

Dose Escalation Trend Analysis for a Multicenter *In Silico* Trial Comparing Photons and Protons for Radiotherapy of Non-Small Cell Lung Cancer (NSCLC)

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Introduction

ROCOCO is an international, multicenter, *in silico* clinical trial in lung, prostate and head and neck cancer using photons, protons and ¹²C-ions. Refer to the information provided online: www.mistir.info

By performing a treatment planning comparison study (hence *in silico*) we aim to demonstrate that proton and ¹²C-ion therapy decrease the amount of irradiated normal tissue, and consequently, the risk of side effects in the surrounding normal tissue and of secondary tumors is also lowered.

In this ROCOCO update, we compare the results of dose escalation with photon and proton radiotherapy for non-selected patients with non-small cell lung cancer (NSCLC).

Material & Methods

Twenty-five consecutive NSCLC patients, stage IA-IIIB, were prospectively included. On 4D-FDG-PET-CT scans, organs at risk (OAR), GTV, CTV and PTV were created at MAASTRO, using individualized set-up margins including breathing motion. The datasets were subsequently uploaded to a secure central database.

After the participants downloaded the datasets, 3D-conformal (3D-CRT) and intensity-modulated (IMRT) radiotherapy photon plans were made at MAASTRO and the NKI, respectively. Passive scattered conformal proton plans (3D-CPT) were designed at MGH. Figure 1 shows three examples of treatment plans for the three modalities.

The plans were created with a prescribed dose of 70 Gy to the tumour in 2 Gy fractions. The TP results were then up- or downscaled to the maximum tolerable dose (MTD), taking critical dose levels into account for the mean lung dose (MLD), spinal cord, oesophagus and heart. These limits were as given below:

- Mean lung dose: 19 Gy
- Max. spinal cord dose: 54 Gy
- Max. oesophagus dose: 80 Gy
- Heart: $V_{60\text{Gy}} < 33\%$, $V_{45\text{Gy}} < 66\%$, $V_{40\text{Gy}} < 100\%$
- Maximum prescribed dose: 150 Gy

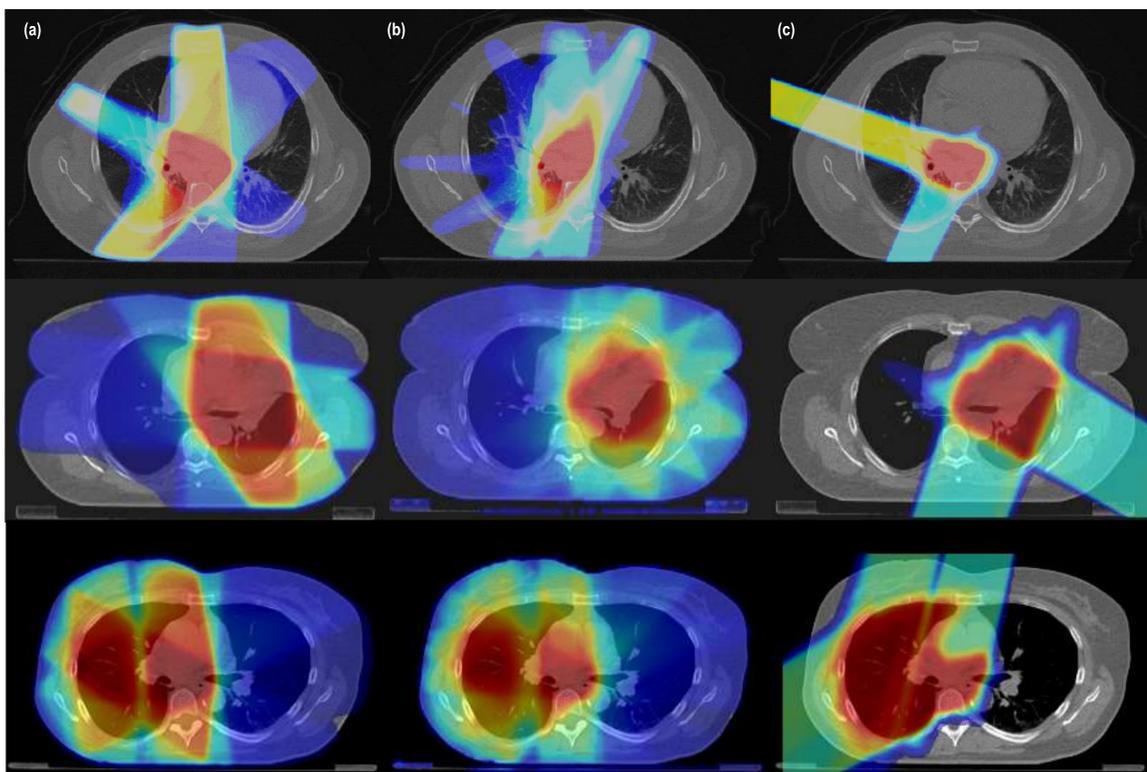


Figure 1 Comparison of dose distributions of 3D-CRT (a), IMRT (b) and 3D-CPT (c) treatment plans of three specific cases.

Statistical testing of differences in the derived dose metrics as given in Table 1 was performed using SPSS (v17, Chicago, IL).

The non-parametric Friedman test was used to determine differences across the three modalities. When significance was shown, the non-parametric, pair-wise Wilcoxon test was used to determine significance between 3D-CRT or IMRT and 3D-CPT. P-values < 0.05 were considered significant.

Results

There were 19 cases available for evaluation. After rescaling the prescribed dose to the critical level of the OAR it increased in 53%, 63% and 58% of the cases for 3D-CRT, IMRT and 3D-CPT, respectively. For the other cases, it had to be lowered or remained the same.

In Table 1, mean doses for the target and OARs are given for the three modalities. The mean PTV

dose considering all 19 cases changed from 71 ± 1 Gy to 71 ± 24 Gy, from 70 ± 1 Gy to 77 ± 21 Gy and from 70 ± 1 Gy to 75 ± 25 Gy for 3D-CRT, IMRT and 3D-CPT, respectively. The mean MLD after rescaling was 16 ± 3 Gy for both the 3D-CRT and IMRT plans and 12 ± 5 Gy for 3D-CPT.

Figure 2 shows the mean dose results when the data is split between Stage I & II (n=7) and Stage III (n=12) groups.

Table 1 Mean dose results for the target and OARs of the 19 cases. Values that proved significant when compare to 3D-CPT were marked with an asterisk (*).

	3D-CRT	IMRT	3D-CPT
MTD	70.3 ± 24.1	77.6 ± 20.7	75.1 ± 25.0
Patient	8.9 ± 3.0*	9.2 ± 3.2*	5.9 ± 2.8
PTV	71.1 ± 23.9	77.2 ± 20.6	75.3 ± 25.0
CTV	71.6 ± 24.1	78.4 ± 21.1	75.5 ± 25.0
MLD	16.1 ± 3.3*	16.1 ± 3.1*	12.2 ± 4.7
Oesophagus	22.8 ± 8.6	24.3 ± 9.7*	20.4 ± 10.7
Spinal cord	9.7 ± 8.0*	13.3 ± 7.1*	6.7 ± 7.1
Heart	12.7 ± 8.3*	13.4 ± 8.5*	7.0 ± 6.8

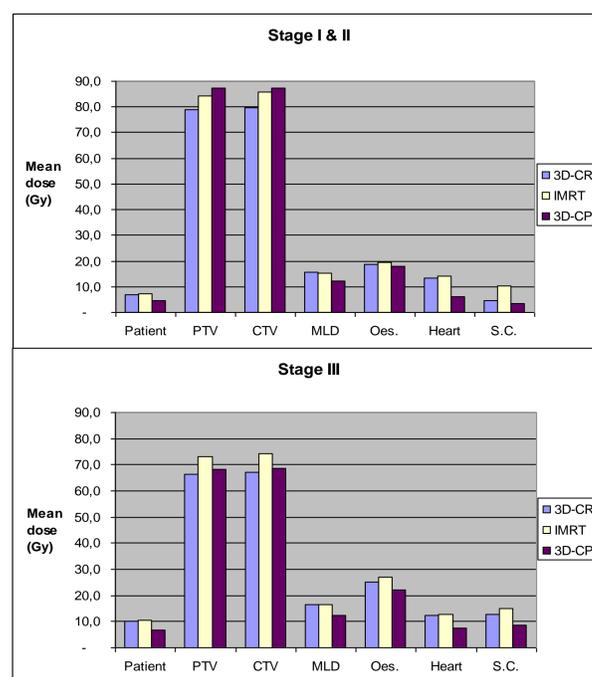


Figure 2 Mean dose values when split into Stage I & II and Stage III groups.

Conclusions

The treatment planning results for these unselected lung cases of the ROCOCO trial show the potential of dose escalation. On average, the largest MTD is seen for IMRT when considering the entire group. When considering Stage I&II this is true for 3D-CPT.

In general, 3D-CPT shows high tumour doses, while keeping the lowest dose to the OAR. This offers a higher therapeutic index (e.g. MTD/MLD) for protons than for photons.

