Material and Methods: In this context, we addressed the in vitro response of colorectal cancer cell lines to X-rays in a radiotherapy setting, alone and combined with L-Asparaginase (L-ASNase), an antimetabolite drug used for acute lymphoblastic leukemia. L-ASNase degrades extracellular asparagine and glutamine, non-essential amino acids for healthy cells, but conditionally essential for cancer cells. Its use in non-haematological tumors is being investigated. Radiobiological data on several endpoints have been collected and integrated with the use of computational biophysical models, in particular related to cell cycle perturbations and to the quantification of the possible synergy.
Preliminary Results: The computational cell cycle model we developed reproduces the percentage of cells in different cell cycle phases and predicts cell growth. The administration of L-ASNase immediately after IR induces a reduced proliferative capability, delays DNA-damage response and reduces the capability to adhere and migrate. In perspective, we provide a model framework to potentially optimize time-delivery in treatment schemes, and our data suggest that a correctly timed combination of X-rays and L-ASNase treatments could represent an advantage in CRC therapy.

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MO-03.6
KNOWLEDGE BASED PLANNING: MODEL ITERATION AND PLAN COMPLEXITY FOR HEAD AND NECK PATIENTS

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Background: Knowledge-Based-Planning (KBP) models are becoming common tools in radiotherapy and are continuously updated and improved using iterative approaches. Purpose of this work was to verify how the iterative learning process used in training KBP models affects plan quality (i)dosimetrically, and (ii) plan complexity and deliverability.
Material and Methods: Twenty-seven VMAT H&N patients were selected. A first KBP model (KBP_M1) was built using clinical plans (CP-set) as training set. A second set of plans (RP1-set) was optimized using the KBP_M1 on the same patients. Another model (KBP_M2) was built using the RP1-set as training set. This was repeated iteratively creating other two sets of plans (RP2 and RP3) and a third model (KBP_M3). The four sets were compared in terms of target coverage and OARs sparing. Plan complexity was evaluated with the Modulation-Complexity-Score (MCS). A total of 108 plans was optimized and delivered. Gamma-Agreement-Index (GAI) was calculated with Dosimetry. GAI and MCS values were reported for each plan set.
Preliminary Results: In RP-sets mean OAR dose was reduced (10%-14%) maintaining an acceptable target coverage (i.e. V95%>95%). In the subsequent iterations the OARs mean dose reduction dropped below 1.2Gy for each iteration. The mean MUs increased by 5% for RP1 compared to CP and remained stable within 1% in subsequent iterations. Compared to the CP, RP-sets showed a significantly ($p<0.05$) lower MCS (i.e. higher complexity). With stricter criteria GAI decreased for the RP compared to the CP-set ($p<0.1$). Correlation between MCS and GAI was R2=0.641. The KBP model iteration does not reduce plan complexity and deliverability with respect to the first KBP model. The use of a KBP model allows a better OARs sparing, iterating this process may improve the dosimetric advantages. MCS and GAI were better for the clinical plans. When evaluating KBP models, Complexity Indexes could help in the deliverability of the plans.

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CLINICAL IMPLEMENTATION OF MRI-ONLY RADIOTHERAPY FOR PROSTATE TREATMENTS: COMMISSIONING AND PATIENT-SPECIFIC QA

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Background: The aim of this work is to present the validation process for clinical implementation of an MRI-only workflow using commercial systems and C-arm Linac (TrueBeam, Varian), to remove the need of a planning CT (pCT).
Material and Methods: This study included 35 patients with prostate cancer. All patients underwent CT and MR simulation (1.5 T, Ingenia MR-RT, Philips) using the same setup. Synthetic-CT (sCT) has been obtained via MRCAT (Philips) using a dedicate MR protocol. To evaluate the dosimetric accuracy of sCT, treatment plans were optimized on pCT and recalculated on sCT images (and vice versa) on Eclipse TPS (Varian), using AcurosXB calculation algorithm. Patient setup accuracy was assessed by performing a hybrid rigid registration (first automatic density based; then manually refined using contours of PTV, rectum and bladder) CBCT to sCT and pCT images, respectively. An offline QA has been carried out to verify both geometric and dose calculation accuracy using daily CBCT (applying an established site-specific procedure) in case the pCT is avoided.
Preliminary Results: Dosimetric accuracy showed on average <0.6% dose difference for target and OARs, with both the CT- and sCT-based plans. No statistically significant differences were found when recalculating the optimized plans on either sCT or CT. The difference between sCT- and CT- based patient positioning was always less than 1 mm in all directions, with mean values of 0.2 mm (AP), 0.1 mm (LL) and 0.4 mm (SI). The QA procedure confirm us the good agreement in terms of dose calculation accuracy. The mean Gamma Index passing rate (2%,2mm) was above 98% [90.5% - 99.8%] with a threshold of 80%, and above 96.5% [88.3%-99.7%] with a threshold of 20%. The MRI-Only workflow as implemented in our department has been demonstrated dosimetrically and geometrically accurate, and ready for clinical use. The dose accumulation process through sCT is still under investigation.

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INVERSE CONSISTENCY ERROR AS A VALIDATION METRIC FOR DEFORMABLE IMAGE REGISTRATION: IMPLEMENTATION RESEARCH WITH DIFFERENT COMPUTATIONAL PHANTOMS

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Background: This work aims to apply the Inverse Consistency Error (ICE) metric on deformable vector fields (DVFs) to evaluate the deformable image registration (DIR) spatial uncertainties in the context of dose warping applications.
Material and Methods: The ground-truth was provided by digital phantoms with known ImSimQA DVFs. The experimental design included the following steps: i) the ground-truth quality was assessed by evaluating the ICE of ImSimQA DVFs; ii) ICE maps were calculated from the RayStation DVFs obtained from phantom DIRs; iii) Ground-Truth Registration Error (GTRE) maps were computed composing the forward ImSimQA DVFs with the backward RayStation DVFs; iv) agreement between RayStation ICE and GTRE maps and correlation between ICE and Mean Distance to Agreement (MDA) have been evaluated on multiple ROIs segmented on anatomical digital phantoms simulating reliable Head-Neck deformations.
Preliminary Results: The ICE of ground truth DVFs was negligible. For Head-Neck phantom deformations, the maximum ground-truth ICE values were below the voxel size (3 mm), respectively 0.073 mm and 2.49 mm, and the maximum ICE of RayStation was always inferior to 3 mm in the clinically relevant regions. Significant correlation was found between the maxima values of ICE and GTRE (R2=0.8667), but the ICE 90th percentile all over the analyzed ROIs highlighted the presence of errors exceeding the voxel size and no correlation with MDA metric (R2=0.0012). For clinically reliable deformations the ICE allows an approximate evaluation of DIR spatial errors at the voxel level. ICE maps, overlaid on patient anatomy, could be used to support the decision maker to evaluate the DIR accuracy in patient-specific QA.

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COMPREHENSIVE COMPARISON OF FOUR AUTOMATIC TOOLS IN OAR SEGMENTATION FOR GYNAECOLOGICAL RADIOTHERAPY

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Background: Latest auto-contouring technologies rely on Deep Learning (DL) to solve one of the typical bottlenecks of radiotherapy workflow thanks to its promising classification performances. This study aims to compare MVISION (MV) and LIMBUS AI (LI) DL auto-contouring performances in cervical cancer (CC) treatments with respect to already known algorithms, Atlas Based Auto Segmentation (STAPLE) and Random Forest algorithm (RF).
Material and Methods: A mono-institutional consecutive series of 40 CC structure sets (rectum, bladder, bowel, femurs) were retrospectively selected. Twenty of them were randomly chosen to be used as atlas set for STAPLE and RF. The remaining 20 structure sets (testing set) were then auto-segmented by STAPLE, RF, MV, and LI and compared, setting manual contouring as the Gold-Standard. Performances have been tested by comparing the resulting 80 sets by means of the Dice Similarity Index (DSC) and the Hausdorff Distance (HD). The Wilcoxon-Mann-Whitney test was performed to assess statistical significance.
Preliminary Results: Rectum and bladder DL results showed a significantly increased DSC with respect to STAPLE and RF (e.g., MV vs STAPLE: DSC_Rectum +25,9%, DSC_Bladder +17,1%; LI vs STAPLE: DSC_Rectum +23,1%, DSC_Bladder +16,4%). STAPLE, RF, and LI bowel contours registered similar DSC and HD, while MVISION metrics were significantly affected by the different cranial delineation limit (e.g. MV vs STAPLE: DSC_Bowel: -18,8%). DL femur contouring resulted in lower indexes because of a different caudal length delineation. Lastly, the median contouring time per structure set was 21,9 minutes [16,8–36,2], 21,0 minutes [18,1–24,7], 0,7 minutes [0,5–1,1], and 1,1 minutes [0,8–1,3] for STAPLE, RF, MV, and LI, respectively. These preliminary results proved the DL higher accuracy in most of CC OARs contouring. Furthermore, DL could significantly reduce contouring time consumption and this time impact has to be evaluated by means of successive manual correction times. These preliminary results will be confirmed on a larger and multi-institutional patient population.

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THREE YEARS OF CLINICAL EXPERIENCE WITH A TRANSMISSION DETECTOR FOR IN VIVO VERIFICATION IN SBRT VMAT RADIOTHERAPY

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Background: Aim of this work is to describe our three years experience in applying in vivo verification in Volumetric Modulated Arc Therapy (VMAT) Stereotactic Body Radiation Therapy (SBRT) treatments using a commercial transmission detector (TRD)
Material and Methods: The Delta4 Discover TRD (ScandiDos, Uppsala, Sweden) is a fluence measurement device designed to monitor dose and MLC position during every treatment fraction. After acceptance and first analysis, the device was introduced 3 years ago into clinical routine for verification of SBRT treatments. 70 SBRT VMAT treatments were analysed. Plans were measured in pre-treatment QA with Delta4 Discover paired to Delta4 Phantom+. Furthermore, treatments were verified with the Delta4 Discover at each daily fraction, for a total of more than 800 in vivo measurements. Dosimetric differences were studied in terms of median dose difference and 2%-2mm global dose-γ passing rate. MLC positioning was evaluated in terms of leaf deviation and 1mm-1° MLC-γ passing rate.
Preliminary Results: The mean leaf deviations for all arcs and leaf banks showed an average value of 0.2 ± 0.15 mm. The average value of the percentage difference in median dose for all VMAT arcs is 0 ±0.5%. 95% of the measured arcs met the criteria for the action level established for dose-γ pass rate (98%). About 10% of measurements showed a value lower than the tolerance level defined for MLC-γ pass rate (93%). Each plan outside the tolerance levels was analyzed and, if appropriate, compared with predefined action level. The study confirms that the transmission detectors can be implemented in the clinical routine with a reduced impact on the workflow and can be effective in detecting delivery errors, so preventing the severe consequences they could have on patient.