Patient individual and regional susceptibility for radiation damage in lung cancer radiotherapy: a dose redistribution concept

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I. Introduction and purpose

Lung toxicity is a limiting factor in current lung cancer radiotherapy treatments. Prediction models currently available in literature however are not discriminative enough for individualized treatment dose prescription[1]. Density change in healthy lung tissue is a known effect of radiotherapy in the chest region. It has been described qualitatively and quantitatively on a population level using CT scans [2-4]. The large variation of interindividual difference in response was pointed out [3-4] but not analysed in detail. This study aims at a patient individual description of radiation-induced lung damage through analysis of the dose effect and identification of prognostic factors. Regional sensitivity within the lungs was subsequently analysed.

II. Material and methods

II.A. Patient individual description of lung density change

110 lung cancer patients were studied: 40 treated with stereotactic ablative radiotherapy (SABR) for stage I (54/18 Gy, 48/12 Gy or 60/7.5 Gy), 40 treated conventionally for stage III (66/2.75 Gy or 66/2 Gy), and an external validation set of 30 conventional treaments (mostly 45/1.5 Gy followed by 24/2 Gy). Follow-up CT scans 3 month after end of treatment were non-rigidly registered to the baseline planning CT. Segmented lung volumes per dose bin of 5 Gy were analysed for their median change in Hounsfield Units (HU). For each patient, linear and sigmoidal fits (parameters HU_{max} (saturation of the effect) and D_{50} (dose corresponding to 50% of saturation level)) of local dose versus HU change were made, both for physical dose (D) and isoeffective dose (EQD2, alpha/beta=4 Gy). Multivariate modelling was performed for D_{50} and HU_{max} using PTV volume, median baseline HU in the V20 region, overall treatment time (OTT), tumour location, left/right lung, follow-up time and heart D_{max}.

II.B. Regional sensitivity and dose redistribution

The aforementioned prognostic model defining sensitive individuals was tested to define sensitive regions within one lung. Therefore, two lung subvolumes with the highest possible difference in density were manually generated close to the tumour (example in Figure 1).

III. Results and discussion

III.A. Patient individual description of lung density change

Sigmoidal fits to EQD2 outperformed the other scenarios for SABR and CONV: median sum of squares (CONV between brackets) of 206.9 (384.3), 311.3 (403.3), 109.0 (198.0) and 106.9 (193.7) for linear fit to D, linear fit to EQD2, sigmoidal fit to D and sigmoidal fit to EQD2, respectively. This finding was successfully validated in the validation set. Table 1

shows the distribution of HUmax and D50 in the different populations. Follow-up time (p=0.04) and heart Dmax (p =0.05) were prognostic for lower D50, while a higher baseline lung density (p=0.04) and shorter OTT (p=0.04) were for higher HUmax.

III.B. Regional sensitivity and dose redistribution

Preliminary results show the expected HU changes in selected lung subvolumes. In the Figure 1 example, no density change was observed in the low density volume and a steep dose response curve in the high density volume. Redistribution IMRT plans avoiding the high density volumes were generated (ensuring similar PTV dose). Approximately 50% of patients from our database seem to have lungs suitable for redistribution planning to be effective.

IV. Conclusions

The sigmoidal description of the per patient local HU change versus dose enhances the damage prognosis. Furthermore, the prognostic model was succesfully translated to regional sensitivity prediction within one lung.

Acknowledgements and potential conflicts of interest

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 601826" (REQUITE project).

D_{50} (Gy)	<10	10-30	30-50	50-70	70-90	>90	Unknown (no effect)	Unacceptable fit (sum of squares >500)
UZ LEUVEN CONV	3.3	14.0	36.7	6.7	0	0	22.5	16.7
MAASTRO CONV	0	33.3	23.3	6.7	0	0	23.3	13.3
UZ LEUVEN SABR	2.9	28.6	5.7	2.9	17.1	2.9	20.0	20.0
HU_{max} (HU increase)	<10	10-30	30-50	50-70	70-90	>90	Unknown (no effect)	Unacceptable fit (sum of squares >500)
UZ LEUVEN CONV	0	40.0	20.0	3.3	0	0	22.5	16.7
MAASTRO CONV	0	30.0	23.3	6.7	0	3.3	23.3	13.3
UZ LEUVEN SABR	8.6	34.3	8.6	2.9	5.7	0	20.0	20.0

Table 1: Distribution of sigmoidal fit parameters of the density changes, in percent of patients.

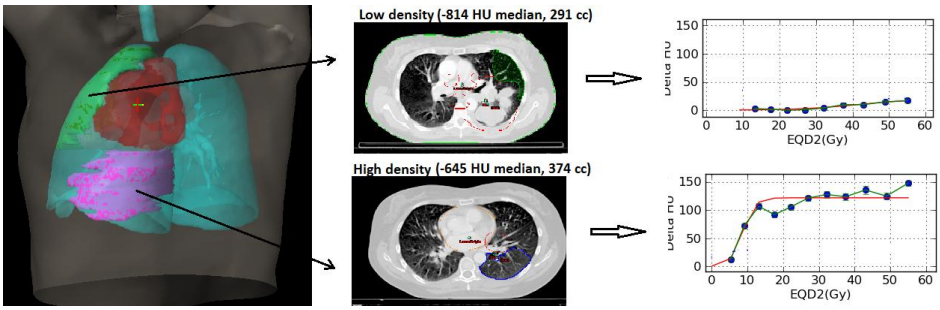

Figure 1 High and low density regions within the lung were defined. The observed change in HU after 3 months being drastically different between both lung regions, supports our model assumption.

References

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