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Purpose/Objective(s): Volumetric modulated arc therapy (VMAT) for lung Stereotactic body radiation therapy (SBRT) has been used effectively in combination with flattening filter-free (FFF) beams with higher dose rates. Robust optimization provides significantly more robust dose distributions to targets and organ at risk (OAR) than the planning target volume (PTV)-based optimization. The fluence of an FFF beam may influence the dosimetric outcome for lung cancer, because a secondary build-up and lateral disequilibrium may affect target coverage. This study aims to assess the differences between 6X- and 10X-FFF beams using PTV-based and robust optimizations for lung cancer patients**.** Lung VMAT SBRT plans incorporating PTV-based and robust optimized plans using 6X- and 10X-FFF beams were generated and evaluated for perturbation doses to the internal target volume (ITV) and lung.

Materials/Methods: Ten lung cancer patients with a breath-holding were selected. All VMAT plans were contoured, optimized, and calculated based on a breath-holding CT image dataset used in the treatment planning system. Four VMAT plans were generated for each patient; namely, an optimized plan based on the planning target volume PTV margin and a second plan based on a robust optimization of the ITV with setup uncertainties, each for the 6X- and 10X-FFF beams. Both optimized plans were normalized by the percentage of the prescription dose covering 95% of the target volume ($D_{95\%}$) to the PTV. The dose prescription was 42 Gy with 10.5 Gy per fraction. All optimized plans were evaluated using perturbed doses by specifying user-defined shifted values from the isocenter. The ITV $D_{99\%}$ and lung doses were evaluated.

Results: As for the robust optimized plans comparison, the $D_{99\%}$ doses to the ITV exhibited statistically significant differences for the 6X- and 10X-FFF beams ($p = 0.010$). The mean dose, V_{20Gy}, and V_{5Gy} to the lung for the 10X-FFF beam were increased by 9.6% ($p = 0.002$), 15.0% ($p = 0.004$), and 14.6% ($p = 0.004$) on average, respectively. The average perturbed $D_{99\%}$ doses to the ITV, compared to the nominal plan, decreased by 7.8% (6X-FFF) and 6.5% (10X-FFF) for the PTV-based optimized plan, and 7.3% (6X-FFF) and 5.8% (10X-FFF) for the robust optimized plan. The standard deviation of the $D_{99\%}$ dose to the ITV for the PTV-based plan with the 6X- and 10X-FFF beams were 163.6 and 158.9 cGy, respectively. The standard deviations of $D_{99\%}$ to the ITV for the robust optimized plan with the 6X- and 10X-FFF beams were 138.9 and 128.5 cGy, respectively.

Conclusion: 10X-FFF beam applied under a robust optimized plan for lung SBRT cancer treatment using a breath-holding technique is a feasible method, despite a slightly higher dose to the lung, compared to a 6X-FFF beam.

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Automated Localization of Lung Nodules from Chest X-rays With Deep Neural Networks

B. Maksudov,[1] S. Kiselev,[1] M. Kholiavchenko,[1] T. Mustafaev,[1,2] R. Kuleev,[1] and B. Ibragimov[1,3]; *[1]Innopolis University, Innopolis, Russian Federation, [2]University clinic of Kazan Federal University, Kazan, Russian Federation, [3]University of Copenhagen, Copenhagen, Denmark*

Purpose/Objective(s): Lung cancer constitutes more than 20% of all cancer deaths in the Russian Federation. About 34.2% of these cases were diagnosed late, which significantly reduces the life expectancy of patients. Chest X-rays are the main screening method for lung cancer in Russia. The small size of nodules and difficult localizations are the reasons why nodules are often missed during routine scanning. The aim of this study is to employ modern deep learning tools for the localization of nodules in chest X-Rays.

Materials/Methods: We assembled a database of chest X-rays, where each X-ray with nodules was accompanied by a mask with Gaussian-shaped nodule heatmaps. We developed a U-net like network for the reconstruction of the nodules heatmaps from original X-rays. Considering the fact that nodules occupy an extremely small part of X-ray, and are often hidden behind clavicles or heart, we also developed a new cost function that computes the mean absolute error between nodule heatmaps and the model output giving more value to area in close proximity to the nodule.

Results: The model was applied to detect nodules from X-rays from a publicly-available JSRT database. The database contains 154 images with nodules. All training samples were heavily augmented using spatial augmentations such as random scale, rotations, flips as well as pixel-level augmentations such as blur and contrast change. We generate candidate nodule locations by extracting connected components from the network output. A 67.8% detection rate with an average of 4 false positives per correctly recognized nodule has been achieved. Our model also achieves a 7 mm error in terms of average distance, between centers of a candidate and a true nodule. Our numbers are comparable or superior to the values reported in the literature.

Conclusion: We demonstrated the potential of deep neural networks to address an important topic of detection of lung nodules from routine X-ray scans for assisting radiologists in the diagnosis of lung cancer.

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Disentangling Contributions from Heart and Lung Anatomical Substructures to Radiation Induced Toxicities: Characterization of Spatial Properties of Dosimetric Data for Voxel-Based Analyses

G. Palma,[1,2] S. Monti,[1] A. Stanzione,[3] T. Xu,[4] M. Durante,[5] R. Mohan,[6] Z. Liao,[7] and L. Cella[1,8]; *[1]National Research Council, Institute of Biostructures and Bioimaging, Napoli, Italy, [2]Hassisto Srl, Napoli, Italy, [3]University of Naples "Federico II", Department of Advanced Biomedical Sciences, Napoli, Italy, [4]Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, [5]GSI Hemholtz Center, Darmstadt, Germany, [6]Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, TX, [7]University of Texas MD Anderson Cancer Center, Houston, TX, [8]National Institute for Nuclear Physics, INFN, Napoli, Italy*

Purpose/Objective(s): Voxel-based analyses (VBAs) in Radiation Oncology have been introduced to evaluate local dose-response patterns via voxelwise statistical analyses on the spatially normalized dose maps (DMs) of patients, classified according to a given outcome [Palma *et al.* 2020]. However, the intrinsic spatial properties of the considered DMs may impact on the dosimetric signatures that can be inferred for a specific outcome. This is particularly relevant for endpoints related to highly interacting organs or substructures, as the cardiopulmonary system. Here, we proposed a strategy for a comprehensive characterization of intrinsic dataset features that impact on VBA results.

Materials/Methods: We spatially normalized the DMs of 178 lung cancer patients treated with photon or proton therapy. The homogeneity of VBA statistical power in different regions is directly related to the uniformity of voxelwise mean μ and standard deviation σ of DMs, which were evaluated across the patients. The spatial correlation between the dose delivered to distinct anatomical subregions directly affects the spatial resolution of the significance map for a given effect. A short correlation length in the DMs ensures that small-scale phenomena could in principle be captured by the VBA. The spatial independence of the irradiation was explored via 2 different analyses: the probabilistic independent component analysis (PICA) [Beckmann & Smith 2005], which blindly infers the number of statistically significant independent maps (model order) that generate the input DMs; and the connectogram [Irimia *et al.* 2012], which represents the relevant links between each pair of substructures according to the Spearman correlation (Rs) between the related mean doses. We analyzed the cardiac substructures defined according to the XCAT digital phantom [Segars *et al.*2010], and the lung subregions segmented by a radiologist.

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