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

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## INTRODUCTION

Voxel-based analyses (VBAs) in radiation oncology have been introduced to evaluate local dose-response patterns via a voxelwise statistical analysis on the spatially normalized dose maps (DMs) of patients, classified according to a given outcome [1]. However, the intrinsic spatial properties of the considered DMs may clearly impact on the dosimetric signatures that can be inferred for a specific outcome. This is particularly relevant when dealing with endpoints related to highly interacting organs or substructures, as the cardiopulmonary system.

## AIM

Aim of our study is to propose a novel strategy for the characterization of DMs properties that impact on significance maps from VBAs evaluating local dose-response patterns via voxelwise statistical analysis on spatially normalized DMs.

## METHOD

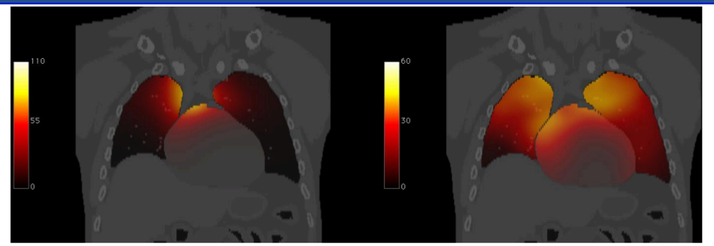
DMs of 178 lung cancer patients, treated with Intensity Modulated Radiation Therapy (IMRT) or Passive Scattering Proton Therapy (PSPT), were normalized on XCAT digital phantom [2]. We analyzed:

1. the uniformity of voxelwise mean (μ) and standard deviation (σ) of DMs over patients, which determines the homogeneity of VBA statistical power;
2. the probabilistic independent component analysis (PICA) [3], blindly inferring the number of statistically-significant independent maps (model order) that generate the DMs;
3. the connectogram [4], linking pairs of substructures by Spearman correlations (Rs) between their mean doses. We analyzed the cardiac substructures included in XCAT and the lung subregions segmented by a radiologist.

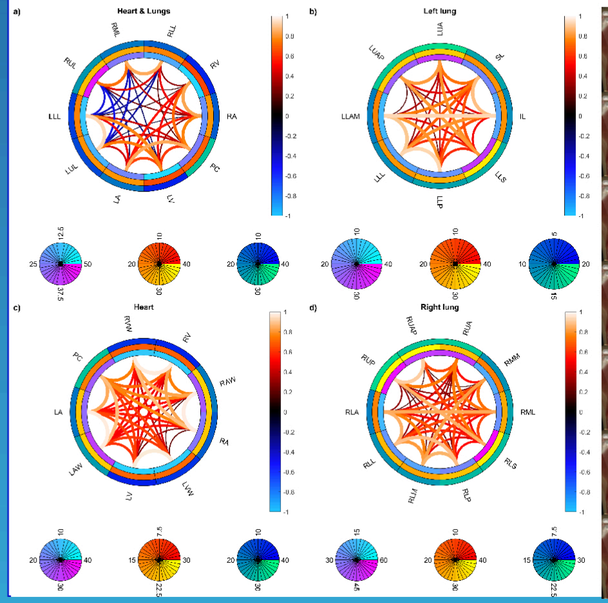
Points 2-3 elucidate the spatial resolution of the significance map from VBA for a given effect.

## RESULTS

The contrast over the 80% of the analyzed volume was 0.8 for μ- and 0.5 for σ-maps. PICA detected 43 dose clusters homogenously spread across the thorax. Connectograms showed that, while doses to main structures (cardiac chambers and lung lobes) were weakly correlated ($Rs^2$<0.2), Rs2 between adjacent lobe segments or chambers and related walls can reach 0.8.




**Above**: Voxelwise mean (left) and standard deviation (right) of biologically effective dose maps. **Below left**: Connectograms showing the Rs coefficients between mean doses to heart and lung substructures. From inside to outside, the circles represent: average of the structure mean doses; standard deviation of the structure mean doses; average of the dose standard deviations within the structure. **Below right**: first 35 PICA components of the analyzed dataset.




## CONCLUSIONS

The homogeneity of the σ map and the spread of PICA clusters suggests a uniform power of possible VBAs on the dataset.
PICA order, comparable with the cohort size, hints that a large number of DMs contributes to split the analyzed volume into independent patches that could highlight via VBAs distinct dose-response correlations.
Connectograms showed that the dataset can barely supports a radiobiological differentiation between the tiniest substructures.
The proposed characterization should be ancillary to any dosimetric VBA for a clear insight on the inference limits.

## ACKNOWLEDGEMENTS

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