

# Modelling the impact of treatment uncertainties in radiotherapy

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# Table of Contents

<b>TABLE OF CONTENTS</b> .....	<b>III</b>
<b>ABBREVIATIONS AND ACRONYMS</b> .....	<b>VIII</b>
<b>SYMBOLS</b> .....	<b>X</b>
<b>LIST OF FIGURES</b> .....	<b>XIV</b>
<b>LIST OF TABLES</b> .....	<b>XVIII</b>
<b>ABSTRACT</b> .....	<b>XIX</b>
<b>THESIS STATEMENT</b> .....	<b>XXI</b>
<b>ACKNOWLEDGEMENTS</b> .....	<b>XXII</b>
<b>CHAPTER 1 GENERAL INTRODUCTION</b>	<b>1</b>
1.1. EXTERNAL BEAM RADIOTHERAPY PLANNING	1
1.2. AIMS OF CURRENT INVESTIGATION	4
1.3. THESIS OUTLINE	5
1.4. PUBLICATIONS	6
<b>CHAPTER 2 A REVIEW OF PATIENT POSITIONING UNCERTAINTY AND ORGAN MOTION AT VARIOUS ANATOMICAL SITES</b>	<b>9</b>
2.1. INTRODUCTION	9
2.2. REVIEW OF ICRU REPORTS 50 AND 62	10
2.3. COMPARISON ACROSS STUDIES	12
2.4. PATIENT POSITIONING (SETUP) ERRORS	14
2.4.1. Defining Patient Positioning Errors	14
2.4.2. Magnitudes of positioning errors at various sites	16
2.4.3. Patient Immobilisation	18
2.4.4. Pelvis	18
2.4.5. Brain	20
2.4.6. Abdomen	20
2.4.7. Head and Neck	20
2.4.8. Breast	21
2.5. ORGAN MOTION	21
2.5.1. Defining organ motion	21

2.5.2.	Magnitudes of organ motion	22
2.5.3.	Prostate Motion	23
2.5.3.1.	<i>Supine versus prone treatment positions</i>	25
2.5.3.2.	<i>Bladder/rectum filling influence on prostate motion (MODprostate)</i>	25
2.5.3.3.	<i>Strategies to account for prostate motion</i>	27
2.5.4.	Abdominal Motion	28
2.5.4.1.	<i>Generalities</i>	28
2.5.4.2.	<i>Kidney Motion</i>	30
2.5.4.3.	<i>Diaphragm Motion</i>	30
2.5.4.4.	<i>Pancreas Motion</i>	31
2.5.4.5.	<i>Breath Holding Techniques</i>	31
2.5.4.6.	<i>Advanced Techniques</i>	31
2.5.4.7.	<i>Patient Orientation during treatment</i>	32
2.6.	PATIENT REPOSITIONING STRATEGIES	32
2.7.	CONTEMPORARY SUGGESTIONS FOR TREATMENT PLANNING	35
2.7.1.	Statistics based treatment margins	35
2.7.2.	Adaptive radiation therapy	39
2.7.3.	Monte Carlo techniques	40
2.7.4.	Convolution techniques	41
2.8.	SUMMARY	42
<b>CHAPTER 3 REVIEW OF RADIOBIOLOGICAL MODELS</b>		<b>43</b>
3.1.	INTRODUCTION	43
3.2.	BIOLOGICAL MODELS	44
3.2.1.	Empirical (Logit and Probit) Models	44
3.2.2.	Theoretical (Poisson/Linear Quadratic) Model	45
3.2.3.	Hyper sensitivity of tumour/normal tissue at low doses	48
3.2.4.	Biological Effective Dose	49
3.2.5.	Standard Effective Dose	50
3.2.6.	Equivalent Uniform Dose	50
3.3.	TUMOUR CONTROL PROBABILITY	51
3.3.1.	Accounting for interpatient radiosensitivity variation in a population of patients	52
3.3.2.	Clonogen density and optimisation	52
3.3.3.	Prostate Carcinoma	54
3.4.	NORMAL TISSUE COMPLICATION PROBABILITY	55
3.4.1.	Dose-Volume effects	55
3.4.2.	Lyman-Kutcher-Burman (LKB) model	56
3.4.3.	Källman k- and s-models	59
3.4.4.	Yaes-Kalend/Fenwick model	60
3.4.5.	Clinical application of NTCP	61
3.4.6.	Rectal complications	62
3.4.6.1.	<i>Grading rectal complications</i>	62
3.4.6.2.	<i>Rectum architecture</i>	62
3.4.6.3.	<i>Dose volume characterisation</i>	64
3.5.	UNCOMPLICATED TUMOUR CONTROL AND OBJECTIVE FUNCTIONS	67
3.6.	SUMMARY	69
<b>CHAPTER 4 MODELLING THE DOSIMETRIC EFFECT OF TREATMENT UNCERTAINTY</b>		<b>71</b>

4.1.	INTRODUCTION	71
4.2.	DOSE UNCERTAINTY	72
4.2.1.	Modelling dose uncertainty	73
4.2.2.	Probability density functions for position and dose	73
4.3.	MONTE CARLO TECHNIQUE	76
4.3.1.	Methods	76
4.3.1.1.	<i>Sampling from distributions, and the dose grid</i>	77
4.3.1.2.	<i>Dose accumulation</i>	78
4.3.1.3.	<i>Clinical example</i>	79
4.3.2.	Results	80
4.3.2.1.	<i>Mean and variance in fractionated dose for single incident beam</i>	80
4.3.2.2.	<i>Impact of margin size</i>	83
4.3.2.3.	<i>Impact of magnitude of patient positioning and organ variations</i>	83
4.3.2.4.	<i>Number of fields and dose gradients.</i>	83
4.3.3.	Discussion	85
4.3.3.1.	<i>Possible margin reductions with multiple pretreatment CT scans</i>	85
4.3.3.2.	<i>Relative importance of systematic and random components</i>	85
4.3.3.3.	<i>Comparison of spatially uniform dose error and positioning errors</i>	86
4.3.3.4.	<i>Dose reporting</i>	87
4.4.	CONVOLUTION TECHNIQUE	87
4.4.1.	Derivation of spatial PDF including systematic organ motion error	88
4.4.2.	Benchmarking against Monte Carlo results	89
4.4.3.	Margin recipe including systematic error	89
4.5.	MULTIPLE CT SCANS	90
4.5.1.	Timing regimes for multiple intra-treatment image acquisition	90
4.5.2.	Results	92
4.6.	MONTE CARLO MODELLING OF 3D DOSIMETRIC IMPACT	92
4.6.1.	Methods	92
4.6.2.	Results	95
4.6.3.	Discussion	97
4.7.	SUMMARY AND CONCLUSION	99

<b>CHAPTER 5</b>	<b>MODELLING DOSE DEPOSITION TO THE DEFORMING RECTUM</b>	<b>101</b>
5.1.	INTRODUCTION	101
5.2.	BACKGROUND	102
5.3.	METHODS	104
5.3.1.	‘Original’ and ‘Initial’ rectum geometries	104
5.3.1.1.	<i>Original geometry</i>	104
5.3.1.2.	<i>Initial Geometry</i>	106
5.3.2.	Modelling rectum deformations	107
5.3.3.	Modelling planning CT image acquisition	109
5.3.4.	Modelling treatment delivery	112
5.3.5.	The input data	113
5.3.5.1.	<i>Geometry</i>	113
5.3.5.2.	<i>Uncertainty parameters</i>	114
5.3.6.	Calculations	114
5.4.	RESULTS	115
5.4.1.	Planned rectum dose distributions	115
5.4.2.	Interfraction variations	117
5.4.2.1.	<i>Systematic error: empty rectum at planning</i>	117
5.4.2.2.	<i>Systematic error: full rectum at planning</i>	120

5.4.3.	Interpatient variations	121
5.5.	DISCUSSION	128
5.6.	CONCLUSIONS	130

## **CHAPTER 6 MODELLING THE RADIOBIOLOGICAL EFFECT OF TREATMENT UNCERTAINTY IN RADIOTHERAPY** **133**

6.1.	INTRODUCTION	133
6.2.	TUMOUR CONTROL PROBABILITY	133
6.2.1.	Background	134
6.2.2.	Method	134
6.2.2.1.	<i>Input data for 1D case</i>	136
6.2.2.2.	<i>Input data for 3D case</i>	138
6.2.2.3.	<i>Calculations</i>	138
6.2.3.	Results	139
6.2.3.1.	<i>Impact of margin size</i>	139
6.2.3.2.	<i>Impact of penumbra steepness</i>	141
6.2.3.3.	<i>Impact of uniform dose uncertainty and interpatient heterogeneity</i>	143
6.2.3.4.	<i>Results using 3D input data</i>	149
6.2.4.	Discussion	151
6.3.	NORMAL TISSUE COMPLICATION PROBABILITY	154
6.3.1.	Background: Incorporating treatment uncertainty into NTCP calculation	154
6.3.2.	Methods	155
6.3.2.1.	<i>Fitting Linear-Quadratic parameters to late rectum complications</i>	155
6.3.2.2.	<i>Modelling individual treatments and patient populations</i>	156
6.3.3.	Results	156
6.3.3.1.	<i>Individual patients</i>	156
6.3.3.2.	<i>Population based results</i>	158
6.3.3.3.	<i>Impact of fluctuations in fractional dose</i>	158
6.3.3.4.	<i>Comparison with mean treatment dose</i>	160
6.3.4.	Discussion	162
6.4.	UNCOMPLICATED TUMOUR CONTROL PROBABILITY (UTCP)	165
6.4.1.	Methods	165
6.4.2.	Results	166
6.4.2.1.	<i>UTCP calculated for an individual patient</i>	166
6.4.2.2.	<i>Population based results</i>	167
6.4.3.	Discussion	171
6.5.	CONCLUSIONS	173

## **CHAPTER 7 TREATMENT PLANNING ALGORITHM CORRECTIONS TO ACCOUNT FOR AND DISPLAY DOSE UNCERTAINTY IN RADIOTHERAPY** **175**

7.1.	INTRODUCTION	175
7.1.1.	Possibilities for future radiotherapy treatment planning	175
7.1.2.	Purpose	176
7.2.	MODIFICATIONS TO DOSE CALCULATION ALGORITHMS FOR PHOTONS	177
7.1.3.	Correction based techniques	177
7.2.1.1.	<i>Input data</i>	177
7.2.1.2.	<i>Dose calculation</i>	178
7.2.1.3.	<i>Including estimations of error</i>	180
7.1.4.	Superposition technique	180

7.2.1.4.	<i>Input data</i>	180
7.2.1.5.	<i>Dose calculation</i>	180
7.2.1.6.	<i>Including estimations of error</i>	181
7.1.5.	Monte Carlo technique	183
7.2.1.7.	<i>Input data</i>	183
7.2.1.8.	<i>Dose calculation</i>	183
7.2.1.9.	<i>Including estimations of error</i>	184
7.3.	REQUIREMENTS FOR DISPLAY INPUT DATA	185
7.1.6.	Standard deviations	185
7.1.7.	Non standard deviations	186
7.4.	TREATMENT PLANNING DISPLAYS	187
7.1.8.	Mean dose and/or standard deviation	187
7.1.9.	Modified dose volume histogram	190
7.1.10.	Mean with estimated standard deviation display	190
7.1.11.	Difference maps	192
7.5.	CRITICAL EVALUATION OF UNCERTAINTY DISPLAY TOOLS	193
7.6.	CONCLUSIONS	196
<b>CHAPTER 8 CONCLUSIONS AND FURTHER RESEARCH</b>		<b>197</b>
8.1.	MAJOR CONCLUSIONS	198
8.2.	FURTHER RESEARCH	201
<b>Appendix A</b>		<b>203</b>
<b>References</b>		<b>223</b>

# Abbreviations and Acronyms

AP	Anterior-Posterior direction
BED	Biological Effective Dose
CL-DVH	Confidence Limited Dose Volume Histogram
CT	Computed Tomography
CTV	Clinical Tumour Volume
DNA	Deoxyribose Nucleic Acid
DSAR	Differential Scatter Air Ratio
DVH	Dose Volume Histogram
DWH	Dose Wall Histogram
EGS4	Electron Gamma Shower version 4
EPID	Electronic Portal Imaging Device
ETAR	Equivalent Tissue Air Ratio
EUBED	Equivalent Uniform Biologically Effective Dose
EUD	Equivalent Uniform Dose
FFT	Fast Fourier Transform
FML	Full Maximum Likelihood
FS	Field Size
FSU	Functional Sub-Unit
FWHM	Full Width at Half Maximum
GTV	Gross Tumour Volume
HDSA	High Dose Surface Area
I-125	Iodine-125
ICRU	International Commission on Radiation Units
IM	Internal Margin
IMRT	Intensity Modulated Radiation Therapy
IPTV	Internal Planning Target Volume
IR	Induced Repair
LET	Linear Energy Transfer
LQ	Linear Quadratic
LR	Left-Right direction
MC	Monte Carlo
ML	Medio Lateral (same plane as left right)



MOD	Mean Organ Displacement
MRI	(nuclear) Magnetic Resonance Imaging
MTPD	Mean Treatment Position Deviation
NAL	No Action Level
NTCP	Normal Tissue Complication Probability
OAR	Organ At Risk
PDF	Probability Density Function
PDV	Prescribed Dose Volume
PTV	Planning Target Volume
RTOG	Radiation Therapy Oncology Group grading system
RTP	Radiation Therapy Planning
SAL	Shrinking Action Level
SD	Standard Deviation
SEAS	Setup Error (averaged) Across Studies
SED	Standard effective dose
SI	Superior-Inferior direction
SM	Setup Margin
SSD	Surface-Skin Distance
TCP	Tumour Control Probability
TERMA	Total Energy Released in the Medium
TPD	Treatment Position Deviation
TPS	Treatment Planning System
UTCP	Uncomplicated Tumour Control Probability

# Symbols

$\bar{x}$	mean organ position
$\bar{x}$	mean patient position based on all measurements for a group of patients
$\bar{r}$	mean rectal wall radius across $N_z$ CT slices
$\bar{r}_{pop}$	mean rectal wall radius across patient population
$\bar{D}$	mean treatment dose
$d_s^*(r)$	perturbed sample fraction dose in spatial element $\Delta r$ located $\Delta r + r$ units from the isocentre
$\Delta \bar{x}_j$	systematic patient positioning error for $j$ th patient
$\tau$	initial action level for possible patient repositioning
$\phi$	proportion of patients with injury uncorrelated to benefit
$\phi_j$	random deviate from Gaussian distribution describing patient position at the $j$ th fraction dose
$\sigma_{m,organ}$	standard deviation in mean organ position
$\sigma_{R,j}$	standard deviation of random error for $j$ th patient
$\Sigma_T$	standard deviation of systematic setup error across a group of patients
$\Delta x_{i,j}$	measured shift in patient position in $i$ th portal image from position at simulation for $j$ th patient
$a$	variable
$A_0$	(original) area of rectal wall segment
$b$	variable
$c_a$	partial score (for treatment plan)
$C_i$	score
$CT_\infty$	infinite CT images used to calculate true mean organ position
$d$	fraction dose
$D$	treatment dose including, for example, 30 fraction doses
$D_0$	planned treatment dose
$D_{50}$	dose that produces a given endpoint in 50% of the population after 5 years
$d_c$	dose limit for induced repair
$d_{eff}$	effective depth
$D_m$	Maximum treatment dose
$d_{max}$	depth of maximum dose

$d_s$	fraction dose sampled from known distribution
$D_s(r)$	sum of $N_{fx}$ sample fraction doses
$d_s^*$	perturbed fraction dose
$d_{st}$	standard dose per fraction (Gy)
$d\Theta$	angle increment
$E$	rotation vector
$erf()$	error function
$F$	objective function
$g$	Gaussian function
$GC$	(absolute) position of geometric centre of rectum
$H$	CTV→PTV margin
$H_p$	primary kernel
$H_s$	scatter kernel
$k$	parameter from Kallman k-model
$m$	parameter from Lyman model
$M$	the total number of voxels
$N$	a number (general)
$n$	parameter from Lyman model
$N_0$	initial number of cells in tumour/organ
$N_{cell}$	number of consecutive cells
$N_{CT}$	the number in CT image acquisitions
$N_F$	number of FSU's in organ
$N_{FSU}$	number of cells per FSU
$N_{fx}$	the number of fraction doses
$n_j$	number of portal images
$N_{pat}$	number of patients in a particular study
$N_S$	number of surviving cells following irradiation
$N_{SD}$	number of standard deviations
$N_z$	number of slices in CT image set
$P$	probability (general)
$P(D,1)$	dose-response function, giving the probability of a given endpoint following irradiation of whole organ volume
$P(D,v)$	dose-response function, giving the probability of a given endpoint following irradiation of partial volume
$P_+$	probability of uncomplicated tumour control

$P_B$	probability of benefit from the treatment
$P_{BI}$	conditional probability for benefit without injury
$P_I$	probability of treatment induced injury
$r$	radius (general)
$r_0$	initial rectal radius
$\xi$	random deviate from Gaussian distribution describing organ position
$r_{def}$	radius of deformed rectal wall
$r_{in}$	inner rectal wall radius
$s$	parameter from Kallman s-model
$S$	surviving fraction
$T$	TERMA (see abbreviations)
$T$	total time of treatment (days)
$T_{1/2}$	half-life for sub lethal damage
$T_k$	kick-off time (days)
$T_{pot}$	potential doubling time of tumour (days)
$U$	Utility of treatment
$u_t$	vector displacement at time, t.
$v$	partial volume ( $\text{cm}^3$ )
$V_{eff}$	effective volume (considering tissue architecture) ( $\text{cm}^3$ )
$V_t$	tumour volume ( $\text{cm}^3$ )
$w$	rectal wall thickness (mm).
$w'$	weighted change in rectal wall thickness
$x$	position along LR axis (mm).
$x_0(v)$	position (absolute) of $v$ at planning (mm).
$x_t(v)$	position (absolute) of $v$ at time, t (mm).
$y$	position along AP axis (mm).
$z$	position along SI axis (mm).
$\gamma$	gradient of dose response function
$\Delta$	deviation or shift (of dose distribution) (mm).
$\Delta r$	change in rectum radius (mm).
$\Delta v$	sub-volume (normally volume of a voxel)
$\Delta w$	change in rectal wall thickness (mm).
$\zeta$	random deviate sampled from Gaussian distribution

$\eta$	co-efficient
$\Theta$	angle
$\mu$	on-going number of measurement
$\xi$	organ position (mm).
$\omega$	a weighting factor
$\Delta_j$	total shift from mean organ position for $j_{th}$ fraction (mm).
$\Delta r'$	weighted change in radius
$\Sigma$	standard deviation between patient variables (systematic error)
$\Sigma_{delin}$	standard deviation in interpatient (systematic) mean delineation error
$\Sigma_{OM}$	standard deviation in interpatient (systematic) mean organ motion error
$\Sigma_{SE}$	standard deviation in interpatient (systematic) mean setup error
$\alpha$	parameter of the Linear Quadratic model for cell killing ( $Gy^{-1}$ )
$\alpha_s$	hyper sensitive cell sensitive at low dose ( $Gy^{-1}$ )
$\beta$	parameter of the Linear Quadratic model for cell killing ( $Gy^{-2}$ )
$\rho$	clonogen density ( $cm^{-3}$ )
$\sigma$	standard deviation in random parameter (general)
$\sigma_{OM}$	standard deviation in interfraction (random) organ motion
$\sigma_p$	standard deviation describing the production of penumbra
$\sigma_{SE}$	standard deviation in interfraction (random) setup error
$\sigma_{TD}$	standard deviation of treatment delivery (random) errors (i.e. interfraction setup errors plus interfraction organ motion error)
$\sigma_\alpha$	standard deviation in interpatient (systematic) cell sensitivity

# List of Figures

Figure 2.1 Definitions of treatment volumes as defined by ICRU-62 (Fig. 2.16) showing their relation by scenarios A, B and C discussed in the text.

Figure 2.2 Cumulative probability distributions as a function of the normalised radius of expansion for three different CTV-PTV margin strategies. From Antolak and Rosen (1999).

Figure 3.1 Plots of Probability of effect following single fraction irradiation to dose, as calculated with the Probit model (solid curve) and Logit model (dashed).

Figure 3.2 Surviving fraction versus dose for early responding tumour tissue and late responding normal tissue. Tumour is characterised by  $\alpha = 0.35 \text{ Gy}^{-1}$  and  $\alpha/\beta = 10$ , while normal tissue is characterised by  $\alpha = 0.15 \text{ Gy}^{-1}$  and  $\alpha/\beta = 3$  (from Metcalfe et al. 1997).

Figure 3.3 Survival fraction versus dose for T98G human glioma cells. The dots with error bars are the experimental data points, the dashed curve is the LQ model prediction, and the solid curve is the IR model prediction. From Joiner et al. (2001).

Figure 3.4 Characteristic sigmoidal TCP versus dose curve derived theoretically and experimentally. (Taken from Webb and Nahum 1994)

Figure 3.5 The dose-volume relationship for a) the (mostly serial) esophagus, b) for (mostly parallel) lung, and c) for the rectum. Taken from Burman et al. (1991) using data from Emami et al. (1991).

Figure 3.6 a) The distribution of rectal surface area irradiated across patients can be separated by the grade of prostate cancer. Taken from Lu et al. (1995) b) The correlation between NTCP and volume is strongest at low partial volumes (less than 0.5) and for full volume delineation. Taken from Dale et al. (1999).

Figure 3.7 A transverse section of the rectum showing different methods of organ delineation for generating histograms. Adapted from Dale and Olsen (1998).

Figure 3.8 Characterisation of the Dose Surface Histogram. From Fenwick et al. (2001).

Figure 4.1 Demonstration of the direct derivation of dose PDF from spatial PDF with static dose distribution. (Adapted from Leong 1987). The spatial PDF (below the half dose profile) is used to allocate probability values (a dose PDF located right of the half dose profile) for a particular element of radius positioned originally at 50% dose. This procedure is repeated for other elements yielding dose PDFs as shown in figure 4-2 below.

Figure 4.2 Dose PDFs within voxels that are positioned at five distances from the central axis, labelled from Figure 4.1. Only odd numbered curves are shown for brevity. Dose PDF curves for distances 3 and 5 cm (corresponding to radii  $r_3$  and  $r_5$  respectively) predict mainly high and low doses respectively because these voxels are centred at the upper and lower position of the dose profile. The dose PDF curve for the voxel centred at 4 cm from the central axis (radius  $r_4$ ) is smeared over a large dose range because its mean location is the midpoint of the penumbra. The value of the positional PDF standard deviation is 0.6 cm.

Figure 4.3 Rayleigh distribution with  $b=2$ .

Figure 4.4 Maxwell probability density function with  $b=2$ .

Figure 4.5 (a) Mean organ position is represented by the  $x,y$  co-ordinate system. In routine treatment, due to CT uncertainty, the planning image represents the organ in an off-set co-ordinate system (the  $x',y'$  co-ordinate system). This co-ordinate system is then used to plan and deliver the dose. The 1D approach in this study uses only the  $x$ -component of these 2D shifts. (b) Organ positions during the treatment delivery (such as  $\phi_1, \phi_2$  and  $\phi_3$  for 3 fractions) are measured in the off-set ( $x',y'$ ) co-ordinate system.

Figure 4.6 (a) Mean dose incorporating uncertainty at both planning and treatment. The dose profile represented by the broken line is the original dose profile and that represented by a solid line includes only the treatment delivery errors. The spatially uniform dose uncertainty follows the original dose profile. (b) Magnified view of penumbra.

Figure 4.7 Dose variation (1 standard deviation of mean treatment dose) scored in voxels ( $\Delta x = 0.1$  cm), using multiple CT scans to estimate mean organ position. The solid line shows dose variation due only to treatment delivery uncertainty. Vertical lines represent position of 95% isodose contour and the dash-dot line represents the spatially uniform dose uncertainty.

Figure 4.8 a) One dimensional profiles of prescribed dose distributions with three margin sizes (0.5, 1.0, 1.5 cm) and b) the associated standard deviations in treatment dose.

Figure 4.9 Standard deviation in treatment dose using the standard deviation in position to be 0.6, 0.8 and 1.0 cm. The value given as 'tumour position' is the standard deviation equal to the quadratic sum of random inter-fraction organ motion and random setup errors.

Figure 4.10 Possible reductions in margin size evident from improving knowledge of mean organ position.

Figure 4.11 Mean treatment dose predicted for 1 and 5 CT scans using the convolution method as compared with MC results. The original dose profile is also shown.

Figure 4.12 Flow chart of regimes for timing multiple imaging

Figure 4.13 Mean dose (A→C) and variance in mean dose (D→F) resulting from incorporating regimes A,B, C into Monte Carlo modelling of the treatment process.

Figure 4.14 Illustration of the prostate gland (GTV), rectum and three dose distributions characterised by margins of a) 0.5 cm b) 1.0 cm and c) 1.5 cm. In each case the 95% isodose indicates the PTV, the green volume is the prostate (GTV & CTV) and the brown volume is the rectal wall.

Figure 4.15 Two views of the mean treatment dose calculated with three original dose distributions (for margins of 0.5, 1.0, 1.5 cm) for three cases. The three cases are an original dose distribution (black solid line), a mean treatment dose calculated based on 1 planning CT scan (blue solid) and a mean treatment dose based on infinite planning CT scans (red dashed line).

Figure 4.16 Iso-standard deviation plots in the transverse plane with a) 0.5 cm and b) 1.5 cm margin.

Figure 4.17 Profiles of one standard deviation in mean treatment dose along the lateral (X) and anterior-posterior (Y) direction for the a) 0.5 cm margin, b) 1.0 cm margin and c) 1.5 cm margin.

Figure 5.1 Schematic of the characterisation of the rectum geometry A rectal wall segment will area,  $A_0$ , subtended by  $d\theta$  of distance  $r_{in}(\theta)$  from the geometric centre, and of thickness,  $w(\theta)$ .

Figure 5.2 Plot of inner rectum wall radius, and wall thickness versus angle for a characteristic slice.

Figure 5.3 Calculated wall thickness (Eq.5.7) with changes of rectal wall radius..

Figure 5.4 Rectum segment has constant area. Dashed segment is original segment.

Figure 5.5 Modelling shifts of the rectum GC is done by shifting the entire organ within a fixed dose grid. A) The rectum GC position in the original CT planning image is compared to b) the position (shifted posteriorly) in a later fraction, or CT image acquisition.

Figure 5.6 Dose surface histograms of the planned dose distributions with CTV-PTV margins of 5, 10, or 15 mm.

Figure 5.7 Dose Surface maps of the planned dose distributions with CTV-PTV margins of a) 5 mm, b) 10 mm, or c) 15 mm. Orientation: Left=0°; Anterior=90°.

Figure 5.8 DSH showing the mean and planned dose distributions modelling an empty rectum at planning with three CTV-PTV margins.

Figure 5.9 Dose Surface Maps showing the difference between rectal dose distributions with empty rectum at planning for a) 5 mm margin, b) 10 mm margin, c) 15 mm margin. Orientation: Left=0°; Anterior=90°.

Figure 5.10 DSH for planned and mean (calculated) dose distributions with 5, 10, and 15 mm margins, including a full rectum at planning.

Figure 5.11 DSM showing where the difference dose occurs for margins of a) 5 mm, b) 10 mm, and c) 15 mm with full rectum at planning. Orientation: Left=0°; Anterior=90°.

Figure 5.12 Dose surface histograms of the rectal wall for dose distributions with a) 5 mm b) 10 mm, and c) 15 mm margin. The three planned dose distributions are solid lines and the 20 DSHs including random and systematic errors are dashed lines. The individual patient DSHs are symmetrical about the planned DSH across the population

Figure 5.13 The standard deviation in rectal wall dose calculated with 5 mm margin and a) one pre-treatment CT scan with, b) two pre-treatment CT scans, and c) infinite pre-treatment CT scans. Orientation: Left=0°; Anterior=90°.

Figure 5.14 The standard deviation in rectal wall dose calculated with 10 mm margin and a) one pre-treatment CT scan with, b) two pre-treatment CT scans, and c) infinite pre-treatment CT scans. Orientation: Left=0°; Anterior=90°.

Figure 5.15 The standard deviation in dose presented as a DSM. A margin of 15 mm is used with a) one, b) two, and c) an infinite number of pretreatment CT scan information. Orientation: Left=0°; Anterior=90°.

Figure 6.1 Isodose contours for typical prostate treatment. The CTV (solid and filled), PTV (dotted), and rectum (brown) are shown, with the oblique and horizontal lines indicating the position of dose profiles used.

Figure 6.2 The dose distribution for 1D TCP calculations.

Figure 6.3 TCP calculated with planned dose distribution versus mean calculated with CTV-PTV margins of 0.5 cm, 1.0 cm and 1.5 cm (incorporating treatment uncertainty). The magnitude of treatment uncertainty is fixed for all cases.

Figure 6.4 TCP calculated with planned dose distribution versus mode calculated with CTV-PTV margins of 0.5 cm, 1.0 cm and 1.5 cm (incorporating treatment uncertainty). The magnitude of treatment uncertainty is fixed for all cases.

Figure 6.5 Mean TCP calculated using dose distribution with steep penumbra compared with the standard dose distribution.

Figure 6.6 Mean tumour control probability for treatments incorporating non-uniform dose uncertainty, uniform dose uncertainty and varying cell sensitivity inter-patient.

Figure 6.7 Standard deviation in mean tumour control probability incorporating spatially non-uniform dose uncertainty, spatially uniform dose uncertainty and varying cell sensitivity inter-patient.

Figure 6.8 Distributions of TCP for three dose levels a) 48 Gy, b) 52 Gy, and c) 56 Gy incorporating dose uncertainty (uniform or non-uniform) and inter-patient cell sensitivity variation. The exact calculated TCP at these dose levels (shown as vertical dashed line) are 0.05, 0.58 and 0.90, respectively.

Figure 6.9 Mode of TCP over a patient population.

Figure 6.10 TCP calculated for an individual patient with (F)ull or (E)mpty rectum in planning CT scan with margins of 0.5 cm, 1.0 cm, or 1.5 cm.

Figure 6.11 Plot of TCP versus cell sensitivity. Two values of cell sensitivity ( $\alpha_1=0.29 \text{ Gy}^{-1}$ ,  $\alpha_2=0.35 \text{ Gy}^{-1}$ ) and the range covered by one and two standard deviations in cell sensitivity are illustrated. See text for further description.

Figure 6.11 Schematics of voxel-based dose allocation from the deformed rectal wall (dashed) to the original wall (solid) following a sampled change of radius. Three cases are shown, where a) the wall thickness does not change, b) the wall thickness is reduced, and c) where the wall thickness increases. See text for further explanation.

Figure 6.13 Mean NTCP calculated for individual patients with either full (F) or empty (E) rectums in the planning CT scan and with margins of 0.5 cm, 1.0 cm, or 1.5 cm. Table 6.4 NTCP across a patient population (N=1000) with D=64 Gy

Figure 6.14 NTCP calculated with planned dose or with a 5% spatially uniform dose error at each fraction of treatment.

Figure 6.15 Comparison between NTCP calculated with the planned dose distribution against NTCP calculated assuming that the planned surface dose (from DSM) is deposited uniformly in each angular rectal wall segment.

Figure 6.16 Comparison of mean NTCP calculated with mean dose against the calculated rectal wall dose. Both sets were calculated for a population of patients, with each patient being planned from a single CT image set.



Figure 6.17 Comparison of mean NTCP calculated with the mean dose against the MC calculated rectal wall dose. Both sets were calculated for a population of patients, with each patient being planned using the mean organ position.

Figure 6.18 NTCP calculated using the mean dose with  $n=0.24$ ,  $m=0.15$  for an individual patient with systematic error.

Figure 6.19 NTCP calculated using the mean dose with  $n=0.12$ ,  $m=0.15$  for an individual patient with systematic error.

Figure 6.20 Mean UTCP calculated for a population of identical patients with fixed systematic error.

Figure 6.21 Mean UTCP (1CT) versus dose for margin sizes 0.5, 1.0, and 1.5 cm.

Figure 6.22 Mean UTCP against margin size at a) 64 Gy and b) 70 Gy..

Figure 7.1 Correction factors for various inhomogeneity correction techniques versus depth in different density media. Taken from Wong and Purdy (1990).

Figure 7.2 The superposition dose calculation technique models primary fluence interactions at  $r'$  and the probability of dose deposition in surrounding voxels, including that voxel centred at  $r$ . Adapted from Metcalfe et al. (1997).

Figure 7.3 The superposition dose calculation overestimates dose in lower density media and underestimates after lower density media. Taken from Metcalfe et al. (1997).

Figure 7.4 Dose PDF at the medial edge of the penumbra.

Figure 7.5 Standard deviation isodoses for a) a liver treatment including random patient positioning errors (Taken from Lujan et al. 1999) and b) a 4-field prostate treatment (reproduced from Chapter 4).

Figure 7.6 a) Mean isodose contours, and b) Confidence limit plot showing the minimum dose received by 90% of the population.

Figure 7.8 The CL-DVH from Mageras et al. (1999) a) for prostate and b) rectum, and b) the DVH accuracy increases with the number of fractions (from Lujan et al. 1999)

Figure 7.9 Schematic of the a) 95% modal isodose, and b) 30% modal isodose with error bars indicating a 95% chance of depositing given dose.

Figure 7.10 Single axial slice showing lateral and AP beam orientation, b) dose difference display:  $\bar{D} - D_0$ . Taken from Lujan et al. (1999).

# List of Tables

Table 2.1 Variation in parameters used for measurement of  $MOD_{prostate}$ . Key: full (F) bladder/rectum, empty (E) bladder/rectum, rectum status Not Considered (NC), insufficient information provided (-). The numbers of images taken per patient refers to the number of images (CT, simulation and portals) used to derive their final measurement. Patients were treated in the supine (S) or prone (P) position, whether patient repositioning was done (yes, Y) or was not done (no, N), and the method used for the measurement (M1 or M2) from the text. In two studies the bladder/rectum content was increased with time (\*), while in another study two time periods for voiding before treatment were examined (\*\*).

Table 2.2 The mean patient displacement averaged across studies (SEAS) and standard deviation  $\delta$  (mm), with the systematic standard deviation  $\delta_s$  (mm) and the random standard deviation  $\delta_R$  (mm).

Table 2.3 Prostate position uncertainty due to the motion not directly attributed to bladder/rectum filling in the anterior-posterior, medio-lateral and superior-inferior directions. References will be bracketed.

Table 2.4 Summary of respiration-induced abdominal motion. The movement of the organ is the positional difference of the organ from inhalation to exhalation, unless otherwise stated. The details of the measurement may include a direction, breathing rate, alternate endpoint, or the condition of the organ at the time of measurement i.e. disease title.

Table 3.1 Magnitudes of parameters  $m, n, D_{50}, s$  and  $k$  used to model normal tissue complications following full volume irradiation for a range of organs. From Burman et al. (1991) and Kallman et al. (1992).

Table 4.1 Summary of typical error magnitudes concerning supine treatment of prostate carcinoma used for modelling. Delineation error ranges are due to uncertainty in apex and seminal vesicles localisation. Systematic set-up errors quoted do not include the use of a correction protocol.

Table 5.1 The parameters defining systematic and random changes in rectum geometry

Table 6.1 The effect of margin size on TCP incorporating treatment uncertainty. The difference between planned TCP and mean TCP with 1 CT, as well as the difference in TCP between the planned and calculated mean TCP are shown.

Table 6.2 The effect of margin size on TCP incorporating treatment uncertainty and steep dose gradient to mimic IMRT. The difference between planned TCP and mean TCP at a 60 Gy dose level, as well as the difference in dose between the planned and calculated mean TCP at two levels of TCP are shown.

Table 6.3 Mean TCP across a patient population for three margin sizes, with error given as one standard deviation in mean TCP.

Table 6.4 NTCP across a patient population (N=1000) with D=64 Gy

Table 6.5 Maximum value of mean UTCP across a population with 1 SD uncertainty. The dose required for maximum UTCP is given in brackets.

# Abstract

Uncertainties are inevitably part of the radiotherapy process. Uncertainty in the dose deposited in the tumour exists due to organ motion, patient positioning errors, fluctuations in machine output, delineation of regions of interest, the modality of imaging used, and treatment planning algorithm assumptions among others; there is uncertainty in the dose required to eradicate a tumour due to interpatient variations in patient-specific variables such as their sensitivity to radiation; and there is uncertainty in the dose-volume restraints that limit dose to normal tissue.

This thesis involves three major streams of research including investigation of the actual dose delivered to target and normal tissue, the effect of dose uncertainty on radiobiological indices, and techniques to display the dose uncertainty in a treatment planning system. All of the analyses are performed with the dose distribution from a four-field box treatment using 6 MV photons. The treatment fields include uniform margins between the clinical target volume and planning target volume of 0.5 cm, 1.0 cm, and 1.5 cm. The major work is preceded by a thorough literature review on the size of setup and organ motion errors for various organs and setup techniques used in radiotherapy.

A Monte Carlo (MC) code was written to simulate both the treatment planning and delivery phases of the radiotherapy treatment. Using MC, the mean and the variation in treatment dose are calculated for both an individual patient and across a population of patients. In particular, the possible discrepancy in tumour position located from a single CT scan and the magnitude of reduction in dose variation following multiple CT scans is investigated. A novel convolution kernel to include multiple pretreatment CT scans in the calculation of mean treatment dose is derived. Variations in dose deposited to prostate and rectal wall are assessed for each of the margins and for various magnitudes of systematic and random error, and penumbra gradients.

The linear quadratic model is used to calculate prostate Tumour Control Probability (TCP) incorporating an actual (modelled) delivered prostate dose. The Kallman s-model is used to calculate the normal tissue complication probability (NTCP), incorporating actual

(modelled) fraction dose in the deforming rectal wall. The impact of each treatment uncertainty on the variation in the radiobiological index is calculated for the margin sizes.

# Thesis Statement

This work contains no material which has been accepted for the award of any other degree or diploma in any University or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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*This thesis is dedicated to my great grandmother, Ethel Jaye 1899-2001*