial turbo-spin-echo fat-suppressed T2-weighted image (Time of repetition (TR) / Time of echo (TE), 4,630/70 msec; field of view, 320 mm; slice thickness, 3 mm and number of excitations, 1); ii) axial turbo-spin-echo T1-weighted image (TR/TE, 736/9.1 msec; field of view, 320 mm; slice thickness, 3 mm and number of excitations, 1); iii) diffusion-weighted images (TR/TE, 5,800/82 msec; field of view, 360 mm; slice thickness, 3 mm and b values 0, 400 and 800 sec/mm²) and iv) measurement of the apparent diffusion-coefficient value.

Two PET/CT scanners [DSTe 8, (GE Medical Systems) and Gemini 64, (Philips Medical Systems)] were used to perform ^{18}F -FDG PET/CT examinations. All the patients fasted for 6 h before scanning and serum glucose levels were measured prior to ^{18}F -FDG injection (DSTe 8, 0.2 mCi/kg and Gemini 64, 0.1 mCi/kg). A CT scan was performed in all the patients 1 h after ^{18}F -FDG injection and images were collected. Each patient was scanned from the base of the skull to the mid-thigh level. Following low-dose CT scanning to correct for attenuation, PET acquisition began immediately in the same anatomical position (3-dimensional mode, 1.5-2.5 min per bed position). The acquired images were reconstructed using an iterative ordered subsets expectation maximization algorithm and then transferred to Advantage Workstation 4.5 (GE Healthcare). According to the methods described in a previous study, the PHL results of the tumors were determined (22). Sonography, MRI and ^{18}F -FDG PET/CT were performed by 3 independent groups. Each group was blinded to the results of the other groups. The quality control of machines was also monitored by radiologists according to widely accepted standards in China (25-27). Quality control consisted of daily, weekly, monthly and seasonally quality examination. Daily and weekly examinations included self-examination of hardware equipment and fast calibration to maintain the accuracy and uniformity of PET/CT. Monthly and seasonally examinations included normalized correction of PET scanner's

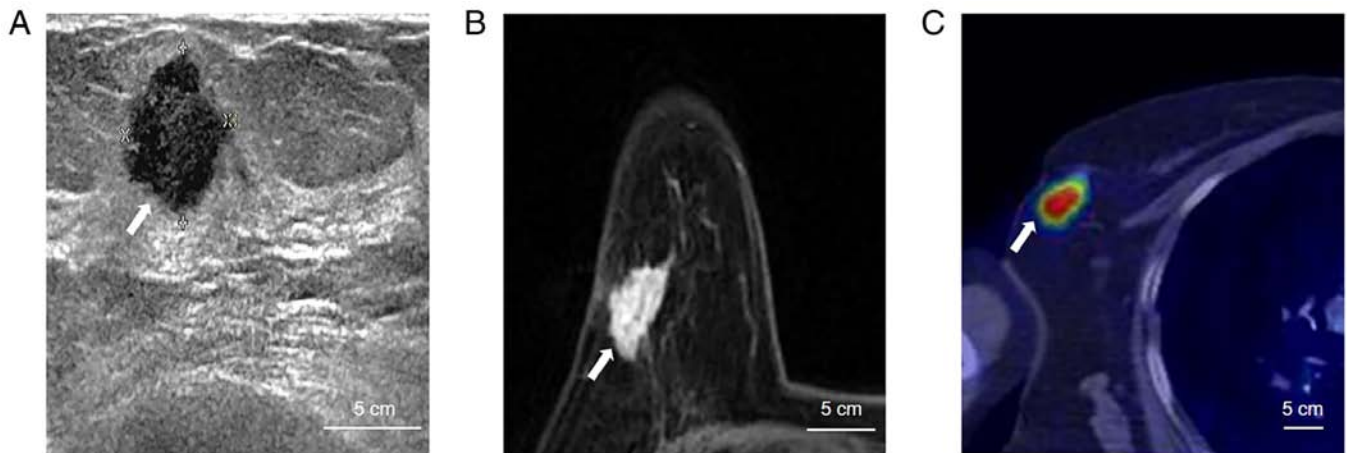


Figure 1. Imaging results of a 54-year-old patient with right breast cancer. (A) Breast sonography, (B) MRI (2 min dynamic image), (C) maximum intensity projection image of ^{18}F -FDG PET/CT. Arrows indicate the position of the tumor. MRI, magnetic resonance imaging; ^{18}F -FDG PET/CT, positron emission tomography/computed tomography using 2-deoxy-2-fluoro-18-fluoro-D-glucose.

sensitivity and image correction using a Well counter. The measurement of tumor size by sonography, MRI and ^{18}F -FDG PET/CT was performed by two independent radiologists in each examination and the average tumor size from two independent radiologists were calculated as final result. Fig. 1 shows an example of sonography, MRI and ^{18}F -FDG PET/CT examination results of the representative case from a 54-year-old patient with right breast cancer.

Concordance between images and pathological results. Tumors were excised according to the direction of largest diameter indicated by previous imaging examination. The largest diameter from 2 edges of the paraffin sample were calculated as the tumor size. Pathological reports were completed by 2 independent pathologists from Department of Pathology, Changxing People's Hospital (Huzhou, China). The average diameter of tumors, recorded by two independent pathologists were defined as the standard of objective tumor size. The most widely accepted cut-off point of 0.5 cm described in previous studies was used in the current study to estimate the results of the imaging modalities (9,28-30). The results were calculated using the image-derived tumor size minus the histopathologically determined tumor size and were considered to be concordant within ± 0.5 cm. Values <0.5 cm were graded underestimated, while those >0.5 cm were graded overestimated regarding tumor size estimation.

Comparison of the results of the different imaging modalities among different subgroups of patients. The reliabilities of ^{18}F -FDG PET/CT, sonography and MRI in terms of tumor size prediction were compared in different subgroups. Tumor size was classified into different subgroups as T1, T2 and T3. The imaging results for different histological subtypes were then compared with histopathologically derived tumor size.

Statistical analysis. All the collected data were described as mean \pm standard deviation. One-way ANOVA followed by Tukey's post-hoc test were performed for the evaluation of differences among 3 groups. Categorical variables were normally tested by the χ^2 test when appropriate. Kappa

statistics were used to evaluate the inter-observer agreement for determination of PHL surrounding each tumor. Associations between pathology and MRI-determined tumor sizes, or between pathology and ^{18}F -FDG PET/CT-determined tumor sizes, were evaluated using linear regression analysis. Intraclass correlation coefficient (ICC) and Bland-Altman analyses were used to examine the concordance and reliability of tumor sizes obtained using MRI and ^{18}F -FDG PET/CT. Two-sided $P < 0.05$ were considered to indicate a statistically significant difference. Statistical analyses were conducted using SPSS v.19.0 software (IBM Corp.).

Results

Patient characteristics. A total of 79 Chinese female patients with breast cancer from Changxing People's Hospital were included in the current study. The clinicopathological characteristics and the results of tumor size estimation based on different imaging modalities are summarized in Table I. The age range of the patients was 42-76 years and the mean age was 53 years. Among all the patients, those with ductal adenocarcinoma were more numerous compared with non-ductal adenocarcinoma, and T2 was the most frequent tumor stage among patients. During ^{18}F -FDG PET/CT examination, the mean standardized uptake value (SUVmax) of the primary tumor was 4.80 (range, 1.12-19.61). The tumor sizes according to the results of sonography, MRI and ^{18}F -FDG PET/CT were 2.65, 3.82 and 2.98 cm, respectively. The mean pathological size of the tumor was 3.05 cm, ranging from 1.28-8.65 cm, which was considered as the final standard size of each tumor.

PHL determination of tumors in patients with breast cancer. PHL, which was determined by 2 radiologist reviewers based on the results of ^{18}F -FDG PET/CT, exhibited good consistency with a contingency coefficient of 0.79 ($P < 0.01$). The PHL of the majority of tumors detected was below the 40-50% band, while the area between 20 and 30% (olive-green color) of the band of SUVmax is the area where the PHL of each tumor was most commonly recorded (24%; data not shown). The PHL exhibited a negative association with the SUVmax of

Table I. Clinical characteristics of patients with breast cancer.

Characteristics	No. of patients/mean (range)
Number of patients	79
Sex	Female
Age, years	53 (42-76)
Pathological type	
Ductal	68
Non-ductal	11
Surgery	48
Breast-conservation therapy	
Mastectomy	31
T stage	
T1	23
T2	37
T3	19
Tumor size, cm	
Pathology	3.05 (1.28-8.65)
Sonography	2.65 (0.95-7.58)
MRI	3.82 (2.87-10.34)
PET/CT	2.98 (1.20-8.72)
SUVmax of primary tumor	4.80 (1.12-19.61)

SUVmax, mean standardized uptake value; T, tumor stage.

separate tumors (Fig. 2), with the exception of 5 cases, as presented in Table II.

Concordance of tumor sizes measured different imaging modalities and pathology. All sonography, MRI and PET/CT examination results had statistically significant associations with pathological measurements regarding tumor size. Using the pathological size of the tumor as the final standard size, there were small differences observed between the imaging and pathology tumor size, namely sonography, -0.78 ± 1.10 cm; MRI, 1.28 ± 1.25 cm and ^{18}F -FDG PET/CT, 0.13 ± 0.90 cm, respectively (data not shown). The linear regression between ^{18}F -FDG PET/CT and pathology measurements ($r^2=0.89$; $P<0.01$) was more significant compared with the linear correlation between sonography ($r^2=0.73$; $P<0.01$) and MRI ($r^2=0.69$; $P<0.01$; Fig. 3).

In addition, ^{18}F -FDG PET/CT demonstrated a smaller bias in tumor size estimation compared with sonography and MRI in Bland-Altman analysis. ^{18}F -FDG PET/CT-derived tumor size exhibited a high concordance with pathological tumor size [0.95; 95% confidence interval (CI), 0.92-0.97] using the ICC test, which was significantly superior to sonography (0.83; 95% CI, 0.81-0.89) and MRI (0.77; 95% CI, 0.65-0.84; Fig. 4).

Association of sonography, MRI and ^{18}F -FDG PET/CT according to pathology T stage in patients with breast cancer. In the analysis of subgroups classified by tumor T stage, ^{18}F -FDG PET/CT compared with sonography or MRI demonstrated significantly lower size differences (vs. pathology) in

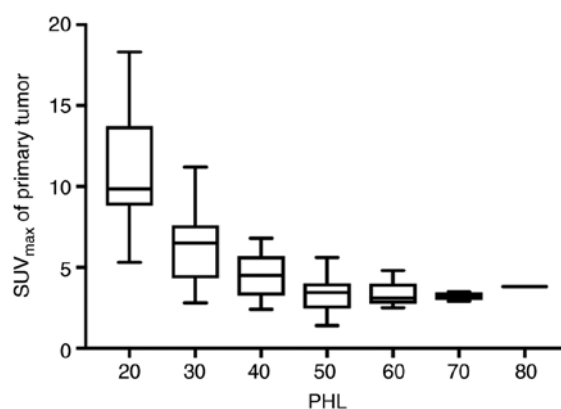


Figure 2. Association between SUVmax of primary tumor and PHL. PHL was calculated using Jun's method (21) by transforming PET/CT image into 10-color scale, based on the SUVmax. PHL refers to the layer between tumor activity and background. PHL, peri-tumoral halo layer; SUVmax, mean standardized uptake value.

T2 and T3 stage tumors ($P<0.05$), but not in T1 stage tumors (Fig. 5). However, there were cases where T stage was wrongly estimated using imaging. Table III presents the T stages and tumor sizes of 12 patients whose T stages were incorrect on sonography, MRI or ^{18}F -FDG PET/CT. For sonography, there were 5 patients whose tumor T stages were overestimated (3 cases were considered T2 instead of T1 and 1 was considered T3 instead of T2; Table III). MRI-assessed T stages were incorrect for 7 patients, of which 5 cases were upstaged (3 cases from T1 to T2; 1 case from T1 to T3 and 1 case from T2 to T3; Table III) while 2 cases were down-staged (1 case from T3 to T2 and 1 case T2 to T1; Table III). A total of 2 patients were upstaged in ^{18}F -FDG PET/CT assessment (1 case was upstaged from T1 to T2 and 1 case from T2 to T3; Table III). Among the mismatched 12 cases, 1 case was incorrectly upstaged from T2 to T3 in sonography, MRI and ^{18}F -FDG PET/CT.

Additionally, ^{18}F -FDG PET/CT also demonstrated a significant advantage in accuracy of predicting tumor size compared with sonography and MRI in different pathological subgroups of tumors. The concordance rates for of sonography, MRI and ^{18}F -FDG PET/CT were 45.4, 31.8 and 69.2%, respectively, in ductal adenocarcinoma, while for non-ductal adenocarcinoma, the concordance rates for sonography, MRI and ^{18}F -FDG PET/CT were 41.2, 29.6 and 72.5%, respectively (data not shown).

Discussion

Previous studies have demonstrated that in early breast cancer, there is no association between long-term survival and mastectomy with tumors of relatively small size (5-9). In addition, complete removal of the tumor reduces the probability of recurrence (1). Thus, estimating the size and area of extension of the tumor accurately is important for chemoradiotherapy decision and surgical treatment. As a non-invasive method, ^{18}F -FDG PET/CT is applied in clinical practice. However, FDG PET/CT is not recommended as a priority option in clinical practice due to poor spatial resolution, which limits clear delineation of the tumor boundary. Studies comparing the reliability of ^{18}F -FDG PET/CT with MRI or sonography in terms

Table II. Discordant cases (n=5) of PHL determined by 2 independent radiologists.

No.	Age	Histologic type	SUVmax of tumor	PHL (%)		Tumor size (mm)			
				Radiologist1	Radiologist2	Sonography	MRI	PET/CT	Pathology
1	53	Ductal adenocarcinoma	8.2	30	20	7.8	8.0	7.5	7.2
2	48	Ductal adenocarcinoma	3.2	70	60	2.4	3.6	2.7	2.9
3	45	Ductal adenocarcinoma	3.8	50	60	3.1	2.9	3.8	3.5
4	62	Non-ductal adenocarcinoma	2.1	70	80	2.2	2.8	2.3	1.8
5	71	Ductal adenocarcinoma	4.6	60	70	4.2	4.3	5.1	4.9

SUVmax, mean standardized uptake value; MRI, magnetic resonance imaging; PET/CT, positron emission tomography/computed tomography; MRI, magnetic resonance imaging; PHL, peri-tumoral halo uptake layer.

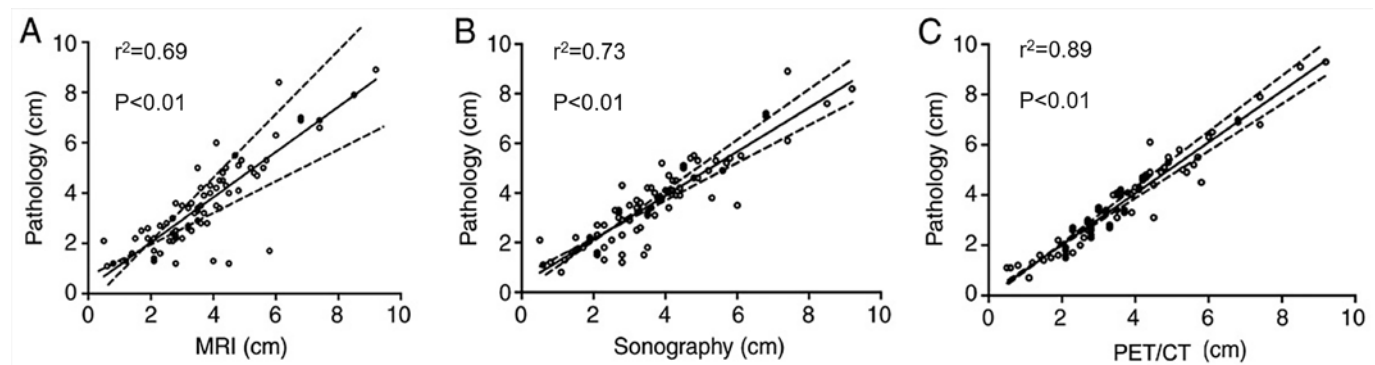


Figure 3. Linear regression analysis for tumor size in patients with breast cancer. (A) pathology vs. sonography, (B) pathology vs. MRI and (C) pathology vs. ^{18}F -FDG PET/CT. MRI, magnetic resonance imaging; ^{18}F -FDG PET/CT, positron emission tomography/computed tomography using 2-deoxy-2-fluoro-18-fluoro-D-glucose.

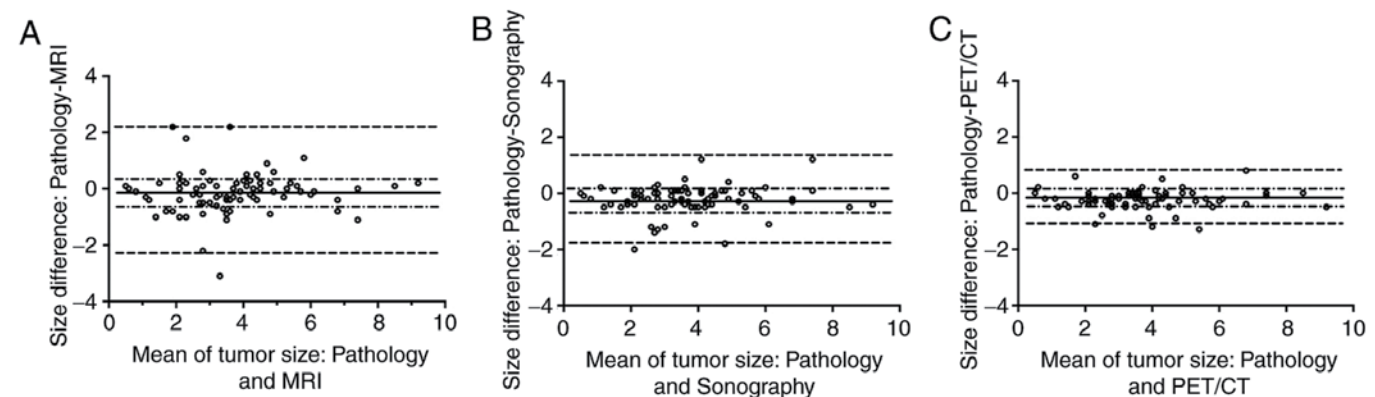


Figure 4. Bland-Altman plot analysis for tumor sizes. The Y axis, the difference between the two paired measurements; the X axis, the average of the two paired measures. (A) MRI vs. pathology; (B) sonography vs. pathology; (C) ^{18}F -FDG PET/CT vs. pathology. MRI, magnetic resonance imaging; ^{18}F -FDG PET/CT, positron emission tomography/computed tomography using 2-deoxy-2-fluoro-18-fluoro-D-glucose.

of tumor size assessment of breast cancer are limited (20). The present study demonstrated that using PHL, the results from the ^{18}F -FDG PET/CT method had a higher accuracy and association with pathological tumor size compared with those obtained by MRI and sonography.

It has been previously reported that tumor size is often underestimated by sonography (31), which was also observed in the current study. Several hypotheses have been proposed

to explain these discrepancies. Hieken *et al* (32), demonstrated that these discrepancies are derived from extensive intraductal in situ components caused by unclear margins of sonography. In the study by Gruber *et al* (31), a novel technique called panoramic mode, which allows a complete image to be built from individual sectional sonographic images, was used in order to obtain more accurate results of the tumor with the diameters exceeding the width of the transducer. This may

Table III. Evaluation of 12 discordant cases of pathological T stage (22).

Serial no.	T stage				Size differences (vs. PET/CT, mm)		
	Pathology	Sonography	MRI	PET/CT	Sonography	MRI	PET/CT
1	T1	T2	T1	T1	0.6	0.3	0.2
2	T1	T2	T1	T1	0.8	0.2	0.2
3	T1	T2	T2	T1	0.4	0.5	0.1
4	T1	T3	T1	T1	1.1	0.3	0.1
5	T2	T3	T3	T3	0.3	0.5	0.3
6	T1	T1	T3	T1	0.2	1.2	0.1
7	T1	T1	T2	T1	0.5	0.8	0.4
8	T3	T1	T2	T3	0.7	0.4	0.2
9	T2	T2	T1	T2	0.6	0.2	0.5
10	T1	T1	T2	T1	0.1	0.5	0.6
11	T2	T1	T2	T2	0.7	0.3	0.2
12	T1	T1	T1	T2	0.3	0.2	0.5

MRI, magnetic resonance imaging; PET/CT, positron emission tomography/computed tomography; T, tumor stage.

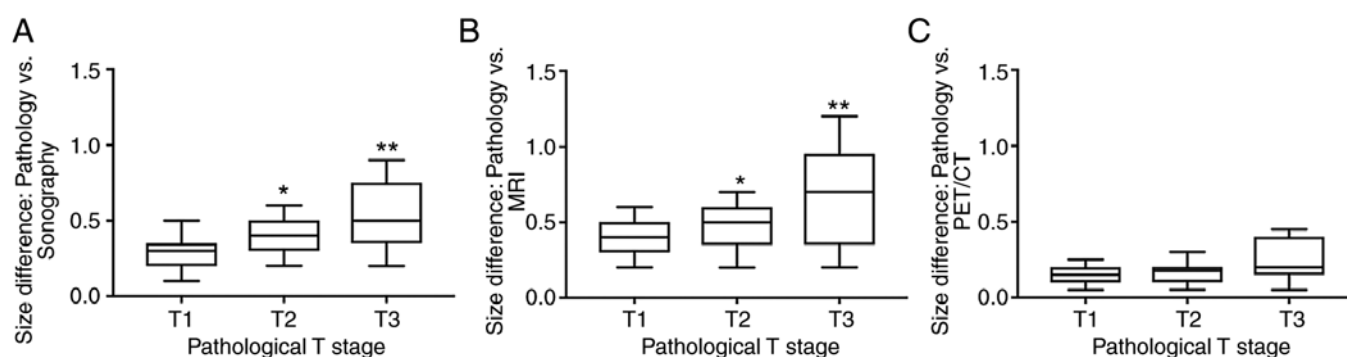


Figure 5. Analysis of tumor size in subgroups of patients with breast cancer classified by tumor stage, according to the 6th Edition of the American Joint Committee on Cancer Staging Manual (22). (A) Sonography, (B) MRI and (C) ^{18}F -FDG PET/CT. Significant differences among 3 groups were tested by one-way ANOVA followed by the post-hoc Tukey's test. * $P<0.05$, ** $P<0.01$, compared with ^{18}F -FDG PET/CT group. MRI, magnetic resonance imaging; ^{18}F -FDG PET/CT, positron emission tomography/computed tomography using 2-deoxy-2-fluoro-18-fluoro-D-glucose; T, tumor stage.

solve the issue of tumor size underestimation with the use of sonography to a certain degree. Regarding MRI, a previously published study revealed that pre-operative MRI was associated with lower re-operation rates for close/positive margins ($P<0.05$) (3), which affirmed the capacity of MRI for breast tumor assessment. However, a previous study reported an overestimation of tumor size using MRI (33), which is consistent with results obtained in the present study. To the best of our knowledge, the present study is so far the first to compare the reliability and association among ^{18}F -FDG PET/CT, MRI and sonography in breast cancer tumor size assessment. The present study, provides further guidance for choosing a more effective diagnostic method for estimating the tumor size in patients with breast cancer.

Since ^{18}F -FDG PET/CT was first recommended as a method to estimate tumor size, there are several studies describing the advantages of ^{18}F -FDG PET/CT for staging breast cancer (34-37). However, only N staging (lymph node detection) and M staging (distant metastasis) were taken into

consideration in these studies, whereas the present study added T stage for tumor size measurement as well. Furthermore, several studies reported ^{18}F -FDG PET/CT to have low concordance with pathology in terms of T stage (38-40), while the present study detected a good consistency with pathology and even a lower bias of tumor size. An unclear tumor margin on ^{18}F -FDG PET/CT, arising from its inherently low resolution and from the confounding factor of surrounding physiological breast uptake, is likely the main reason why PET/CT is not used for tumor size evaluation (20). Recently, a method using PHL has been reported as reliable for measuring tumor volume in cases of thyroid cancer (41). A recent report suggested that PHL can enhance tumor margin detection on ^{18}F -FDG PET/CT (41).

In the present study, the longest tumor diameters obtained with ^{18}F -FDG PET/CT scan compared with MRI and sonography, exhibited statistically significant smaller differences and more linear associations with pathological tumor size. This demonstrated that tumor size estimation by ^{18}F -FDG

PET/CT scan can be more accurate than by sonography and MRI and can provide a reliable reference for the decision of an appropriate surgical strategy and prognostic prediction. In T stage assessment, MRI and sonography displayed higher sizes differences (vs. pathology) compared with ^{18}F -FDG PET/CT in T2 and T3 stage tumors, but not in T1 stage tumors. Furthermore, MRI assessments resulted in 2 patients being incorrectly upstaged as T3, while this error was avoided in ^{18}F -FDG PET/CT assessments. Size differences by ^{18}F -FDG PET/CT were also smaller compared to MRI and sonography in 12 incorrectly staged patients. Overestimation of tumor size can be a serious mistake, as it may deprive patients of the opportunity of undergoing breast-conservation therapy, which is a simpler and more superficial type of therapy compared with mastectomy (4). Thus, tumor size estimates using ^{18}F -FDG PET/CT may be more reliable in guiding surgical strategy for large-sized tumors and ^{18}F -FDG PET/CT could be recommended as a better imaging modality in breast cancer tumor estimation compared with other imaging methods.

The present study has several limitations. First, as all the patients are enrolled from a single institution, this may lead to a lack of appropriate representation and selection bias. However, this may not affect the results severely, since the purpose of the present study was simply to evaluate and compare the reliability of a tumor size measurement method using PHL and the included cases exhibited various tumor sizes. Second, investigator influence during malignancy assessment of the results due to previous knowledge of the results derived from other imaging techniques cannot be excluded. Third, the pathological size that was used as a reference standard was solely based on previous pathological reports, while there may be changes in pathological measurement during preservation and preparation of each tissue specimen. Additionally, the bias during sonography should be taken into consideration as it is more likely to be operator-dependent. Last, because of the flat character of imaging analysis and the non-planar growth form of the tumors, only the larger diameter could be measured with the image. Despite the aforementioned limitations, the results of the present study suggest that the ^{18}F -FDG PET/CT-based PHL method was superior to breast ultrasound and MRI.

In conclusion, the present study has demonstrated that ^{18}F -FDG PET/CT-based PHL can accurately estimate tumor size in patients with breast cancer. Despite the fact that this method may overestimate small size tumors, it is superior to sonography and MRI, with greater association and reliability for pathological tumor size assessment in breast cancer.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YW performed patient enrollment according to the exclusion and inclusion criteria of the study, performed experiments and analyzed the data. YL and CX performed experiments, analyzed the data and drafted the manuscript. BL designed and conceived this study. All authors have read and approved the manuscript.

Ethics approval and consent to participate

The retrospective study was approved by The Ethics Committee of Changxing People's Hospital (Huzhou, China; approval no. CPH 201505). All patients provided signed informed consent.

Patient consent for publication

All patients enrolled in this study have provided consent for the publication of their examination information.

Competing interests

The authors declare that they have no competing interests.

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