CT characteristics allow to identify patient-specific and regional susceptibility for radiation-induced lung damage

Gilles Defraene¹, Wouter van Elmpt³, Wouter Crijns¹,², Pieter Slagmolen⁴, Dirk De Ruyscher¹,²

¹KU Leuven - University of Leuven, Department of Oncology, Experimental Radiation Oncology, B-3000 Leuven, Belgium ²University Hospitals Leuven, Department of Radiation Oncology, B-3000 Leuven, Belgium ³Department of Radiation Oncology (Maastro-Clinic), Maastricht University Medical Centre ⁴Department of Electrical Engineering (ESAT/PSI), KU Leuven, Belgium

**PURPOSE**
- Existing models predicting radiation-induced lung toxicity typically have low AUC values (smaller than 0.7)
- Dyspnea as primary endpoint is influenced by many causes other than mean lung dose (MLD), e.g. heart dose
- Moreover, the huge difference in radiosensitivity of lungs between patients, is not taken into account in these models
- The present study aims to quantify patient-specific and regional radiosensitivity based on a single pre-treatment CT scan

**METHODS AND MATERIALS**
- 70 patients with standard fractionation treatments (CONV group), stage I-IV: 40 from UZ Leuven (CONV1), 30 from MAASTRO (CONV2)
- 60 patients with stereotactic fractionations (SABR group), stage I NSCLC: 30 from UZ Leuven (SABR1), 20 from MAASTRO (SABR2)
- Nonrigid registration (MMI) of follow-up CT at 3 months (CT₃₆₅) and baseline planning CT (CT₀)
- Image analysis (MeVisLab): median density change (HU₀-HU₃₆₅) calculated locally (lung regions defined per dose bin of 5 Gy)
- EQD₂ doses derived using LQ formula with β = 6 Gy and a repopulation rate of 0.4 Gy/day

**RESULTS**

**Step I Individual dose-response relation**
- Sigmoidal fits (ΔHUₘₐₓ and D₅₀) outperformed linear fits

**Step II Importance for the dyspnea endpoint**
- CONV datasets merged
- Dyspnea score increase at 6 months (CTCAE 4.0)
- Δdyspnea ≥ 2 in 14.8% of patients
- MLD-model: AUC=0.65
- MLD-model incorporating patient-specific D₅₀: AUC=0.83 (p=0.05)

**Step III Heterogeneity within one lung**
- Hypothesis: denser regions are more prone to damage
- Subregions maximally differing in density on planning CT₀ are manually defined in 12 CONV cases retrospectively

**Step IV Radiation dose redistribution planning**
- Maximally sparing high-risk subregions
- Same PTV and OAR constraints (identical MLD!)
- Result: possible mean dose reduction to high-risk subregions by 6.6 Gy in 12 retrospectively planned cases

**CONCLUSION**
- The presented lung damage description on CT could permit patient individual treatment selection as
  - The damage endpoint proves to be less multifactorial (AUC=0.77) and could be externally validated
  - A simple planning CT characteristic is as a surrogate of radiosensitivity
  - A significant improvement of the classical MLD-based dyspnea prediction model could be shown
- Dose redistribution planning, avoiding radiosensitive subregions of lung, should be validated for its clinical relevance in a randomized study

This work was partly funded by the European Union’s Seventh Framework Programme under grant agreement no 601826: REQUITE project

**e-mail:** gilles.defraene@kuleuven.be

This work was partly funded by the European Union’s Seventh Framework Programme under grant agreement no 601826: REQUITE project