

**COMPARING “TRIANGULAR”, “V” AND CONVENTIONAL PATTERNS OF DOSE  
DELIVERY IN OPTIMIZING CELL KILL WHEN APPLIED TO TUMOUR TYPES WITH  
LOW  $\alpha/\beta$  RATIOS**

By

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## Declaration

I declare that the study, Comparing “triangular”, “V” and conventional patterns of dose delivery in optimizing cell kill when applied to tumour types with low  $\alpha/\beta$  ratios, is my own work and that all the sources I have used or quoted have been indicated and acknowledged by means of complete references and that this work has not been submitted before for any other institution.

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Ms Elsie Neo Seane

.....

Date



## Dedication

This dissertation is dedicated

To my late sister

***Mrs Ditshebo Khutswane,***

*“I feel blessed to have had a sister like you who always supported me in all my endeavours. I am saddened that you are not here to share my success, but I know you are always with me in spirit. You might be physically gone, but your encouragement and motherly love will stay with me forever.”*

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## Abstract

**The aim:** To compare mean inactivation doses between the triangular and the V-shaped; the triangular and conventional; and V-shaped and conventional patterns of dose delivery on prostate tumour cells, with  $\alpha/\beta$  ratios of 1 Gy, 1.5 Gy and 3 Gy.

**Design and method:** A total of 45 treatment plans created for prostate tumours, using conformal radiotherapy techniques, six treatment fields, and dose per fraction of 2 Gy were sequentially collected. The beam weightings and treatment field positions used in the creation of these treatment plans, as well as prostate tumour cell kinetic parameters from literature, were then used to perform computational simulations, using the Virtual Cell Radiobiology programme Version 2 to calculate tumour cell survival. The mean inactivation doses for each  $\alpha/\beta$  ratio and for each dose delivery pattern were calculated.

### Results:

For the comparison between: (i) the triangular and conventional dose delivery patterns across the three  $\alpha/\beta$  ratios, the results showed a non-significant difference, with  $p=0.5436$ ; (ii) for the triangular and V-shaped patterns of dose delivery across the three  $\alpha/\beta$  ratios, the results indicate that the triangular pattern is not statistically different from the V-shaped pattern, with  $p=0.5436$ ; and (iii) for the V-shaped and conventional patterns of dose delivery, a non-significant difference with  $p=0.5436$  was observed.

**Discussion:** The observed non-significant differences in mean inactivation dose from the different dose delivery patterns is attributed to 1) treatment times that are shorter than the sub-lethal damage repair half times; (2) high dose rates used in conformal radiotherapy techniques; and (3) the small size of individual dose fields.

### Conclusions:

The study demonstrated that the suggested triangular and V-shaped patterns of dose delivery do not result in different biological effect when implemented to 3-D conformal treatment techniques.

**Keywords:** beam sequencing, triangular pattern of dose delivery, V-shaped pattern of dose delivery, mean inactivation dose, prostate cancer.

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## List of Abbreviations

3-D: three-dimensional

$\alpha/\beta$  : alpha beta

BED: Biologically equivalent dose

CKM: Cell Kinetics Model

CLRP: Cell Repair Parameters

DNA: Deoxyribonucleic Acid

DRM: Damage Repair Model

DSB: Double-strand Break

FL: Fatal Lesions

GF: Growth Fraction

HRS: Hyper-radiosensitivity

IAEA: International Atomic Energy Agency

ICRU: International Commission of Radiation Units and Measurement

I.E.: That is

IMRT: Intensity Modulated Radiation Therapy

IRR: Increased Radio Resistance

keV: Kiloelectron Volt

LAO: Left Anterior Oblique

LDR: Low Dose Radiosensitivity

LET: Linear Energy Transfer

LPO: Left Posterior Oblique

LPL: Lethally and Potentially Lethal

LQ: linear quadratic

MCDS: Monte Carlo Damage Simulation

MCER: Monte Carlo Excision Repair

MCNP: Monte Carlo N-particle

MeV: Megaelectron Volt

MID: Mean Inactivation Dose

NID: Normalised Iso-effective Dose

NTCP: Normal Tissue Complication Probability

OER: Oxygen Enhancement Ratio

QECK: Quasi-Exponential Cell Kinetics

RAO: Right Anterior Oblique

RBE: Relative Biologic Effectiveness

RHT: Repair Half Time

RL: Right Lateral

RMR: Repair-misrepair Model

RPO: Right Posterior Oblique

SSB: Single Strand Break

TCP: Tumour Control Probability

TLK: Two Lesions Kinetic Model

VC: Virtual Cell

XBRT: External Beam Radiation Therapy

## Glossary of Terms

### **3-D conformal radiation therapy**

A treatment technique where the radiation treatment beams used are shaped to conform to the shape and size of the target volume.

### **$\alpha/\beta$ ratio**

The ratio of the parameters  $\alpha$  and  $\beta$  in the linear quadratic model. It is used to characterise the radiation sensitivity of normal tissue, as well as tumours.<sup>1, 21, 55</sup>

### **Aberration**

Atypical development or growth.<sup>1</sup>

### **Acentric chromosome**

A chromosome fragment without a centromere.<sup>1</sup>

### **Algorithm**

In mathematics and computer science, it is an effective method expressed as a finite list of well-defined instructions for calculating a function.

### **Base pair**

A pair of complementary nitrogenous bases in a DNA molecule, adenine pairs with thymine, and guanine pairs with cytosine. It is also the unit of measurement for DNA sequences.<sup>21</sup>

### **Beam weighting**

The individual dose contribution from each treatment field.

### **Chromosomal aberration**

Any change resulting in duplication, deletion, or rearrangement of chromosomal material.<sup>1, 21</sup>

### **Cell survival fraction**

The fraction of cells that survive a dose of radiation.<sup>1</sup>

### **Dicentric chromosome**

A chromosome with two centromeres.<sup>1, 21, 65</sup>

### **Differential equation**

Mathematical equation for an unknown function of one or several variables.

### **Dose rate**

The radiation dose delivered per unit time, for instance, in grays per hour.<sup>1, 21</sup>

### **Double-strand break (DSB)**

A break in both strands of a DNA molecule.<sup>1, 21, 55</sup>

### **Gray (Gy)**

A unit of absorbed dose. 1 Gy = 1 J per kg.<sup>1, 21, 55</sup>

### **He La cells**

A cell type in an immortal cell line used in scientific research. It is the oldest and most commonly used human cell line.<sup>61</sup>

### **Hypofractionation**

A reduction in the number of fractions with increase in fraction size within a similar overall time.<sup>21</sup>

### ***In vitro***

In glassware, normally in a laboratory or in an artificial environment outside the living body.<sup>1, 21</sup>

### ***In vivo***

In the living; occurring within the living body of an organism.<sup>1, 21, 55</sup>

### **Isocentric dose**

Radiation dose delivered to the isocentre. The isocentre is a common point in the target volume where all the treatment beams converge.

### **Iso-effect dose**

The total dose of radiation for a given effect.<sup>21</sup>

### **Lethal damage**

Damage that cannot be repaired.<sup>1, 21, 55</sup>

### **Linear Energy Transfer (LET)**

The rate at which radiation energy is deposited as a charged particle travels through matter.<sup>1</sup>

### **Linear Quadratic (LQ) model**

The model in which the effect (E) is a linear quadratic function of dose (d):  $E = \alpha d + \beta D^2$ .

For cell survival:  $S = \exp(-\alpha d - \beta D^2)$ .<sup>21, 55</sup>

### **Low dose radiosensitivity (LDR)**

The increased sensitivity to radiation caused by low doses.<sup>3</sup>

### **Nucleotide**

The three components of a DNA molecule, including a nitrogenous base, a 5-carbon sugar and phosphoric acid.<sup>21</sup>

### **Radiation treatment fractionation**

Extension of the total radiation dose in radiation therapy over a period of time, ordinarily days or weeks, in order to minimise radiation effects on normal tissues.<sup>21</sup>

### **Radiosurgery**

A radiotherapy treatment technique where only a single fraction is given, using high doses.

### **Sub-lethal damage**

Non-lethal damage that either can be repaired or can accumulate and become lethal if further doses are given.<sup>1</sup>

### **Time dose effects**

The dependence of the iso-effective radiation dose on the duration (and number of fractions) in radiotherapy.<sup>21</sup>

### **Type 1 damage**

Creation of lethal single tract lesions.<sup>19</sup>

### **Type 2 damage**

Creation of sub-lethal lesions which will interact with sub-lethal lesions that are created later during the same fraction to form lethal lesions.<sup>19</sup>

### **Type 3 damage**

Creation of sub-lethal lesions which interact with sub-lethal lesions formed during a previous fraction, to form lethal lesions.<sup>19</sup>