SP-0461 Spatial dose signature in lung or head and neck radiation induced morbidity

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Abstract text

The risk of radiation-induced morbidity (RIM) in patients treated with radiation therapy (RT) for lung or head and neck (HN) cancer is historically estimated by condensing the 3D dose distribution into a monodimensional dose-volume histogram (DVH) that disregards spatial information of the dose. Increasing evidences, however, suggest that a voxel-based approach (VBA) allows to identify unprecedented correlations between RIM and local dose release, and accordingly unveils the spatial signature of radiation sensitivity in inhomogeneous organs – such as the lungs – or in composite regions – such as the HN district.

A first key issue of any kind of VBA (ranging from neuroimaging to dose map processing) is represented by the spatial normalization of the analyzed patients to a common anatomical reference. In the context of lungs or HN RIM analyses, several studies showed the excellent performance of the inter-patient diffeomorphic log demons image registration, which allows for a robust match of anatomical structures both from a pure geometrical point of view and in terms of dose-organ overlap (see [Palma *et al.*, Int J Radiation Oncol Biol Phys 2016] for the lungs and [Monti *et al.*, Sci Rep 2017] for the HN). This appears particularly noteworthy in the HN district, due to the high number of elusive structures, whose contouring may be challenging even for an experienced radiologist. Of note, the B-spline parameterization approach was also exploited in the spatial normalization of a cohort of lung cancer patients included in a survival analysis [McWilliam *et al.*, Eur J Cancer 2017].

Next, the voxel-based statistical analysis to test regional dosimetric differences between patients with and without RIM can be performed according to different schemes, ranging from a classical voxelwise *t*-test to several methods counteracting the multiple comparison problem inherent in the task. In particular, our previous researches showed that a non-parametric permutation test [Holmes *et al.*, J Cereb Blood Flow Metab 1996] based on the Threshold Free Cluster Enhancement [Smith & Nichols, NeuroImage 2009] of a maximum-*T* statistics allows for an excellent compromise between the sensitivity of the analysis and the control over imagewise Type I errors.

The application of this pipeline to a cohort of Hodgkin Lymphoma survivors for the study of late radiation-induced lung damage led to the discovery that a significantly higher dose (~ 6 Gy) was consistently delivered to patients with RIM in voxel clusters near the peripheral medial-basal portion of the lungs in low dose parenchymal regions.

Analogously, in a cohort of patients treated for HN cancer, two voxel clusters located in correspondence of the cricopharyngeus muscle and cervical esophagus were found to receive a significantly higher dose (~ 48 Gy) in patients developing severe radiation-induced acute dysphagia. Interestingly, in both cases, the mean dose released to the significant clusters was found to be a good classifier of RIM (AUC of 0.7-0.8).

An effort to put the VBA in a clinical perspective has led to the definition of an avoidance region in correspondence of the significant clusters. In particular, Monti *et al.* proposed to constrain the mean dose to clusters not to exceed the first percentile of the corresponding doses received by RIM patients.

It should be stressed, however, that neither the described voxel-based dose difference analysis nor the criterion proposed for the avoidance regions provide any insight on actual Normal Tissue Complication Probability (NTCP) models including full dose spatial info. In this respect, we are currently defining a new formalism to fill this gap and to develop a space based NTCP (SpNTCP). An explorative implementation of the developed formalism has been trained on the above cohort of thoracic patients, with encouraging results measured by an AUC of 0.72, compared to the AUC of 0.61 achieved by a traditional Lyman-Kutcher-Burman (LKB) model.

In summary, both grounds of Treatment Planning expediency in complex regions and even more evidences of inhomogeneous radiosensitivity of organs recommend a shift in perspective on the way we should deal with dose analysis of RIM in the future. In this sense, we believe that a prompt effort at the standardization of the VBA approaches should be warranted, in order to foster the spread of these tools in the Radiation Oncology community, following the virtuous example of neuroimaging.

Symposium: Dose mapping and dose accumulation

SP-0462 Do the current software solutions serve our needs?

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Abstract text

Accurate and consistent segmentation of tumor and normal tissues is essential for dose mapping and dose accumulation in radiotherapy (RT) in order to avoid sub-optimal treatment plans with systematic dose errors throughout the treatment fractions. The performance of commercial segmentation solutions has improved given the access to atlas-based approaches, and may further improve using deep learning segmentation. Residual segmentation inadequacy beyond what is clinically acceptable can, however, still be expected, but few efforts have investigated the consequence of this in terms of dose and associated dose-response relationships. In this presentation, published results from commercial solutions on segmentation, dose mapping and dose accumulation in central tumor sites are summarized. In addition, the segmentation performance of two atlas-based software solutions is compared to ground-truth segmentations, and the magnitude of volume/distance disagreements with respect to the ground-truth segmentations are studied in 'dose space' including their potential impact on generated dose-response relationships. Lastly, not yet commercially available post-processing steps to improve segmentation performance, and results from deep learning segmentation are being discussed.

SP-0463 Dose mapping from the target point of view

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Abstract text

In this talk relevant aspects for dose accumulation/ mapping for target volumes will be discussed. The interplay of registration errors and dose gradient will be explored as well as its relevance to mapping dose distributions for target volumes; e.g., uniform irradiation vs. dose painting. In particular for tumors that change volume, we will demonstrate that using non-rigid registration is not always the best approach since different type of tumor changes happen, i.e. tumor

erosion vs. tumor shrinkage. Furthermore, even if the registration is perfect, radiobiological effects such as tumor hypoxia should be accounted for. Multidisciplinary research is essential to further study and develop methods for dose accumulation to properly support outcome modeling, adaptive radiotherapy and reirradiation planning.

SP-0464 Dose mapping from the organ at risk point of view

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Abstract text

In this talk, relevant aspects for dose accumulation/ mapping, from the organ at risk point of view, will be discussed. The interplay of registration error and dose gradient will be explored as well as its relevance to mapping dose distributions for organs at risk. In particular, we will explore how organs at risk can change shape during treatment, both intra- and inter-fraction and that using non-rigid registration is not always the best approach, i.e. tissues that show elasticity or for sliding tissues. Even though dose mapping is not perfect in these situations we will explore the pro's and con's of using such information in an online adaptive workflow. Finally, we will move from intra-patient dose mapping to inter-patient dose mapping and ask the question, can we use dose mapping for organs at risk, across large cohorts of patients, to inform how to better treat future patients? This approach allows us to retain spatial information of the dose distributions and has the power to highlight sub-regions of organs at risk which show a stronger dose-response relationship.

Symposium: Stereotactic RT and radiosurgery

SP-0465 SBRT in the management of oligometastatic disease

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Abstract text

Stereotactic body radiotherapy (SBRT) has emerged as a novel treatment modality for patients with oligometastatic disease. Historically, the management of metastactic disease focused on systemic treatment given with palliative intent. Over the last decade, new developments in systemic and targeted biologic cancer therapies have markedly improved patients' prognosis and lengthened the overall survival. In light of this, aggressive local management of metastases including surgical resection, radiofrequency ablation and SBRT is becoming increasingly important, particularly in the oligometastatic setting where the disease may not yet have developed the ability to broadly disseminate.

SBRT is a treatment approach utilising advanced highly precise radiotherapy techniques to deliver ablative doses of radiation to tumours. This allows for local dose escalation at the site of the targeted tumours while sparing surrounding normal tissues. The wider use of SBRT in the treatment of oligometastases is supported by numerous comprehensive clinical studies. Evidence has been gathered suggesting that SBRT for oligometastases is safe and effective, with high local control rates ranging from 70% to 90%. With a robust body of data to inform treatment decisions, the radiation oncology community can ensure that SBRT is used to provide optimised outcomes for patients with oligometastases. This presentation aims to discuss the clinical rationale and evolving evidence of using SBRT in the management of oligometastases. Examples on clinical implementations of SBRT in treating oligometastases of different tumour types and anatomical locations will be presented.

SP-0466 Intracranial lesions and dedicated Linac radiosurgery

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Abstract text

This presentation will start with a general introduction of intra-cranial stereotactic radiotherapy (SRT) and stereotactic radiosurgery (SRS). A historic overview will be presented how SRT/SRS evolved from a frame-based to a frameless radiation technique. In this overview the currently available dedicated SRT/SRS treatment units will be reviewed including the robotic CyberKnife and the GammaKnife systems. An important aspect of SRT/SRS is the precision that is required to deliver safely high doses in one or a limited number of treatment fractions. Common sources of error that can occur in each part of the treatment chain will be stated and mitigation measures will be discussed. In particular, the role of margins in SRT/SRS to account for these errors will be elucidated. Treatment plan generation, prescription and reporting can differ significantly from conventional fractionated radiotherapy. Those differences will be discussed. This will be done in the context of the recent ICRU 91 report on Prescribing, Recording, and Reporting of Stereotactic Treatments with Small Photon Beams.

SP-0467 Stereotactic Radiotherapy for Benign Disease

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Abstract text

The majority of our work in the field of Radiation Therapy is the treatment of oncology patients with malignant disease, however, radiation therapy can also be a valuable tool in the treatment of a variety of benign conditions. Historically radiation therapy has been commonly used for this purpose, often with a low dose approach, nonetheless there are some indications for high dose RT in non-malignant scenarios. Due to recent developments in technology, along with the advent of widespread availability of stereotactic techniques, we can now deliver with great accuracy, highly conformal dose distributions. This approach may be particularly appropriate when irradiating a benign condition as minimal exposure is key.

This talk will provide an overview of the current indications for SRS/SBRT in benign disease with a focus on the commonly treated intra-cranial sites. The role of the RTT will be examined in relation to the non-cancer patient pathway. Late toxicity and quality of life following SRS for benign disease will be examined. Finally, some novel potential future directions of stereotactic radiotherapy for benign disease will be highlighted.