

Министерство науки и высшего образования Российской Федерации
 федеральное государственное автономное
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 «Национальный исследовательский Томский политехнический университет» (ТПУ)

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Отделение ядерно-топливного цикла

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Современные вычислительные методы для планирования и оптимизации лучевой терапии.

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School of Nuclear Science & Engineering

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Specialization: Nuclear medicine

MASTER THESIS

Topic of research work
Modern computational methods to plan and optimize radiological therapy

UDC 615.849:519.6

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Competence code	Competence name
Universal competences	
UC(U)-1	Ability to make critical analysis of problem-based situations using the systems analysis approach, and generate decisions and action plans.
UC(U)-2	Ability to run a project at all life-cycle stages.
UC(U)-3	Ability to organize and lead the teamwork and generate a team strategy to achieve the target goal.
UC(U)-4	Ability to use modern communication technologies to realize academic and professional interaction.
UC(U)-5	Ability to analyse and account for cultural diversity in the process of intercultural interaction.
UC(U)-6	Ability to set and pursue individual and professional activity priorities and ways to modify professional activity based on the self-esteem.
General professional competences	
GPC(U)-1	Ability to formulate goals and objectives of the research study, select assessment criteria, identify priorities for solving problems.
GPC(U)-2	Ability to apply modern research methods, evaluate and present the results of the performed research.
GPC(U)-3	Ability to present research outcomes in the form of articles, reports, scientific reports and presentations using computer layout systems and office software packages.
Professional competences	
PC(U)-1	Ability to maintain medical and technical documentation related to medico-physical aspects of radiation therapy, interventional radiology and radionuclide diagnostics and therapy.

PC(U)-2	Ability to ensure radiation safety of personnel, public, and the environment, to carry out monitoring of radiation exposure levels of patients, personnel, public, and the environment.
PC(U)-3	Ability to operate and maintain equipment and tools applied for the medical use of radiation.
PC(U)-4	Ability to manage the quality of physical and technical aspects within radiation therapy, diagnostics, interventional radiology and radionuclide diagnostics and therapy departments in accordance with the specific equipment requirements, regulatory requirements and staffing of a medical organization.
PC(U)-5	Ability to conduct and organize dosimetry planning, clinical dosimetry, quality assurance procedures for radiotherapy, interventional radiology, and radionuclide diagnostics and therapy.
PC(U)-6	Ability to apply knowledge of natural sciences, fundamental laws in the field of nuclear physics and technology, clinical and radiation standards, hygienic measures in nuclear medicine, which is sufficient to study issues associated with medical physics using modern equipment and information technology relying on the latest Russian and international experience.
PC(U)-7	Ability to develop reference books, tables and software containing data for clinical use in dosimetric planning of radiation therapy, radionuclide diagnostics and therapy.
PC(U)-8	Ability to take part in the design and physical and technical equipment development for radiation therapy, diagnostics, interventional radiology and radionuclide diagnostics and therapy, and radiation safety divisions.
PC(U)-9	Ability to conduct training sessions and develop instructional materials for the training courses within the cycle of professional training programs (bachelor degree programs).

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**ASSIGNMENT
for the Graduation Thesis completion**

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Topic of research work:

Modern computational methods to plan and optimize radiological therapy	
Approved by the order of the Director of School of Nuclear Science & Engineering (date, number):	№ 32-6/c dated February 1, 2022

Deadline for completion of Master Thesis: 06.06.2022

TERMS OF REFERENCE:

Initial date for research work:	The results of the work will be a comparison of the dose volume histograms and dosimetric indices of plans from matRad and Monaco treatment planning systems.
--	---

List of the issues to be investigated, designed and developed	<ul style="list-style-type: none"> -To generate treatment plans with matRad -To deliver a powerful dose of radiation that will kill the cancer but to do it as precisely as possible so that minimal damage happens to the healthy tissue around it. -To reduce the treatment time. -Compare open source with commercial software
List of graphic material <i>(with an exact indication of mandatory drawings)</i>	
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School of Nuclear Science & Engineering
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 Specialization: Nuclear medicine
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Nuclear Fuel Cycle Division
 Period of completion: spring semester 2021/2022 academic year

Form of presenting the work:

Master Thesis

**SCHEDULED ASSESSMENT CALENDAR
for the Master Thesis completion**

Deadline for completion of Master’s Graduation Thesis:	06.06.2022
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Assessment date	Title of section (module) / type of work (research)	Maximum score for the section (module)
27.01.2022	Preparation of technical specifications and selection of research areas	10
24.02.2022	Development of a common research method	10
23.03.2022	Selection and study of materials on the topic	10
13.04.2022	Experimental research	20
27.04.2022	Processing received data	20
18.05.2022	Registration of the work performed	15
30.05.2022	Preparation for defending the dissertation	15

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**ЗАДАНИЕ ДЛЯ РАЗДЕЛА / TASK FOR CHAPTER
«ФИНАНСОВЫЙ МЕНЕДЖМЕНТ, РЕСУРСОЭФФЕКТИВНОСТЬ И
РЕСУРСΟΣБЕРЕЖЕНИЕ» / «FINANCIAL MANAGEMENT, RESOURCE EFFICIENCY AND
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Уровень образования / Level of qualification	Master degree	Направление / Field of study	14.04.02 Ядерные физика и технологии / Nuclear Physics and Technology

Initial data for chapter «FINANCIAL MANAGEMENT, RESOURCE EFFICIENCY AND RESOURCE SAVING»:

1. <i>The cost of scientific research resources: material, technical, energy, financial, informational and human</i>	<i>Project budget 450 thousand rubles: The cost of purchasing equipment - 64 thousand rubles, the cost of a salary for a supervisor - 131 thousand rubles, the cost of a salary for a student - 82 thousand rubles. etc.</i>
2. <i>The system of taxation used, tax rates, volumes of payments, discounts and loans</i>	<i>According to clause 3 of subclause 16 of Art. 149 of the Tax Code of the Russian Federation, this project is not subject to taxation. Based on Chapter 34 of the Tax Code of the Russian Federation, since 2016, the rate of 30.2% of the wage fund has been used to calculate contributions to extra-budgetary funds.</i>

Problems to research, calculate and describe:

1. Project initiation	Project goals and results, project structure, assumptions and limitations, planning, budgeting, etc.
2. Economic model development	Calculation of initial investment, calculation of funds obtained from fuel savings, calculation of cash flows over 20 years
3. Determining the effectiveness of projects	Net Present Value Calculation and Sensitivity Analysis
4. Final decision making	Selecting and evaluating criteria, weighing the criteria and calculating the most appropriate solution

Graphic materials:

1. *Competitive power of the project*
2. *SWOT matrix*
3. *Plan of investments. The budget for scientific and technical research*
4. *Project Efficiency indicators*
5. *«Portrait» of the consumer*
6. *Assessment of the prospects of a new product*

Assignment date

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Level of qualification	Master degree	Field of study	14.04.02 Nuclear Physics and Technology

Topic of research work:

Modern Computational Methods to Plan and Optimize Radiological Therapy

Initial data for section «Social Responsibility»:

<p>1. Information about object of investigation (matter, material, device, algorithm, procedure, workplace) and area of its application</p>	<p><i>The object of investigation modern computation methods to plan and optimise radiotherapy. The different algorithms used in optimising radiotherapy plans will be discussed and an open source treatment planning system will be compared to a commercial one.</i></p>
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List of items to be investigated and to be developed:

<p>1. Legal and organizational issues to provide safety:</p> <ul style="list-style-type: none"> – Special (specific for operation of objects of investigation, designed workplace) legal rules of labour legislation; – Organizational activities for layout of workplace. 	<ul style="list-style-type: none"> – Labour code of Russian Federation #197 from 30/12/2001 GOST 12.2.032-78 SSBT – Sanitary Rules 2.2.2/2.4.1340-03. Hygienic requirements for PC and work with it
<p>2. Work Safety:</p> <p>2.1. Analysis of identified harmful and dangerous factors</p> <p>2.2. Justification of measures to reduce probability of harmful and dangerous factors</p>	<ul style="list-style-type: none"> – Enhanced electromagnetic radiation level – Insufficient illumination of workplace – Excessive noise – Deviation of microclimate indicators – Electric shock
<p>3. Ecological safety:</p>	<ul style="list-style-type: none"> – Indicate impact of the devices used in research on hydrosphere, atmosphere and lithosphere
<p>4. Safety in emergency situations:</p>	<ul style="list-style-type: none"> – Fire safety;

Date of issuance of the task for the section according to the schedule	
---	--

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Abstract

Master's Graduation work 100 pages, 15 figures, 31 tables and 51 sources.

Keywords: Optimisation, dose distribution, radiation therapy, matRad, dose-volume histogram.

Topic of research: Modern computational methods to plan and optimize radiological therapy

This aim of this research is to analyse the possibilities of implementations of recent mathematical methods to create and optimise radiological plans. The main objective focuses on comparative analysis of open-source matRad software against a set of cases validated in commercial software.

During the course of study, the literature was reviewed; generation of treatment plans of three cancer cases for the head and neck localisation using both Monaco v.5.11.03 treatment planning system and matRad Blaise v 2.10.1.

As a result of the study, an assessment of dose loads on both the target and critical organs was carried out using the DVH and dosimetric indices. The results showed that matRad is a platform that can be used to optimise treatment plans just as good as the commercial systems.

Scope: in education centres like universities for innovation of new techniques and oncology centres for research.

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List of Acronyms and Abbreviation

RT- Radiotherapy

PTV- Planning Target Volume

DVH- Dose Volume Histograms

CTV- Clinic Target Volume

GTV- Gross target Volume

BED- Biological Effective Dose

EUD- Equivalent Uniform Dose

TCP- Tumour Control probability

NTCP- Normal Tissue Control Probability

PB- Pencil Beam

MC- Monte Carlo

CT- Computer Tomography

TPS- Treatment Planning System

RBE- Radiobiological Effectiveness

GUI- Graphical User Interface

HI- Homogeneity Index

CI- Conformity Index

NLP- Non-Linear Programming

LP- Linear Programming

D- Dose

Max- Maximum

Min-Minimum

IMRT- intensity Modulated Radiation Therapy

VMAT- Volumetric Modulated Arc Therapy

1.0 Introduction

Radiation therapy (RT) is a major procedure for treating cancer and is recommended for over 50% of all cancer patients (Delaney et al.,2005)

The aim of radiotherapy treatment is to deliver a powerful dose of radiation that will kill the cancer but to do it as precisely as possible so that minimal damage happens to the healthy tissue around it. Attaining a precise and fast dose distribution calculation is indeed among the most difficult tasks in modern RT.

Modern conformal radiation therapy should not only aim to conform the treated volume to the PTV, i.e. improve the ability to sculpt isodoses in the planning of treatment and execution but also to conform the PTV to the CTV, i.e. reduce geometric variations in the treatment chain, and to conform the CTV to the GTV, i.e. improve clinical visualization methods of tumour cells.

Improvements in dose calculation accuracy could positively affect the effectiveness of treatments, mainly in highly heterogeneous tissues, such as the adipose tissue, where detailed secondary particle tracking is required.

An oncologist and physicist determine an appropriate set of beam angles and beam weights that results in an acceptable treatment plan through a continuous process of trial and error. Beam angles, beam intensities, and anticipated dose distribution make up the plan for treatment. Treatment planning models and optimization are used to find the delivery machine instructions necessary to produce a desirable dose distribution. A treatment planning system is a software package that assists treatment planners in determining machine instructions for delivery.

Treatment planning systems are at the core of radiation therapy (RT) and are a key to improved patient outcomes. Once image datasets are loaded and the tumours are identified, the systems develop a complex plan for each beam line route for how the therapy system should deliver radiation. The software also computes the expected distribution of dose in the tissue, including variables such as tissue energy level penetration influenced by the type of tissue the beam lines encounter.

When a patient is diagnosed with cancer and radiotherapy is considered as a treatment, images are taken of the patient to help the clinician to plan the mode of delivery of the treatment and delineating the tumour and the vital organs.

The system uses the geometry delineated to simulate radiation delivered to the patient. While treating the plan can always be revised according to the intended treatment outcomes.

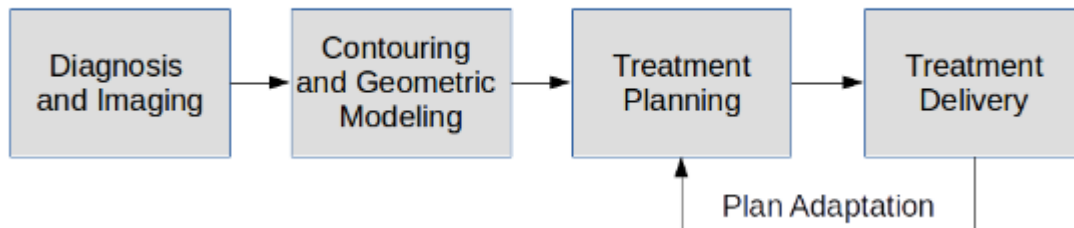


Figure 1.1- steps involved in radiotherapy

Modern TPSs employ an inverse optimization algorithm to arrive at clinically acceptable treatment plans, where the planner defines clinical dose-volume constraints and objectives for the target and tissues which are healthy to form a cost function. Utilizing a gradient-based searching technique, the optimizer returns a set of radiation beam parameters which produce a dose distribution that minimizes this cost function.

The treatment planning process should be done carefully and accurately because a small deviation in absorbed dose of only a few percent from the intended one might thus mean a reduced probability for tumour control or an increased probability for normal tissue complications.

Treatment planning has two different approaches namely;

The forward planning technique

This technique is mostly deployed in radiotherapy treatment planning process using external beams. For example, a medical physicist determines the beam angles in the treatment planning software to maximize tumour dose when sparing the healthy tissues. This type of planning is used for the majority of external-beam radiotherapy treatments, but is only useful

for relatively basic cases in which the tumour has a simple shape and is not in the vicinity of any critical organs.

Inverse planning

This is a technique used to inversely design radiotherapy treatment plans. The critical organs and tumours of a patient are defined by the radiation oncologist. The dosimetrist then provides target doses to each organ. The treatment plan that best matches all input criteria is then found using an optimization algorithm. This type of trial-and-error planning process is time and labour intensive [1].

Aim

This research focuses on comparative analysis of open-source matRad software against a set of cases validated in commercial software.

Objectives

- To generate treatment plans with matRad
- To deliver a powerful dose of radiation that will kill the cancer but to do it as precisely as possible so that minimal damage happens to the healthy tissue around it.
- To reduce the treatment time.
- Compare open source with commercial software

1.1 Factors considered in a treatment plan.

In recent years, the field of radiation physics has grown significantly. Radiotherapy is becoming even more precise thanks to new localization and fixing techniques, dose calculation algorithms, and treatment approaches. With deeper understanding of the concepts of factors such as the normal tissue complication probability, biological effective dose, equivalent uniform dose, α/β ratio and tumour control probability biological responses can possibly be translated into a means for radiation physics optimization [2].

1.1.1 Biologically Effective Dose (BED)

Physical dose distributions-based radiotherapy plans do not always accurately reflect biological impacts under various fractionation schemes. The linear-quadratic model has evolved as a useful tool for quantifying biological effects in radiotherapy over the last decade [2].

BED is a measure of the actual biological dose delivered to a certain tissue by a specific combination of total dose and dose per fraction, as determined by a particular α/β ratio.

$$\frac{E}{\alpha} = (nd) \times \left(1 + \frac{d}{\alpha/\beta}\right)$$

where **E**-biological effect

nd- n is well-separated fractions of dose *d*,

α and **β** are linear and quadratic constants

E/ α is the biologically effective dose –the quantity by which different fractionation regimens are intercompared [4].

BED = total dose \times relative effectiveness

1.1.2 Equivalent Uniform Dose (EUD)

When it comes to tumours, the equivalent uniform dose is the biologically equivalent dose that, if delivered uniformly, will result in the same cell kill throughout the tumour volume as the actual nonuniform dose distribution [3].

EUD can be a useful end point in evaluating treatment plans with nonuniform dose distributions for 3D conformal radiation and intensity-modulated radiotherapy. The outcomes of the study reveal that EUD-based optimization can improve the sparing of key structures beyond the requirements. The target dose distributions are also shown to be more inhomogeneous in the absence of limitations on the maximum target dosage, with large hot spots inside the target volume [3].

1.1.3 Tumour Control Probability (TCP)

The tumour control probability is a formalism derived to compare various treatment regimens of radiation therapy, based on the probability that given a prescribed dose of radiation, a tumour has been eradicated or controlled considering its specific biological cells. The ‘TCP’ is used in planning treatment as a tool to differentiate among treatment plans[4].

1.1.4 Normal Tissue Complication Probability (NTCP)

The likelihood that a given dose of radiation will cause an organ or structure to experience complications considering the specific biological cells of the organ or structure[5].

NTCP models attempt to reduce complicated dosimetric and anatomic information to a single risk measure. Most models fall into one of three categories: DVH-reduction models, tissue architecture models, and multiple-metric models. The main objective of radiotherapy is to achieve a high probability of local tumour control at a low risk of normal tissue complications.

1.2 Algorithms in Treatment Planning

The precision of calculating dose using a treatment planning software is important in radiation therapy to achieve tumour control while sparing normal tissue. An ideal dose calculation algorithm can perfectly reflect the actual distribution of dose within a real patient, which in turn reduces the uncertainty during the appraisal of treatment plans.

Commercially available TPS systems use different algorithms in planning and optimizing radiotherapy. In this section we shall look at the different algorithms being used in treatment planning.

1.2.1 Pencil Beam Algorithm

The PB algorithm is a correction-based algorithm that calculates dose on an infinitely thin pencil beam dose distribution. In order to determine the absorbed dose, dose kernels are collected in a homogenous media such as water. A large variety of pencil beam algorithms (PBAs) exist in commercial TPSs and re-search software. Their varying degrees of

complexity balance the trade-offs between precision and computational times. These analytical calculations are based on the parametrization of each pencil beam, describing the longitudinal depth dose distribution (DDD), as well as the lateral extent which is at right angle to the axis of the centre beam. Typically, the DDD is derived from MC calculations and verified against measurements.

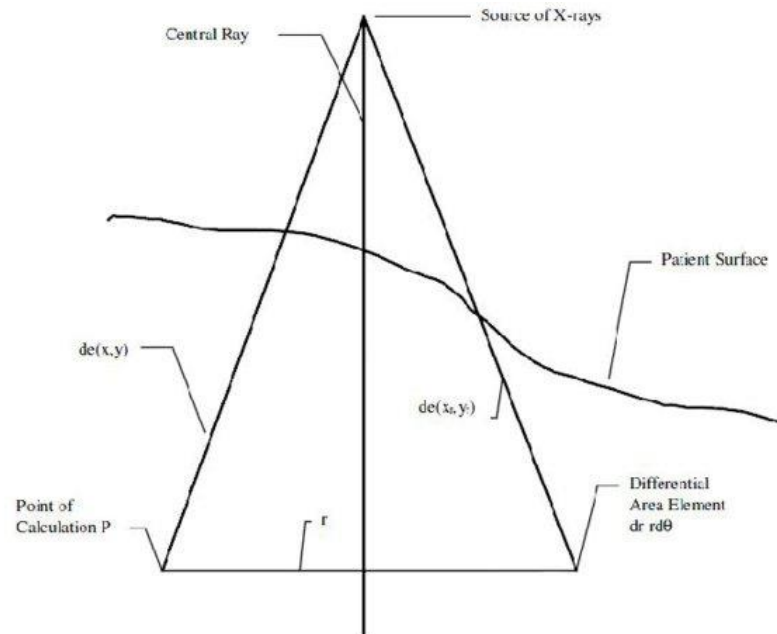


Figure 1.2 – Pencil beam algorithm

While PB algorithm is very fast, the limitations of PB algorithms in inhomogeneous media are well known. This is because PB uses a one-dimensional density correction, which does not accurately represent the secondary electrons distribution in materials with varying densities [7].

1.2.2 Collapsed Cone Algorithm

A collapsed cone-based dose calculation algorithm is based on a separation of primary photon transport and secondary transport of photons and electrons.

This algorithm is commonly applied in intensity modulated radiotherapy so as to calculate dose, especially for beams originating from a point source of radiation. This method was first introduced by [7].

This approach can decrease the time taken to compute without any loss of accuracy the doses in a convolution process. With a TERMA value all three spatial dimensions, the algorithm

assumes the kernel to be partitioned into various tens of collapsed cones emanating from a centric voxel. TERMA is the total energy released per unit mass which represents the primary photon transport. The algorithm is demonstrated in the figures below;

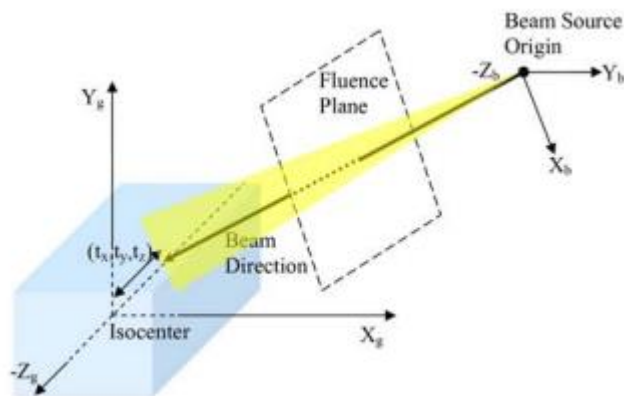


Figure 1.3 – Collapsed cone algorithm

(Color online) Global (“patient”) coordinates and beam coordinates: X_g , Y_g , and Z_g indicate the axes in global coordinates, and X_b , Y_b , and Z_b indicate the corresponding axes in beam coordinates.

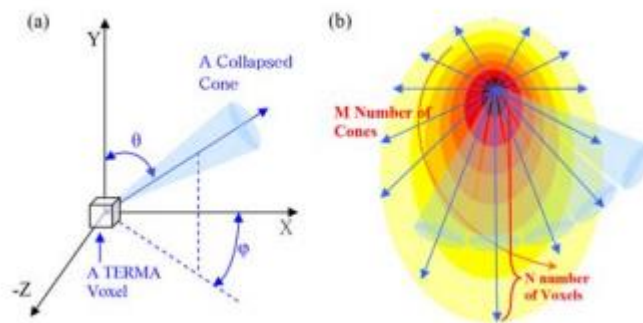


Figure 1.4 – Collapsed cones concepts: (a) The transferred energy in a cone-shaped area at azimuthal and altitudinal angles ϕ and θ respectively is represented by the axial line in a collapsed cone. (b) M number of collapsed cones is used to quantify the kernel's area. The number of voxels N quantize each cone line [8].

The distribution of dose in a 3D volume was defined as the convolution of the TERMA distribution and the kernel distribution. To sum and calculate the doses, only the voxels which were traversed by axial lines in the collapsed cones were used.

1.2.3 Monte Carlo Algorithms

MC simulations are extensively used in medical physics. MC algorithms are based on a statistical model that calculates the dose distribution given a limited set of particle interaction types and their probabilities. The probability for a certain interaction is given by the linear attenuation coefficient [9].

MC accurately handles heterogeneous material, scattering and fragmentation, at the cost of a considerably higher computational effort.

Despite the proven Monte Carlo algorithm precision and the ability for improved dose distribution to influence treatment results, the lengthy computational times earlier associated with MC simulation rendered this algorithm unfeasible for daily clinical treatment planning [12]. MC simulations are now available on linear accelerators, patient treatment planning and detectors. Simulation using Monte Carlo is currently the most sophisticated and accurate algorithm. Monte Carlo is used in radiotherapy;

- Fluence and spectrum calculations.
- Dosimetric parameters (stopping power)
- Treatment head simulations
- Treatment planning dose calculations
- Beam delivery and dosimetry verification

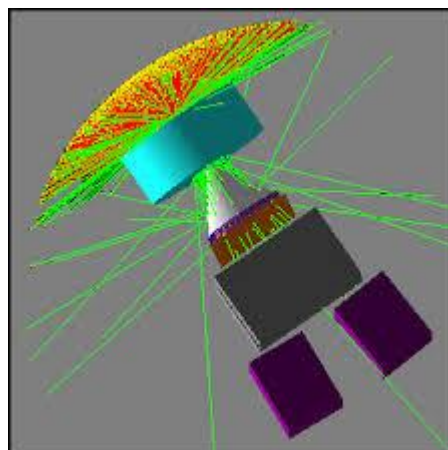


Figure 1.5 – An image showing Monte Carlo simulation

1.3 Optimization of radiation therapy

Developments in radiation therapy have led to the advancement of delivery systems with a high grade of computer control in the last few years. The approaches open up plenty of new possibilities for radiation therapy delivery. Due to the complexities of the treatments, an optimization method is required to design the best treatment plan unique to each patient. Over the years, clinicians have developed insight for what I “optimal” for a particular cancer in a particular location. Due its complexity, optimization needs important attention of all the parameters so that the clinician output a suitable treatment plan.

The difficulty of finding an appropriate technique for optimising each treatment plan uniquely was tackled using a mathematical programming approach. MATLAB was utilised in this study because of its competence in both advanced graphic visualisation and numeric computation.

1.3.0 Optimization Approaches

A patient is treated with huge number of radiation beamlets during radiotherapy [13] a computer-based optimization strategy is necessary to create every patient's ideal treatment plan due to the huge number of beams and range of intensities involved. Cumulative dose volume histograms are often used by physicists to appraise the quality of the plan of treatment. A cumulative dose volume histogram shows the volume portion of the patient organs that gets at least a specified level of dose.

The position of the vital organs and the tumour are defined first in the generation of a treatment plan, and then the dose from each individual beamlet is calculated. The sum of dose delivered to a patient's transverse cross section is represented by the matrix D, which is the summation of all the beamlets p of the beam weight multiplied by the matching dose matrix D_p .

$$D_{ij} = \sum_{p=1}^n w_p D_{ij}^p$$

n is the amount of beamlets, j and i are the pixel coordinates, and w the beamlet weights [14]. The convolution/superposition technique was utilized to compute the dose matrices. This technique has the capability to precisely model dose distributions that are complex.

The dose optimizations are done using algorithms in matRad and sequences provided the Optimization Toolbox of MATLAB.

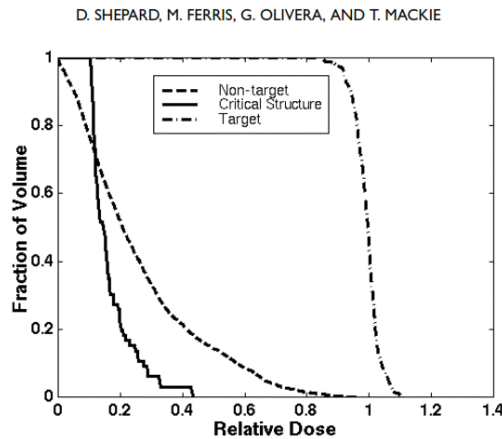


Figure 1.6 – A DVH from a treatment plan that is optimised.

During the optimization process many approaches are used;

1.3.1 Linear Programming Approaches.

The linear program is without a doubt the most extensively used mathematical programming formulation. The linear programming problem is of the form

$$\begin{aligned} \text{Min} \quad & C^T x \\ \text{Subject to} \quad & Ax \geq b, \\ & \ell \leq x \leq u, \end{aligned}$$

where x is the vector of continuous decision variables, $c^T x$ describes the linear objective function, $Ax \geq b$ represents the set of constraints, and l and u are vectors of upper and lower bounds on the variables [15].

There are several linear programming approaches are used to optimise radiotherapy dose. One linear programming formulation is to reduce the total integral dose while maintaining the dose to the tumour constant. The integral dosage is calculated by multiplying the total dose by the number of pixels.

1.3.2 Nonlinear Programming Approaches.

A summarised mathematical explanation of the nonlinear programming (NLP) problem is as below [16];

$$\begin{aligned} \min \quad & f(x) \\ \text{Subject to} \quad & g(x) \leq 0, \\ & \ell \leq x \leq u. \end{aligned}$$

Here, x is a vector of variables that are continuous real numbers, $f(x)$ is the objective function, and $g(x)$ represents the set of constraints. ℓ and u are vectors of lower and upper bounds placed on the variables [14,16].

The main advantage of employing such an approach is that it permits for the development of many complicated objective functions and constraints; however, the disadvantage of using this approach is that increasing the complexity of the formulation often results in more time-consuming optimizations [11].

1.4 matRad TPS

matRad is a free software tool for designing radiation therapy plans with a modulated beam of photons, carbon ions and protons. Its name derives from the combination of two words: MATLAB + Radiation = MatRad. It was developed by scientists at the Cancer Research Centre, German.

matRad is a multi-modality treatment planning toolbox that is open source which was completely written in the interpreted numerical programming language MATLAB and covers a wide range of functionalities from DICOM import, scanned proton, photon and scanned carbon ion dose calculation, dose optimization to plan visualization. matRad's code base corresponds to a flexible and modular set of functions containing well established radiotherapy algorithms with clearly structured function interface [12].

matRad was created for the purpose

- to support gaining experience with radiation therapy treatment planning,
- to allow for algorithmic developments on top of the basic toolkit,
- to be used as a learning and teaching tool, and
- to enable its application in research.

1.4.1 Requirements for installing matRad

In order to run MatRad, it's is advised to use a computer system at least 64-bit processor with 1GHz, 4 GB RAM and 100 MB hard disk space. Besides the image processing tool

which is required for the DICOM import, no other MATLAB toolbox is required to run MatRad in its entirety including inverse optimization.

matRad models a radiotherapy treatment planning workflow by consecutive function calls and organizes the relevant data for treatment planning in multiple structures in the base workspace of MATLAB as illustrated in Table 1.1.

Table 1.1 – matRad variables as of version 3.0.0.

Variable name	Description
Ct	Ct images and ct meta information
Cst	Segmentation along with constraints and objectives for dose optimisation
Pln	Treatment planning information
Stf	Beam geometry information
Dij	Dose influence information
resultGUI	Dose distribution with corresponding bixel/pencil beam weights.

Patient data can either be imported using matRad’s import interface or by loading one of the existing open-source patient data sets. Two variables (`ct`, `cst`) have to be existing in the MATLAB workspace in order to proceed.

The next step, meta treatment planning parameters, e.g. the beam angles, radiation modality and bixel spacing, have to be well-defined in the `pln` structure array by the operator before the beam geometry information is generated in `matRad_generateStf` and stored in the `stf` structure array [15].

when the beam geometry information is established, particle or photon dose calculations in water for unit fluences can be performed(`matRad_calcPhotonDose` or

matRad_calcParticleDose). The dosage computation function returns a structure array(dij), which contains the dose contribution for each bixel/pencil beam. [15]. Next, the fluence optimization function (matRad_fluenceOptimization) can be called in order to optimize individual bixel/pencil beam weights such that the resulting dose distribution produces a minimal objective function value according to given constraints and objectives. The optimised dose distribution is ultimately stored in a structure array called resultGUI, which allows plotting the computation of quality indicators and dose volume histograms, such as maximum and mean dose. If the optimization does not produce acceptable results, a re-optimization using different parameters can be carried out up to when the distribution of dose is deemed suitable.

Figure 1.7 presents the complete source code for an intensity-modulated scanned proton treatment plan that consists of dose calculation, inverse dose optimization and visualization.

```

load('TG119.mat'); % Load ct and cst
%% define treatment plan
pln.radiationMode = 'protons';
pln.machine       = 'Generic';
pln.numFractions = 30;
pln.propStf.bixelwidth = 5;
pln.propStf.gantryAngles = [0 45 315];
pln.propStf.couchAngles = [0 0 0];
pln.propStf.numOfBeams = 3;
pln.propOpt.bioOptimization = 'const_RBExD';
pln.propStf.isoCenter = ones(3,1) * ...
matRad_getIsoCenter(cst,ct,0);
%% generate geometrical steering information
stf = matRad_generateStf(ct,cst,pln);
%% perform dose calculation
dij = matRad_calcParticleDose(ct,cst,stf,pln);
%% perform optimization
resultGUI = matRad_fluenceOptimization(dij,cst,pln);
%% start visualization
matRadGUI

```

Figure 1.7 – matRad code generating a proton treatment plan on phantom TG119

In principle, there are three different ways to run matRad. The first possibility is given by executing scripts directly from the command prompt in the integrated development environment (IDE) of MATLAB. For instance, users can start the script matRad.m in the root folder of matRad, which defines a default intensity-modulated photon treatment

planning workflow. Alternatively (or complementary), users may want to work with the GUI by executing `matRadGUI` from the command prompt.

The second option to run MatRad is given by using GNU Octave instead of MATLAB.

The third option is intended for users not familiar with the scripting language or users who do not intend to make code changes. For this group of users, we provide a `matRad` standalone executable for Windows 7, 8, and 10, which is able to run all functionalities via the GUI.

The standalone does not require a MATLAB product license.

The algorithms that is for carbon/photon/proton dose calculation, ray tracing, multi-leaf collimator sequencing and fluence optimization follow techniques that are well-established and depend on clinically appropriate bixel and voxel resolution. `matRad` includes all base as well patient data as required for all computations.

For photons, `matRad` employs a singular value decomposed pencil beam algorithm, whereas for particles, a pencil beam algorithm allowing a single Gaussian to estimate the lateral dose profile is used [19,13].

1.4.2 Source code

<http://e0404.github.io/matRad> is an online Git repository where the `matRad` source code can be gotten [19]. People can either utilise the functionalities of the repository on Git to get the code and add to its development directly, or download the whole source code as a zipped file. Via GitHub error reports and requests can both be filed [20]. Users can submit modification to `matRad`'s development team via the open Git repository. `matRad`'s GitHub representation has been expanded to comprise steadfast wiki documentation. The `MatRad` toolset includes MATLAB workspace files for the CORT dataset [21], which includes CT scans and segmentations for three cancer cases and an AAPM TG119 phantom [22]. This freely available data can be directly experimented with by users.

1.4.3 Standalone installation

If you do not have MATLAB installed on your PC you are restricted to use `matRad`'s standalone application. For this option a MATLAB installation is not required. The installer is available for Windows, Mac and Linux with the latest `matRad` release.

Steps for installation:

- Download the matRad installer of the latest Release to your system (Win64, Mac64, Linux64)
- Run the respective installer for your system
- Run matRad by clicking on the desktop icon formed after installation.

1.4.4 The matRad GUI

The GUI is utilized for the treatment plan visualization and the adjustment of the plan and optimization parameters. It is possible to execute the matRad script using only the GUI [21].

The matRad GUI consists of 6 main sections:

Table 1.2 – six main sections of the GUI

Section	Content
Workflow	Includes the main steps that need to be executed for treatment planning.
Plan	Here the plan parameters like beam direction and radiation mode can be selected.
Command Window	Here the output of the Command Window is displayed inside the GUI.
Objectives & constraints	Using the optimization parameters, the constraints of the VOIs can be adjusted.
Visualization	Here the visualization can be adjusted to show different planes/slices of plot types.
Viewing	The information specified in the Visualization Parameters is displayed in this section.

Prior to producing the dose-influence-matrix utilised in the GUI, plan parameters are adjusted in the work flow. The parameters are shown in table 1.3.

Table 1.3 – Parameters in the GUI

Parameter	Description
bixel width	<i>Photons:</i> width of a photon bixel. <i>Particles:</i> lateral spot distance. Default value: 5 mm
Gantry angle	Here the set of desired gantry angles (in degree) can be specified. For the separation of the values you can either use ',' or a space ' '.
Couch angle	Here the set of desired couch angles (in degree) can be specified. For the separation of the values you can either use ',' or a space ' '. Make sure that you always have the same amount of couch and gantry angles.
Radiation mode	You can choose between carbon ions, photons and protons
Machine	Actual machine name as string to identify the base data set during runtime.
IsoCenter	Use this to set the isocenter (in mm).
# Fractions	Here you can specify the required number of fractions.
Biological optimization	A biological optimization can be used for carbon ions. You can choose for a biological effect optimization ('effect') or an RBE-weighted dose optimization ('RBExD').
Run Sequencing	Check this if you want to run a MLC sequencing. The number of stratification levels can be adjusted.
Run Direct Aperture Optimization	Check this if you want to run an additional direct aperture optimization.

The optimization parameters regarding the volumes of interest are stored in the variable *cst*. Using the GUI you can adjust the settings. To add or delete volumes you can use the '+' and '-' buttons. Below are the optimization parameters [21].

Table 1.4 – Optimization parameters

Field	Description
VOI name	Via a drop-down menu, you can select a VOI by clicking its name.
VOI type	You can specify whether the VOI is an organ at risk or a target volume.
OP	<i>Overlap</i> . This value defines how overlapping structures are handled during optimization. Consider two structures A and B with priorities p_A and p_B . If A and B both include voxel <i>i</i> , voxel <i>i</i> will be treated to belong only to structure A if $p_A < p_B$. If $p_A = p_B$ the voxel will be considered for both structures. An extension to more than two structures is trivial.
Function	<i>Objective Function</i> . This field allows you to specify how the VOI will be considered during the optimization. You can choose between <i>Squared Underdosing</i> , <i>Squared Overdosing</i> , <i>Squared Deviation</i> , <i>Mean Dose</i> , <i>EUD</i> , <i>Max DVH</i> , <i>Min DVH</i> , <i>DVH constraint</i> , <i>Min/Max dose constraint</i> or <i>mean dose constraint</i> . You can find more detailed information about this in the section 'Dose objectives' of the page: The <i>cst</i> cell
P	<i>Penalty</i> . For the objective function value, a weighted sum is calculated. The penalty value corresponds to the weighting factor for this VOI with respect to the defined constraint (e.g. overdosing). By adjusting this value, you can stress the importance of these constraints with respect to each other.
Parameters	For <i>Squared Underdosing</i> , <i>Squared Overdosing</i> and <i>Squared Deviation</i> this value tallies with the threshold dose above/below which the penalty will apply. For the <i>Mean Dose</i> -option, this value is not needed, as the mean dose within this VOI will be minimized. For the <i>EUD</i> method, the parameter corresponds to the exponent.

After the optimization, the treatment plan is visualized within the GUI. Using the visualization parameters, you can change the view. The radio buttons can be used to turn off/on, among others, the plotting of contours, dose (isolines) and isoline labels.

Below are the display options:

Table 1.5 – GUI display options

Type of plot	Display option	Plane
Intensity	dose	Axial
		Sagittal
		Coronal
	effect	Axial
	RBEWeightedDose	Axial
	RBE	axial
	alpha	axial
	beta	axial
	RBETruncated10Perc	axial
Profile		lateral
		longitudinal

1.4.5 Work flow

matRad simulates the workflow of radiation therapy treatment planning using a series of function calls that can be activated using either MATLAB's command line prompt or matRad's graphical user interface [15].

- **patient information loading**

The patient data, which consists of a CT dataset (`ct`) and segmentations(`cst`), is loaded initially in the workflow. The DICOM or binary import interfaces can be used to load data, or patient data stored in matRad's unique format can be directly imported. To define the

radiation modality, beam angles, and number of fractions, among other things, treatment plan parameters are specified within a Matlab structure (`pln`) [15].

– **Setting up parameters**

Following the previous step, the beam geometry (`stf`) is generated, which describes the positioning of bixels/beamlets for photons or individual pristine pencil beams for charged particles [15].

– **Calculation of dose**

After the beam geometry has been established, the dose calculation function can be used to generate a dose influence structure (`dij`) that contains the dose contribution from each bixel/pencil beam [15].

The dose calculation engine's core is made up of two nested loops, the outer loop running over the number of beams and the inner loop processing all rays from the current beam. An additional inner loop is responsible for calculating the dose deposition of multiple pencil beams per ray for charged particles. A ray tracing algorithm is used by `matRad` to calculate the radiological depth for the entire irradiated volume. Standard matrix vector algebra is used to calculate geometrical distances from the virtual radiation source and lateral distances to the core ray [15].

$$d(x, y, z_{rad}) = \sum_i z_i(z_{rad}) \iint \partial x' \partial y' \Psi(x', y') F(x', y') k_i(x' - x, y' - y)$$

– **Reverse planning technique to visualise the plan.**

`MatRad` employs the dose influence matrix approach for optimization, in which the dose d_i in voxel i can be calculated using a matrix vector product according to;

$$d_i = \sum_j D_{ij} w_j \quad \text{or} \quad \vec{d} = D \vec{w}$$

The dose contribution to voxel i from bixel/pencil beam j at unit intensity is stored in matrix D , and w_j corresponds to the weight of bixel/pencil beam j . Matlab's built-in double precision sparse matrix format is used to store the dose influence matrix D [22].

matRad calculates the optimal radiation fluence by minimising a weighted sum of objective functions that can be constrained further [22]:

$$\begin{aligned} \min_{w \in \mathbb{R}^n} f(w) &= \sum_n p_n f_n(w) \\ c'_k &\leq c_k(w) \leq c_k^u \\ 0 &\leq w \end{aligned}$$

In this case, $f(w)$ denotes the overall objective function, which is made up of individual components. $f_n(w)$ with relative weighting (also called penalty) p_n . c_k^l and c_k^u denote lower and upper bounds on the k -th constraint function $c_k(w)$. Only positive radiation fluences are considered due to the positivity constraint $0 \leq w$.

The goal of the fluence optimization is to find a set of bixel/spot weights which produce the best possible distribution of dose based on the clinical objectives and constraints governing the radiation treatment.

During mathematical optimization, these clinical objectives and constraints have to be translated into mathematical objectives and constraints. matRad supports the mathematical optimization of objectives with a weighted sum to help finding an optimal trade-off between acceptable normal tissue saving and target coverage for an individual as well as the formulation of constraints. The individual objectives and constraints are defined per structure and can be chosen by the user and include, among others:

- squared overdosage objective,
- squared underdosage objective,
- squared dose deviation objective,
- mean dose objective,
- equivalent uniform dose objective,
- min/max dose constraints,
- DVH point objectives and constraints.

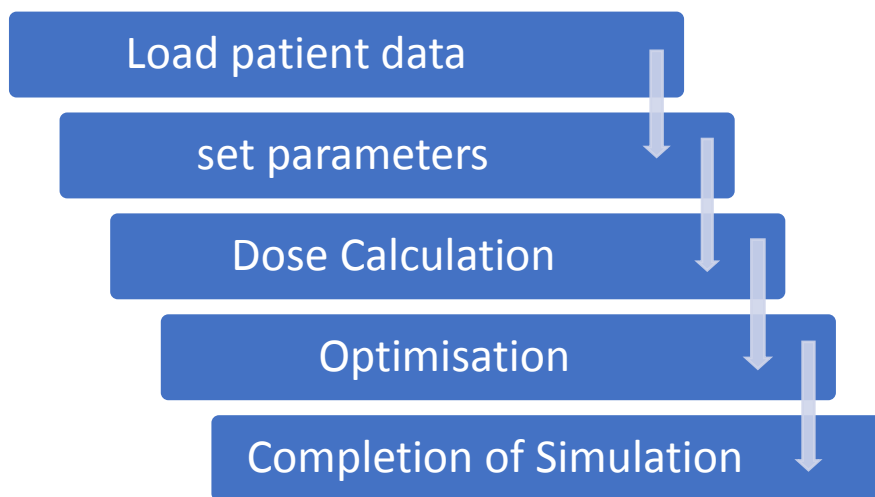


Figure 1.8– Work flow of matRad.

1.5 Other open-source treatment planning systems.

There are several open-source software projects, including PPlanUNC [23], FoCa [24], REGGUI, CERR [25] and SlicerRT [26], including the proton dose engine, that address the limited availability of flexible technology platforms in radiation oncology. However, most existing opensource solutions are limited to a particular radiation modality and focus on certain radiation therapy planning phases such as image processing and plan analysis and/or dose computation and optimization [15]. matRad provides clinically appropriate resolution therapy treatment planning for scanned carbon ions photon and scanned protons. For both study and education, matRad offers a high level of accessibility and flexibility [15].

1.5.1 Foca

FoCa is an in-house modular treatment planning system, developed entirely in MATLAB, which includes forward dose calculation of proton radiotherapy plans in both active and passive modalities as well as a generic optimization suite for planning inverse treatment. The software has a dual education and research purpose. From the educational point of view, it can be an invaluable teaching tool for educating medical physicists, showing the insights of a treatment planning system from a well-known and widely accessible software platform.

From the research point of view, its current and potential uses range from the fast calculation of any physical, radiobiological or clinical quantity in a patient CT geometry, to the development of new treatment modalities not yet offered in commercial treatment planning software. The physical models in FoCa were compared with the datasets from the institution and show an excellent correlation in depth dose distributions and longitudinal and transversal fluence profiles for both active scanning and passive scattering modalities. Three Dimension distributions of dose in patient and phantom geometries were compared to a treatment planning software from the market, yielding a gamma-index pass rate of above 94% (using FoCa's most accurate algorithm) for all cases considered. Finally, the inverse treatment planning suite was used to produce the first prototype of intensity-modulated, passive-scattered proton therapy, using 13 passive scattering proton fields and multi-leaf modulation to produce a concave dose distribution on a cylindrical solid water phantom without any field-specific compensator [19].

1.5.2 PLUNC

PLUNC was one of the earliest 3D radiotherapy treatment planning (RTP) systems to be operational. Since 1985, the Radiation Oncology Department at the North Carolina University (UNC) has been developing this RTP system for research and educational purposes. PLUNC is freely distributed to the area of radiation oncology for research and educational use under special license agreement. In this study, PLUNC 3D treatment planning software has been installed and implemented for research and educational utilisation in the field of health physics. A 3D treatment plan has been created and analysed in a typical patient CT image for educational demonstration purpose. Based on this analysis, it has been determined that the PLUNC 3D TPS could be successfully used for research and education purposes in M Sc/PhD thesis works of students from medical physics discipline [23].

1.5.3 CERR

CERR addresses four major research requirements in treatment planning [25]:

- (a) It offers a simple and powerful software platform for generating and prototyping treatment planning ideas.
- (b) It's as a software integration environment for combining treatment planning software built in a variety of languages (C/C++, FORTRAN, JAVA, MATLAB and so on) with treatment plan data (CT scans, RT structures, dose distributions, digital films, etc.),
- (c) it uses the commonly accessible AAPM/RTOG archiving method for extracting treatment plans from various planning systems, and also provides an effective and simple way to share and reproduce treatment planning research findings. The following functional components, as well as source code, are currently being distributed:

In conclusion, CERR provides a powerful, simple, and standardised framework that enables researchers to compare and exchange study findings by utilising common patient data sets [24].

1.5.4 3Dslicer

3D Slicer has a tonne of features for visualising and analysing a variety of datasets, including anatomical/functional images, image segmentation results, surface models, point sets, and rigid/nonrigid transformations. It includes cutting-edge algorithms such as image segmentation and registration, which are also important tools in RT research (deformable, rigid and affine). It can import and export data from a variety of common file formats, including DICOM [29].

3D Slicer is free and open-source software with a BSD-style licence that permits it to be used for commercial purposes. Since 2003, it has been utilised in over 100 different research projects by a wide and continuously rising user group. More than 40 000 people have downloaded the software [25].

Chapter 4: Financial Management

4.0 Introduction

Radiotherapy, surgery, and chemotherapy constitute the three pillars of cancer treatment. One key element of radiotherapy which involves a heavily computer-aided process known as radiation treatment planning. Commercially developed radiotherapy treatment planning software is proprietary and closed-source, which limits its value to researchers working to advance treatment planning technology. Open source research-oriented calculation environments facilitate discovery and testing of new approaches and algorithms for radiotherapy planning. Unfortunately, open source software is not validated as thoroughly as the commercial one. Moreover, new algorithms are not necessary outperform well-known standard procedures. This research focuses on comparative study of new algorithms implemented in open-source matRad software against a set of cases validated in commercial software. In this research treatment plans generated with matRad were compared with those by commercial treatment planning systems for uniform dose distribution, homogeneity and sparing of the organs at risk.

The essence of this research is show that matRad an open source software can be used for innovations and research in treatment planning. Monaco a commercial software was compared with matRad for three different patient cases of head and neck. The dose volume histograms from both software were compared and the results showed that matRad can be used to produce quality treatment plans as other commercial software.

4.1 Financial management, resource efficiency and resource saving

Financial Management is a vital activity for any project within any organization. It is the process of planning, organizing, controlling and monitoring financial resources with a view to achieve the organizational goals and the project objectives successfully. Proper management of an organization's finance ensures the efficient functioning of the whole organization. If finances are not properly managed, the organization with all of its projects will face barriers that may have severe repercussions on its growth and development. Therefore, both in industry and in research, it is extremely important.

The purpose of this section discusses the issues of competitiveness, resource efficiency and resource saving, as well as financial costs regarding the object of study of this Masters' thesis. Competitiveness analysis is carried out for this purpose. SWOT analysis helps to identify strengths, weaknesses, opportunities and threats associated with the project, and give an idea of working with them in each particular case. The development of the project requires funds that go to the salaries of project participants and the necessary equipment, a complete list is given in the relevant section. The calculation of the resource efficiency indicator helps to make a final assessment of the technical decision on individual criteria and in general.

4.2 Pre-research analysis

The perspective of scientific research is determined not so much by the scale of discovery, which is difficult to estimate at the first stages of the life cycle of a high-tech and resource-efficient product, but by the commercial value of the development. Assessment of the commercial value of the development is a necessary condition when searching for sources of financing for scientific research and commercialization of its results. This research is meant for hospitals and clinics in low-income countries which cannot afford to pay for licenses for treatment planning systems. Intern physicists can learn and improve their planning skills on this free software, this will be beneficial for such facilities because the money for license can be used to buy other equipment or pay staff better. Researchers and students can also benefit from this research because they can use it for innovations and publications which are restricted in commercial software. Other open source software like FOCA, CERR, SLICE RT are the competitors when it comes to this research. These other open-source software mentioned also are doing the same investigations but matRad has an edge over them because it cooperates particle therapy. The developers of matRad, dkfz (German Cancer research Centre) are working to add more possibilities with the software so as to make it as competitive as possible.

In conclusion matRad is a better option.

4.3 Potential consumers of the research results

To study consumers of research results, it is necessary to segment the market.

The target market that would be interested in the outcomes of this research investigations will include cancer institutes, oncology research departments in universities and clinical software manufacturers.

4.4 Competitiveness analysis of technical solutions

In order to find sources of financing for the project, it is necessary, first, to determine the commercial value of the work. Analysis of competitive technical solutions in terms of resource efficiency and resource saving allows to evaluate the comparative effectiveness of scientific development. Strengths and weaknesses of competitors should be evaluated realistically and impartially.

This analysis is advisable to carry out using an evaluation card.

First of all, it is necessary to analyse possible technical solutions and choose the best one based on the considered technical and economic criteria.

Evaluation map analysis presented in Table 4.1. The position of your research and competitors is evaluated for each indicator by you on a five-point scale, where 1 is the weakest position and 5 is the strongest. The weights of indicators determined by you in the amount should be 1. Analysis of competitive technical solutions is determined by the formula:

$$C = \sum P_i \cdot W_i,$$

C - the competitiveness of research or a competitor;

W_i – criterion weight;

P_i – point of i-th criteria.

Radiotherapy planning is the core to cancer treatment in clinics. The success of radiotherapy depends on giving the maximum dose to the tumor while sparing the organ at risk.

For the competitive analysis of technical solution, two treatment planning software were considered. These are:

- matRad - P_i
- Monaco - P_f

matRad is an open source software used in treatment planning, the study is to compare it to commercially used treatment planning systems to check its viability in real life treatment plans for cancer treatment.

The competitor here is other commercial software because if the data shows little difference or even better results in dose distribution and sparing of the organs at risk.

Table 4.1– Evaluation card for comparison of competitive technical solutions

Evaluation criteria <i>example</i>	Criterion weight	Points		Competitiveness Taking into account weight coefficients	
		P_f	P_i	C_f	C_i
1	2	3	4	7	8
Technical criteria for evaluating resource efficiency					
1. Data processing time	0,12	4	3	0,62	0,3
2. Dose homogeneity	0,13	5	4	0,56	0,5
3. Dose on organs at risk	0,2	4	3	0,8	0,39
4. Ease of planning	0,14	3	4	0,5	0,6
5. Accuracy of dose delivery	0,1	5	4	0,8	0,56
Economic criteria for performance evaluation					
1. Competitive methods	0,08	5	4	0,5	0,4
2. Market penetration rate	0,07	4	4	0,35	0,35
3. Development cost	0,1	5	4	0,6	0,34
4. popularity of the software	0,06	3	5	0,2	0,24
Total	1	38	35	4,93	3,68

Conclusion

This analysis suggests that the study is effective because it provides acceptable quality results. Further investment in this development can be considered reasonable. matRad is preferable for the intended target institutions.

4.5 SWOT Analysis

Complex analysis solution with the greatest competitiveness is carried out with the method of the SWOT analysis: Strengths, Weaknesses, Opportunities and Threats. The analysis has several stages. The first stage consists of describing the strengths and weaknesses of the project, identifying opportunities and threats to the project that have emerged or may appear in its external environment as presented in figure 5.1.

The second stage consists of identifying the compatibility of the strengths and weaknesses of the project with the external environmental conditions. This compatibility or incompatibility should help to identify what strategic changes are needed. SWOT analysis is intended to specify the objectives of the business venture or project and identify the internal and external factors that are favourable and unfavourable to achieving those objectives. Usually, users of a SWOT analysis often ask and answer questions to generate meaningful information for each category to make the tool useful and identify their competitive advantage. SWOT has been described as the tried-and-true tool of strategic analysis, and in this case of course is considered for the works of this thesis.

The description of each step for executing the SWOT analysis should be accurate and following the meaning of each topic, as;

Strengths: Factors that characterize the competitive side of the research project. It shows a specific advantage or a special resource in terms of competition, that means is the resources or opportunities for achieving the main objective. **Weaknesses:** Limitation of a research project that hinders the achievement of its objectives, or basically the insufficient capabilities or resources compared to competitors. **Opportunities:** Occurrence of environmental situations that may interfere in the project, which may improve the

competitive position of the project. Threat: Situation not expected and not desired, may be destructive or threatening for the project competitiveness. All analysis is presented in the Table 4.2.

Table 4.2– SWOT analysis

	<p>Strengths: S1. Reducing the dose load on critical organs S2. High precision of dose delivery S3. Licence free hence cheap</p>	<p>Weaknesses: W1. Relatively high data processing time for particle therapy. W2. Need of power computational hardware W3. Additional licensed software.</p>
<p>Opportunities: O1. RBE optimisation leading to better treatment plans O2. Applying of new software to a different set of data. O3. Gaining skills in treatment planning.</p>	<p>Strategy which based on strengths and opportunities: <i>1. Reduced dose loads on critical organs and local increases will reduce interest in standard treatments;</i> <i>2. The possibility of using the measurement results in further research in various fields of science.</i></p>	<p>Strategy which based on weaknesses and opportunities: 1. Training of medical physicists to work with the planning program. 2. The ability to adapt new software for less powerful computers</p>
<p>Threats: T1. The difficulty of convincing the implementation in medical institutions</p>	<p>Strategy which based on strengths and threats: <i>1. Improving the quality of radiation therapy will increase competitiveness in the market</i></p>	<p>Strategy which based on weaknesses and threats: 1. Creation of a statistical database showing the comparison matRad and other commercial software. 3. Additional research in this area will increase interest in the software and increase demand.</p>

Based on the results of the analysis of this matrix, it can be concluded that

the difficulties and challenges that this research project may face are offset by the existing strengths of the research.

4.6 Project Initiation

In the initiation processes, the initial purpose and content of the project are determined. The initial financial resources are fixed. The internal and external stakeholders of the project are determined, which will interact and influence the overall result of the research project are determined.

4.6.1 Project Goals and Results

This section describes the project stakeholders, the hierarchy of project objectives and the criteria for achieving the objectives. Project stakeholders refer to individuals or organisations that are actively involved in the project or whose interests may be affected positively or negatively during project implementation or completion. Information about project stakeholders are provided in Table 4.3.

Table 4.3– Stakeholders of the project

Stakeholders of the project	Stakeholders of the project expectations
Cancer hospitals/clinics	Free software no need to pay for license. Better treatment plans with RBE optimization.
Research Institutions	Convenient in usage; New studies to due availability of software
Tomsk Polytechnic University (TPU)	The acquired results could be a ground breaking finding for research in TPU.
Patients with cancer	Reducing the risk of late radiation reactions in the body. Reduced recovery time after radiation treatment, due to reduced radiation load

Table 4.4 shows information on the hierarchy of project objectives and criteria for achieving the objectives.

Table 4.4 – Purpose and results of the project

Purpose of project:	This research focuses on comparative study of new algorithms implemented in open-source matRad software against a set of cases validated in commercial software.
Expected results of the project:	<ol style="list-style-type: none"> 1.Improving the accuracy of dose delivery to the target and reducing the dose on normal tissues 3. Comparison of radiation therapy of the standard method with voxel-based analysis
Criteria for acceptance of the project result:	The dose distribution of matRad should be better or almost similar to the commercial software.
Requirements for the project result	<ol style="list-style-type: none"> 1.The research carried out under this project should be completed on time. 2. The results obtained must meet the criteria for accepting the project result 3. If unsatisfactory results are obtained, additional studies should be conducted using received results

4.6.2 Organizational Structure of the Project

In this section, we define the personnel who will be part of the working group of this project, determine the role of each participant in this project, and prescribe the functions of the participants and their number of labour hours in the project. Two major participants are going to be involved as shown in the table below:

Table 4.5– Project Working Group

№	Name	Role in the Project	Functions	Hours spent (working days (from table 4.7) × 6 hours)
1	Brazovskii Konstantin Stanislavovich, professor, Research School for Chemical and Biomedical Technologies	Supervisor	Responsible for the project implementation within the set resource constraints, coordinates the activities of the project participant.	102
2	Peter Kisembo, student	Project Executor	Work on project implementation.	720
Total:				822

4.6.3 Project Limitations

Limitations and assumptions are summarized in table below.

Table 4.6– Limitations and assumptions

Factor	Limitations/assumptions
1. Project budget - for design	450529 RUB
1.1 Source of budgeting	TPU
2. Project timeline:	1 March 2022 – 01 June 2022
2.1 Date of approval of the project management plan	10 March 2022
2.2 Project completion date	01 June 2022

4.6.4 Project Schedule

As part of planning a science project, you need to build a project timeline and a Gantt chart.

Table 4.7 – Project Schedule

No	Job title	Duration, working days	Start date	Date of completion	Participants
1	General Technical supervision	10 days	01/03/2022	10/03/2022	Supervisor
2	Consultations	14 days	11/03/2022	24/03/2022	Supervisor/ Student
3	Literature review	15 days	25/03/2022	08/04/2022	student
4	Learning how to use matRad	10 days	09/04/2022	18/04/2022	student
5	Optimization and treatment planning	25 days	19/04/2022	13/05/2022	Supervisor/student
6	Summary of results	3 days	14/05/2022	16/05/2022	Supervisor/student
7	Synthesis and evaluation of results	3 days	17/05/2022	19/05/2022	Supervisor/student
8	Preparing for Defence	10 days	20/05/2022	29/05/2022	Supervisor/student
	Supervisor	Total 65 days			
	student	Total 80 days			

A Gantt chart, or harmonogram, is a type of bar chart that illustrates a project schedule. This chart lists the tasks to be performed on the vertical axis, and time intervals on the horizontal axis. The width of the horizontal bars in the graph shows the duration of each activity.

Table 4.8 – Gantt chart showing the timeline of the project

№	Activities	Participa nts	T _c , day s	March			April			May		
				1	2	3	1	2	3	1	2	3
				1	General Technical Supervisor	Supervis or	10	▨				
2	Periodic meetings and discussion	Supervis or/studen t	14		▨	▨						
3	Literature review	student	15			▨						
4	Learning how to use matRad	student	10				▨					
5	Optimization and treatment planning	student	25					▨	▨	▨		
6	Summary of results	Supervis or/studen t	3								▨	
7	Synthesis and evaluation of results	Supervis or/studen t	3									▨
8	Preparing for Defense	Supervis or/studen t	10									▨



Supervisor



Student

The duration of the project in calendar days for a student is 80 days, and for a supervisor is 65 days. The total number of working days is 90.

4.6.5 Scientific and technical research budget

The amount of costs associated with the implementation of this work is the basis for the formation of the project budget. This budget will be presented as the lower limit of project costs when forming a contract with the customer.

To form the final cost value, all calculated costs for individual items related to the manager and the student are summed.

In the process of budgeting, the following grouping of costs by items is used:

- material costs of scientific and technical research;
- costs of special equipment for scientific work (Depreciation of equipment used for design);
- basic salary;
- additional salary;
- labour tax;
- overhead.

4.7 Calculation of material costs

The calculation of material costs is carried out according to the formula:

$$C_m = (1 + k_T) \cdot \sum_{i=1}^m P_i \cdot N_{consi}$$

where m – the number of types of material resources consumed in the performance of scientific research; N_{consi} – the amount of material resources of the i -th species planned to be used when performing scientific research (units, kg, m, m^2 , etc.);

P_i – the acquisition price of a unit of the i -th type of material resources consumed (rub./units, rub./kg, rub./m, rub./ m^2 , etc.);

k_T – coefficient taking into account transportation costs.

Prices for material resources can be set according to data posted on relevant websites on the Internet by manufacturers (or supplier organizations).

Table 4.9 – Material costs

Name	Unit	Amount	Price per unit, rub.	Material costs, rub.
Electricity: Average computer consumes 0.2 kW per hour	kW/hr	0.2kW/ hr * 90 days *6 hours	4.81	0.2*90*6*4.81= 519.48
Papers	unit	200	1	200
Printing on A4 sheet	unit	500	7	3500
Pen	unit	1	150	150
Internet	Month	3	1000	3000
Transportation and procuring expenses	0	0	0	0
Total for materials	unit			7369.48
Total				7369.48

4.7.1 Costs of special equipment

This point includes the costs associated with the acquirement of special equipment (instruments, stands, devices and mechanisms) necessary to carry out work on a specific topic [43]

Table 4.10 a – Costs of special equipment (+software)

№	Equipment identification	Quantity of equipment	Price per unit, rub.	Total cost of equipment, rub.
1.	An core i5, 8 Gb Ram, 2Gb GPU laptop computer	1	60000	60000
2.	Matlab software with license	1	4179.85	4179.85

4.7.2 Calculation of the Depreciation

Calculation of the depreciation: Depreciation is not charged if an equipment cost is less than 40 thousand rubbles; its cost is taken into account in full.

If you use available equipment, then you need to calculate depreciation:

$$A = \frac{C_{\text{перв}} * H_a}{100}$$

A - annual amount of depreciation;

$C_{\text{перв}}$ - initial cost of the equipment;

$$H_a = \frac{100}{T_{\text{сл}}} - \text{rate of depreciation};$$

$T_{\text{сл}}$ - life expectancy.

Table 4.10 b – Depreciation of special equipment

№	Equipment identification	Quantity of equipment	Total cost of equipment, rub.	Life expectancy, year	Depreciation for the duration of the project, rub.
1.	A core i5, 8 Gb Ram, 2Gb GPU laptop computer	1	60000	10	6000

4.7.3 Basic Salary

This section includes the basic salary of participants directly involved in the implementation of work on this research. The value of salary costs is determined based on the labour intensity of the work performed and the current salary system.

The basic salary (S_b) is calculated according to the formula:

$$S_b = S_a \cdot T_w,$$

where S_b – basic salary per participant;

T_w – the duration of the work performed by the scientific and technical worker, working days;

S_d - the average daily salary of a participant, rub.

The average daily salary is calculated by the formula:

$$S_d = \frac{S_m \cdot M}{F_v},$$

where S_m – monthly salary of an participant, rub .;

M – the number of months of work without leave during the year: at holiday in 48 days, $M = 11.2$ months, 6 day per week;

F_v – valid annual fund of working time of scientific and technical personnel (251 days).

Table 4.11– The valid annual fund of working time

Working time indicators	Student	Supervisor
Calendar number of days	365	365
The number of non-working days	-	-
- weekend	52	52
- holidays	14	14
Loss of working time		
- vacation	48	48
- isolation period	-	-
- sick absence		
The valid annual fund of working time	251	251

Monthly salary is calculated by formula:

$$S_{month} = S_{base} \cdot (k_{premium} + k_{bonus}) \cdot k_{reg},$$

Where S_{base} – base salary, rubles;

$k_{premium}$ – premium rate;

k_{bonus} – bonus rate;

k_{reg} – regional rate.

Table 4.12 – Calculation of the base salaries

Performers	S_{base} , Rubles	k_{reg}	S_{month} , rub.	W_d , rub.	T_p , work days (from table 4.7)	W_{base} , rub.
Supervisor	35120	1,3	45656	2029,16	65	131895,4
Student	17890		23257	1033,64	80	82691,2
Total						214586,6

4.7.4 Additional salary recount

This point includes the amount of payments stipulated by the legislation on labour, for example, payment of regular and additional holidays; payment of time associated with state and public duties; payment for work experience, etc.

Additional salaries are calculated on the basis of 10-15% of the base salary of workers:

$$W_{add} = k_{extra} \cdot W_{base},$$

Where: W_{add} – additional salary, rubles;

k_{extra} – additional salary coefficient (10%);

W_{base} – base salary, rubles.

Table 4.13 – Additional salary

Participant	Additional Salary, rubles
Project manager	13189,54
Project executor	8269,12
Total	21458.66

4.7.5 Labour tax recount

Tax to extra-budgetary funds are compulsory according to the norms established by the legislation of the Russian Federation to the state social insurance (SIF), pension fund (PF) and medical insurance (FCMIF) from the costs of workers.

Payment to extra-budgetary funds is determined of the formula:

$$P_{social} = k_b \cdot (W_{base} + W_{add})$$

where k_b – coefficient of deductions for labor tax.

In accordance with the Federal law of July 24, 2009 No. 212-FL, the amount of insurance contributions is set at 30%. Institutions conducting educational and scientific activities have rate – 30.2 %.

Table 4.14 – Labour tax

	Project leader	Student
Coefficient of deductions	30,2 %	
Salary (basic and additional), rubles	145084,94	90960,32
Labor tax, rubles	43815,65	27470

4.7.6 Overhead costs

Overhead costs include other management and maintenance costs that can be allocated directly to the project. In addition, this includes expenses for the maintenance, operation and repair of equipment, production tools and equipment, buildings, structures, etc.

Overhead costs account from 30% to 90% of the amount of base and additional salary of employees.

Overhead is calculated according to the formula:

$$C_{ov} = k_{ov} \cdot (W_{base} + W_{add})$$

where k_{ov} – overhead rate.

Table 4.15 – Overhead recount

	Project leader	Student
Overhead rate	30%	
Salary, rubles	145084,94	90960,32
Overhead, rubles	43525,48	27288,1

Other direct costs

Energy costs for equipment are calculated by the formula:

$$C = P_{el} \cdot P \cdot F_{eq},$$

$$C = 5.8 * 0.2 * 720 = 835.20 \text{ rubles}$$

Where P_{el} – power rates (5.8 rubles per 1 kWh);

P – power of equipment, kW;

F_{eq} – equipment usage time, hours.

Formation of budget costs recount

The calculated cost of research is the basis for budgeting project costs.

Determining the budget for the scientific research is given in the table 4.16

Table 4.16 – Items expenses grouping recount

Name	Cost, rubbles
1. Material costs	7369,48
2. Equipment costs	64179,85
3. Basic salary	214586,6
4. Additional salary	21458,68
5. Labour tax	71285,65
6. Overhead	70813,58
7. Other direct costs	835.20
Total planned costs	450529

4.8 Evaluation of the comparative effectiveness of the project

Determination of efficiency is based on the calculation of the integral indicator of the effectiveness of scientific research. Its finding is associated with the definition of two weighted average values: financial efficiency and resource efficiency.

The integral indicator of the financial efficiency of a scientific study is obtained in the course of estimating the budget for the costs of three (or more) variants of the execution of a scientific study. For this, the largest integral indicator of the implementation of the technical problem is taken as the calculation base (as the denominator), with which the financial values for all the options are correlated.

The integrated indicator of resource efficiency of variants of execution of the object of research can be defined as follows:

$$I_{pi} = a_i b_i$$

where I_{pi} – integral resource efficiency index for the i-th variant of development execution;

a_i – development weighting factor;

b_i^a, b_i^b -an evaluation of the i-th variant of the development's execution is set by the expert by the selected evaluation scale. The calculation of the integral resource efficiency index of this study is presented in the form of Table 4.17.

Table 4.17 – Comparative assessment of the characteristics of the project implementation options

Criteria	Parameter weighing factor	Current project	Commercial Treatment planning systems
Computing time	0,2	4	5
Computation power	0,2	4	4
Planning accuracy	0,3	5	3
Treatment results	0,3	5	4
Total	1	4,5 (average)	4 (average)

Assessment of dose volume histograms of two plans of the same patient produced by matRad and Monaco. This helps compare the dose distribution in both the target volume and the organs at risk.

The integral financial measure of development is defined as:

$$I_f^p = \frac{F_{p_i}}{F_{max}}$$

where I_f^p – integral financial indicator of current project;

F_{p_i} – price of i-th variant of execution;

F_{max} – the maximum cost of execution of the research project (including analogues).

In this project, $F_{p_i} = 450529$. It is assumed that, $F_{max} = 460000$.

Hence, the integral financial indicator is:

$$I_f^p = \frac{450529}{460000} = 0,98$$

The obtained value of the integral financial measure of development reflects the corresponding numerical increase in the budget of development costs in times (the value is greater than one), or the corresponding numerical reduction in the cost of development in times (the value is less than one, but greater than zero).

The integrated index of efficiency of development variants (I_{fin}^p) and analogues (I_{fin}^{a1}) is determined on the basis of the integrated index of resource efficiency and integrated financial index by formulas:

$$I_{fin}^p = \frac{I_m^p}{I_f^p} = \frac{4,5}{1} = 4,5$$

$$I_{fin}^{a1} = \frac{I_f^{a1}}{I_f^p} = \frac{4}{1} = 4$$

Comparison of the integral performance indicator of the current project and its analogues will allow to determine the comparative efficiency of the project (see Table 4.18).

Comparative effectiveness of the project:

$$C_{eff} = \frac{I_{fin}^p}{I_m^p} = \frac{4,5}{4,5} = 1$$

Table 4.18 – Comparative efficiency of the project

Indicators	Project	Commercial software
Integral resource efficiency indicator	4,5	4
Integral performance indicator for variants	4,5	4
Comparative performance of the variants	1	1

Based on the calculation of the integral indicator with the definition of two weighted average values: financial efficiency and resource efficiency of scientific research, we can conclude that the comparative assessment of the current project is relatively higher than commercial software.

4.8.1 Conclusion

Thus, in this section was developed stages for design and create competitive development that meet the requirements in the field of resource efficiency and resource saving.

These stages include:

- development of a common economic project idea, formation of a project concept;
- organization of work on a research project;
- identification of possible research alternatives;
- research planning;
- assessing the commercial potential and prospects of scientific research from the standpoint of resource efficiency and resource saving;
- determination of resource (resource saving), financial, budget, social and economic efficiency of the project.

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