Supplementary material for Santiago A. et al. Changes in the radiological depth correlate with dosimetric deterioration in particle therapy for stage I NSCLC patients under high frequency jet ventilation. Acta Oncol 2015; doi:10.3109/0284186X.2015.1067716.

Supplementary materials

WEPL calculations

1. Both datasets, planning and localization CT scans, were coregistered according to the shift values calculated with Pinnacle³.
2. To simplify the calculation of the water equivalent path length, the CT images were rotated in order to align the CT voxels with the beam direction.
3. The Hounsfield units (HU) of the planning and localization CT scans were converted to relative stopping powers in water according to the default look-up table built in TRiP98, which was also used for the planning.
4. The voxel-based differences between the relative stopping powers of both CT datasets were calculated and converted to mm, scaling with the voxel size. Absolute values of the differences calculated this way were extracted.
5. A PTV binary mask (created with the tool trip2png [19]) was overlaid to visualize the absolute value of the local WEPL differences inside the PTV region. Examples of these WEPL difference maps are displayed in Fig. 2.
6. For the correlation of the variations in PTV V95% between planning and dose recomputation, the mean values of the absolute values of the local WEPL differences inside the PTV region were calculated.

Homogeneity and Conformity of the proton and carbon ion plans

All values of the homogeneity and conformity for the proton as well as the carbon ion plans are listed in Table I. Changes of the field configuration alone (i.e. a beam at 0° together with second beam at 45°, 90° and -45° respectively) resulted in small CI and HI changes only. A decrease in CI_{95} and CI_{98} was seen for increasing values of the lateral virtual contour extension, since more dose is allowed outside the PTV. At the same time an increase in V95% was seen for larger values of contour extension, illustrating that a better coverage typically involves compromises in the conformity. Since the peripheral, early stage tumors presented in this study have no critical normal tissue structures in the vicinity of the PTV, with exception of the chest wall and ribs partly encompassed by the PTV in tumors close to these structures, decreases in CI indexes due to large contour extension values had a lower priority in this study, in comparison to a satisfactory PTV coverage. HI values generally decrease with a larger value of the contour extension as well as plans with a larger number of fields. Larger contour extension values lowered the risk of underdosage at the PTV border while a larger number of fields had the potential to flatten the dose distribution and lower the inhomogeneity due to the increased pencil beam overlap within the PTV. Using energy step sizes of 3 mm yielded slightly worsened conformity values, lower coverage and an increase in the HI by a factor of almost 2 for both proton and carbon ion plans. This fact shows that the homogeneity and coverage within the target both depend more markedly on the energy step size, while the conformity of the plans is less dependent on this parameter. The larger the energy step size, the more dose will be given outside of the PTV at the proximal and distal edges, where the actual extent of excess dose will depend on the location of the PTV and the available energy steps from the accelerator.

Supplementary Table I. Summary of planning settings, and median (range) dosimetric indexes for the previously published proton plans in Santiago et al, presented here in order to compare with the dosimetric summary in Table I.

Plan Nr	Plan settings	V ₉₅ PTV [%]	ΔV_{95} GTV [%]	ΔV_{98} GTV [%]
Hv1*	2FA, 8, 3-3, 2, 1.5	99.6 (98.4-99.9)	0.1 (-0.1-8.9)	3.9 (-0.6-14.1)

* From Santiago et al.

Supplementary Table II. Summary of CI and HI indexes for the proton plans, median [range].

Plan Nr	Plan settings	CI95 PTV [%]	HI PTVplan [%]	HI GTVplan [%]	HI GTVloc [%]
Hv5	2FA, 8, 3-3, 2, 0.9	0.69 (0.57-0.73)	15.2 (13.8-18.4)	12.0(8.8-14.0)	15.2 (9.0-49.2)
Hv4	2FA, 8, 3-3, 2, 1.2	0.60 (0.44-0.64)	8.3 (6.7-10.3)	6.2 (4.7-9.4)	8.9 (5.0-49.4)
Hv1*	2FA, 8, 3-3, 2, 1.5	0.49 (0.29-0.51)	5.0 (3.4-8.6)	3.6 (2.1-8.5)	5.6 (3.4-49.2)
Hv7	2FA, 8, 3-3, 2, 1.8	0.33 (0.19-0.39)	3.5 (1.8-7.9)	3.1 (1.0-8.0)	4.0 (1.6-48.6)
Hv6	2FA, 8, 3-3, 3, 1.5	0.44 (0.30-0.52)	10.2 (5.6-17.7)	8.8 (2.9-16.6)	11.9 (5.9-50.8)
Hv2	2FB, 8, 3-3, 2, 1.5	0.46 (0.34-0.54)	5.8 (3.2-8.5)	4.6 (1.9-7.3)	5.4 (2.6-9.0)
Hv3	2FC, 8, 3-3, 2, 1.5	0.43 (0.30-0.54)	4.8 (2.9-9.3)	3.5 (1.8-8.6)	4.0 (1.8-8.6)

* From Santiago et al.

Supplementary Table III. Summary of CI and HI indexes for the carbon ion plans, median [range].

Plan Nr	Plan settings	CI95 PTV [%]	HI PTVplan [%]	HI GTVplan [%]	HI GTVloc [%]
C12v16	2FA, 5, 2-2, 2, 1.2	0.52(0.47-0.63)	2.2 (1.2-4.8)	1.3 (0.7-2.7)	2.3 (0.7-43.4)
C12v7	2FA, 5, 2-2, 3, 0.9	0.69(0.62-0.77)	7.2 (4.0-14.8)	2.7 (1.7-13.2)	8.2 (1.7-44.4)
C12v8	2FA, 5, 2-2, 3, 1.2	0.55(0.50-0.65)	3.9 (2.1-9.3)	2.1 (1.3-13.0)	3.6 (1.2-44.9)
C12v9	2FA, 5, 2-2, 3, 1.5	0.48(0.40-0.58)	2.9 (1.7-7.1)	2.0 (1.2-13.0)	2.7 (1.2-44.7)
C12v4	2FA, 6, 2-2, 2, 0.9	0.65(0.62-0.77)	4.7 (2.6-8.9)	2.0 (1.1-3.5)	6.1 (1.1-43.0)
C12v5	2FA, 6, 2-2, 2, 1.2	0.51(0.45-0.62)	1.9 (1.1-3.7)	1.3 (0.7-2.4)	2.0 (0.6-42.9)
C12v6	2FA, 6, 2-2, 2, 1.5	0.39(0.34-0.50)	1.5(0.9-2.5)	1.2 (0.6-2.3)	1.4 (0.6-42.2)
C12v0	2FA, 6, 2-2, 3, 0.6	0.76(0.71-0.84)	20.4 (12.0-32.0)	8.8 (3.6-17.2)	22.0(4.2-45.0)
C12v1	2FA, 6, 2-2, 3, 0.9	0.68(0.64-0.76)	7.7 (4.0-18.3)	3.2 (1.6-13.7)	7.7 (1.6-44.1)
C12v2	2FA, 6, 2-2, 3, 1.2	0.54(0.48-0.64)	3.5 (2.0-6.9)	2.1 (1.2-12.6)	3.3 (1.2-44.1)
C12v3	2FA, 6, 2-2, 3, 1.5	0.42(0.37-0.52)	2.6 (1.5-5.5)	1.9 (1.1-10.1)	2.6 (1.1-43.5)
C12v13	2FA, 8, 2-2, 2, 0.9	0.60(0.54-0.71)	3.8 (2.7-5.7)	2.0 (1.2-4.0)	4.8 (1.2-42.7)
C12v14	2FA, 8, 2-2, 2, 1.2	0.44(0.39-0.55)	1.7 (1.1-2.6)	1.3 (0.7-2.2)	1.7 (0.7-42.2)
C12v15	2FA, 8, 2-2, 2, 1.5	0.32(0.26-0.44)	1.4(0.8-2.0)	1.2(0.6-2.0)	1.4 (0.6-41.6)
C12v10	2FA, 8, 2-2, 3, 0.9	0.63(0.57-0.73)	5.6 (3.9-8.8)	2.8 (1.6-13.6)	6.0 (1.7-43.9)
C12v11	2FA, 8, 2-2, 3, 1.2	0.47(0.41-0.57)	3.0 (1.8-5.5)	2.0 (1.2-9.7)	2.9 (1.2-43.2)
C12v17	2FB, 8, 2-2, 2, 1.2	0.50(0.40-0.56)	1.59 (0.93-2.61)	1.16 (0.59-2.13)	1.30 (0.69-5.87)
C12v18	2FC, 8, 2-2, 2, 1.2	0.45(0.40-0.50)	1.68 (1.06-3.00)	1.01(0.68-2.48)	1.28 (0.71-3.45)

Multivariate analysis of the influence of planning settings in the carbon ion plans

We systematically analyzed the influences of the different scanning beam and planning setting variables on the dosimetric coverage loss for the subset of approved carbon ion plans, i.e. with a PTV V95% of at least 98%, which are visually represented in Fig. 1. Linear models were run for each of the different parameters and the correlations for the univariate models as well as for the two best multivariate models are represented in the following table:

Supplementary Table IV.

Correlation of CTV Δ V95% with:	R^2 ($p < 0.05$)
Patient (0)	0.53
Δ WEPL (1)	0.40
Volume PTV (2)	0.20
Contour extension (3)	0.10
FWHM (4)	n.s.
Energy Step (5)	n.s.
Grid size	NA
Linear model ~ (1) + (2)	0.49
Linear model ~ (1) + (2) + (3)	0.58

Single-beam plan calculations

Dose contributions from each individual field for four selected directions, namely 45°, 0°, -45°, and -90° were calculated separately, four single beams for each patient. Spearman's correlations between CTV V95% and V98% of single beams and Δ WEPL in the respective beam directions were calculated for each patient.

Supplementary Table V. Spearman's correlation between CTV Δ V95 or Δ V98 versus Δ WEPL for the protons and carbon ion plans..

Spearman's R ($p < 0.05$) all patients	Carbon ions	Protons
Δ V95%	0.45	0.45
Δ V98%	0.40	0.47

Dosimetric deterioration of 2F proton plans

Supplementary Fig. 1. Isodose lines for proton plans calculated on the planning CT and localization CT respectively for two selected patient cases and the three selected beam angle configurations presented in Table I. The 2FA plans have been published before in [12] but are plotted here as well for the convenience of the readers. The corresponding WEPL changes to the beams directions in these plans are represented in Fig. 2.