4D Dynamic Contrast-Enhanced Breast CT: Evaluation of quantitative accuracy

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ABSTRACT

Four-dimensional dynamic contrast-enhanced breast CT (4D DCE-bCT) holds potential for high spatio-temporal-resolution imaging for characterization and monitoring of breast tumors. This study presents a dedicated phantom-based evaluation of the accuracy of dynamic iodine concentration quantification in 4D DCE-bCT.
A breast CT (bCT) system was adapted for extended acquisition times, and the x-ray spectrum was optimized (65 kV/0.25 mm Cu). Additionally, reconstruction and correction algorithms were developed for accurate iodine quantification. The imaging sequence involved a 10-second pre-contrast scan with 360 projections, followed by two 100-second post-contrast scans, each with 400 projection images over 10 rotations, with 10 seconds between each scan.
In this experiment, we aimed to quantitatively assess the changes in iodine concentration, while a time-varying concentration of iodine (range 0.5 to 10 mg I/mL) was pumped through a 5 mm diameter tube in an olive-oil breast phantom. Pre- and post-contrast images were scatter-corrected and reconstructed using a polychromatic iterative reconstruction (IMPACT) combined with PICCS.
This process yielded a 38-framevirtual monoenergetic (30 keV) image sequence at 5-second intervals. To verify the perfusion curve accuracy, a 5 × 5 × 10 voxel VOI was compared against the known true iodine concentration. Linear fits to the results showed good precision with some under-estimation of the true concentration (wash-in: slope = 0.7530, offset = +0.5208, R^2 = 0.985; wash-out: slope = 1.012, offset = -0.8295, R^2 = 0.987). These findings indicate the 4D DCE-bCT's potential to provide quantitatively accurate estimates of iodine concentration.

Keywords: 4D dynamic contrast-enhanced breast CT; Iodine quantification; Perfusion accuracy.

1. INTRODUCTION

Building on the foundational work by Prionas et al. (2010) on enhancing lesion detection through contrast-enhanced dedicated breast CT (CE-bCT)[1] and the advancements by Caballo et al. (2019) in 4D dynamic contrast-enhanced breast CT (4D DCE-bCT) for high-resolution imaging,[2] our study introduces an experiment to evaluate the quantitative accuracy of dynamic iodine imaging within 4D DCE-bCT.
By combining the enhanced detection capabilities of CE-bCT with novel imaging techniques, we have optimized a breast CT system for extended scanning periods and refined the x-ray spectrum to accurately quantify iodine concentrations.

2. METHODS

2.1 Breast CT system

A state-of-the-art dedicated bCT system, (Koning Corp., Norcross, GA, USA), was modified to enable long-duration scans. The system is equipped with a pulsed x-ray tube (M-1581, Varian Medical System, Salt Lake City, UT), which can operate at a maximum voltage of 70 kV, and a flat-panel detector (Xineos 3030HS, Teledyne Dalsa, Waterloo, ON, CA), mounted on a rotating gantry.
Pre- and post-contrast scans can be continuously acquired and independently adjusted within the same sequence for tube current, scan duration, and the number of pulses per revolution. The spectrum was optimized for iodine detection, with a tube voltage of 65 kV, 0.25 mm copper filtration, and 5 ms pulse width.

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2.2 Breast perfusion phantom setup

A simplified breast perfusion phantom was fabricated using 3D printing. Its design was based on the dimensions of an existing bCT quality control phantom, incorporating the typical 1.5 mm thickness of breast skin.[3] The phantom was printed from PLA material, selected for its x-ray attenuation properties similar to human skin, and filled with olive oil to simulate fatty breast tissue.

The perfusion setup of the phantom comprised a programmable syringe pump for time-varying concentration of iodine (range 0.5 to 10 mg I/mL), a 30 mL container (initially filled with water) with a mixer for fluid blending, and tubing (Ø = 5 mm) that connects the phantom to an extraction syringe pump (Figure 1).

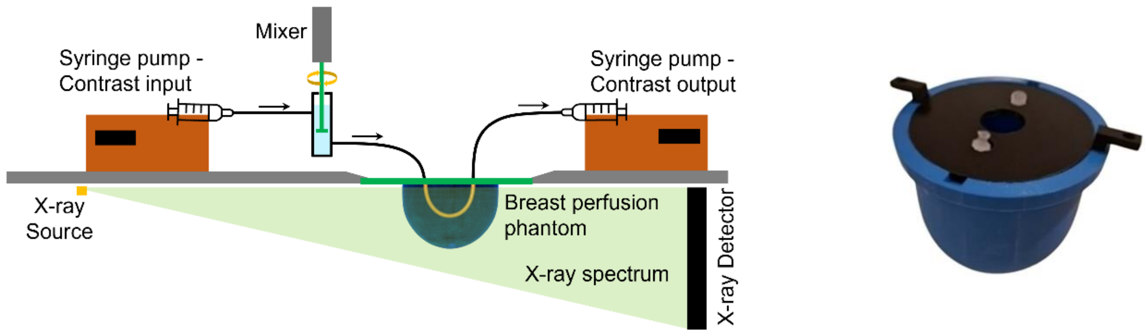

Figure 1: Schematic of the breast perfusion phantom setup for 4D DCE-bCT, with the breast perfusion phantom design depicted on the right.

2.3 Image acquisition

The pre-contrast acquisition sequence consisted of 360 pulses over a 10-second revolution, with each pulse automatically set at 80 mA by the system's automatic exposure control. This was followed by a 10-second pause. Then, two post-contrast scans were performed, each comprising 400 pulses over 10 revolutions (40 pulses per 10-second revolution), at a tube current of 32 mA, determined experimentally as the lowest feasible value. The first post-contrast scan was designed to monitor the 'wash-in' phase, while the second scan, following another 10-second pause, aimed to capture the 'wash-out' phase of the iodine perfusion curves.

2.4 Contrast dynamics in 4D DCE-bCT scanning

Wash-in and wash-out phases were programmed on the syringe pump. During the post-contrast scans, the mixer's speed was set to 800 RPM to ensure homogeneous mixing and prevent vortex formation. The contrast medium, with an iodine concentration of 10 mg/mL, was administered at a flow rate of 40 mL/min. Adjustments to the syringe pump's injection speed were made to create a defined perfusion curve shape, which will then be used for comparison with the curve obtained from the 4D DCE-bCT.

2.5 Image reconstruction

Pre- and post-contrast images were scatter-corrected using a previously-validated Monte Carlo simulation algorithm.[4] The pre-contrast image was reconstructed employing a single energy polychromatic iterative reconstruction method (IMPACT)[5] with decomposition parameters tailored for the energy range of 10 to 65 keV and breast anatomy, completed in 75 iterations.

This resulted in a high-quality prior image free of cupping artifacts. Each post-contrast image was reconstructed using PICCS[6] together with IMPACT, setting $\alpha = 0.95$ and employing total variation as a sparsifying transformation over 25 iterations. This procedure produced a sequence of 38-virtual monoenergetic images (30 keV), each with a 0.25 mm isotropic voxel size, generated at 5-second intervals.

2.6 Quantitative accuracy assessment

To assess the quantitative accuracy of 4D DCE-bCT, a $5 \times 5 \times 10$ voxel volume of interest (VOI) was analyzed. Measurements were taken at the proximal and distal extremes and the center inside the tube part of the breast perfusion phantom during the wash-in and wash-out phases and the mean and standard deviation were calculated.

This analysis yielded linear attenuation values, which were subsequently converted to iodine concentration values using a pre-established calibration curve. This curve, derived from static measurements of iodine concentration ranging from 0.5 to

10 mg I/mL, is described by the equation: $\mu = 0.001239\ \times C + 0.0307$, where μ represents the x-ray linear attenuation in mm^{-1} and C the concentration values in mg I/mL.

These concentration values were then compared with the theoretical concentrations set in the pumping sequence. To assess the accuracy, linear regression analysis and Bland-Altman plots were performed for the wash-in and wash-out phases at the tube's center.

3. RESULTS

In Figure 2, the VOI at the proximal (In) and distal (Out) extremes, as well as the center inside the tube, is shown. Additionally, the mean and standard deviation for both the wash-in and wash-out phases are plotted. Figure 3 shows the theoretical iodine concentration curve alongside the bCT-estimated concentration values.

Figure 4 shows linear fits applied to the results, indicating good precision, though with some underestimation of the true concentration. In the wash-in phase, the slope is 0.7530 with an offset of +0.5208, and an $R^2 = 0.985$. In the wash-out phase, the slope is 1.012 with an offset of -0.8295, and an $R^2 = 0.987$. In Figure 5, Bland-Altman plots show that the difference between respective pairs ranges from -0.98 to 2.12 mg I/mL for the wash-in phase and from 0.32 to 1.24 mg I/mL for the wash-out phase.

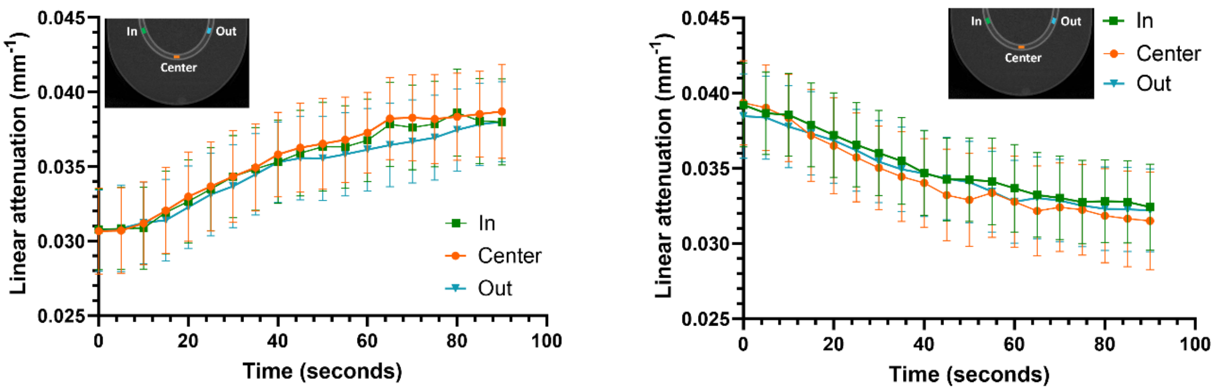

Figure 2: Linear attenuation over time for the 'wash-in' (left) and 'wash-out' (right) phases at different locations within the tube.

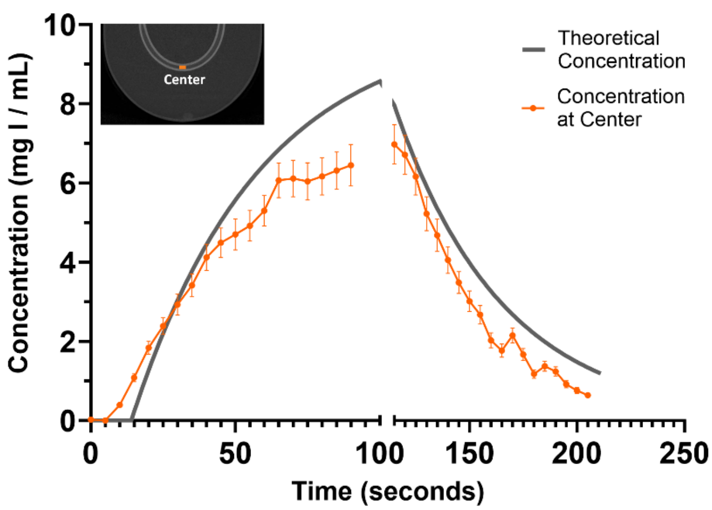

Figure 3: Comparative analysis of iodine perfusion using 4D DCE-bCT. The graph displays the measured iodine concentration at the center of the tube over time (orange line), alongside the theoretical perfusion curve (gray line). Error bars represent the standard deviation, indicating variability in the concentration measurements.

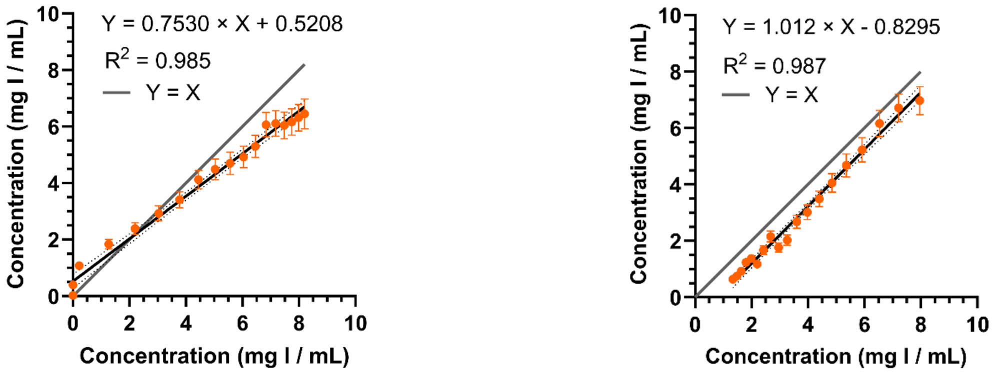

Figure 4: Linear regression analysis showing the correlation between known iodine concentrations and those center-measured, for the 'wash-in' (left) and 'wash-out' (right) phases.

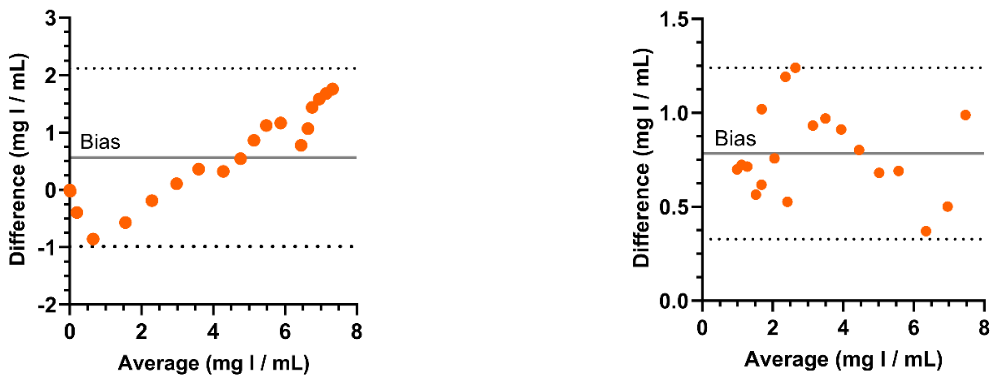

Figure 5: Bland-Altman plots for the 'wash-in' (left) and 'wash-out' (right) phases assessing the agreement between center-measured and known concentrations, indicating the system's bias in estimating iodine concentration. Dashed lines represent the limits of agreement (95% confidence interval).

4. CONCLUSIONS

While reconstructed values tracked the wash-in and wash-out of iodine concentration, this was with a steadily increasing bias over the duration of the scan sequence. This was caused by ever increasing detector lag that went undetected in experiments involving shorter acquisition times, possibly combined with incomplete convergence of the reconstruction. Further experiments are planned to determine the exact causes and the algorithms needed to correct for these will be developed. Nevertheless, the initial findings indicate the 4D DCE-bCT's potential to provide quantitatively accurate estimates of iodine concentration once we correct for these issues.

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