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**Evaluation of an adaptive radiation therapy workflow for
hypofractionated prostate cancer treatment based on synthetic
cone-beam computed tomography**

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Hypofractionated stereotactic body radiation therapy of prostate cancer has experienced an increasing use during the last years, requiring higher accuracy during every treatment fraction. This can be achieved by harnessing the full potential of daily acquired images such as cone-beam computed tomography (CBCT) which are currently limited by insufficient image quality. Hence, the aim of this work was to overcome this drawback by generating synthetic CT (sCT) from CBCT based on a novel cycle-generative adversarial network and validating the accuracy of the obtained pelvic synthetic CT model for the following core components of an online adaptive workflow: image quality, image segmentation and dose calculation. Having been priorly trained with an independent collective of prostate cancer patients' pelvic CT data, the neural network-based model allowed for a conversion of CBCT into sCT in 30 ± 3 s for 15 tested patients. It accomplished image uncertainties being close to the related treatment planning CT with mean errors of 5.4 ± 4.6 Hounsfield units. Afterwards, image segmentation was performed with a deformable image registration-based method that provided a structure set within 30 ± 5 s, showing a satisfying mean dice similarity coefficient of $85.9\pm 3.3\%$ for the prostate compared to manual references. Dose calculations on sCT were determined as sufficiently accurate with dosimetric deviations not exceeding $\pm 1.5\%$ and $\pm 1.0\%$ for target and organ-at-risk structures. Based on this validation, different adaptive replanning strategies were evaluated in respect of dosimetric benefits over conventional image-guided radiation therapy and regarding clinical feasibility. Three different replanning approaches on sCT ranging from segment aperture morphing-based warm start optimization with segment-weights and additional segment-shape modification to a full re-optimization were analyzed for the hypofractionated treatment regimen of the PACE-C trial for 32 patients each having 5 CBCT. All three replanning approaches were proven to gain substantial dosimetric benefits over the image-guided approach, especially for the planning target volume and rectum. Additional plan quality scoring revealed that dosimetric benefits were either focused on increasing target coverage or sparing organs-at-risk, thus guiding the decision on the most suitable adaptation strategy.

With all evaluated approaches being executable within 7.1 ± 1.8 min in one software environment, crucial steps towards the clinical implementation of online adaptive radiation therapy methods at CBCT-based C-arm linear accelerators were accomplished. If combined with techniques of online quality assurance and intrafractional tracking, the presented image conversion, segmentation and replanning approaches are ready for use in clinical routine.