

**Purpose:** To systematically evaluate, in phantom and patient, differences obtained between using free-breathing CT (FBCT) and average CT (AVGCT) as the reference dataset for daily treatment localization with cone-beam CT (CBCT).

**Methods:** Five displacement curves generated from Varian's RPM patient data were inputted into motion platform varied amplitudes and irregularities. FBCTs and 4DCTs were acquired under programmed motion conditions. CBCTs were acquired for phantom on Trilogy equipped with cone-beam CT. Beam-on information from RPM isolated appropriate platform motion for each curve studied. Manual registrations between FBCT/CBCT and AVGCT/CBCT were performed in Eclipse's Registration Workspace. Volumes and registration results were compared. Seven early-stage lung cancer patients (mean ITV volume = 21.5 +/- 22.4 cc) were studied. CBCTs (2-4/patient, n=26) were registered to both AVGCT and FBCT, evaluating 52 registrations overall.

**Results:** In phantom, mean differences between using AVGCT and FBCT for CBCT localization were 0.01 +/- 0.24 mm, 0.24 +/- 0.23 mm, and 1.55 +/- 6.12 mm in lateral (LAT), anterior-posterior (A-P), and superior-inferior (S-I) directions, respectively. In one case, FBCT registration was 1.2 cm superior to that of the AVG-CT. Over 52 patient registrations, mean differences between using AVG-CT and FBCT as reference for CBCT registration were 0.4 +/- 1.3 mm, 0.2 +/- 2.0 mm, and 1.6 +/- 2.0 mm LAT, A-P, and S-I directions, respectively. Largest discrepancy between registrations was for small mobile tumor (6.2 mm S-I) with FBCT at end-exhale. Another case revealed 6.2 mm anterior shift between AVGCT and FBCT, which corresponded to obvious CT intensity differences.

**Conclusions:** CBCT registration differences between the AVG-CT and FBCT can be marked. FBCT as the reference image for daily CBCT on-line image guidance, especially for SBRT, should be exercised with caution, and should be verified to ensure it is not representative of an extreme phase of patient breathing.