

Purpose: Accuracy of direct dose calculation on CBCT datasets is compromised by inaccuracy of reconstructed Hounsfield unit (HU) numbers in CBCT. Establishing HU to electron density (ED) calibration curves for CBCT can improve dose calculation accuracy on CBCT images. The goal of this study is to investigate effects of phantom volume and radial positions of inserting materials on HU-to-ED calibration for CBCT and evaluate impact of the calibration on dose calculation accuracy on CBCT datasets. **Method and Materials:** Catphan 600 and Gammex RMI 467 phantoms were used to characterize HU-to-ED calibration curves for both FBCT and CBCT. The effect of scatter volume on the HU-to-ED calibration was evaluated using the Catphan phantom fitted with annuli and the Gammex phantom in water. The CBCT HU-to-ED calibration was conducted by varying the radial positions of inserts in the Gammex phantom. The determined calibration curves were input into the Pinnacle TPS to calculate dose for an anthropomorphic pelvis phantom. **Results:** The scatter volume has negligible effects on the HU-to-ED calibration for FBCT. The CBCT HU-to-ED calibration curves vary significantly with the scatter volume and differ largely from that of FBCT. Large deviations of 330 HU and 700 HU in high density materials are observed for CBCT with the use of the modified Catphan and Gammex phantoms. In comparison to FBCT, the HU numbers on the CBCT HU-to-ED calibration curves are larger and smaller for materials less dense and denser than water, respectively. Radial position variations of inserts can cause HU number to change by up to 200 HU. The doses computed based on FBCT and CBCT of the pelvis phantom agree to within 3%. **Conclusion:** The CBCT and FBCT HU-to-ED calibration curves differ significantly. A fairly good dose calculation accuracy can be achieved using a single CBCT HU-to-ED calibration curve.