Voxel-based analysis for pericardial effusion and mortality in patients treated with photons and protons for non-small-cell lung cancer

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INTRODUCTION

A wide range of dosimetric parameters have been associated to pericardial effusion (PCE) development and worse overall survival (OS) after thoracic cancer radiation therapy (RT); though producing conflicting results.

AIM

Aim of our study is to investigate the thoracic dose-response patterns for PCE and mortality in patients treated for locally advanced Non-Small-Cell Lung Cancer (NSCLC) by Intensity Modulated RT (IMRT) or Passive Scattering Proton Therapy (PSPT) with concurrent chemotherapy [1].

METHOD

We analyzed 178 patients treated with proton or IMRT to prescribed doses of 66 or 74 Gy (2 Gy/fraction) with concurrent chemotherapy (CHT).

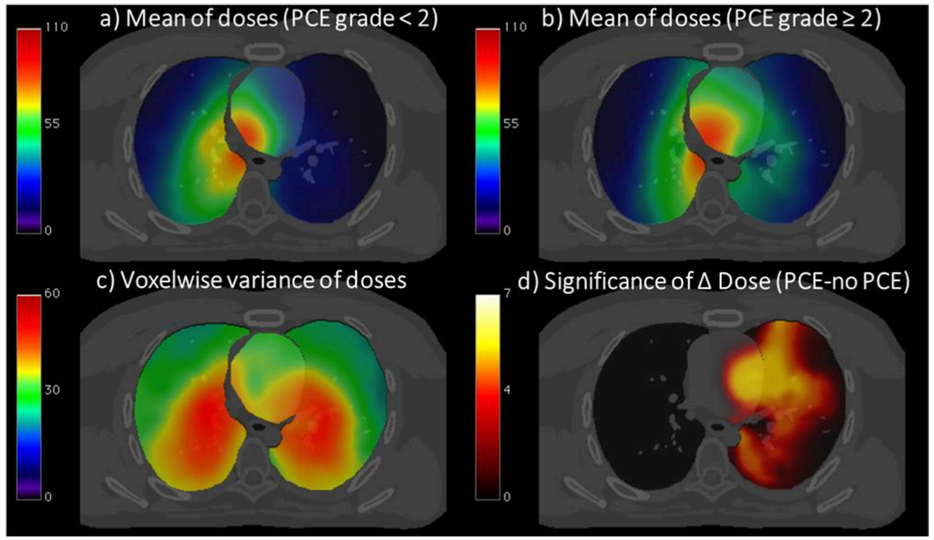
We considered four endpoints: PCE of CTCAE grade≥2 and mortality at 12 and 24 months from irradiation, with patients censored for follow-up.

Voxel-Based Analysis (VBA) of local dose differences between patients classified according to each endpoint was performed according to Palma et al. 2019 [2].

Clusters with dose differences correlated with outcomes at $p<0.05$ ($S_{0.05}$) were generated, and associated mean doses (MD) extracted.

Impact of clinical variables and of PCE on Overall Survival (OS) was analyzed by Cox regression with time-dependent covariates.

RESULTS



Figure

Axal CT views fused with mean biologically effective dose maps for NSCLC patients: a) without 2-years PCE, b) with 2-years PCE, c) the corresponding variances of doses, and d) the significance map (-log *p*) of dose differences.

One- and 2-year PCE occurrence were 32% (45/139) and 47% (42/90). The multivariable analysis (MVA) showed a significant correlation between adjuvant CHT with 1-year PCE ($p=0.05$), and between age and 2-year PCE ($p=0.004$).

One- and 2-year mortality were 28% (49/176) and 48% (79/166). MVA selected pre-treatment cardiac disease ($p=0.04$), age ($p=0.03$), GTV size ($p=0.001$) and weight ($p=0.02$) for 1-year mortality, and age ($p=0.05$) and GTV size ($p=0.036$) for 2-year mortality.

On Cox analysis, only GTV size ($p<0.001$) and age ($p=0.028$) were correlated with OS.

The VBA identified two largely overlapping clusters associated with 1- and 2-years PCE in the heart and in the lungs,

$S_{0.05}$ for 1-year PCE was 410 cc, with MD_{PCE}= [42±30] Gy vs MD_{noPCE}=[25±22] Gy. $S_{0.05}$ for 2-years PCE was 390 cc with MD_{PCE} = [42±37] Gy vs MD_{noPCE}= [21±23] Gy (**Figure**).

The VBA did not highlight significant dose-patterns related to mortality endpoints.

CONCLUSIONS

The VBA highlighted dose-patterns associated with PCE in both heart and lungs, opening new perspectives on the analysis of multi-organ contribution to thoracic toxicities.
Tumor volume and older age were the only significant factors for OS, which seems not associated with PCE or dose to heart or pulmonary healthy tissues.

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