

THE EFFECT OF DOSE CALCULATION ALGORITHMS ON THE NORMAL TISSUE
COMPLICATION PROBABILITY VALUES OF THORACIC CANCER

by

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CERTIFICATE

This is to certify that the dissertation entitled "The effect of dose calculation algorithms on the normal tissue complication probability values of thoracic cancer" is the bona fide records of research work done by Noor Ashikin Binti Ahmad during the period February 2015 till June 2015 under our supervision

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LIST OF ABBREVIATION

GTV	Gross Tumor Volume
PTV	Planning Target Volume
CTV	Clinical Target Volume
DVH	Dose Volume Histogram
LKB	Lyman-Kutcher-Burman
RS	Relative Seriality
NTCP	Normal Tissue Complication Probability
TCP	Tumor Control Probability
TPS	Treatment Planning System
OMP	Oncentra Masterplan
RTOG	Radiation Therapy Oncology Group
CT	Computed Tomography
ICRU	International Commission on Radiation Unit and Measurements
MLC	Multi Leaf Collimator
FSU	Functional subunits
IV	Internal Volume
TV	Target Volume

ABSTRACT

Purpose: To identify the effect of dose calculation algorithms on the Normal Tissue Complication Probability values of thoracic cancer. **Materials and Methods:** NTCP values from BIOPLAN software is calculated based on standard DVH data. Dose distributions of treatment plans are calculated by using two different algorithms of Oncentra Masterplan (OMP) treatment planning system (TPS) which are Collapse Cone and Pencil Beam. Four treatment plans are created and DVHs are evaluated based on criteria of acceptance level. NTCP values for thorax plan one and two are evaluated by using different algorithm. **Results:** The coverage of the target volume for all treatment plans has achieved the desired isodose for at least 90% of isodose at 100% of volume. Collapsed cone shows better calculation in three beam but pencil beam is better in 5 beams calculation. The NTCP values of the LKB model are slightly higher than RS model for both cases even though using different kind of algorithm. **Conclusions:** There is no difference between pencil beam and collapsed cone algorithms in term of NTCP values. NTCP values are due to physical and biological effects. Mathematically, both treatment plans have higher probability to develop the complication but the numbers in this paper are not wholly based on clinical or even experimental data. It may due to patient-related factors, patient history or the modalities used in treatment delivery.

ABSTRAK

Tujuan: Untuk mengenal pasti kesan algoritma pengiraan dos terhadap nilai Normal Tisu Kebarangkalian Komplikasi kanser toraks. Bahan dan Kaedah: Nilai NTCP daripada perisian BIOPLAN dikira berdasarkan data DVH standard. Dos pengagihan pelan rawatan dikira dengan menggunakan dua algoritma yang berbeza di dalam 'Oncentra Masterplan' (OMP) sistem perancangan rawatan (TPS) iaitu 'Collapsed Cone' dan 'Pencil Beam'. Empat pelan rawatan yang dicipta dan DVHs adalah dinilai berdasarkan kriteria tahap penerimaan. Nilai NTCP untuk pelan toraks satu dan pelan toraks dua dinilai dengan menggunakan algoritma yang berbeza. Hasil: Liputan jumlah sasaran bagi semua pelan rawatan telah mencapai isodos yang dikehendaki sekurang-kurangnya 90% . 'Collapsed Cone' menunjukkan pengiraan yang lebih baik dalam tiga rasuk tetapi 'pencil beam' yang lebih baik 5 pengiraan rasuk. Nilai NTCP model LKB adalah lebih tinggi sedikit daripada model RS untuk kedua-dua kes walaupun menggunakan pelbagai jenis algoritma. Kesimpulan: Tiada perbezaan antara algoritma 'pencil beam' dan 'collapsed cone'. Nilai NTCP adalah disebabkan oleh kesan fizikal dan biologi. Secara matematik, kedua-dua pelan rawatan mempunyai kebarangkalian yang lebih tinggi untuk membangunkan komplikasi tetapi nombor dalam kertas kerja ini adalah tidak secara keseluruhannya berdasarkan data klinikal atau eksperimen. Ia mungkin disebabkan oleh faktor-faktor yang berkaitan dengan pesakit, sejarah pesakit atau kaedah yang digunakan dalam penyampaian rawatan.

CHAPTER 1

1.0 INTRODUCTION

1.1 Background of the study

The successful delivery of external beam radiotherapy involves a number of complex processes beginning with the decision by the clinical oncologist to use radiotherapy as part of the patient's cancer management, through the preparation and planning of the patient's treatment, to the verification of the patient position and radiation dose delivered at the time of treatment (Hoskin, 2012).

The aim of radiotherapy is to deliver a homogenous radiation dose to tumor inside the patient, whilst minimizing dose to all other parts of the body, in particular to organs which are especially radiosensitive or in close to proximity to the tumor. In order to begin to achieve these aims, detailed information is required about the tumor position, size, and shape within the patient and the location of radiosensitive organs at risk. This is achieved from three-dimensional patient images, usually CT scans. The various structures are outlined on a series of axial slices to produce three-dimensional (3D) volumes. Once this has been done, a radiotherapy plan can be designed for the individual patient to meet treatment goals by using treatment planning system, which is a detailed computer model of the way radiation dose will be deposited within the patient anatomy (Hoskin, 2012)

Treatment planning has evolved from the early use of radiation for therapy, where the distribution of radioactive sources was decided by applying a set of rules, to present-day planning techniques that rely on complex computer modeling of the dose distribution from patient data and external radiation beam parameters. The overall aim of the planning process remains the translation of the therapeutic requirements of the oncologist into a set of treatment instructions that will enable the patient to be treated accurately. The treatment plan does not only provide a set of instructions for the radiographer but also give information about the distribution of dose that enables the oncologist to assess the adequacy of the beam arrangements (Cherry, 2009).

The basic principal steps involved in treatment planning are localization of the tumor and a dimensional description of the target volume by the oncologist, followed by the identification of any critical structures to be avoided during the planning process. Next, measurement of patient data such as body contours, dimensions, and tissue densities are required to enable the target volume to be defined within planar usually transverse contours of the body (Cherry, 2009).

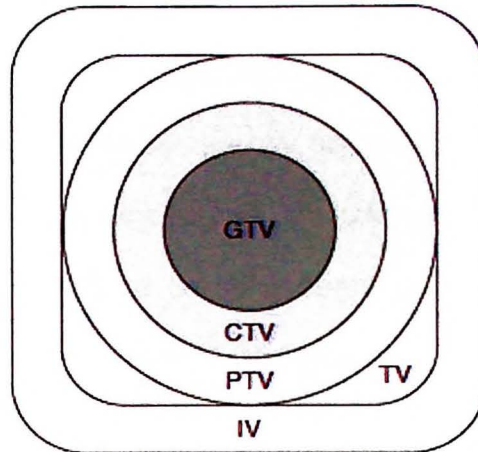


Figure 1 Volume definitions in radiotherapy according to the International Commission on Radiation Units and Measurements (ICRU, 1999) Report 62 (ICRU,1999)

Apart from that, the treatment planner will determine the optimum arrangement of radiation fields to obtain a uniform dose distribution which is +7 and -5% of the prescribed dose determined by the constraints set by the clinical requirements such as dose to sensitive organs. The dose distribution is calculated and displayed in single or multiple planar views to allow assessment of the plan and adjustment of field parameters to achieve optimization. The oncologist prescribes a fractionated time and dose to a reference point within the treatment volume and a set of treatment instructions is produced to allow the plan to be delivered (Cherry, 2009).

The International Commission on Radiation Units and Measurements (ICRU) produced a report in 1987 on the use of computers in treatment planning and subsequently produced a report on prescribing, recording and reporting procedures in external beam photon therapy followed by a supplement to these 6 years later. These reports are of particular importance to treatment planning in describing the parameters of volume and dose when prescribing radiotherapy treatments (Cherry, 2009).

The publications ICRU50 and its supplement ICRU62 give clear recommendations about reporting of absorbed dose distributions and set out the level of complexity of dose evaluation from basic planning techniques to complex 3D dose computation. ICRU50 gives clear and concise definitions of gross tumor volume (GTV), clinical target volume (CTV) and planning target volume (PTV), which are marked on the CT images of the patient before beam placement and calculation of the plan. The supplement publication, ICRU62 develops the concept of treatment margins that can account for geometrical changes in the CTV due to anatomical uncertainties (internal margin) and those added to account for uncertainties on patient position (set-up margin).

Radiotherapy planning is almost exclusively performed using computer-based treatment planning systems, apart from some single field and parallel pair treatments for which no dose distribution is required and

central axis depth doses are obtained from charts. The earliest planning systems, which became available in the 1970s were required to calculate 2D dose distribution for simple square or rectangular fields on a single patient contour. Advances in patient imaging and radiotherapy delivery techniques have driven the development of more sophisticated dose calculation algorithms.

The introduction of CT imaging to the radiotherapy planning process enabled more accurate localization of the target volume. Meanwhile, the subsequent development of beam-shaping technology such as the MLC allowed the shape of treatment fields to be more accurately matched to that of the target. The advent of such conformal radiotherapy techniques introduced a new challenge for dose computation that is 3D calculation of dose from highly irregular fields. The other important impact of CT was visualization of inhomogeneities within the patient and the need to accurately account for them in the dose calculation.

There are many types of algorithm to be used in dose calculation such as pencil beam and collapsed cone. A pencil beam kernel describes the deposition of energy around a very narrow beam and typically represents the scatter distribution due to the primary photon fluence and secondary electron scatter. Collapsed cone convolution is the most commonly used and widely accepted algorithm class in radiotherapy planning systems.

Primary photons are treated separately from scattered photons and electrons set in motion. (DesRosiers C., 2013)

Plan evaluation tools allow fast appraisal and optimization of dose distributions in order to determine whether the tolerances for the target volume and critical structures have been achieved. An alternative method of summarising the 3D dose distribution common to all modern treatment planning systems is the dose-volume histogram (DVH). The DVH for a target volume can be used to easily determine the percentage of that volume receiving a dose above and below the required tolerances. A weakness of DVH is that it does not provide positional information such as the target DVH may show a certain volume of tissue receiving a dose below the lower tolerance but it does not indicate where that tissue is situated within the target (Joiner, 2009).

The responses of normal tissues to therapeutic radiation exposure range from those that cause mild discomfort to others that are life-threatening. The speed at which a response develops varies widely from one tissue to another and often depends on the dose of radiation that the tissue receives. A major development in the radiobiology of normal tissues during the 1980s was the realization that early and late normal-tissue responses are differently modified by a change in dose fractionation (Joiner, 2009).

A cell's response to radiation is modified by four factors which are Repair, Re-assortment, Repopulation and Reoxygenation. These factors are known as "four R's of radiobiology". This concept helps to describe the differential that exists between tumor cells and normal ones. The normal tissues can be repaired by dividing up a dose radiation into a number of smaller fractions. The external beam radiation delivered to tumor invariably passes through normal tissues and in some instances either partially or fully through adjacent body organs. These normal tissues are called organ at risk. They may become the limiting factor in delivering the desired dose to tumor successfully. Normal tissues can be divided into early responding tissues and late responding tissues. Late responding tissues are those that start proliferating months rather than weeks after radiotherapy while, early responding tissues are those which start proliferating within a few weeks of starting a course of radiotherapy (Colin, 2005).

The concept of tissue radiation tolerance based on functional subunits (FSUs), which may be considered as anatomical structures such as bronchioli, or simply as tissue stem cells. Per definition, a FSU is the largest tissue volume, or unit of cells, that can be regenerated from a single surviving clonogenic cell. Functional subunits are sterilized independently by irradiation. This results in structural damage within the exposed volume. The number of FSUs that are sterilized, and hence the

severity of the damage, depends on their intrinsic radiosensitivity, and on dose and other radiobiological parameters, such as overall treatment time. With suitable procedures (e.g. radiological imaging) the changes can be diagnosed. However, the clinical consequences are dependent on the arrangement of the FSU within the exposed organ. Similar to the connection of elements in an electrical circuit, the FSU can be arranged either in parallel or in series. In organs with a parallel structure, FSUs function independently. Hence, a clinical radiation effect is observed only if the number of surviving FSUs is too low to sustain the physiological organ function. Hence, a threshold volume must be considered in treatment planning, which must not be exceeded but within which large doses may be administered. The risk of complications depends on the distribution of the total dose within the organ rather than on individual 'hot spots'. Examples of organs with a (predominantly) parallel architecture are lung, kidney, and liver. In contrast, in organs with a serial the function of the entire organ depends on the function of each individual FSU which is inactivation of only one FSU results in clinical side-effects in a binary response. In these organs, the risk of complications is highly dependent on 'hot spots', while the dose distribution within the entire organ is less relevant. Examples of (mainly) serially structured organs are spinal cord, intestine and oesophagus (Joiner, 2009).

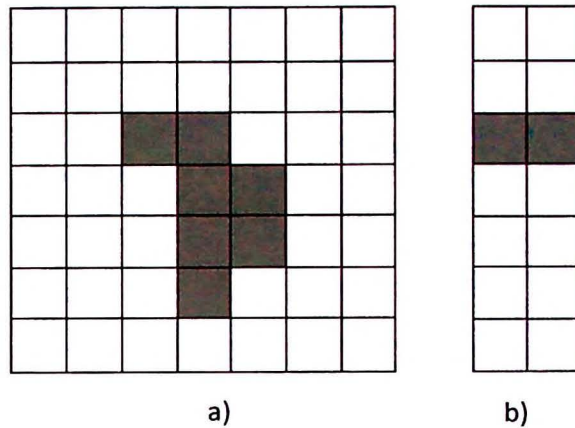


Figure 2 a) Parallel and b) serial organization of functional subunits (FSUs) in normal tissues.

Distributions of absorbed dose do not provide any information on the biological response of tissues either tumor or organs at risk to irradiation. BIOPLAN (BIOplan evaluation of PLANs) has been conceived and developed as a PC based friendly software that allows the user to evaluate a treatment plan from the more objective point of view of the biological response of the irradiated tissue, providing at the same time flexibility in the use of models and parameters. It requires on the Dose Volume Histograms (DVH) and can accept a number of different formats (including DVH files from commercial treatment planning systems). BIOPLAN provides a variety of tools such as Tumor Control Probability (TCP) calculations using Poisson model and Normal Tissue Complication Probability (NTCP) calculation (Sanchez-Nieto, 2000).

CHAPTER 2

2.0 LITERATURE REVIEW

In an analysis conducted by Tine B. Nielsen et al. (2011), they investigated the differences in calculated doses and normal tissue complication probability (NTCP) values between different dose algorithms. Six dose algorithms from four different treatment planning systems were investigated which are Eclipse AAA, Oncentra MasterPlan Collapsed Cone and Pencil Beam, Pinnacle Collapsed Cone and Xio Multigrid Superposition, and Fast Fourier Transform Convolution. Twenty NSCLC patients treated in the period 2001-2006 at the same accelerator used for treatments were modeled in the different systems. The treatment plans were recalculated with the same number of monitor units and beam arrangements across the dose algorithms. Dose volume histograms of the GTV, PTV, combined lungs (excluding the GTV), and heart were exported and evaluated. NTCP values for heart and lungs were calculated using the relative seriality model and the LKB model, respectively. Furthermore, NTCP for the lungs were calculated from two different model parameter sets. Calculations and evaluation were performed both including and excluding density corrections. There are found statistical significant differences between the calculated dose to heart, lung, and targets across the algorithms. Mean lung dose and V_{20} are not very sensitive to change between the investigated dose calculation algorithms. However, the

different dose levels for the PTV averaged over the patient population are varying up to 11%. The predicted NTCP values for pneumonitis vary between 0.20 and 0.24 or 0.35 and 0.48 across the investigated dose algorithms depending on the chosen model parameter set. The influence of the use of density correction in the dose calculation on the predicted NTCP values depends on the specific dose calculation algorithm and the model parameter sets. Calculated NTCP values for pneumonitis are more sensitive to the choice of algorithm than mean lung dose and V_{20} which are also commonly used for plan evaluation.

In a study reported by Bo Zhao et al. (2010), they investigated a new software tool for radiotherapy treatment plan evaluation. The goal of this work is to develop an enhanced treatment plan evaluation tool which incorporates biological parameters and retains spatial dose information. A software system is developed which provides biological plan evaluation with a novel combination of features. It incorporates hyper-radiosensitivity using the induced-repair model and applies the new concept of dose convolution filter (DCF) to simulate dose wash-out effects due to cell migration, bystander effect, and/or tissue motion during treatment. The concept of spatial DVH is introduced to evaluate and potentially optimize the spatial dose distribution in the target volume. Generalized equivalent uniform dose is derived from both the physical dose distribution (gEUD)

and the distribution of equivalent dose in 2 Gy fractions ($gEUD_2$) and the software provides three separate models for calculation of tumor control probability (TCP), normal tissue complication probability (NTCP), and probability of uncomplicated tumor control (P+). TCP, NTCP, and P+ are provided as a function of prescribed dose and multivariable TCP, NTCP, and P+ plots are provided to illustrate the dependence on individual parameters used to calculate these quantities. 10 plans from two clinical treatment sites are selected to test the three calculation models provided by this software.

In a study conducted by Colin (2005), TCP and NTCP potentially offer the capability of being able to better optimize treatments for an individual patient's tumor and normal anatomy. But, from their introduction and even up to present time, TCPs and NTCPs have not been used to predict the actual outcomes of treatment. The aim of the research is to see whether TCP and NTCP can be correlated with the measured clinical outcomes of prostate cancer radiotherapy. The results produced by this research represent a qualified 'yes' to that question with six rectum and five bladder wall related side effects (a total of 11 toxicities) being identified that were reasonably correlated to the calculated NTCP for that particular organ. The outcome of any analysis to determine whether a TCP can be a predictor for observed clinical outcomes of prostate irradiation is in part subject to the a/B that is used in the TCP calculation. This needs

to be representative of the true radiosensitivity of prostate tumors for the TCP to have some accuracy. The unexpected finding of a lower predicted tumor control when utilizing IMRT cannot be confirmed clinically by this research with too few observed relapses to do any correlation. The TCP model also needs to be validated on another data set to permit some credibility regarding its predictions of lower tumor control for a given dose when using IMRT and should be investigated further. Independent of the calculated TCP predictions in relation to the use of an IMRT technique, this research does raise the question of whether one of the prostate radiation techniques compared to the other might be related to better observed clinical outcomes. This research was able to show that the maximum dose and/or the mean dose received by the two outlined OARs in prostate irradiation are related to a calculated NTCP but in themselves were not a reliable predictor of complications.

In an analysis conducted Kupchak, C. et al. (2007), it presents a novel technique for mapping normal tissue complication probabilities (NTCP) onto regions of dose-volume space with statistical considerations of risk. Mapping is done for DVHs specific to one treatment technique for one disease site. In this study, the method is illustrated for simplified intensity modulated arc therapy of prostate and the resulting NTCP values apply complications in the rectum. The method consists of implementing a Monte Carlo algorithm that creates a large set of DVH curves by

simulating random walks through dose-volume space. The walks are guided by a base set of clinical DVHs. Grid points in the dose-volume space have an associated NTCP spectrum for curves passing above right of the grid point of interest. After a DVH is simulated and the NTCP estimate calculated using the Lyman model, dose-volume points located to the bottom left of the curve are scored with this NTCP value and contributed to the spectrum of each point. A NTCP tolerance value is then selected and the risk of violating this tolerance is identified by a gray-scale map in regions of dose-volume space. The generated maps distinguish technique-specific, high-risk regions, a feature which is advantageous over fixed single-point dose-volume constraints commonly used. The maps also provide a visualization tool to help select safe and robust treatment plans and open the possibility for improving the efficiency of biologically based plan optimization by focusing on the more critical sections of DVH curves.

In a study conducted by Hussein, M. et al. (2012), the aim of this study was to investigate the effect of 6 and 15 MV photon energies on intensity-modulated radiation therapy (IMRT) prostate cancer treatment plan outcome and to compare the theoretical risks of secondary induced malignancies. The methods used were separate prostate cancer IMRT plans were prepared for 6 and 15 MV beams. Organ equivalent doses were obtained through thermoluminescent phantom. The neutron dose

contribution at 15 MV was measured using polyallyl-diglycol-carbonate neutron track each detectors. Risk coefficients from the International Commission on Radiological Protection Report 103 were used to compare the risk of fatal secondary induced malignancies in out-of-field organs and tissues for 6 and 15 MV. For the bladder and the rectum, a comparative evaluation of the risk using three separate models was carried out. Dose-volume parameters for the rectum, bladder and prostate planning target volume were evaluated, as well as normal tissue complication probability (NTCP) and tumour control probability calculations. Results are there is a small increased theoretical risk of developing a fatal cancer from 6MV compared with 15MV, taking into account all the organs. Dose-volume parameters for the rectum and bladder show that 15MV results in better volume sparing in the regions below 70 Gy, but the volume exposed increases slightly beyond this in comparison with 6MV, resulting in a higher NTCP for the rectum of 3.6% vs 3.0% (p50.166). The choice to treat using IMRT at 15MV should not be excluded, but should be based on risk vs benefit while considering the age and life expectancy of the patient together with the relative risk of radiation-induced cancer and NTCPs.

CHAPTER 3

3.0 OBJECTIVE OF THE STUDY

3.1 Aim

To investigate the effects of dose calculation algorithm on the normal tissue complication probability (NTCP) values on thorax patients.

3.2 Specific objectives

The objectives of this research are:

- To calculate NTCP values from bioplan based on DVH data.
- To compare dose distributions of planning using Collapse Cone and Pencil Beam algorithms
- To evaluate the NTCP values of plans with different algorithms

CHAPTER 4

4.1 MATERIALS

4.1.1 Treatment planning data

Volume calculations performed by 3D treatment planning systems provide a large quantity of dose information, which can be difficult to interpret and evaluate when it is displayed as isodose curves on several transverse, sagittal, and coronal planes. It is much simpler to condense the 3D dose distribution data to a graph, which displays the radiation distribution within a specifically defined volume of interest, so that summarizing and analyzing the 3D data is possible. Such a graphical representation is called a dose volume histogram (DVH).

The DVH can be expressed as the summed volume of elements receiving dose in a specified dose interval, against a set of equally spaced dose intervals. This is differential DVH and shows the absolute or relative volume in each dose interval (bin) directly. More frequently used, however are cumulative dose volume frequency distributions, which are plots of the volume receiving a dose greater than, or equal to, a given dose, against dose. The volume accumulates starting at the highest dose bin continuing towards zero dose, eventually reaching 100% of the total volume. Normally volumes are expressed as a percentage of the total volume but in some situations the absolute volume may be more appropriate.

DVHs can be used during the planning process to check whether the dose is adequate and uniform throughout the target volume, and the extent and value of any hot spots in adjacent normal tissue. However, because they do not display positional information, they should not be only method used. Their main use is as a plan evaluation tool. They can be used as a method of comparing different treatment plans on a single graph, for specifically identified structures and target volumes. DVHs were used originally for analysis of the effect of sophisticated treatment equipment or for charged particle therapy. They are now a method of choice in the evaluation and optimization of all external-beam conformal plans (Mayles 2007).

4.1.2 BIOlogical Evaluation of Plans (BIOPLAN) Software

BIOPLAN was initially designed using Microsoft Visual Basic (a Windows development language) ver 3.0 but the most recent tools have been added using VB 5.0 professional edition. It runs on a PC (486DX/66Mhz or higher processor) with the Microsoft Windows 95 (or higher) or NT operating system. BIOPLAN is a menu-driven application. It responds to keyboard or mouse events by displaying windows and dialog-boxes. The results (numbers or plots) are displayed on the screen either in text or graphics windows which can be printed out or saved on disk.

The major advantage of BIOPLAN is its flexibility. It allows the user to really exploit the potential that DVH information may provide and also plan inter-comparison. By simply looking at the DVHs of the rival plans plotted together (in both differential and cumulative format and using either absolute or relative values) one may guess the optimal plan. However, these plots are not often conclusive as the DVHs may cross each other. BIOPLAN provides a new insight into the problem by calculating the TCP and NTCP values associated with the rival plans. Thus, a decision can be taken according to these predictions (Sanchez-Nieto 2000).

Apart from the plan inter-comparison it is possible to analyze or enhance a particular treatment through the prism of the biological response. Thus, it is possible to assess the effect of a particular non-uniform dose distribution upon the probability of controlling the tumor, the effect of the dose prescription on TCP and NTCP (specifically compute the individualized prescription dose which would produce a certain level of complications), and how the fractionation regime affects the outcome for a particular patient.

Normal Tissue Complication Probability (NTCP)

Two different models have been implemented in BIOPLAN are the Lyman-Kutcher-Burman model (empirical) and the relative seriality model (mechanistic).

The Lyman-Kutcher-Burman model

This model, also called normal or probit model, calculates the probability of complication of a partially uniformly irradiated critical organ. The equations for the model are:

$$\text{basic LKB equation is }^{23}: NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^t e^{-t^2/2} dt$$
$$v = \frac{V}{V_{ref}} \quad t = \frac{[D - TD_{50}(v)]}{[m \cdot TD_{50}(v)]}$$
$$TD(v) = TD(1) \times v^{-n}$$

Where V = volume of organ irradiated to uniform dose d per fraction for t fractions
 V_{ref} = reference volume (ie whole organ)
 v = fraction of volume irradiated
 $TD_{50}(v)$ = dose to partial volume leading to 50% complication probability
 $TD_{50}(1)$ = dose to reference volume leading to 50% complication probability
 n = parameter describing volume dependence
 m = parameter describing the slope of NTCP vs. dose

Figure 3 Calculation of NTCP value based on Lyman-Kutcher-Burman model

In order to incorporate into Lyman's model the more likely situation of a non-uniform irradiation of the critical organ, Kutcher and Burman gave a reduction scheme to reduce the DVH to an effective fractional volume uniformly irradiated to the maximum dose. Lyman model required three parameters TD_{50} refer to dose sensitivity, m refers to the slope and n refer

to the volume dependence. The parameters affect the model predictions for same dose distribution. RS model is used to describe the probability of damage of normal tissue based on the binomial statistics (Colin 2005).

4.1.3 Oncentra MasterPlan (OMP) Treatment Planning System

The OMP system has two kind of models, which are pencil beam convolution/superposition and collapsed cone convolution. The models are based on energy fluence including head scatter modeling. The first model is based on a two-dimensional pencil beam convolution for volume integration. Inhomogeneties are handled by an equivalent path length correction for the primary dose contribution and a one-dimensional convolution along fan lines with an exponential for scattered radiation. The second model is a CC convolution approach in which a ray-trace procedure through the irradiated object is utilized to get the total energy released by photon per unit mass (TERMA) at all points in the dose calculation matrix. The TERMA is separated into a primary part (collision kerma) and a scatter part, each of which are transported separately along 106 lines from the interaction point. The energy from each voxel intersected by a fan line in the irradiated medium is collected and deposited according to the elemental composition of the medium and density variations along the fan line. (Kim, Kim et al. 2010)

4.2 METHODS

4.2.1 Installation of BIOPLAN software

The library MSVBVM50.DLL and file GRID32.OCX are copied in the \windows\system directory (Figure 4). The grid control is registered by using RegSvr32.EXE(Figure 5). The command line (you can do that from 'run' menu in windows) is

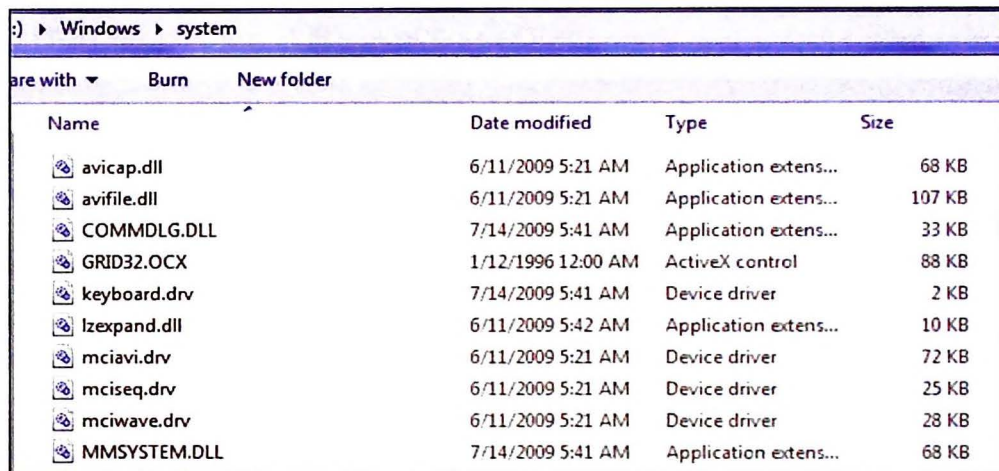


Figure 4 Directory to copy library MSVBVM50.DLL and file GRID32.OCX

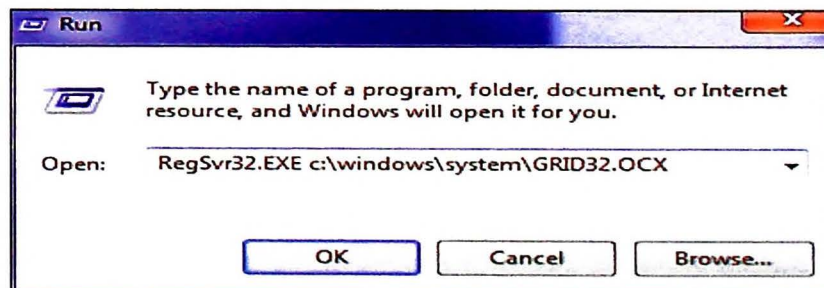


Figure 5 Run menu to register the grid control

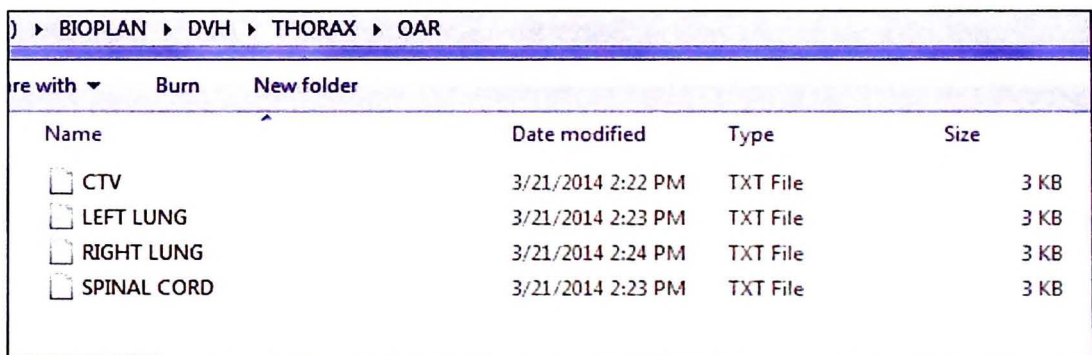
A directory called c:\BIOPLAN is created. Next, the executable program BIOPLAN.EXE is copied on it. A subdirectory c:\BIOPLAN\DVH is created. It is advisable to create new subdirectories in the DVH directory for the different structures. For example:

c:\BIOPLAN\DVH\GTV (for GTVs)

c:\BIOPLAN\DVH\OAR\rectum (for rectum)

c:\BIOPLAN\DVH\OAR\bladder (for bladder)

The DVH files in the corresponding subdirectory of the DVH directory are copied. (Figure 6)



Name	Date modified	Type	Size
CTV	3/21/2014 2:22 PM	TXT File	3 KB
LEFT LUNG	3/21/2014 2:23 PM	TXT File	3 KB
RIGHT LUNG	3/21/2014 2:24 PM	TXT File	3 KB
SPINAL CORD	3/21/2014 2:23 PM	TXT File	3 KB

Figure 6 Subdirectory of the DVH directory where the DVH files are copied

Next, change the configuration setting. This step is very important as it might affect the calculation of NTCP. The steps are on SETTING - CONTROL PANEL - REGIONAL SETTING, check that regional settings are in English (British). Next, under the tab NUMBER, the decimal are defined by "." (point) and thousand separator by "," (commas).

4.2.2 Calculation of NTCP values

BIOPLAN needs DVHs in ASCII format because the DVHs could not be transferred directly into the BIOPLAN software. Those files must be transferred into the Microsoft Excel first, then save as "Text (Tab delimited) (*.txt)". Those files can be checked on directory and they have been saved in ASCII format.

In order to run the BIOPLAN, the parameters of organ main menu items must be selected appropriately. Firstly, select FILE and then DVH FILE. A DVH file for thorax plan is selected. One structure of organ at risk is chosen on file name. Then, the differential and cumulative format will be plotted automatically and all picked files will appear in the DVH files window. After that, the dose considered as the centre of the first bin is entered. The input dose for the first bin is given. It can be calculated by using this formula: