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## Articulated patient model in high-precision radiation therapy

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In modern high precision radiotherapy, changes in the anatomy of the patient over the course of treatment pose a major challenge. An accurate assessment of occurring anatomical variations is the key requirement to enable an adaptation of the treatment plan for ensuring a highly precise treatment. Comparison of commonly used deformable image registration shows large discrepancies regarding the quality of anatomical alignment, benchmarked on a common data pool. One of the main reasons is found in widely used transformation models, insufficiently reflecting the actual deformation behaviour of the underlying tissue. Thus, especially in the highly heterogeneous head and neck area, which is characterized by many organs at risk being in proximity to the tumor as well as posture changes induced by the interplay of several bones, an accurate assessment of anatomical changes is essential for a successful adaptive radiotherapy. A physically meaningful transformation model offering a high biofidelity is required to provide an accurate anatomical alignment in such area. In this work, a novel biomechanical deformation model based on kinematics and multi-body physics for the whole head and neck area is introduced to guarantee the representation of physically meaningful transformations.

The developed kinematic model is individually tailored to each patient as it is based on the delineated bones extracted from the computer tomography scan. It encompasses all bones relevant for head and neck cancer treatment, including bones of the proximal upper extremities, the shoulder girdle, cranial region, the rib cage and the vertebral column. Moreover, the model is designed to be easily extendible to other body regions. All bones are connected by ball and socket joints, which are automatically localized based on their individual geometries. A kinematic graph maintains the hierarchy of the connected bones across the whole skeleton to enable the propagation of local transformations to other body regions by inverse kinematics. Accuracy, robustness and computational efficiency of the kinematic model were retrospectively evaluated on patient datasets representative for typical inter-fractional variations as well as separately acquired image scans with large arms-up to arms-down posture changes. Using landmarks defined by multiple observers as reference, the overall mean accuracy of the kinematic model in reproducing postures in the image scans was found to be around 1 millimetre, which is settled slightly above the inter-observer variation. In detail, the assessed accuracy revealed potential for improvement regarding the automated positioning of the intervertebral joints in the region of the cervical spine. Due to the complex shape of the vertebrae, a relocation of the joint rotation centres towards the line connecting the centres of the intervertebral disks seems beneficial. Moreover, the use of ball and socket joints for the acromioclavicular joints has shown to be insufficient for mimicking the large arms-up to arms-down posture change due to the lack of representing translational offsets, observed in the image scans. The strong regularization of the permissible deformations in the skeletal anatomy leads to a higher robustness against conflicting input such as flawed or mixed-up anatomical feature points. Furthermore, such a physical-object-oriented transformation model requires even less input to describe meaningful deformations. With the

total degrees of freedom of the kinematic head and neck model limited to those specified by the joints, the computation of new arbitrary skeletal postures is achieved within less than 50 milliseconds.

With such efficient computation on the one hand and the strong regularization of deformations on the other hand, the kinematic model seems suitable for its application in a registration approach. In addition, it was demonstrated how the kinematic model can be successfully embedded into a registration approach as a transformation model to enable the fully automatic extraction of anatomical variations from image scans. This was accomplished by coupling the model to an extended simplex downhill optimizer and an overlap based similarity metric. The anatomy of pre-selected bones is aligned following a hierarchical optimization scheme.

In conclusion, the novel developed kinematic model guarantees a deformation modelling of high biofidelity and efficiency, thus promising an assessment of anatomical changes without the need of an extensive visual inspection of the results as otherwise expected. To date, successful application of adaptive radiotherapy especially for tumors in regions characterized by a high anatomical flexibility is hampered by a lacking reliability of conventional deformation models. While associated uncertainties can be compensated at the cost of extended safety margins for photon therapy, prevailing range uncertainties when using particles currently impede the treatment of tumors in such areas. The dissemination of the proposed kinematic deformation model into the clinics provides a way to lay the foundation towards broadening the spectrum of patients eligible for treatment with particles, carried out at the increasing number of particle therapy centres worldwide.