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Building tools for image-guided adaptive radiotherapy of bladder cancer

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Summary

One of the major factors limiting the precision of radiotherapy for bladder cancer is organ motion. The inter- and intra- fractional movement of the bladder wall can be as much as 3 cm due to changes in volume of bladder and adjacent organs. The clinical introduction of a Cone Beam CT (CBCT) device mounted on the treatment machine enables image-guided radiotherapy (IGRT) and image-guided adaptive radiotherapy (IGART) for bladder cancer to compensate for the rigid and deformable organ motion during radiotherapy.

The objectives of this thesis were to study the feasibility of lipiodol markers to enable image guidance of focal radiotherapy of bladder cancer and to develop tools for computer-aided generation of multiple-plans and plan selection for IGART of the whole bladder.

In **Chapter 2**, the behavior of lipiodol markers during IGRT for partial bladder treatment was investigated. The 15 analyzed patients had 2.3 marker injections on average. The lipiodol spots were well visible on CT and CBCT and had significant higher intensity than the surrounding bladder tissue. The lipiodol markers were automatically registered by a chamfer matching algorithm. Although lipiodol marker diffusion was negligible, significant relative movement of marker caused by tumor deformation was found, in particular for tumors with an elongated shape. Therefore, lipiodol markers are feasible to track bladder tumor position and deformation changes with online CBCT for the partial bladder radiation.

Since bladder volume change is a main driving force causing pelvic organ deformation, and to understand the nature of this deformation, in **Chapter 3**, a biomechanical model was constructed to simulate pelvic organ motion caused by bladder filling. A 3D finite element (FE) method was used to model the specific geometries of 10 healthy volunteers and simulate the interaction between the bladder and adjacent pelvic organs. The simulation results showed realistic anisotropic deformation of the bladder wall: the bladder became more elongated in the cranial and anterior directions with increasing bladder volume. The simulated bladder shapes agreed well with the real bladder shape (DICE overlap ranging from 0.79 to 0.93 for the ten volunteers). The prediction errors for the bladder wall position of all volunteers with 200 ml mean bladder volume changes were on average 0.31 ± 0.29 cm (SD). The accuracy of the bladder model depended on the magnitude of bladder volume change, and was mostly limited by inaccuracies in material properties and sliding between organs that had not been modeled. This FE based bladder model can potentially be used to improve IGART for the whole bladder, e.g. by generating multiple plans with different bladder volume from one planning image and predicting short-term bladder deformation.

Two factors, however, prevent clinical application of FE based bladder models: (1) the manual labor required to construct a FE model with high quality mesh and (2) long computation time needed to solve the FE equations. In **Chapter 4**, these issues were addressed by constructing a low-resolution voxel-based FE bladder model directly from the binary segmentation images. FE models with a low-resolution non-uniform hexahedral mesh were constructed on the same data set as the FE model with

tetrahedral mesh in Chapter 3. The algorithm directly generated regular hexahedral elements from the voxels of interest in binary segmentation images. The low-resolution voxel-based hexahedral mesh yielded comparable accuracy in bladder shape prediction (<1% difference in mean dice similarity coefficient to manual contours and <0.02 cm difference in mean SD of residual errors) and speeded up the computation time to 3 min as opposed to 1 hour for the standard tetrahedral mesh in Chapter 3. This approach makes clinical application of the FE method to model bladder deformation more feasible, for instance to generate multiple plans from one planning CT for IGART of the whole bladder.

After multiple plan generation, IGART of bladder cancer can be performed by online selection of the best fitting plan from this library of plans. The complexity of the patient anatomy and the low contrast of CBCT, however, make manual decision making at the treatment console immediately before treatment challenging, and very few clinics have therefore implemented this technique in practice. To facilitate the more widespread clinical implementation, computer aided plan selection is highly desirable. Therefore, in **Chapter 5**, an automatic bladder segmentation method using a patient-specific bladder model was developed for plan selection. Principal component analysis (PCA) was applied to bladder contours of the planning CT and the first five CBCT images to model the patient-specific bladder deformation patterns. The PCA modes were then used to deform the segmentation candidate to fit the bladder edge of online CBCT. The automatic bladder segmentation method yielded a 78.5% mean conformity index (CI) between manually and automatically segmented bladders, which was similar to the inter-observer variability of bladder delineation on CBCT. The agreement between plan selections made by manually and automatically segmented bladders was 77.6%, which was similar to the reported agreement between different observers. The segmentation method using a patient-specific model is robust and allows for fast and reliable automatic segmentation of the bladder on CBCT for selecting the optimal plan from a library.

Drawbacks of the segmentation method in Chapter 5 are that it can only work after the first five CBCT images are collected for each patient, and that it requires manual delineation of five bladder contours. In addition, it is not applicable for multiple plan ART strategies that start from the first treatment day. In **Chapter 6**, a bladder segmentation method using a population based bladder shape model combined with spherical harmonic expansion was developed. Contrary to the method in Chapter 5, the method in Chapter 6 uses a single generic bladder model for all patients instead of having to build a patient-specific model over and over again. The new method produced automatic bladder segmentation in a short time with moderate accuracy (70.5% mean CI overlap). In addition, a fast manual correction method was provided to correct those bladders that were poorly segmented. In this method, the user adds a small number of landmarks on the bladder surface which are subsequently used as extra constraints for bladder segmentation. This step improved the mean CI overlap of bladder segmentation to 77.7%, which was slightly better than the inter-observer variability. The semiautomatic strategy with manual correction resulted in 80.7% plan selection agreement, which was higher than the reported agreement between different observers. This method further improves the feasibility of computer aided plan selection technique for bladder IGART.

From this thesis, we can conclude that the injection of lipiodol markers into the bladder wall is a feasible method to track bladder tumors for IGRT of partial bladder. We succeeded in developing a biomechanical bladder model and bladder segmentation methods for online CBCT, which are useful tools for computer-aided plan generation and selection techniques for IGART of bladder cancer. Clinical implementation of the IGART of bladder cancer is the next step to be taken.