

## CONTENTS

1.	RELATIVE BIOLOGICAL EFFECTIVENESS IN ION BEAM THERAPY.....	1
1.1.	Introduction .....	1
1.1.1.	Role of radiation therapy in the treatment of cancer ...	1
1.1.2.	Present situation and future trends .....	2
1.1.3.	Rationale for ion therapy .....	3
2.	BIOLOGICAL WEIGHTING OF ABSORBED DOSE: THE SPECIFIC ISSUE OF RBE IN ION BEAM THERAPY....	8
2.1.	Absorbed dose .....	8
2.2.	Need for weighting factors .....	9
2.3.	Reference irradiation conditions .....	10
2.3.1.	Radiation quality .....	10
2.3.2.	Reference fractionation scheme .....	10
2.4.	Fractionated external photon therapy .....	11
2.4.1.	Weighting factor for differences in dose per fraction ...	11
2.4.2.	Example .....	12
2.5.	Brachytherapy and differences in dose rate .....	12
2.6.	Influence of overall time .....	13
2.7.	Radiation quality and RBE .....	14
2.7.1.	The RBE concept .....	14
2.7.2.	Application of the RBE concept in radiation therapy .....	14
2.7.2.1.	RBE and dose prescription .....	15
2.7.2.2.	Selection of the most clinically relevant RBE or weighting factors for ions .....	18
2.7.2.3.	Selection of $W_{ion}$ based on the linear quadratic model .....	19
2.7.2.4.	Evaluation of $WI_{soE}$ from clinical considerations or outcomes .....	22
2.7.3.	Ion RBE in therapy applications: Summary .....	23
3.	QUANTITIES AND UNITS .....	26
3.1.	Absorbed dose, $D$ .....	26
3.2.	Biological weighting factor, $W_B$ .....	27

3.2.1.	Fractionated photon beam therapy .....	27
3.2.2.	Brachytherapy .....	28
3.2.3.	External beam therapy with non-conventional radiation quality .....	28
3.3.	Biologically weighted absorbed dose, $D_B$ .....	29
3.4.	Recommendations for reporting .....	30
3.4.1.	Reporting the isoeffective dose weighting factor, $W_{IsoE}$ .....	30
3.4.2.	General recommendations for reporting radiation therapy .....	31
3.4.3.	Review of some current practices for weighting and reporting weighted dose and isoeffective dose in centres using particle irradiations .....	31
3.4.3.1.	Proton beam therapy .....	31
3.4.3.2.	The Darmstadt-Heidelberg approach in carbon ion therapy .....	32
3.4.3.3.	The Chiba approach in carbon ion therapy ...	32
3.4.3.4.	Equivalent dose .....	32
3.4.4.	ICRU/IAEA recommendations for reporting the isoeffective dose, $D_{IsoE}$ .....	33
4.	<b>RADIOBIOLOGY OF HIGH LET RADIATION: NEUTRONS AND IONS</b> .....	36
4.1.	Radiobiological rationale for the use of high LET radiation .....	36
4.1.1.	Increased RBE .....	36
4.1.2.	Reduction in the oxygen enhancement ratio with increasing LET .....	39
4.1.3.	Reduction of the variation in radiosensitivity related to the position of the cell in the mitotic cycle ...	40
4.1.4.	Reduced repair with high LET radiation .....	41
4.1.5.	Effect of tumour differentiation and growth rate .....	43
4.2.	Patient selection for high LET radiotherapy .....	45
4.3.	Rationale for ion therapy .....	46
5.	<b>CLINICAL EXPERIENCE WITH NEUTRONS AND IONS</b> ...	51
5.1.	Clinical experience with fast neutrons .....	51
5.1.1.	Salivary gland tumours .....	51
5.1.2.	Prostatic adenocarcinomas .....	52

5.1.3.	Other tumour sites or types .....	54
5.2.	Clinical experience with ion beams .....	55
5.2.1.	The Berkeley ion programme .....	55
5.2.2.	The Chiba programme .....	56
5.2.3.	The Darmstadt programme .....	58
5.2.3.1.	Chordomas and low grade chondrosarcomas of the base of the skull .....	58
5.2.3.2.	Sacrococcygeal and spinal chordomas and low grade chondrosarcomas .....	59
5.3.	Conclusions from clinical experience with high LET radiations .....	60
5.3.1.	Summary of clinical experience .....	60
5.3.2.	Clinical and biological considerations for selecting patients for ion therapy .....	62
6.	RECOMMENDATIONS FOR REPORTING ION BEAM THERAPY .....	65
6.1.	Reporting: An essential tool for exchanging information ....	65
6.1.1.	Three levels for reporting .....	65
6.1.2.	Reporting radiation treatment .....	65
6.1.3.	Reporting versus prescribing .....	66
6.1.4.	Points and volumes used for reporting .....	66
6.1.4.1.	Gross target volume .....	67
6.1.4.2.	Clinical target volume .....	67
6.1.4.3.	Planning target volume .....	67
6.1.4.4.	Anatomical volumes relating to normal tissues .....	68
6.1.4.5.	Treated volume .....	68
6.1.4.6.	Reference volume .....	69
6.2.	Specific recommendations for reporting a therapeutic ion beam irradiation .....	69
6.2.1.	Irradiation conditions .....	69
6.2.2.	Quantities and factors to be reported .....	69
6.2.2.1.	Absorbed dose .....	69
6.2.2.2.	Isoeffective dose weighting factor in radiation therapy .....	70
6.2.2.3.	Isoeffective dose in radiation therapy .....	70
6.2.3.	Reference points and volumes for reporting .....	71

6.2.3.1.	Reference points .....	71
6.2.3.2.	Volumes for reporting .....	71
ANNEX I:	RESPONSE IN VIVO TO HIGH LET RADIATION ...	75
ANNEX II:	MODELLING THE INCREASED BIOLOGICAL EFFECTIVENESS OF HEAVY CHARGED PARTICLES FOR TUMOUR THERAPY TREATMENT PLANNING .....	93
ANNEX III:	MEASUREMENT OF RBE OF CARBON IONS FOR CELLS, TUMOUR RESPONSE AND TISSUE REACTIONS IN EXPERIMENTAL SYSTEMS .....	120
ANNEX IV:	CLINICAL RBE DETERMINATION SCHEME AT NIRS-HIMAC.....	135
	CONTRIBUTORS TO DRAFTING AND REVIEW.....	153