**Purpose:** To compare different image-guidance (IG) strategies in the alignment of prostate cancer patients. Using data from patients that were treated with daily IG, the remaining set-up errors for several different strategies were retrospectively calculated.

**Method and Materials:** Alignment data from 74 patients treated with helical tomotherapy were analyzed, resulting in a dataset of 2252 fractions during which a megavoltage CT image was used for image-guidance. Given the daily positional adjustments, a variety of protocols differing in imaging frequency and methodology were studied retrospectively. The residual set-up errors on days imaging would not have been performed were determined for each protocol.

**Results:** As expected, systematic errors were effectively reduced with increasing imaging frequency. However, the random errors were unaffected. Even when image guidance was performed every other day with a running mean of the prior displacements, residual set-up errors exceeding 5 mm occurred in 24% of instances. This frequency increases to about 40% if setup errors larger than 3 mm are scored.

**Conclusion:** Set-up errors increased with decreasing frequency of image guidance. However, residual errors are still significant even at the 5 mm level if the patient is imaged every other day. This suggests that it is beneficial to use daily IG in the set up of prostate cancer patients during a course of external beam radiotherapy.

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