Exploring the correlation between 3D spatial dose distribution and toxicity in normal tissue

Radiotherapy efficacy is often limited by normal tissue toxicity. Standard models to estimate Normal Tissue Complication Probability (NTCP), such as Lyman-Kutcher-Burman (LKB), often rely on parameters derived from the dose-volume histograms (DVHs) which consider organs and tissues to be completely homogeneous with equal sub-volume radiation sensitivities. As a result, they neglect any potential variation in radiosensitivity within the organ(s) at risk. Therefore, we adopted an atlas based approach for identifying potentially critical anatomic structures utilizing the full spatial dose distribution [1, 2]. This was achieved by deforming 3D dose distributions from a patient cohort onto a single “Reference Patient” as illustrated in Fig 1.

Fig. 1. The workflow diagram summarizes the steps to construct spatially co-registered dose maps from a patient cohort onto a “Reference Patient”.

In order to demonstrate the validity of this approach, we analyzed a cohort of 37 right-sided H&N cancers of the oropharynx regarding the endpoint of trismus (12 pts with Grade >=1). CT-scans, RT-Structs, and 3D prescription doses were deformed onto a reference patient selected arbitrarily. Model selection based on DVH parameters, derived from the four pairs of mastication muscles, using cross validation leave-one-out (LOO) techniques in DREES showed that a two parameter model as the most predictive model yielding a Spearman correlation of 0.45 (p<0.05).
Fig. 2 (a) & (b) Maximum intensity projection of the 3D Spearman correlation coefficient along the sagittal and transverse planes respectively. A line profile, as indicated by the white dotted line along the sagittal view in the bottom panel (c), shows no correlation between the variation in the dose and Spearman correlation.

The 3D Spearman map was computed based on the dose to each voxel through the entire voxel space of the reference patient. A maximum intensity projection of the Spearman map along the sagittal and transverse view reveals regions of high correlation as shown in fig. 2 (a) & (b). In order to rule out any correspondence between dose variation and Spearman correlation a line profile, across the sagittal view in fig. 2 (c), clearly indicates no association between the two values.

Impact: This technique preserves the spatial information of the dose distribution and provides an unbiased approach to identify critical anatomic structures since it does not require prior assumptions about the organs at risk.
