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2 Milisievert Low Dose Dedicated Breast CT with Iterative Model Reconstruction Technique in Evaluation of Breast Mass: Feasibility Study in Comparison with MRI

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Abstract: Objective To investigate the feasibility of low dose dedicated computed tomography (CT) with IMR technique compared with magnetic resonance imaging (MRI) in preoperative evaluation of breast cancer. Methods Dedicated CT and breast MRI were performed in 21 patients with diagnosed breast mass for preoperative evaluation. A dedicated protocol combined with chest diagnostic CT and dynamic scans of breast was developed with the use of IMR technique as well as optimization of scan parameters to ensure acceptable radiation dose. Image quality evaluations of CT images were performed using a five-point scale. The number, site and size (maximum diameter) of breast lesion were recorded respectively in CT and MRI images. The enhancement patterns of breast lesion were classified to 3 types (washout, plateau, and persistence) according to time intensity curve derived from CT and time signal curve derived from MRI, respectively. Pearson's correlation, Bland-Altman analysis, and Cohen's kappa test were used for statistical assessment. Results The mean effective radiation dose of dedicated breast CT, with the image quality diagnostic acceptable for evaluation of breast lesion and pulmonary structures, was (2.15±0.39) mSv, which was no more than a routine chest diagnostic CT. Results of breast lesion number and lesion site obtained by CT and MRI was consistent, with a total of 24 lesions detected in 21 patients. The mean lesion size was (26.5±12.1) mm in CT and (26.1±12.9) mm in MR, respectively. CT showed an excellent correlation with MRI for lesion size ($r=0.99$, $n=24$, $p<0.0001$). Limits of agreement determined by Bland-Altman analysis for lesion extent was (-3.0mm, 3.8mm). Good agreement was observed between CT and MRI for lesion enhancement patterns (kappa value = 0.936, $p=0.000$). Conclusion Dedicated breast CT imaging with acceptable radiation dose enabled diagnostic image quality and showed good agreement with breast MR imaging in preoperative evaluation of breast cancer.

Keywords: Breast Cancer, Computed Tomography, Low Radiation Dose, Iterative Reconstruction

1. Introduction

A breast mass is one of the most common presenting features of breast cancer but may not exhibit distinctive physical findings [1]. Diagnostic mammography and breast ultrasound are used as first line modalities to characterize the nature of the mass before biopsy [2]. For those lesions with biopsy-proven malignancy in non-fatty tissue, magnetic resonance (MR) imaging is considered more sensitive than mammography or ultrasound for evaluating the extent of disease [3]. In nowadays clinical practice, MR imaging has emerged as a useful modality for preoperative evaluation of cancer localization and extension in patients with diagnosed breast cancer [4]. On the other hand, computed tomography (CT) imaging has also been found to have high diagnostic efficacy in evaluation of breast tumoral lesions [5-8] and enlarged lymph nodes [9], meanwhile plays an important role in preoperative evaluation in patients with breast cancer who cannot undergo MRI because of contraindications such as claustrophobia. However, CT breast imaging is not preferred due to its high radiation exposure.

In view of CT radiation exposure, iterative reconstruction techniques were introduced to achieve low-dose CT scans with diagnostic image quality during last decade. Recent studies [10-13] reported that iterative model reconstruction (IMR) technique was able to reach dramatically radiation dose reduction as well as improved low-contrast detectability in chest, abdomen, cardiovascular and brain CT examinations. Among which, sub-milisievert chest CT with better delineation of lesion margins have been achieved with iterative model reconstruction (IMR) technique, compared to routine dose scans with conventional reconstruction techniques [10]. Theoretically, it is predictable of IMR technique in CT breast imaging to help reduce radiation dose and potentially improve image quality.

According to clinical guidelines [14], chest diagnostic CT imaging is suggested in breast cancer patients with pulmonary symptoms at clinical stage I-IIB and patients at clinical stage IIIA for preoperative evaluation. For these patients who are referred for chest diagnostic CT imaging, a dedicated protocol combining with chest diagnostic scans and breast dynamic scans for comprehensive evaluation of breast mass is able to be practiced in low radiation dose, considering the use of IMR technique enables substantial radiation dose reduction. In this way, the dedicated CT imaging for breast cancer can provide more information of breast mass itself in addition to pulmonary information before surgery, which may be partially alterative to MR imaging in preoperative evaluation of breast mass, meanwhile has the potential to optimize the workflow of preoperative breast imaging. Thus, we designed this study to investigate the feasibility of a dedicated CT imaging protocol for preoperative evaluation of breast cancer using IMR technique at a 2mSv dose level by comparison of MR imaging in lesion detection, lesion size and characterization of lesion nature.

2. Materials and Methods

The prospective study received Institutional Review Board approval; prior informed consent was obtained from all patients.

2.1. Study Population

21 patients were prospectively enrolled to our study between December 2015 and August 2016. The inclusion criteria were 1) diagnosed as solitary breast nodule or mass by ultrasound and/or mammography, with a grade no less than 4 according to BI-RADS criteria [15]; 2) were referred for chest diagnostic CT and breast MRI examinations for pre-operative evaluation. Exclusion criteria included allergy to contrast medium, renal insufficiency (estimated glomerular filtration rate < 40 ml/min/1.73m^{-2}), unstable clinical condition and inability to perform a breath hold. All patients received CT and MRI scans with an interval no more than 3 days.

2.2. CT Acquisition, Image Reconstruction and Dose Management

All CT examinations were performed on a 256-slice CT scanner (Brilliance iCT; Philips Healthcare, Cleveland, OH) according to a dedicated protocol. A total of six scans were performed before and 1min, 2min, 3min, 4min, 6min after the intravenous bolus injection of contrast medium, with the patients in a supine position. The scans at 2min time point were used as chest diagnostic scans in addition to dynamic scans, with a range from bilateral clavicular fossa to diaphragm, and the scans at other time points were only used as dynamic scans for kinetic characteristic evaluation, with a range merely covering bilateral breast area. The scan parameters were as follows: 0.5s of rotation time, 0.304 of pitch, and 61 mAs as reference of tube current using automatic tube current modulation (ATCM, DoseRight, Philips Healthcare) at the 2min time point scan; 0.75s of rotation time, 0.99 of pitch, and 10mAs of tube current at the other scans. The other scan parameters were identical for each scan: detector configuration, 128*0.625mm; FOV, 350mm; slice thickness, 1.0mm; slice increment, 0.5mm, matrix 512*512; tube voltage, 80 kVp when BMI less than 24kg/m^2 otherwise 100kV. A total of 80 mL of contrast medium (iopromide, ultravist 320; Schering, Berlin, Germany) was injected via the right antecubital vein at a rate of 4ml/s, followed by 15ml saline flush. All the image were reconstructed with IMR technique using identical parameters of 1mm thickness at 0.5mm increment.

Machine-generated CT dose index volume ($CTDI_{vol}$), scan length, and dose-length product (DLP) values were recorded for each patient. Estimated effective dose (ED) was calculated from DLP using a revised normalized effective dose constant of 0.014[16].

2.3. MR Acquisition

All breast scans were performed at a 3.0T system (Signa HDXT, GE Healthcare, Milwaukee, USA), using a 4 channel phased array breast coil, with the patients in a prone position. A total of seven to nine dynamic acquisitions were performed with VIBRAN sequence (TR/TE = 4.7/2.2 ms, TI = 16 ms), one before and six to eight immediately after an intravenous bolus injection of contrast medium (Magnevist; Schering, Berlin, Germany) equal to 0.1mmol/kg body weight, followed by 20ml flush, with a slice thickness of 2.4mm and a matrix of 384x320. The scan time was 88 s per dynamic acquisition.

2.4. Image Analysis

All breast lesions were evaluated and compared for their morphologic and kinetic characteristics in both CT and MRI images. CT images were reviewed and interpreted on a Philips EBW4.5.2 workstation. Image quality assessment was performed by two thoracic radiologists in all six series on reconstructed 3.0mm thick axial images firstly, using a five-point scale in which 5 (excellent) = images neither noisy nor artifactual, lung structures and breast lesion contours clear, useful diagnostic information; 4 (good) = image slightly noisy or artifactual, clear structure and contours, sufficient diagnostic information; 3 (fair) = image noisy and artifactual, structure and contour partially obscured, acceptable diagnostic information; 2 (poor) = image very noisy and artifactual, insufficient information for diagnosis; and 1 (unacceptable) = severe noise and artefacts, image non-assessable. When they disagreed, a third thoracic radiologist with more than 15 years' experience was asked to adjudicate the differences in order to obtain a consensus score. The final results were used for statistical analysis. Afterwards, post processing including maximum intensity projection (MIP) and multi-planar reformation (MPR) were performed on images acquired in 2min CT scans, to evaluate the morphologic characteristics of breast lesion in addition to pulmonary information. MR images were transferred to a GE AW4.4 workstation for post processing including subtraction and MIP to evaluate lesions.

The number, site and disease extent (maximum diameter) of breast lesion were recorded for morphologic characteristics evaluation. Moreover, time density curve (TDC) derived from CT as well as time-signal intensity curve (TIC) derived from MR were used for kinetic characteristics evaluation. Region of interest (ROI) was placed in the lesion in each dynamic scans and the CT attenuation of each ROI were recorded for drawing TDC, while the signal intensity of lesion in MR images per dynamic scans were recorded for drawing TIC. The enhancement patterns were classified according to the shape of TDC or TIC [17]: A type was defined as washout, with early quick enhancement then quickly decline; B type was defined as plateau, with early significant enhancement and in the middle and late period the offset maintained within 10% of the enhancement peak; C type was defined as persisting, with a gradual enhancement and in the late continuous or slow enhancement. The enhancement pattern of each lesion according to TDC and TIC were recorded, respectively.

2.5. Statistical Analysis

All continuous values were expressed as mean ± standard deviation (SD). The subjective scores were compared using the Friedman test, and if there was a significant difference, pairwise comparisons would be performed with the Steel–Dwass test. Inter-observer agreement for subjective image scores was measured using Kappa test. The Bland-Altman analysis was used to examine the agreement of lesion size in CT and MR image, and Cohen's kappa test was used to examine the agreement of enhancement pattern derived from CT and MR images. In addition, the Pearson correlation coefficient was employed to examine the relationship between the measurements of lesion size in CT and MR images. All statistical analyses were performed with commercially available software (MedCal 15.2). A value of $P<0.05$ was considered a statistical significant difference.

3. Results

3.1. Demographics and CT Radiation Dose

A total of 21 patients with 24 breast lesions were investigated in our study. All patients were female with a mean age of 50.9±9.2 and a mean BMI of 24.5±2.8 kg/m^2. All the lesions were confirmed by biopsy and/or surgery, of which 20 invasive ductal carcinoma, 3 fibroadenoma, and 1 fibrocystic disease. Axillary lymph nodes enlargement was observed in 4 cases and one pericardial nodule was observed in 1 case. No thoracic metastases were found in all cases.

The mean effective radiation dose was 2.15mSv±0.39 for the dedicated breast scans including all six series, 1.55mSv±0.32 for the 2min time point series which were used as chest diagnostic imaging, and in total of 0.60mSv±0.18 for the other five series, with 0.12mSv±0.03 per series. Details are summarized in Table 1.

Table 1. *Radiation dose of CT series.*

Parameters	$CTDI_{vol}$ (mGy)	Scan length (cm)	DLP (mGy*cm)	ED (mSv)
Series 1	0.33±0.10	25.97±6.49	8.57±2.14	0.12±0.03
Series 2	0.33±0.10	25.97±6.49	8.57±2.14	0.12±0.03
Series 3	#3.52±0.73	#31.45±6.47	#110.71±22.8	#1.55±0.32
Series 4	0.33±0.10	25.97±6.49	8.57±2.14	0.12±0.03
Series 5	0.33±0.10	25.97±6.49	8.57±2.14	0.12±0.03
Series 6	0.33±0.10	25.97±6.49	8.57±2.14	0.12±0.03
In total	5.14.±1.02	25.97±6.49	154.05±27.84	2.15±0.39

*$CTDI_{vol}$, CT dose index volume; DLP, dose-length product; ED, effective radiation dose.

** Series 1 to 6 represented the scan series that acquired before and 1min, 2min, 3min, 4min, and 6min after the contrast medium injection, in which the series scanned at 2min time point (Series 3) were used for chest diagnostic imaging in addition to breast dynamic imaging, while the other series were only used for breast dynamic imaging.

Significant difference compared to other series

3.2. Image Quality Assessment of CT Images

There was no significant disagreement between the 2 radiologists (k=0.708–0.919). All the subjective image assessment score for each algorithm of both groups are summarized in Table 2 and Figure 1.

Table 2. *Image quality scores of all CT series.*

Parameters	Reader 1	Reader 2	Final	Kappa Value
Series 1	0/10/10/1/0	0/11/10/0/0	0/10/11/0/0	0.826
Series 2	0/9/11/0/0	0/10/10/1	0/10/10/1/0	0.904
Series 3	#0/0/0/4/17	#0/0/1/2/18	#0/0/0/3/18	0.708
Series 4	0/9/11/1/0	0/10/10/1/0	0/10/11/0/0	0.919
Series 5	0/9/11/1/0	0/10/10/1/0	0/9/11/1/0	0.919
Series 6	0/10/10/1/0	0/9/12/0/0	0/9/12/0/0	0.825
P	n/a	n/a	<0.001	n/a

* Data show the frequency of numerical scores given in each category (grade 1/2/3/4/5).

** Series 1 to 6 represented the scan series that acquired before and 1min, 2min, 3min, 4min, and 6min after the contrast medium injection, in which the series scanned at 2min time point (Series 3) were used for chest diagnostic imaging in addition to breast dynamic imaging, while the other series were only used for breast dynamic imaging.

Significant difference compared to other series

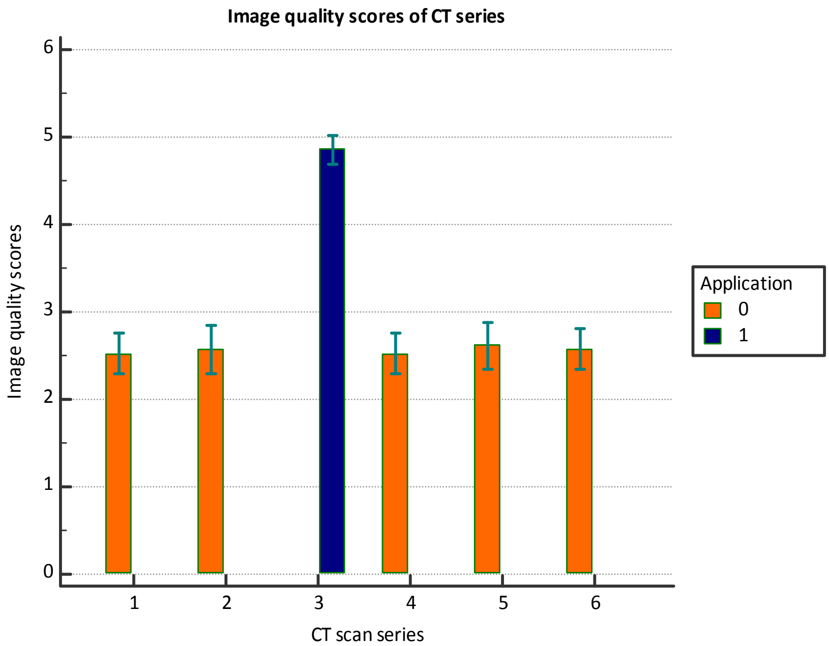

Figure 1. *Image quality scores of CT series. Series 1 to 6 represented the scan series that acquired before and 1min, 2min, 3min, 4min, and 6min after the contrast medium injection, in which the series scanned at 2min time point (Series 3) were used for chest diagnostic imaging in addition to breast dynamic imaging (Application 1), while the other series were only used for breast dynamic imaging (Application 0).*

Series 3 demonstrated significant better image quality than the other five series.

Images at 2min scans demonstrated significant better score comparted to images of the other five series ($p<0.001$). No significant difference was found among the other series ($p=0.327$).

3.3. Comparison of Lesion Evaluation in CT and MR

All the 24 breast lesions were both detected on CT and MR images, with exactly the same number and location, the representative case was shown in Figure 2.

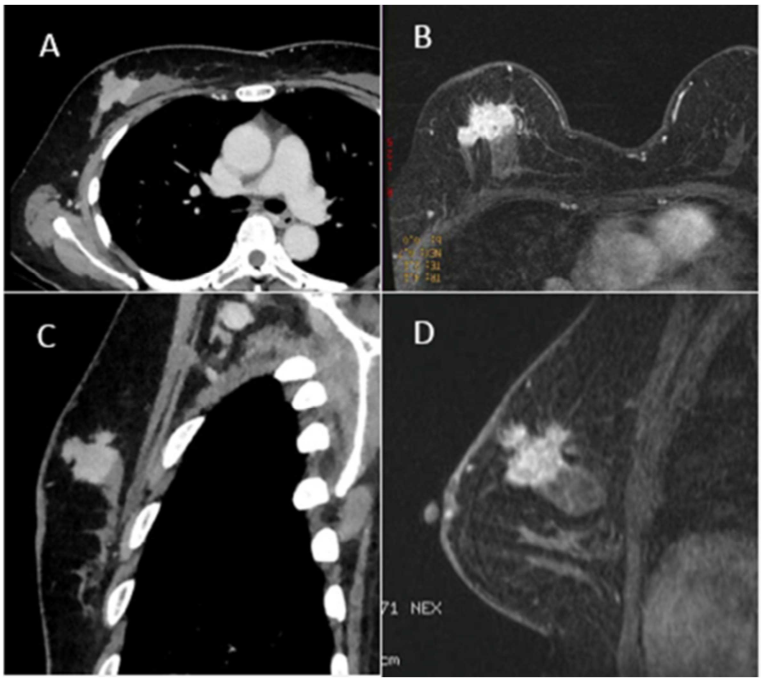

Figure 2. *Comparison of representative breast lesion in CT (chest diagnostic series) and MR images. A 56 years' old women with diagnosed invasive ductal carcinoma by biopsy, BMI = 24.5kg/m^2. A lobulated breast mass with spiculate edge was observed in CT axial images (A), MR axial images (B), CT sagittal images (C), and MR sagittal images (D). The site, disease extent, and enhancement pattern of the breast lesion are similar in CT and MR images, the maximum diameter of the lesion is 35mm in CT and 32mm in MR.*

The mean lesion extent was 26.5mm±12.1 in CT and 26.1mm±12.9 in MR, which presented an excellent correlation between the two (r=0.99, n=24, p<0.0001, Figure 3), as well as a good agreement, with the 95% limits of agreement determined by Bland-Altman analysis of (-3.0mm, 3.8mm), Figure 4.

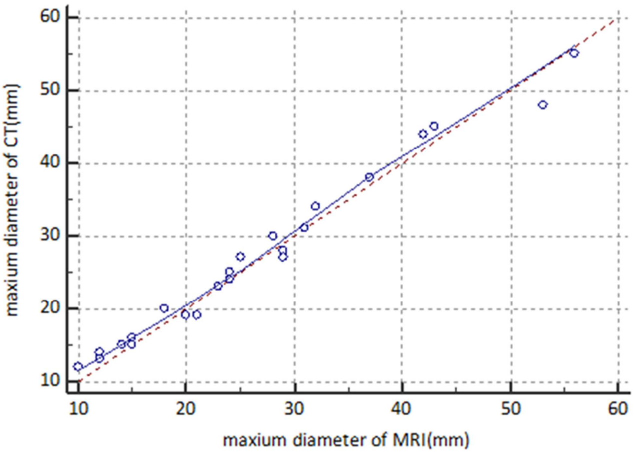

Figure 3. *Correlation of lesion extent (maximum diameter) between CT and MR. Excellent correlation were presented (r =0.99, n=24, p<0.0001).*

In evaluation of enhancement pattern according to CT, 13 lesions (12 invasive ductal carcinoma and 1 fibrocystic disease) were observed as A type, 9 lesions (8 invasive ductal carcinoma and 1 fibroadenoma) were observed as B type, and 2 lesions (both fibroadenoma) were observed as C type; meanwhile according to MR, 12 lesions (11 invasive ductal carcinoma and 1 fibrocystic disease) were observed as A type, 10 lesions (9 invasive ductal carcinoma and 1 fibroadenoma) were observed as B type, and 2 lesions (both fibroadenoma) were observed as C type. Good agreement were showed between CT and MR for the enhancement pattern evaluation (kappa value=0.936, p=0.000), the representative case was shown in Figure 5.

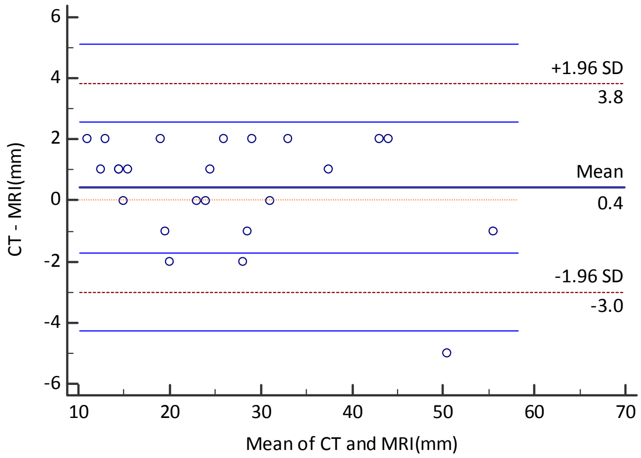

Figure 4. *Bland-Altman analysis of lesion extent (maximum diameter), with the 95% limits of agreement of (-3.0mm, 3.8mm).*

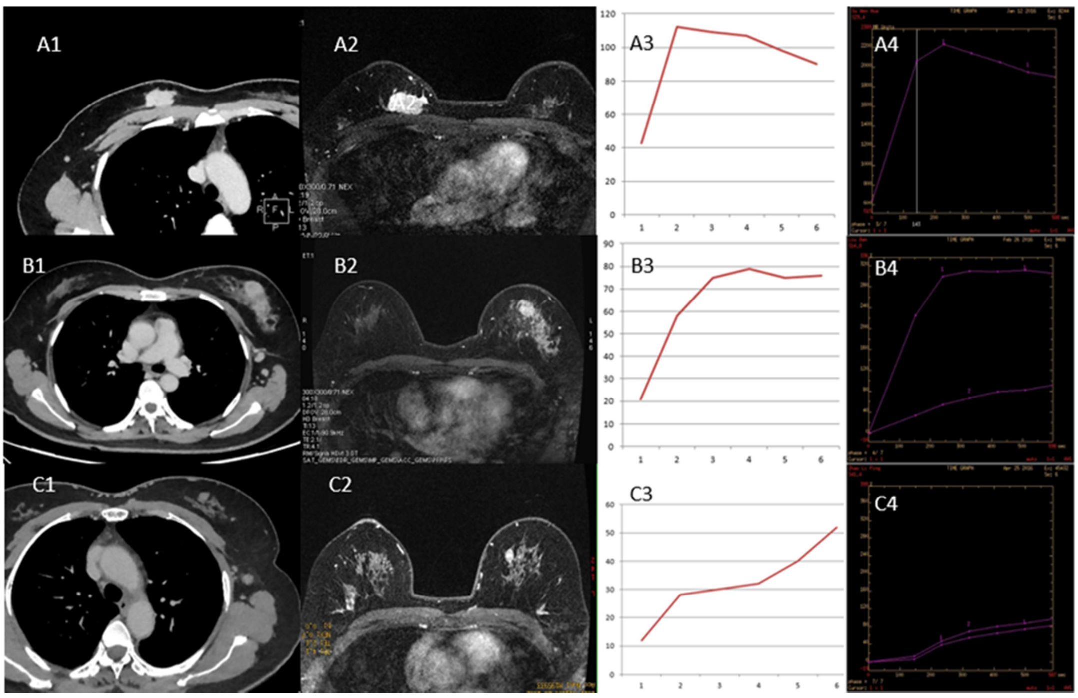

Figure 5. *Comparison of enhancement pattern demonstrated by TDC and TIC:*

A|48 years' old women with breast mass histologically diagnosed as invasive ductal carcinoma, solitary mass was observed in right breast in CT (A1) and MR (A2) images, both TDC (A3) and TIC (A4) illustrated a washout type of enhancement pattern.

B|50 years' old women with breast nodule histologically diagnosed as invasive ductal carcinoma, solitary nodule was observed in left breast in CT (B1) and MR (B2) images, both TDC (B3) and TIC (B4) illustrated a plateau type of enhancement pattern.

C|50 years' old women with breast nodule diagnosed as BI-RADS category 4 by ultrasound, and confirmed as fibroadenoma by histology after surgery, solitary nodule was observed in left breast in CT (C1) and MR (C2) images, both TDC (C3) and TIC (C4) illustrated a persisting type of enhancement pattern.

4. Discussion

The dedicated CT breast imaging that we proposed demonstrated diagnostic image quality for both breast and pulmonary structures at an effective radiation dose of around 2mSv, which is equivalent to that of low dose chest CT scans in National Lung Screening Trial (NLST)[18], meanwhile far less than that of routine diagnostic chest imaging. The CT series used for diagnostic information exhibited excellent image quality at an effective radiation dose of around 1.5mSv by use of IMR due to the noise and artifacts reduction capability of IMR, while the other dynamic series with merely 0.12mSv per series enabled kinetics characteristics obtaining of breast lesion despite exhibiting lower image quality.

The dedicated breast CT imaging exhibited excellent agreement with MR imaging in both morphologic and kinetics characteristics evaluation. In our study, the number and site of detected breast lesions were identical between CT and MR imaging, and the lesion extent were strongly correlated between CT and MR imaging, with a correlation coefficients of 99%, as well as its 95% limits of agreement was no more than 4mm, which indicated CT exhibited similar accuracy compared to MR imaging in preoperative evaluation for breast cancer thus to help formulate the surgical plans. Moreover, CT an MR demonstrated good agreement in enhancement pattern determined by TDC/TIC. In both CT and MR images, 20 lesions of invasive ductal carcinoma were observed as washout or plateau type, 3 lesions of fibroadenoma were observed as plateau or persisting type, and the one fibrocystic lesion was observed as washout type, which is consistent with previous study [17] and indicate that malignant lesions such as invasive ductal carcinoma tend to be washout and plateau type, while benign lesions such as fibroadenoma tend to be persisting type, meanwhile reveals that CT has similar ability with MR to identify the benign and malignant of breast lesions.

As described above, the dedicated breast CT imaging in our study demonstrated high accuracy in evaluation of breast lesions, which can be alternative or partial alternative to MR for preoperative evaluation of breast cancer. Furthermore, CT can also provide chest diagnostic information in addition to breast lesion evaluation. For patients who are referred for chest diagnostic CT according to guidelines, the dedicated breast CT imaging enables one-stop examination combining both breast and pulmonary evaluation, thus to potentially improve the imaging workflow of preoperative breast cancer. Finally, the incidental enhancing foci [19] that often observed in MR are rarely seen in CT imaging [7], which is also an advantage of CT imaging in breast evaluation as conducive to identify the nature of breast lesions.

Our study has several limitations. First, patients were scanned with a supine position in CT but with a prone position in MR, the change of scan position may lead to changes in location and shape of breast lesions due to relatively greater degree of breast activity, but it should not influence the study results. In addition, the supine position that in CT scans is closer to the surgical state and may be more accurate for surgical positioning. Second, all lesions included in our study were BI-RADS grade 4 and above, which tend to be malignant with the enhancement pattern mostly of washout and plateau type. Lesions of low BI-RADS grades need to be evaluated in further studies for a more complete view. Third, we didn't evaluate the diagnostic performance such as accuracy, sensitivity and specificity of CT and MR imaging in breast lesions evaluation according to the histological results as reference, due to relatively small sample size.

5. Conclusion

In conclusion, by use of IMR technique, the dedicated breast CT imaging enabled diagnostic image quality in both breast lesions and pulmonary structures for preoperative evaluation of breast cancer, with an acceptable radiation dose, potentially providing the possibility of one-stop evaluation before surgery for patients with breast cancer.

Compliance with Ethical Standards

(In case of Funding) Funding: All authors have no conflict of interest.

(And/or in case humans were involved) Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

(In case humans are involved) Informed consent: Informed consent was obtained from all individual participants included in the study.

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