

Purpose: The prostate can be localized automatically on daily cone-beam CT (CBCT) images by means of intensity-based 3D/3D image registrations. The goal of this study is to evaluate nine different similarity metrics for the best localization accuracy.

Methods and Materials: Seven prostate patients were retrospectively selected with natural prostate calcifications, which resulted in a dataset of 220 CBCT and 7 simulation CT (SimCT) images. On each SimCT image, a region of interest (ROI) was defined by expanding the treatment planning prostate structure by 6 mm and subtracting the rectum with 10 mm expansion. The expansions were chosen empirically. Then, all CBCT images were registered to the corresponding SimCT images by maximizing the similarity within the defined ROI. Downhill simplex method was employed for optimization with full 6D rigid-body transformation. The pixel values corresponding to bone and air were also excluded from similarity calculations. After each registration, the calcification mismatch was recorded as a measure of prostate localization error. The registrations were repeated for each similarity metric. The nine similarity metrics investigated were: normalized cross-correlation (**NCC**), entropy of difference (**EOD**), mutual information (**MI**), correlation ratio (**CR**), sum of absolute difference (**SAD**), sum of squared difference (**SSD**), gradient correlation (**GC**), gradient difference (**GD**), and pattern intensity (**PI**).

Results: The absolute error means (\pm standard deviations) were $2.1(\pm 1.6)$ mm for **GD** and **GC**, $2.6(\pm 2.8)$ mm for **PI**, $3.9(\pm 4.3)$ mm for **NCC**, and $6.4 (\pm 8.0)$ mm for **MI**. The others showed over 10 mm mean errors. The directional errors of **GD** were $-0.1(\pm 0.5)$ mm, $0.1(\pm 1.4)$ mm, and $-0.2(\pm 2.1)$ mm in the left-right, anterior-posterior, and superior/inferior directions respectively.

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Conclusions: Among the investigated similarity metrics, registrations using **GD** and **GC** showed the most accurate prostate localizations on daily CBCT images.