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Preliminary Clinical Analysis with Dose-Averaged LET Calculation for Head and Neck Cancer Patients Treated by Using Carbon-Ion Radiotherapy

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INTRODUCTION

- A new irradiation methods of optimizing dose-averaged linear energy transfer (LET_d) within target, which are directly related to relative biological effectiveness (RBE), have recently been highlighted[1,2].
- Clinical data are needed to determine how much LET_d affects targets and normal tissues in heavy particle therapy.

AIM

- For head and neck cancer patients treated with carbon-ion radiotherapy (CIRT), normal tissues such as brain and optic nerves are close to the irradiation field such that those may receive radiation damage.
- In order to estimate their clinical results, a LET_d calculation tool was developed. We focused on the usefulness of LET_d in the clinical analysis.

METHOD

- Patient: From October 2006 to December 2013, 99 adenoid cystic carcinoma (ACC) patients treated with CIRT at National Institute of Radiological Science (NIRS, Japan) were selected (see Table 1). In-house Heavy Ion Plan (HIPLAN) treatment planning system was used in the CIRT with a wobbler-scattering method[3].
- We developed the LET_d and its standard deviation (LET_dSD) calculation tool, and implemented in the HIPLAN:

$$LET_d(r) = \frac{\sum_i (n_i \times D_i(r) \times LET_i(r))}{\sum_i (n_i \times D_i(r))}$$

$$LET_dSD(r) = \sqrt{\frac{\sum_i (n_i \times D_i(r) \times LET_i(r)^2)}{\sum_i (n_i \times D_i(r))} - LET_d(r)^2}$$

r : Point of interest
n_i: Number of fraction beams i
$D_i(r)$: Physical dose of beam i
$LET_i(r)$: LET of beam

- In this study, we clinically analyzed RBE-weighted dose, LET_d, and LET_dSD of 99 ACCs and 128 optic nerves using the analysis tool for local control and optic neuropathy.

Table 1. Patient, treatment, and tumor and normal tissue characteristics

Characteristics	Value (%)
Number of patients	99
Sex, Male/Female	39 (39)/60 (61)
Age, Median/range	59/22–28
Fractionation (fx)	16 fx (4 fx per week)
Irradiation field, Median/range	5/22–28
RBE-weighted dose 57.6 Gy/16 fx 64 Gy/16 fx	 31 (31) 68 (69)
Gross tumor volume (ml), Median/ range 57.6 Gy/16 fxs 64 Gy/16 fxs	 46.1/1.1–255.3 38.5/2.0–193.1
Optic nerve volume (ml), Median/range	1.1/0.5–2.2

Abbreviations: RBE = relative biological effectiveness.

RESULTS

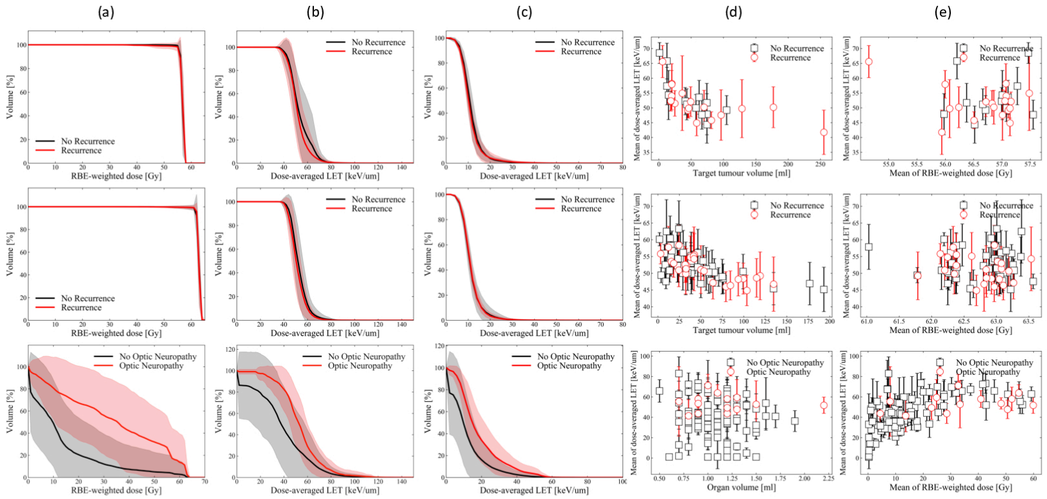

Figure 1. Volume histograms of (a) RBE-weighted dose, (b) LET_d, (c) LET_dSD; (d) Mean of LET_d vs volume; (e) Mean of LET_d vs mean of RBE-weighted dose (First row: GTV (57.6 Gy); Second row: GTV (64 Gy); Third row: Optic nerves).

Table 2. Mean and standard deviations of mean RBE-weighted dose, mean LET_d, and mean LET_dSD for GTV (57.6 and 64 Gy) between recurrence and non-recurrence.

	GTV (57.6 Gy)	GTV (64 Gy)
RBE-weighted $dose_{NoRecur}$ (Gy)	56.8 ± 0.5	62.8 ± 0.4
RBE-weighted $dose_{Recur}$ (Gy)	56.7 ± 0.7	62.8 ± 0.4
P value	0.443	0.874
$LET_{d,NoRecur}$ (keV/μm)	53.3 ± 6.7	52.8 ± 4.4
$LET_{d,Recur}$ (keV/μm)	51.5 ± 5.2	51.3 ± 3.7
P value	0.425	0.154
$LET_dSD_{NoRecur}$ (keV/μm)	5.7 ± 1.2	5.3 ± 1.6
LET_dSD_{Recur} (keV/μm)	5.6 ± 2.6	5.5 ± 1.5
P value	0.961	0.541

Table 3. Mean and standard deviations of mean RBE-weighted dose, mean LET_d, and mean LET_dSD for optic nerves between with and without optic neuropathy (ON).

	Optic nerves
RBE-weighted $dose_{without\ ON}$ (Gy)	13.2 ± 13.6
RBE-weighted $Dose_{with\ ON}$ (Gy)	33.9 ± 17.2
P value	<0.001
$LET_{d,without\ ON}$ (keV/μm)	38.3 ± 20.1
$LET_{d,with\ ON}$ (keV/μm)	53.6 ± 8.0
P value	0.006
$LET_dSD_{without\ ON}$ (keV/μm)	9.4 ± 6.6
$LET_dSD_{with\ ON}$ (keV/μm)	13.6 ± 7.3
P value	0.030

CONCLUSIONS

- For tumors, mean of LET_d was not significant for recurrence and non-recurrence.
- For optic nerves, optic neuropathy occurred even at low RBE-weighted dose (10 Gy or less), when the mean of LET_d was over 40 keV/μm.
- There is a need for a method to analyze LET_d separately from dose. Especially, it is necessary to accurately predict the effects of high LET_d at the low RBE-weighted dose.
- We will continue to analyze clinically more patients in the future.

REFERENCES

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