lower dose in the higher dose regions as well. **Conclusion:** This work indicated the feasibility of outcome-based planning optimization algorithm for reducing risk of injury and improving chance of recovery from xerostomia. This was done by reducing dose to the salivary glands and oral cavity while maintaining target coverage.

This study is funded by ROI institute and Johns Hopkins Radiation Oncology Discovery Award.

TH-A-SAN2-07

Deep-Learning Based CBCT Image Correction for CBCT-Guided Adaptive Radiation Therapy

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Purpose: Adaptive radiation therapy (ART), where dose delivery is changed daily based on patient setup and anatomy, has been a goal in most clinics since the introduction of cone-beam CT (CBCT) since its introduction to the radiation therapy workflow. However, the large scatter-to-primary ratio typical of CBCT leads to degraded image quality and the loss of quantitative information in CBCT images. In this work, we propose a deep-learning method to correct CBCT artifacts and restore HU levels to those typical of planning CT images. **Methods:** The proposed method learns a mapping from a CBCT HU distribution to a planning CT HU distribution. The powerful cycle-consistent generative adversarial network (cycle-GAN) framework is used. During training, a generator is continually optimized to produce corrected CBCT (CCBCT) images, while a discriminator is optimized to identify the differences between a CCBCT image and a planning CT image. As these two are pitted against each other, convergence of the overall network optimization is improved. Compared with a GAN, a cycle-GAN includes an inverse transformation from CBCT to CT images, which constrains the model by forcing calculation of both a CCBCT and a synthetic CBCT. The proposed algorithm was evaluated using 24 brain patient datasets and 20 pelvis patient datasets. **Results:** Overall, mean absolute error, peak signal-to-noise ratio, normalized cross-correlation and spatial nonuniformity were 18 HU, 37.18 dB, 0.99 and 0.05 for the proposed method, improvements of 45%, 12%, 1%, and 65%, respectively, over the CBCT image. The proposed method showed superior image quality as compared to a conventional scatter correction method, reducing noise and artifact severity. **Conclusion:** The authors have developed a novel deep learning-based method to generate high-quality corrected CBCT images. With further evaluation and clinical implementation, this method could lead to quantitative adaptive radiation therapy.

This research is supported in part by the National Cancer Institute of the National Institutes of Health under Award Number R01CA215718 (XY).

TH-A-SAN2-08

Vasculature Anatomy Change in Nonsmall Cell Lung Cancer Patients Post Radiation Therapy

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Purpose: To investigate the impact of radiation dose to the lung on pulmonary vasculature anatomy and analyze the response dependence on fractionation method. **Methods:** A cohort of 32 patients were recruited as part of an IRB approved clinical trial analyzing pulmonary function following radiation therapy. Jerman vesselness filtration was performed on two sets of two 4DCTs taken before and 3 months post-RT, respectively. The filtration produced a vesselness map indicating the probability of a vessel being located in each voxel of the 4DCT. Using the known voxel size, an integration over the entire lung mask was taken to analyze the predicted volume of vessels in the lung at each timepoint. Additional analysis was done to compare the relationships between predicted vessel volume with the treatment fractionation scheme and PTV volume respectively. **Results:** A statistically significant ($P = 0.017$) decrease in vasculature was observed between pre-RT and 3-month follow-up scans for patients treated with standard-fractionation. On average, these patients experienced a 4.7 $\pm$ 0.07% decrease in vasculature volume. The hypo-fractionation group did not experience significant changes in vasculature 3 months post-RT. The PTV volume showed weak correlation to the change in predicted vessel volume ($R^2 < 0.04$). **Conclusion:** This work indicates anatomical reduction in pulmonary vasculature at 3 months following standard-fractionation RT. Results from 6 and 12-months post RT imaging and correlation with contrast perfusion scans are needed to demonstrate these changes are permeant and correlated with changes in lung perfusion function. Ultimately, the hope is that this work will aid in developing a perfusion/dose response model derived from a 4D noncontrast scan that can be used for functional avoidance radiation therapy.

R01 CA166703.

TH-A-SAN2-09

Mid-Treatment Gd-EOB-DTPA-Enhanced MRI and Interleukin 6 Cytokine as Biomarkers of Radiation-Induced Liver Toxicity in Metastatic Liver Patients

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Purpose: In the era of precision medicine and personalized radiation treatment (RT), there is an ever-growing need to find predictive biomarkers of treatment response in patients. Here we investigate the potentials of using mid-treatment MR images and inflammatory cytokines as biomarkers of liver toxicity. **Methods:** Eleven intrahepatic metastatic patients who had proton stereotactic body radiotherapy (SBRT) to the liver lesion were retrospectively analyzed. Two Gd-EOB-DTPA (a hepatobiliary-directed contrast agent)-enhanced MR scans as well as three inflammatory cytokines (interleukin 6 [IL-6], IL-8, and tumor necrosis factor α [TNF- α]) were acquired during the RT course. Deformable image registrations were done among mid-treatment (fx4 and 5) MR images and the planning CT. MR signal changes and delivered dose were then calculated for each voxel. Mid-treatment changes in the expression of the cytokines were calculated with respect to the pretreatment baseline. Liver toxicity was assessed at 3 months post-RT, using Child-Pugh (CP) and ALBI score. Patients were subsequently classified into high-risk (HR) and low-risk (LR) groups. Statistical analysis was performed to compare the changes in the MR signals and cytokine expressions between these groups. **Results:** On average, high-risk patients had lower high-dose/low-dose mid-treatment signal changes (i.e., decreased/increased signal in high-dose/low-dose). In CP classification, there was a significant difference in MR signal change between two group means (0.61 and 1.04 for HR and LR groups; $P = 0.005$). The ALBI classification showed more pronounced difference (0.61 vs 1.11, $P = 0.002$). High-risk patients also showed larger IL-6 changes during their treatment (86% vs 0.33%, $P = 0.01$). **Conclusion:** Using mid-treatment MR scans and interleukin 6 as biomarkers, it is possible to predict the risk of acute liver toxicity, already during the RT course. This biomarker information can be potentially used for adaptive planning and RT plan personalization.

TH-A-SAN2-10

Adaptive Margins with An Early Warning System for Motion-Tracking Errors in Liver SBRT

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Purpose: To estimate patient-specific PTV margins for liver SBRT with motion-tracking based on a dry-run session prior to planning (mock treatment), and provide warnings when relatively large errors are predicted during treatment. **Methods:** Using log file data for 118 courses (104 patients), 22 features from their first Synchrony model (emulating the mock treatment) including motion-compensation errors are calculated. A support vector machine (SVM) classifier is trained using mock data to predict root-mean-square errors for the subsequent treatment models to facilitate patient-specific margins. For the warning system, the only data used is what is available to the CyberKnife Synchrony system up until the most recent X-ray image is acquired. These data include all manual user interactions such as removing invalid model points. 56 features are calculated including statistics concerning morphological LED time-trace features. A warning system is created via a linear SVM classifier, trained with mock data and X-ray data to predict high errors (≥ 3 mm) during the treatment. The classifiers are evaluated by confusion matrix and receiver operating characteristic metric. **Results:** The mock model gives an accuracy of 89% ± 9% (5-fold cross-validation) to predict if root-mean-square errors for subsequent treatments are above 2 mm for all courses. The variation of errors, linearity between internal target motion and external marker motion, and target motion amplitudes from mock data are important for classifying two groups (errors ≥ 2 mm and <2 mm). For 84% of the time, the warning system can give warnings of an incoming error above 3 mm evaluated via group 5-fold cross-validation. **Conclusion:** The mock data can be used to predict errors to provide patient-specific margins prior to planning. It is possible to build a warning system to predict when errors above a predefined threshold will occur during the treatment.

This work was supported by the Ontario Consortium for Adaptive Interventions Radiation Oncology, a research grant from Accuray Inc., CA, Ontario Graduate Scholarship, and John Lyndhurst Kingston Scholarship.

TH-A-SAN2-11

Real-Time 3D Scintillation Imaging Enables Rapid End-To-End Verification of Online Adaptive Replanning On MR-Linac

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Purpose: Online adaptive replanning (OARP) in magnetic resonance guided radiotherapy offers unprecedented ability to improve beam targeting precision. The OARP workflow cannot accommodate measurement-based patient-specific quality assurance (QA). Instead, the re-optimized plans are verified against an independent Monte Carlo-based dose calculations. Due to the complexity of the re-planning process, a comprehensive end-to-end verification of software QA is pivotal. The purpose was to assess performance of volumetric scintillation imaging system for end-to-end OARP QA as a part of real-time scintillation-based 3D dosimetry solution. **Methods:** A multitarget plan was delivered by ViewRay MR-linac (0.34T, 6MV FFF) to a water-based scintillator phantom (1 g/L quinine sulphate, ø127 × 300 mm). Intensified, gated CMOS camera recorded projected scintillation images through the base of the phantom at 20 Hz framerate. Cumulative scintillation image served as surrogate to the projected dose distribution. First, gamma pass-rate was evaluated between the measured scintillation image and CT-based dose plan. Second, MR image of the phantom was recorded by MR-Linac and used for dose calculation with an artificially modified structure set. The adapted MR-based plan was delivered to the phantom and gamma pass-rate between scintillation image and MR-based dose image was evaluated. Finally, 3D geometrical beam volume was reconstructed from scintillation images and multileaf collimator position logs in order to allow 3-dimensional gamma and dose volume histogram (DVH) analysis. **Results:** 2D gamma pass-rate of the measured dose distribution compared against the calculated CT-based dose was 96% at 3%/3 mm criteria. The pass-rate of MR-based optimized plan dropped to 94%. The majority of nonpassing pixels were found in the sub-surface area, most likely caused by an electron-return effect. **Conclusion:** Scintillation images of both original and re-planned deliveries agreed with treatment planning system calculations. Scintillation surrogated dose real dose distribution and enabled high-resolution, rapid QA of online adaptive replanning, as well as a 3D DVH comparisons.

This work has been sponsored by NIH research grant R01EB023909. B Pogue is the president and co-founder of DoseOptics LLC. P Bruza is the principal investigator in SBIR subaward B02463 (prime award NCI R44CA199681, DoseOptics LLC). This work was not financially supported by DoseOptics.

TH-A-SAN2-12

A Framework of Automatic Contour Quality Validation for MRI-Guided Online Adaptive Radiation Therapy

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Purpose: Rapid and accurate segmentation is essential for online adaptive radiation therapy (OART). This study aims to develop a framework to automatically evaluate contour quality using quantitative MRI texture and shape features for MRI-guided OART. **Methods:** The framework includes: (a) preprocessing images, (b) extracting texture and shape features on a slice-by-slice basis in the contours to be checked and feature changes between 4-mm inner/outer shells and a core region, (c) ranking all the features using a recursive feature elimination method and selecting top-ranked features, and (d) building and testing supervised classification models for contour validation. A variety of contours of the pancreatic-head generated on 22 sets of T1-weighted noncontrast MRIs of 11 patients was utilized to demonstrate the framework. Three sets of contours were created: (a) ground truth, (b) auto-generated contour using deformable image registration, and (c) modified contour from that in (b). The contour on a slice from set #2 or 3 was labeled as accurate if Dice similarity coefficient ≥ 0.85, mean distance to agreement ≤ 1.5 mm, and 95% of distance to agreement ≤ 5 mm, as compared to the ground truth. A total of 754 accurate and 650 inaccurate contour slices were used, where 80% of these contour slices were used for the model training and 20% for testing. **Results:** A total of 132 features were extracted from each slice and ranked. The top-ranked 30 features were selected for model building where 12 different classification models were trained and compared. The best performing model yielded average sensitivity of 91% and specificity of 89% on the testing data after 5-fold cross-validation. **Conclusion:** The newly-developed framework can automatically identify accurate and inaccurate contours on a slice-by-slice basis on MRI with high sensitivity and specificity, thus, can be implemented for quick contour check in MRI-guided OART.

Multi-Disciplinary Scientific Session — Room 225BCD

Deformable Image Registration

TH-A-225BCD-01

Integrating Computer Vision and Nonlinear Optimization for Automated Deformable Registration of Three-Dimensional Medical Images

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Purpose: Deformable image registration (DIR), is a challenging task with many important clinical applications. Commonly used DIR techniques chiefly rely on nonlinear optimization. Various semi-dense feature-based methods drawing inspiration from mammalian systems as the basis for 2D visual processing have been implemented for automated wide baseline registration and object detection applications with great success. Extension to the 3D case could be adapted, in theory, to allow precise semi-dense global optimization. **Methods:** 3D image features were detected, oriented, and described using modified biologically-inspired 2D computer vision algorithms extended to the 3D case. Features were matched using Euclidean distance thresholded by first-to-second best distance ratio, followed by topological analysis. This algorithm was hybridized with a second stage normalized correlation-based nonlinear optimizer, and benchmarked with publically available 4D computed tomography (CT) datasets against published results for commercial packages. Further characterization was performed with actual clinical 3D CT images containing truncated data and very large deformations. A method for estimating registration error in the absence of ground truth was derived. **Results:** The feature-based algorithm reliably and repeatedly detected distinct semi-dense 3D image features with sub-voxel localization accuracy and with high matching rates. The hybrid algorithm significantly improved landmark displacement error on the benchmark cases (mean improvement 0.91 mm, range −0.13 to 4.78, $P < 0.00001$). Difficult clinical cases showed significant qualitative improvements. **Conclusion:** The hybrid algorithm, dubbed Constrained Robust Affine Feature Transform (CRAFT), incorporates paradigms from various computer-vision techniques to combine aspects of the human visual pathway with well-characterized nonlinear optimization methods to automate general deformable registration with unprecedented robustness. This hybrid technique is able to estimate registration confidence and can serve as the basis of machine perception of 3D medical images for machine learning.

This work was performed at the University of Cincinnati. The author is a founder of Pymedix, Inc and serves as Chief Technology Officer.