Peer Review File

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Reviewer A:

Comment 1: The title needs to indicate both accuracy and concordance between CBBCT and MRI and the old standard of pathological tumor size.

Reply 1: Thanks for your professional comment. This study was conducted to compare the accuracy of CBBCT and MRI for breast tumor size measurements using measurements of pathological gross specimens as the gold standard, as well as to analyze the factors affecting the accuracy of tumor size measurements by CBBCT and MRI. In this study, we intend to explore a new way that can be relied upon for preoperative imaging assessment of breast cancer. We have made it clear in the "Methods" section of the manuscript that pathological results are the gold standard (Page 7-8, Line 171-172). In order to highlight the focus of this study and to express the authors' intention as concisely and accurately as possible, we adopted the current title "Accuracy of cone-beam breast CT for assessing breast cancer tumor size - comparison with breast MRI". If you still feel the need to make changes, please let us know and we will make the changes as quickly as possible. Thank you.

Changes in the text: None.

Comment 2: The abstract needs some revisions. The background did not indicate why the focus on the concordance and inconsistency between CBBCT and MRI is clinically important. The methods need to describe the inclusion of subjects and the gold standard of the tumor size. The results need to briefly summarize the clinical characteristics of the study sample. The conclusion needs comments for the clinical implications of the findings.

Reply 2: Thanks for your professional suggestions. The main purpose of this study is to analyze the concordance between CBBCT-pathology and MRI-pathology in measuring the tumor size and to investigate the influencing factors that lead to the discordance between CBBCT-pathology and MRI-pathology. Although the accuracy of CBBCT and MRI in measuring tumor size is also compared, the focus is on the differences between the two and pathology. Therefore, the clinical importance of concordance and non-concordance between CBBCT and MRI was not expressed in the Background of the Abstract. In addition, we have made corresponding revisions in the Methods, Results, and Conclusions sections of the Abstract in accordance with the reviewers' comments.

Changes in the text: We have modified our text as advised (see Page 3, Line 43-45, 54-55; Page 4, Line 67-68).

Comment 3: In the introduction of the main text, the authors has reviewed that the

selection of CBBCT and MRI depends on certain conditions, so why there is a need to compare their consistency and inconsistency. The authors need to clearly explain the potential clinical needs for such comparisons, as well as the factors associated with inconsistencies.

Reply 3: Thank you very much for your professional opinion. Excessive tumor size is one of the main reasons for failure of breast-conserving surgery or conversion to mastectomy. Therefore, accurate preoperative assessment of breast cancer tumor size is very important to develop an individualized treatment plan for the patient. MRI is currently the most reliable imaging technique for preoperative evaluation of breast cancer and has the highest accuracy in measuring tumor size. However, MRI has the disadvantages of more clinical contraindications and high cost, etc. CBBCT is a new 3D breast imaging technique, and its clinical value in breast cancer diagnosis and treatment has been increasingly recognized. Based on the above background, we would like to explore whether CBBCT can be used as an effective technique to assess tumor size, thus providing a new alternative route for patients who cannot tolerate MRI. The potential clinical significance of this study we have described in the Introduction section (see Page 5, Line 81-83, Page 6, Line 99-100). In addition, the influencing factors that lead to discordance between CBBCT-pathology and MRI-pathology measurements are what we mainly wanted to analyze in this study, and are therefore described mainly in the Results and Discussion section. If you feel that our description is not clear and precise enough, please let us know and we will make adjustments immediately.

Changes in the text: None.

Comment 4: The methodology of the main text needs to accurately describe the clinical research design, sample size estimation, and data collection of clinical and pathological factors. In statistics, please split the current text into two parts: analysis on the consistency and inconsistencies. It would be helpful to analyze how the inconsistencies would affect the treatment outcome or selection of treatments.

Reply 1: We thank you for your professional comments and have modified the Statistical analyses section of the Methods accordingly.

Changes in the text: We have modified our text as advised (see Page 9, Line 185-186 and 192-193).

Comment 5: Please cite several related papers:

1. Gong W, Zhu J, Hong C, Liu X, Li S, Chen Y, Zhang B, Li X. Diagnostic accuracy of cone-beam breast computed tomography and head-to-head comparison of digital

mammography, magnetic resonance imaging and cone-beam breast computed tomography for breast cancer: a systematic review and meta-analysis. Gland Surg 2023;12(10):1360-1374. doi: 10.21037/gs-23-153.

2. Li X, Chen Y, Liu J, Xu L, Li Y, Liu D, Sun Z, Wen Z. Cardiac magnetic resonance imaging of primary cardiac tumors. Quant Imaging Med Surg 2020;10(1):294-313. doi: 10.21037/qims.2019.11.13.

3. Chilla GS, Tan CH, Xu C, Poh CL. Diffusion weighted magnetic resonance imaging and its recent trend—a survey. Quant Imaging Med Surg 2015;5(3):407-422. doi: 10.3978/j.issn.2223-4292.2015.03.01.

Reply 2: We have added the above references to the manuscript as 10th, 11th, and 15th.

Changes in the text: We have modified our text as advised (see Page 5, line 85-86; Page 6, Line 92).

Reviewer B

1. Abbreviations in all figures, tables and legends should be explained.

Reply 1: We have added.

2. In figure 2, it is -1.97 not -1.96.

Fig. 2, where the mean difference between CBBCT pathology was 0.37 (95% CI: -1.96, 2.70) cm, the mean difference between MRI pathology was 0.61 (95% CI: -2.17, 3.40) cm and the mean CBBCT-MRI difference was 0.25 (95% CI: -0.78, 1.27) cm.

Reply 2: We have corrected. Thank you!

3. It seems the p values mentioned in the main text are inconsistent with that in Figure 4.

group exhibited non-mass enhancement (NME) (48.6% (17/35) vs. 13.8% (11/80) (Fig. 4.a), $p<0.001$),

and lesions in the discordant group were also more likely to show calcifications (62.9% (22/35) vs. 37.5% (30/80, $p=0.012$) (Fig. 4.b).

Based on MRI measurements of breast cancer tumor size, a total of 73 lesions (63.5%, 73/115) were classified in the concordant group, and 42 lesions (36.5%, 42/115) were classified in the discordant group. The pathological maximum diameter of breast cancers was larger in the discordant group than in the concordant group (2.3 (1.6, 2.9) cm vs. 1.8 (1.4, 2.2) cm, $p=0.002$). Fatty infiltration was more frequently observed in the concordant group than in the discordant group (84.9% (62/73) vs. 69.0% (29/42)). In terms of MRI features, 50.0% (21/42) of breast cancers in the discordant group exhibited NME, whereas the vast majority of the concordant group exhibited mass-type lesions (90.4%, 66/73) ($p < 0.001$) (Fig. 4.a).

In addition, this study compared the differences in breast cancer tumor size based on CBBCT and MRI measurements with those based on pathology specimens. Overall, the difference between CBBCT and pathology (0.1 (-0.1, 0.4) cm) was significantly smaller than that between MRI and pathology (0.3 (0.0, 0.6) cm) ($p=0.008$) (Fig. 4.c). In breast cancer lesions containing calcification, the difference between CBBCT and pathology was smaller than that between MRI and pathology (0.2 (-0.1, 0.5) cm vs. 0.4 (0.1, 1.0) cm, $p=0.021$), suggesting that CBBCT has an advantage over MRI in assessing the size

Reply 3: We have corrected. Thank you!

4. Please provide description for the y-axis of Figure 4a and 4b.

Reply 4: We have added. Thank you!

5. Please check and confirm the highlighted percentage.

Table 1 The clinical characteristics of patients and lesion subtypes

Clinical and pathological characteristics		Value [a]/ N [b] (%)
Age (years)		49.63 ± 8.26
Malignant lesions		115 (86.47%)
	Invasive ductal carcinoma	97 (84.35%)
	Ductal carcinoma in situ with microinvasion	7 (6.09%)
	Mucinous Carcinoma	4 (3.48%)
	Invasive lobular carcinoma	3 (2.61%)
	Invasive micropapillary carcinoma	3 (2.61%)
	Ductal carcinoma in situ	1 (0.87%)

[a] Data are the mean ± standard deviations

[b] N, Number of the lesions

Reply 5: We have corrected. Thank you!

6. It is 0.983 not 0.938 in Table 2. Please also check Table 4.

Based on ICC analyses, the agreement of tumor size measurements by the two reviewers based on both CBBCT and MRI was excellent, with ICC values of 0.983 (95% CI: 0.976-0.988) and 0.973 (95% CI: 0.938-0.986), respectively. The agreement between CBBCT and MRI was also excellent, with ICC

CI: 1.229, 10.045, p=0.019) were the main predictive factors for the difference between CBBCT and pathological assessment of tumor size, with NME having a stronger association. For MRI-based tumor size measurements, NME (OR=6.002, 95% CI: 2.058, 17.5055, p=0.001) was also a significant predictor of discrepancies between MRI and pathology (Table 4).

Reply 6: We have corrected. Thank you!