TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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

Инженерная школа ядерных технологий
Направление подготовки 14.04.02 Ядерные физика и технологии
Отделение ядерно-топливного цикла

МАГИСТЕРСКАЯ ДИССЕРТАЦИЯ

Тема работы
Влияние технических параметров планов стереотаксической радиохирургии (SRS) на дозиметрическую и радиобиологическую оценку

УДК 539.16.08:617-089:615.849

Студент

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School of Nuclear Science & Engineering
Field of training (specialty): 14.04.02 Nuclear Science and Technology
Specialization: Nuclear medicine
Nuclear Fuel Cycle Division

MASTER THESIS

Topic of research work
The influence of the technical parameters of the SRS plans on the dosimetric and radiobiologic evaluation

UDC 539.16.08:617-089:615.849

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Section “Social Responsibility”

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Associate Professor	Dan A. Verigin	PhD		

ADMITTED TO DEFENSE:

Programme Director	Full name	Academic degree, academic rank	Signature	Date
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Tomsk – 2021

LEARNING OUTCOMES

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 analyze 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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School of Nuclear Science & Engineering
Field of training (specialty): 14.04.02 Nuclear Science and Technology
Specialization: Nuclear medicine
Nuclear Fuel Cycle Division

APPROVED BY:
Program Director
_____ Verkhoturova V.V.
«____» _____ 2021

ASSIGNMENT
for the Graduation Thesis completion

In the form:

Master Thesis

For a student:

Group	**Full name**
0AM9M	Sagov Islam Ruslanovich

Topic of research work:

The influence of the technical parameters of the SRS plans on the dosimetric and radiobiologic evaluation	
Approved by the order of the Director of School of Nuclear Science & Engineering (date, number):	№ 29-49/c dated January 29, 2021

Deadline for completion of Master Thesis:	05.06.2021

TERMS OF REFERENCE:

Initial date for research work: *(the name of the object of research or design; performance or load; mode of operation (continuous, periodic, cyclic, etc.); type of raw material or material of the product; requirements for the product, product or process; special requirements to the features of the operation of the object or product in terms of operational safety, environmental impact, energy costs; economic analysis, etc.)*	In this study is investigated the influence of the technical parameters of the SRS plans on the dosimetric and radiobiologic evaluation. The purpose was to see how technical parameters can influence and change SRS plans, and which way it can lead this change to.

List of the issues to be investigated, designed and developed *(analytical review of literary sources with the purpose to study global scientific and technological achievements in the target field, formulation of the research purpose, design, construction, determination of the procedure for research, design, and construction, discussion of the research work results, formulation of additional sections to be developed; conclusions).*	1. Create SRS dosimetric plans of brain tumors using VMAT technique. 2. Evaluate the influence of technical parameters on SRS plans of brain tumors based on dosimetric and radiobiologic criteria. 3. To carry out a comparative analysis of radiation exposure when planning SRS of brain tumors.
List of graphic material *(with an exact indication of mandatory drawings)*	Table of cost function of VMAT The DVHs of VMAT ArcCHECK's QAs

Advisors to the sections of the Master Thesis
(with indication of sections)

Section	Advisor
Financial Management, Resource Efficiency and Resource Saving	**L. Y. Spicyna**
Social Responsibility	**D.A. Verigin**

Date of issuance of the assignment for Master Thesis completion according to the schedule	

Assignment issued by a scientific supervisor / advisor (if any):

Position	Full name	Academic degree, academic status	Signature	Date
Associated Professor	E.S. Sukhikh	PhD		

Assignment accepted for execution by a student:

Group	Full name	Signature	Date
0AM9M	Sagov Islam Ruslanovich		

TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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School of Nuclear Science & Engineering
Field of training (specialty): 14.04.02 Nuclear Science and Technology
Specialization: Nuclear medicine

Level of education: Master degree program
Nuclear Fuel Cycle Division
Period of completion: spring semester 2020/2021 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:	05.06.2021

Assessment date	Title of section (module) / type of work (research)	Maximum score for the section (module)
15.03.21	Developing technical specification	5
20.03.21	Selection of research direction	5
23.03.21	Searching and selection materials of the topic	10
02.04.21	Scheduling activities of the project	5
06.04.21	Obtaining results	15
10.05.21	Preforming calculation	20
17.05.21	Analyzing results	20
24.05.21	Verification results	10
29.05.21	Preparing for submitting	10

COMPILED BY:
Scientific supervisor:

Position	Full name	Academic degree, academic status	Signature	Date
Associate professor	E.S. Sukhikh	Ph.D.		

APPROVED BY:

Program Director	Full name	Academic degree, academic status	Signature	Date
Nuclear medicine	Vera V. Verkhoturova	PhD		

Task for section
«Social responsibility»

To student:

Group	Full name
0AM9M	Sagov Islam Ruslanovich

School	School of Nuclear Science and Engineering	**Department**	Division for Nuclear-Fuel Cycle
Degree	Master	**Specialization**	Nuclear medicine

Title of graduation thesis:

The influence of the technical parameters of the SRS plans on the dosimetric and radiobiologic evaluation	
Initial data for section «Social Responsibility»:	
1. Information about object of investigation (matter, material, device, algorithm, procedure, workplace) and area of its application	Object of investigation is stereotactic radiosurgery plans. Application area: stereotactic radiosurgery on linear accelerator
List of items to be investigated and to be developed:	
1. Legal and organizational issues to provide safety: – Special (specific for operation of objects of investigation, designed workplace) legal rules of labor legislation; – Organizational activities for layout of workplace.	– 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
2. Work Safety: 2.1. Analysis of identified harmful and dangerous factors 2.2. Justification of measures to reduce probability of harmful and dangerous factors	– Enhanced electromagnetic radiation level – Insufficient illumination of workplace – Excessive noise – Deviation of microclimate indicators – Electric shock – Ionizing radiation
3. Ecological safety:	– Indicate impact of linear accelerator on hydrosphere, atmosphere and lithosphere
4. Safety in emergency situations:	– Fire safety;

Assignment date for section according to schedule	

The task was issued by consultant:

Position	Full name	Scientific degree, rank	Signature	Date
Assistant professor	Verigin D.A.	Cand.of Sc.		

The task was accepted by the student:

Group	Full name	Signature	Date
0AM9M	Sagov Islam Ruslanovich		

ASSIGNMENT FOR THE DIPLOMA PROJECT SECTION «FINANCIAL MANAGEMENT, RESOURCE EFFICIENCY AND RESOURCE SAVING»

Student:

Group	Name
0AM9M	Sagov Islam Ruslanovich

School	School of Nuclear Science & Engineering	**Department**	Division for Nuclear-Fuel Cycle
Educational level	Master	**Specialization**	14.04.02 Nuclear Science and Technology

Initial data for the section "Financial Management, Resource Efficiency and Resource Saving":	
1. The cost of scientific research resources: material, technical, energy, financial, informational and human	*Budget of research not higher than 852595 rubles, salaries of executors not higher than 83190 rubles*
2. Norms and standards for spending resources	*Supervisor' salary – 45500 rubles per month; engineer' salary – 22503 rubles per month*
3. The system of taxation used, tax rates, volumes of payments, discounts and loans	*Coefficient of incentive bonuses 10%, coefficient of incentives for the manager for conscientious work activity 10%; contributions for social funds are 30% totally*
Problems to research, calculate and describe:	
1. Assessment of the commercial potential of engineering solutions	*Comparison of the condensers' types*
2. Planning of research and constructing process and making schedule for all periods of the project	*Calendar plan of the project*
3. Requirement for investments	*Costs calculations*
4. Budgeting an engineering project	*Creation of the project budget*
5. Calculation of resource, financial, social, budgetary efficiency of an engineering project and potential risks	*List of resource requirements*
Graphic materials	
1. «Portrait» of the consumer *2. Competitive power of the project* *3. SWOT matrix* *4. Assessment of the prospects of a new product* *5. Plan of investments. The budget for scientific and technical research* *6. Project Efficiency indicators* *7. Project risks*	

Assignment date	

Consultant:

Position	Name	Academic degree	Signature	Date
Associate Professor Division for Social Sciences and Humanities School of Core Engineering Education	Spicyna Luibov Yurievna	PhD		

Student:

Group	Name	Signature	Date
0AM9M	Sagov Islam Ruslanovich		

Abstract

This master's thesis consists of 109 pages, 30 figures, 46 tables, 30 literature sources and 3 appendixes.

Key words: STEREOTACTIC RADIOSURGERY, INTENSITY-MODULATED RADIATION THERAPY, BRAIN TUMORS, TECHNICAL PARAMETERS, EVALUATION INDICES, CONFORMAL INDEX, HOMOGENEITY INDEX, DOSIMETRIC EVALUATION, RADIOBIOLOGIC EVALUATION.

The object of this investigation is technical parameters using during Stereotactic Radiosurgery to treat brain tumors.

The purpose of this investigation is search the influence of the technical parameters of the SRS plans of brain tumors on the dosimetric and radiobiologic evaluation.

In this study we investigate influence of technical parameters on SRS dosimetric plans, based on data of two patients who had brain tumors.

Results showed that non-coplanar plans have higher quality of covering target and able to decrease dose to OAR. Various values of increment supplies well covering of a target.

List of Notations and Abbreviations

WHO – World Health Organization;

3D-CRT – 3 Dimensional Conformal Radiation Therapy;

IMRT – Intensive Modulated Radiation Therapy;

SRS – Stereotactic Radiosurgery;

VMAT – Volumetric Modulated Arc Therapy;

DNA – Deoxyribonucleic Acid;

EBRT – External Beam Radiation Therapy;

CT – Computed Tomography;

GTV – Gross Tumor Volume;

CTV – Clinical Tumor Volume;

PTV – Planning Tumor Volume;

OAR – Organ At Risk;

ICRU – Intonation Commission of Radiation Units and Measurements;

TPS – Treatment Planning System;

SRS – Stereotactic Body Radiation Therapy;

MLC – Multi-Leaf Collimator;

PET – Positron Emission Therapy;

MRI – Magnetic Resonance Imaging;

SPECT – Single Photon Emission Computed Tomography;

MC – Monte Carlo;

CI – Conformal Index;

PCI – Paddic Conformal Index;

HI – Homogeneity Index;

DGI – Dose Gradient Index;

RTOG – Radiation Therapy Oncology Group;

QA – Quality Assurance;

DD – Dose Difference;

DTA – Distance To Agrement;

BED – Biological effective dose;

NTCP – Normal Tissue Complication Probability;

TCP – Tumor Control Probability;

LQ – Linear Quadratic;

LQL – Linear Quadratic Linear;

USC – Universal Survival Curve;

PLQ – Pade Linear Quadratic;

LQC – Linear Quadratic Cubic;

AVM – Arteriovenous Malformation;

GRS – Gamma Knife Surgery.

Content

Introduction

Radiation therapy plays the decisive role in treatment primary and secondary brain tumors. According to World Health Organization (WHO) 8% -10% oncologic patients have metastasis in brain [1]. For the last few decades of radiation therapy, there were progress in all aspects of treatment including improvement immobilization of patients, visualization of dosimetric planning and carrying of treatment planning. Achievement in visualization and technology radiotherapy made possible to do step from 3-dimentional conformal radiotherapy (3D-CRT) to intensive modulated radiotherapy (IMRT) and stereotactic methods. Stereotactic radiotherapy based on medical linear accelerators have been for many years taking on eye of radiation society. The basic advantage of Stereotactic Radiosurgery (SRS) is possibility to accurately deliver dose in localization, that reduce irradiation with high doses to the health brain tissues, and minimizing long term consequences of treatment.

The planning of radiotherapy for tumors is to use factors such as the use of which leads to the maximum therapeutic effect with minimal radiation exposure to normal organs and tissues. High isodose gradient can be improved by varying beam modulation, gantry position, couch angles and arch length in Volume Modulated Arc Therapy (VMAT). The dosimetry planning system uses a two-step process to optimize dose distribution. As a rule, in the first stage, the ideal beam distribution is optimized. At the second stage, the planning system includes the possibility of delivering one of the two segments, includes the calculation of the shape and weight of all segments. Changes in technical parameters in the treatment planning system also affect the optimization of the plan and, consequently, its quality.

In this study we investigated two patients with brain tumors and who were treated with SRS. To describe how precise doses were delivered, we evaluated metrics which can show us quality of SRS, such as Homogeneity index, Conformity index, Paddick Conformity index and two Gradient indices.

Chapter 1. Review

1.1 Radiotherapy

Radiotherapy is the delivery of ionizing radiation to tissue with the goal of killing the diseased subunits of the tissue. Radiation kills cells by causing irreparable DNA damage. The main predictor on the amount of DNA damage to tissue receiving ionizing radiation is the mean energy absorbed by the medium per unit mass. This quantity is measured in joules per kg (unit Gray), which for its significance in treatment outcomes in radiotherapy, is also referred to simply as “dose”. In photon-based external beam radiation therapy (EBRT), radiation dose is delivered by directing a beam of high energy photons at the treatment site. These photons have typical energies of 4 MeV to 18 MeV. They are delivered with a linac which produces a focused beam of high energy photons which are directed at the target from multiple directions. The photons used in radiotherapy do not deliver dose directly, but instead impart their energy to electrons which subsequently deposit their energy in the tissue, causing DNA damage.

Metastasis in brain is always a grade IV tumor. The majority of secondary brain tumors are caused by hematogenous spread of tumor cells from the primary tumor. Most metastatic in brain (for adults) are lungs tumors (45% cases), mammary cancer (15%), renal cell carcinoma (7%), nasopharynx and colon carcinomas (6%), unknown focus tumors and melanoma (5-13%). Secondary brain tumors come out in 10-20% of adult population with oncologic disease. The prognosis in patients with brain metastasis is poor: median overall survival doesn’t exceed 2 months without treatment [2].

As a rule, stereotactic radiosurgery is performed simultaneously. However, some experts recommend multiple sessions of radiation therapy, especially for large tumors about 3 to 4 cm in diameter. This technique with the appointment of 2-5 treatment sessions is called fractionated stereotactic radiotherapy. However, at the moment the concept of radiosurgery in different clinics is understood as any fractionation mode for irradiation of brain tumors. Therapeutic protocols of the hypofraction technique (hypofractional radiosurgery), including the modes of

summing up 21 Gy for 3 fractions, 24 Gy for 4 fractions, 30 Gy for 5 fractions, 25 Gy for 5 fractions. Good tolerance of the technique and good local control are noted. Radiosurgery is becoming the choice for the treatment of both single and multiple BMs due to good local tumor control and low complication rates. Stereotactic radiosurgery for lesions no more than 2.5–4 cm in size, the patient's general status (Karnofsky index) is not less than 70%. Doses used in stereotactic radiosurgery have a volume of 24 Gy with a maximum diameter of 2 cm, 18 Gy - from 2 to 3 cm, 15 Gy - from 3 to 4 cm [3].

1.1.1 The main stages of Stereotactic Radiosurgery process

SRS processes are unique to every facility practicing radiosurgical procedures. Figure 1.1 shows an example of a process map or a process tree for a patient undergoing linac-based SRS treatment. The trunk of the tree, as shown by the central arrow, depicts the main process of SRS treatment, whereas the branches show the subprocesses that feed into the main process. Each of the subprocesses can then be subdivided into many smaller steps that constitute the subprocesses. For the execution of a successful SRS treatment, each step in each of these subprocesses will need to be executed successfully. This particular process tree consists of 18 subprocesses.

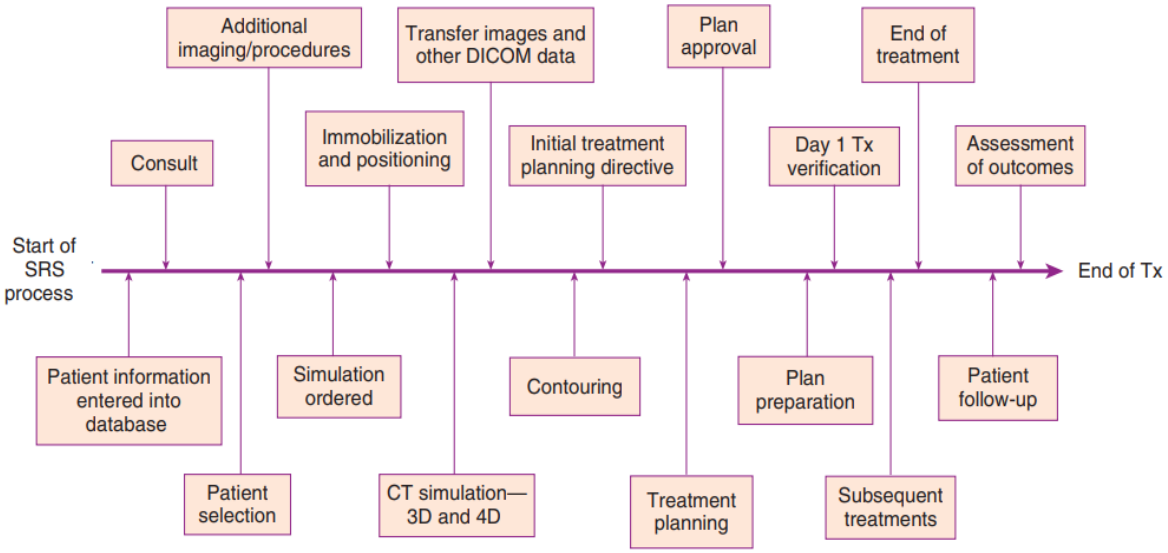

Figure 1.1_Main stages in SRS process

The process of radiation therapy will be customized for patients, depending on which form of radiation therapy patients and their physicians choose as their options. Basic steps include initial consultation, simulation, treatment planning, treatment delivery and post treatment follow-up [4]:

1. Start of SRS process. Patient referred to radiation oncology;

2. Patient information entered into database;

3. Consult (may include one or more discussions between the patient and the physician);

4. Patient selection;

Case reviewed with multidisciplinary team. Lesion type/size/location/stage confirmed to be appropriate for SRS. Role for concurrent systemic therapy determined. Patient ability to tolerate treatment/immobilization assessed

5. Additional supplemental imaging/procedures required for treatment/treatment planning;

Supplemental imaging ordered and performed (e.g., MRI for fusion).

6. Simulation/imaging for treatment planning ordered;

Patient position specified. Immobilization specified. Imaging protocol(s) specified, including use of contrast, slice thickness, and interslice gap.

7. Immobilization and positioning;

Immobilization devices created/configured as needed.

8. Simulation/imaging for treatment planning;

Images obtained using imaging protocols as ordered and with positioning/immobilization/motion management as ordered. Patient marked/tattooed if needed and associated point on the image set defined

9. Transfer images and other Digital Imaging Communication in Medicine (DICOM) data;

Images transferred to treatment planning system; transfer includes marked/tattooed point(s) as well as images.

10. Contouring tumor volume and organ at risk;

11. Initial treatment planning directive;

Treatment parameters specified, including total dose, dose per fraction, number of fractions, treatment site, modality, beam energy, and allowable target dose heterogeneity. Normal tissue constraints specified. All other planning-related constraints specified

12. Treatment planning;

Objectives created for inverse planning. Beam arrangement determined. Dose calculation grid size set appropriately. Additional planning structures created if/as required for inverse planning. Dose calculated. Dose distribution normalized so that the 100% isodose line corresponds to the plan maximum dose. Dose–volume histograms (DVHs) created and compared with prescription and constraints. Conformity evaluated. Dose distribution reviewed on treatment planning image set.

13. Plan review and approval;

Plan reviewed by physician with treatment planner. Plan revised if/as needed. Final plan approved by physician. Written prescription finalized by physician.

14. Pretreatment preparation and Quality Assurance treatment plan;

15. Day 1 treatment;

Patient set up in immobilization device(s) on table. Patient positioned to marks/tattoos/fiducials. Patient position verified (This includes performing any pretreatment image guidance and, if the patient is shifted from the original position based on this guidance, verifying the shift. Physician confirms patient position). Portal imaging performed, if appropriate. Machine settings verified Includes external collimators; jaw and multileaf collimator (MLC) leaf positions; energy; monitor unit (MU) settings. Required personnel present in control area.

1.1.2 Immobilization of patient

Stereotactic radiation therapy rests on the idea that improved localization of target structures will permit the use of smaller treatment planning margins than those used in conventional external beam radiation therapy. These smaller target volumes will in turn allow higher fractional radiation doses to be delivered safely. To reduce planning margins, however, extreme care must be taken in patient setup and positioning for treatment. Effective immobilization is critical in minimizing

intrafraction motion of the patient, which could result in catastrophic consequences in high-dose fraction delivery. In addition, stereotactic immobilization should be stable and relatively comfortable for long treatment times.

Immobilization devices are intended to prevent movement of the patient during treatment and replicate patient's position from CT-scans.

We can mark out three types of immobilization devices for brain tumors:

1) Intracranial immobilization

Early stereotactic radiosurgery systems almost exclusively used rigid, invasive skull fixation systems that incorporated a stereotactic coordinate system in the frame. The use of image-guided radiation therapy (IGRT) has allowed the use of nonrigid, relocatable frames often very similar to those used for conventional radiation therapy.

Intracranial immobilization can be divided into two main types: invasive and noninvasive fixation. Invasive, rigid frames provide the most accurate localization, but require the entire process of immobilizing, scanning, planning, and treating the patient to be completed in a single day. Noninvasive, relocatable frames may provide nearly equivalent accuracy, in particular when combined with IGRT, and allow the planning process to be done over several days; they also allow for fractionated treatment. Both invasive and noninvasive immobilizations for cranial SRS are capable of 1 mm accuracy.

Thermoplastic mask (fig. 1.2) provides positioning and immobilization of patient during imaging and treatment. This mask is elastic when it is heated and can reproduce patient's head contour.

For this purpose, to immobilize patient, we can also use Leksell helmet (fig. 1.3). These devices align precisely the head and the positioning of the isocenter site of linear accelerator. It consists in four screws fixed to patient scalp and a ring fixed to the helmet, thus it also called bloody immobilization device.

It is notable to say that in our study we resorted to use thermoplastic mask as immobilization device and didn't use bloody immobilization devices.

Figure 1.2_Thermoplastic mask

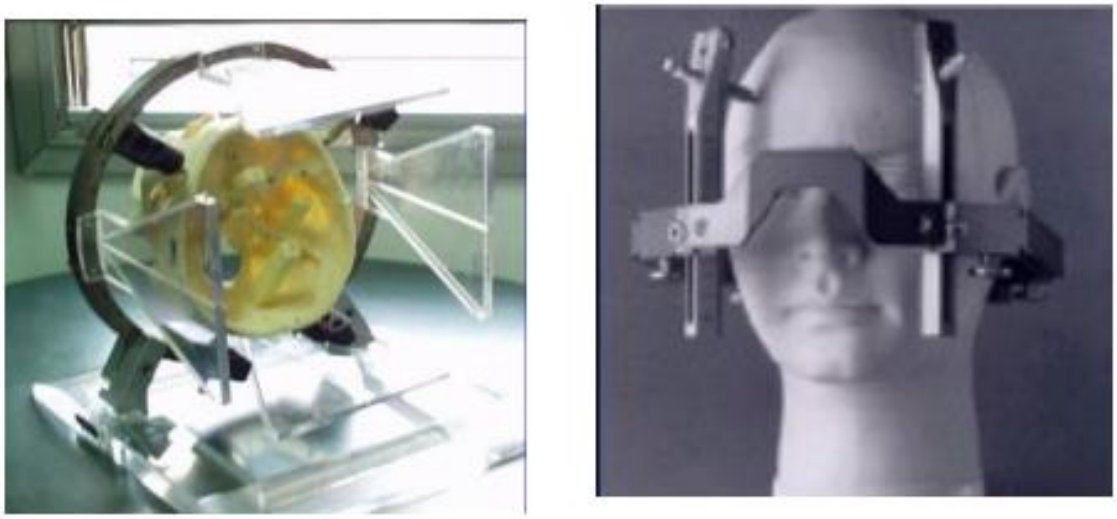

Figure 1.3_Leksell helmet

2) Head support

Head support (fig. 1.4) provides enhanced repositioning and patient comfort. Head support is device shaped to fit comfortable under the patient's head, enabling the patient lie relaxed on the treatment couch.

Figure 1.4_Head support

3) Baseplate, extension or overlay board

Baseplate, extension or overlay board (fig. 1.5) provide foundation for the system.

Figure 1.5_Overlay board

1.1.3 Definition of volumes

Target definition in SRS is typically performed by the physician only, on the basis of detailed 3D imaging of the patient, often in multiple imaging modalities.

There are three main volumes to be considered in radiotherapy planning, though only the first two of these volumes are of real interest to diagnostic colleagues (fig. 1.6).

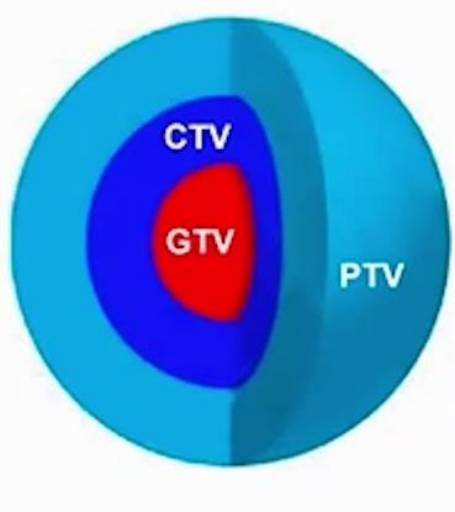

Figure 1.6_Diagram to illustrate the main radiotherapy planning volumes, taken from ICRU Report 50

The International Commission on Radiation Facilities and Protection (ICRU) Report 50 in 1993 [5] first described the concept of GTV and CTV volumes. In addition, this report also described the offset value for various uncertainties or PTVs. And then in 1999, in the report ICRU 62 [5], the concept of PTV was consolidated, and information about organs of risk (OAR) was also added to the report.

The first volume is Gross Tumor Volume(GTV). This tumor is visible one that we can see on image or palpate.

The second volume is Clinical Target Volume(CTV). This is volume of GTV and plus additional value of margin for case of spreading single cells around tissues.

Next comes the third volume and this is the Planned Target Volume (PTV). This volume takes into account various uncertainties that arise for reasons. In fact, this volume is needed to deliver the exact prescribed dose to CTV. This volume has nothing to do with the anatomical patient, but is associated with the isocenter of the linear accelerator and this volume can go beyond the anatomical limits [6]. The volume of PTV is made up of the volumes of GTV and CTV and the limit of this volume will depend on the parameters of the linear accelerator, but usually this volume is taken more than CTV by 1-3 mm.

OAR are health tissues which radiation sensitivity influences treatment planning or the prescribed radiation dose.

When contouring target volumes and organ at risk by hand, it is important to review the target volume in multiple plane views, including sagittal and coronal views, to confirm that the volume has been consistently defined in three dimensions. When contouring on thin CT slices, it is easy to create “jagged” volumes in three dimensions by slightly altering the position of the contour from slice to slice. These “jagged” volumes are more difficult to conform dose to, because of the finite beam-shaping resolution of multileaf collimators (MLCs).

1.1.4 Radiotherapy techniques

Stereotactic radiosurgery is radiotherapy where the dose must be delivered precisely and accurate to the target. The target must receive a conformal dose and at

the same time, we must preserve critical organs at single or hypofractional high doses.

For these purposes, high-precision and modern radiotherapy systems are needed. And ideal systems should have the following criteria: firstly, it should have a high dose rate, it is necessary to reduce the time of patient treatment and thereby reduce the uncertainties that may arise due to patient movement; a sharp decrease in the dose gradient at the periphery of the target; equipment for obtaining 3D images in real time, so that constant monitoring of the patient during treatment can be carried out, and the latter is uninterrupted output radiation during the rotation of the gantry, the movement of the collimator and the change in the dose rate. Modern devices designed for SRS should be suitable for these purposes [7].

Some types of delivery systems can achieve these aims and each of them have their limitations and traits.

One of these types is gamma-ray systems that were the first SRS delivery systems, which is still valid today. These systems are known as Leksell Gamma Knife or simply gamma knives. These systems are used only for intracranial SRS as a source, they use the radioactive element Co-60. Melon radiation sources are positioned in the gamma knife so that they can be screened or collimated depending on the location of the organs and the geometry of the radiation. Since all radiation from all sources is directed into one beam.

Figure 1.7_Gamma Knife.

One of the main disadvantages of gamma-ray systems is the lack of flexibility in use and the regulation of the handling of radioactive sources of radiation made these systems unattractive for most clinics.

The second type of SRS delivery systems are linear accelerator systems. Unlike systems based on gamma radiation, linear accelerators do not use radioactive materials and can be used for many tasks. Therefore, it was logical to use systems based on linear accelerators to deliver SRS, and in the 1980s, systems optimized for SRS were developed; they had MLC collimators and could deliver powerful doses.

The dose delivery techniques for SRS can be dynamic conformal-arc therapy, volumetric-modulated arc therapy (VMAT) and intensity-modulated radiotherapy (IMRT). Modern commercial treatment planning systems (TPS) that can plan for SRS have implemented advanced optimization algorithms. Beam orientation is an important factor for a planner to consider in the SRS planning process.

The goal of beam orientation optimization in SRS planning is to avoid sensitive organs and to select short beam paths whenever possible. Mechanical constraints and collision risks imposed by the equipment must be considered. Generally, more radiation beams lead to more conformal target dose distribution and more isotropic dose gradient outside of the target volume, especially for centrally located targets. When an SRS plan contains a sufficient number of beams, the choice of beam orientation becomes insignificant. However, for shallow or irregularly shaped targets, multiple-angle IMRT may still be preferable. It is generally desirable to keep the entrance dose as low as possible to prevent acute skin reactions.

Rotational therapy such as VMAT is generally superior to its static field counterparts in producing conformal dose distributions to cover the target, spare critical structures, and reduce treatment times. In many cases, a uniform dose fall-off with VMAT is desirable, but in some cases the treatment target is in close proximity to one or more critical structures, a sharper dose fall-off may be required in some particular directions, which may be achieved by selecting more perpendicular beam angles.

1.1.5 Linear accelerator Elekta Synergy

The creation of Elekta Synergy was driven by the need to visualize internal structures. Elekta Synergy system (fig. 1.8) was the first linear accelerator to bring 3D image guidance into the treatment set up process.

Figure 1.8_Elekta Synergy linear accelerator

The system is equipped with imaging tools that help clinicians visualize tumor targets and normal tissue, and their movement between and during fractions. The integration of this technology in the Elekta Synergy gantry enables physicians to perform imaging with the patient in the treatment position at the time of treatment, to optimize patient setup before therapy.

Key imaging tools include 3D and 4D* volumetric cone-beam imaging for soft tissue visualization; 2D real-time, fluoroscopic-like imaging for targets that move frequently; and 2D kV imaging for standard and orthogonal planar imaging. Elekta Synergy also features sophisticated ultra-low leakage field shaping with a fully integrated multileaf collimator, in addition to a 40 x 40 cm uninterrupted field size to simplify and refine treatment of larger-field targets.

Table 1.1_Specification of Elekta Synergy

Photon energy (MV)	4,6,8,10,15,18 and 25
Electron energy (MV)	4,6,8,9,10,12,18 and 20

Gantry angle (left and right)	0…180º
MLC	80 MLC (Field size 40x40cm leaf thickness – 10 mm) Optional: 160 Agility
Treatment delivery	3D, IMRT, VMAT, SRS/SRS (optional)
Wight (kg)	5500
Nominal size (mm) Length Width Height	 3558 3868 2488

1.2 Treatment planning of radiotherapy

Once the necessary stereotactic images have been acquired and transferred to the treatment-planning computer, the next step is to plan the precise delivery of radiation. This is accomplished through the use of a computer workstation and specialized treatment planning software "tools." Treatment planning, as the name implies, entails the development of a plan of attack on a targeted tumor. The number and nature of treatment beams to be used as well as the shape, size, orientation, and direction of these beams all must be carefully determined in order to achieve the goal of doing maximum possible damage to the tumor while simultaneously minimizing damage to adjacent healthy organ systems and tissues. In most ways, treatment planning for stereotactic treatments has the same goals and challenges as any other form of treatment planning but with potentially higher stakes, and therein lies the most important difference.

An ideal radiation treatment plan would deliver 100% of the desired dose to the treatment target and none to the normal brain. This is not possible in reality, but the primary goal of radiosurgery treatment planning is to achieve a plan that conforms to the target as closely as possible, as defined by radiation isodose shells. Isodose shells are volumes bounded by surfaces that receive the same radiation dose

– expressed as a specified percentage of the maximum radiation dose. Another goal of dose planning is to adjust the dose gradient such that critical brain structures near the target receive the lowest possible dose of radiation. In addition, most LINAC radiosurgeons strive to produce a treatment dose distribution that maximizes uniformity (homogeneity) of dose throughout the entire target volume.

1.2.1 Monaco TPS

Monaco treatment planning is designed to support all conventional linacs. However, when used with Elekta linear accelerators Monaco offers exclusive features that further enhance plan quality and faster delivery time.

In the Monaco system, the dose is calculated using the Monte Corlo method. This algorithm is used as the gold standard in radiotherapy. Monte Carlo generates particles and tracks their movement, collisions and the generation of secondary electrons, thus simulating a dose in tissue. The interactions of these pseudo particles is determined by generating random numbers which leads to a stochastic process. The stochastic process introduces static uncertainty in the dose calculation, which can be reduced by increasing the number of generated histories, but this will lead to an increase in the dose calculation time. [8].

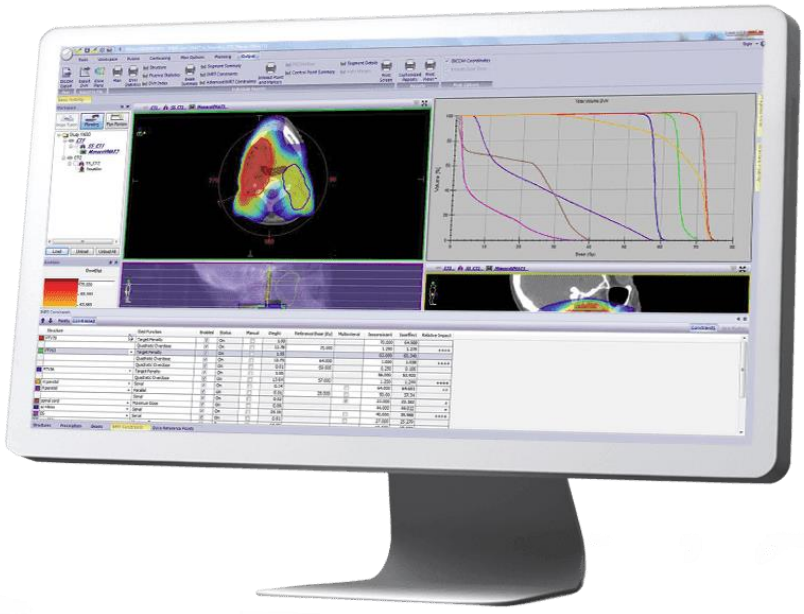

Figure 1.9_Monaco TPS.

Monaco TPS is based on two properties: the biological properties of tissues and the physical properties of radiation. It combines biological constraints such as

Target EUD, serial and parallel, as well as physical constraints such as overdose DVH, quaratic overdose, quadratic uder dose, under dose DVH and maximum dose. In this TPS, the user is given the opportunity to set the sensitivity of tumor cells and establish which organs he works with serial or parallel.

1.2.2 Constrained optimization

This TPS is a template-based planning system. Templates store beam geometry, calculation parameters, calculation settings, physician's intent, IMRT constraints, and so on and thus it decreases time to build plans. Templates can be used to create alas solution; a method of standardizing planning approaches across a whole clinic. And they can be stored by delivery type and anatomical site.

Monaco 5.11 templates further increase efficiency by allowing users to easily import and export treatment plans, facilitating best practice sharing across departments and organizations. The ability to create multiple prescription plans simultaneously reduces overall planning time as well. Improved data sharing creates opportunities to optimize individual treatment plans.

Constrained optimization is a more structured and has logical way to plan. There is an order in which cost function objective or constraints must be met. Some of them, such as Quadratic Overdose, will be used in conjunction with target coverage and this can add a little confusion. The order of constraints and objective is next:

1st Order Constraints

- Goal will always be met.
    - Serial, Parallel, Quadratic Overdose, Max Dose

2nd Order Constraints

- Goal will be met UNLESS there is a 1st Order constraint.
    - Quadratic Under Dose, Under Dose DVH

1st Order Objective

- Goal will be met unless a 1st or 2nd Order Constraints prevents this.
    - Target EUD, Target Penalty

2nd Order Objective

- Goal will be met or succeeded unless Constraints prevent and UNLESS 1storder objectives are not met.
  - Cost functions that have “Multi Criterial” option

Next we shortly describe how we produce a plan and how Monaco tells us where the conflicts are. System in two stages. At the first stage, a certain volumetric amount of calculation is used in all outlined systems. After this system, it combines all the volumes of targets with a certain margin. The sector on which the system divides the light beam depending on the length of the arch. The width of the Beamlet is set as the length that is the length of the MLC lobe. The system uses an advanced "pencil beam" algorithm for open field calculations. Then the optimization of the energy flux density begins, where the energy flux density occurs simultaneously. Unconditional problems are solved by the conjugate gradient algorithm. After the unconditional optimization is complete, if necessary, the system changes the relative weight of each cost function so that the optimizer is consistent with the isoconstraints, and restarts the unconditional optimization problem. Optimization in the first step continues until all constraints are satisfied. The accuracy of the doses at the end of the first stage is limited due to the algorithm is based on a 2-dimensional kernel method, especially in the presence of inhomogeneities [9].

Structure	Cost Function	Enabled	Status	Manual	Weight	Reference Dose (Gy)	Multicriterial	Isoconstraint	Isoeffect	Relative Impact
GTV	Target Penalty	☑	On	☐	1.00			24.000	24.283	
	Quadratic Overdose	☑	On	☐	0.03	25.800		0.100	0.112	+
	Target EUD	☑	On	☐	1.00			24.000	25.534	
PTV25	Target Penalty	☑	On	☐	1.00			23.800	23.379	
	Quadratic Overdose	☑	On	☐	0.21	25.500		0.100	0.077	++
brainstem	Maximum Dose	☑	On	☐	0.23			7.500	7.691	+++
optic nerve R	Maximum Dose	☑	On	☐	0.04			10.000	9.807	+
	Serial	☑	On	☐	0.01		☐	10.000	7.100	
lens R	Maximum Dose	☑	On	☐	0.01			5.000	4.386	
cochlea R	Maximum Dose	☑	On	☐	10.00			15.000	16.063	++++
optic nerve L	Maximum Dose	☑	On	☐	0.01			7.000	7.007	
lens L	Maximum Dose	☑	On	☐	0.01			5.000	1.786	
Patient	Serial	☑	On	☐	0.02		☐	17.500	17.289	+

Figure 1.10_IMRT constraints table.

The second stage of optimization is the adjustment of the dose to the capabilities of the linear accelerator. It takes each flux density map and arranges it so that it is distributed over the source sector which it represents. The trajectory of the collimator leaves is determined based on the dose to the target that the user prescribes. If we choose the Segment Shape Optimization (SSO) method, then the

system will be able to mom to choose the right dose. The system then optimizes this dose based on the capabilities of the accelerator. And the dose will be calculated based on the Monte Carlo voxel method. The user can change some parameters and thereby adjust the calculation time and accuracy [9].

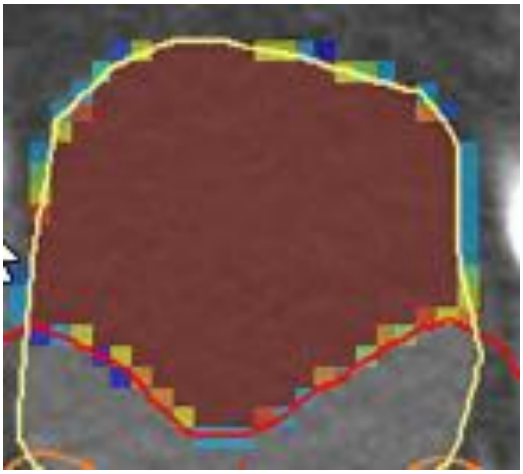

Figure 1.11_Voxels look like in Monaco system.

Monaco is a voxel-based planning system (fig 1.11). The entire volume is split tiny voxel. The advantage is being able to control voxel and not structures. The voxel extends out from isocenter and are based on the grid size, the finer the grid size, the greater the number of voxels.

1.3 Evaluation of treatment plans

1.3.1 Dose Volume Histogram

One of the evaluation instrument of dosimetric plans is Dose Volume Histogram (DVH), which widely used in radiotherapy. DVH illustrates graphical dose distribution inside of structure. DVH can be visualized in one of two ways: cumulative DVH or differential DVH.

In differential DVH, the height of the bar or column indicates the volume of the structure that received the dose given by the bin. Each bin shows the dose received by the organs. Differential DVH provides information on the maximum and minimum imaging doses [10].

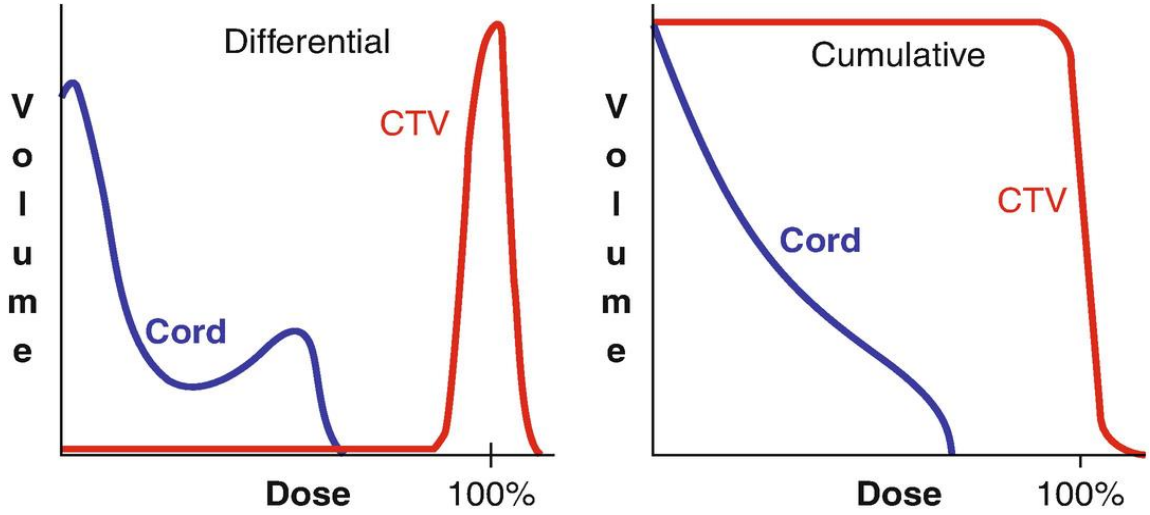

Figure 1.12_Differential and cumulative DVH.

The cumulative DVH is plotted with bin doses along the horizontal axis, as well. The cumulative DVH presents how many doses received by that or another structure and in which volume that doses were gotten. [10].

The ideal DVH for target volume is when 100% of volume receive description dose, but this case occurs rarely.

Visual examination of histograms helps to reveal clinical indicators of absorbed dose distribution (but not location), such as the presence of high or low absorbed dose or other inhomogeneities in absorbed doses. Dose statistics provide quantitative information about the volume of the target or critical structure and the dose received by these volumes. Since there may be different distributions in different irradiated areas, the dose distribution can be estimated using the following most informative parameters: minimum dose (D_{min}), maximum dose (D_{max}) and mean dose (D_{mean}). According to ICRU 83 [11], which describes recommendations IMRT planning, for plan's dose distribution evaluation suggested use next parameters: D_{98}, D_{50} and D_2. First of all, it is notable to mark maximum dose of target volume. In ideal case it should not exceed 5-7% from description dose. The same way we should take note on minimum dose of target volume, since dose lack in tumor can lead to a poor control under tumor. The critical maximum dose can subsequently cause serious complications, regardless of the plan that meets the prescribed parameters. Ideally, the so-called hot spots should be within the PTV and not in the area of the critical organ. Ideally, hot spots should be located inside the

GTV. Further, the tolerance doses of critical organs are compared with the average or maximum dose, depending on whether they are serial or parallel structures.

The main disadvantage of the dose-volume histogram is that the dose distribution is reduced to a one-dimensional histogram, while the spatial details of the dose distribution are lost. Therefore, it would be wise to assess for each plans the conformal index (CI) and the homogeneity index (HI) of the dose distribution to cover the target. To evaluate the dose gradient from the target periphery to normal tissues, the Dose Gradient Index (DGI) could be assessed.

1.3.2 Plan evaluation indices

According to International Commission on Radiation Units and Measurements (ICRU) to evaluate HI can be used next formula:

$$HI = \frac{(D_2 - D_{98})}{D_{50}}, \qquad (1.1)$$

where D_2, D_{50}, D_{98} are doses distributed to 2, 50 and 98 percent of volume respectively.

The CI is defined as the quotient of the prescription dose volume (V_{pi}) and the target volume (V_{PTV}), as follows:

$$CI = \frac{V_{pi}}{V_{PTV}} \qquad (1.2)$$

The PCI is defined as the reciprocal of the modified Paddick Conformity index [12] as follows:

$$PCI = \frac{V_{PTV} * V_{pi}}{(V_{PTV,pi})^2}, \qquad (1.3)$$

Herein, V_{PTV} is the planning target volume, V_{pi} is the body volume of the patient covered by the prescribed dose, and $V_{PTV,pi}$ is the partial volume of the PTV covered by the prescribed dose.

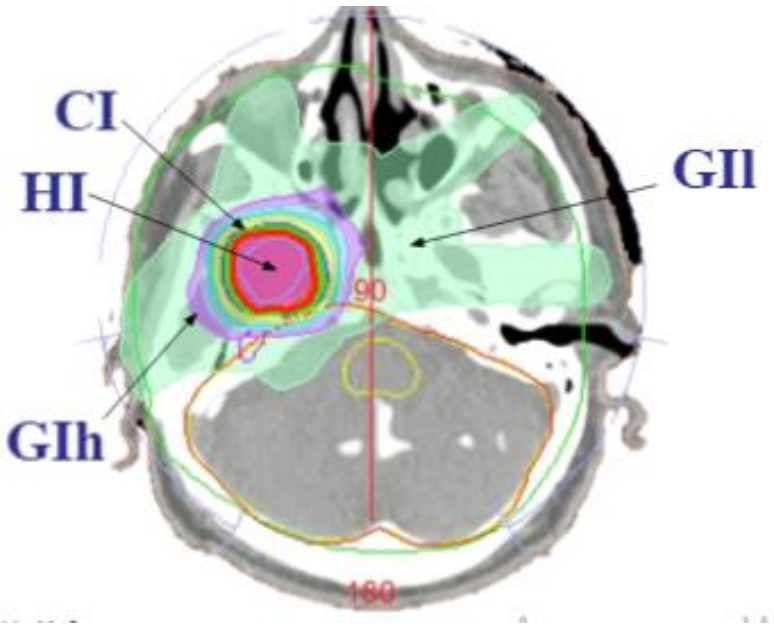

Figure 1.13_ Plan evaluation indices: CI – Conformity index, HI – Homogeneity index, GIl – Gradient low index, GIh – Gradient high index.

According to the RTOG guidelines, ranges of conformity index values have been defined to determine the quality of conformation. If the conformity index is plotted between 1 and 2, the treatment is consistent with the treatment plan; an index of 2 to 2.5 or 0.9 to 1 is considered a minor violation, and when the index value is less than 0.9 or greater than 2.5, the protocol violation is considered serious, but may nevertheless be deemed acceptable [13].

Two gradient indexes, as described by Paddick et al. and modified by Stieler et al. can be calculated to assess dose falloff outside the target volume [14]:

$$GI_{low} = \frac{V_{25}}{V_{50}} \qquad (1.4)$$

and

$$GI_{high} = \frac{V_{50}}{V_{90}} \qquad (1.5)$$

where V_{25} is volume receiving at least 25% dose of the prescription dose; V_{50} is volume receiving at least 50% dose of the prescription dose; V_{90} is volume receiving at least 90% dose of the prescription dose.

The goal of radiation therapy is to optimize therapeutic ratios by delivering tumoricidal doses to targets while maximally sparing organs-at-risk. Mostly, the quality of a radiation treatment plan is judged by isodose distribution and dose-

volume-histograms. Typically, the biological outcomes in terms of tumor control and normal tissue complication are not estimated when evaluating a plan.

1.4 Radiobiology models for SRS/SRS

Recent advances in the technology of radiotherapy have enabled the development of new therapeutic modalities that deliver radiation with very high accuracy, reduced margins and high dose conformation, allowing the reduction of healthy tissue irradiated and therefore minimizing the risk of toxicity. The next step was to increase the total tumor dose using conventional fractionation (which remains the best way to relatively radioprotect healthy tissues when large volumes are treated) or to use new fractionation schemes with greater biological effectiveness. Stereotactic radiotherapy delivers high doses of radiation to small and well-defined targets in an extreme hypofractionated (and accelerated) scheme with a very high biological effectiveness obtaining very good initial clinical results in terms of local tumor control and acceptable rate of late complications. In fact, we realize a posteriori that it was not feasible to administer such biologically equivalent dose in a conventional fractionation because the treatment could last several months [16].

So far, these new therapeutic modalities have been developed due to technologic advances in image guidance and treatment delivery but without a solid biological basis. It is the role of traditional radiobiology (and molecular radiobiology) to explain the effects of high doses of ionizing radiation on tumor and normal tissues. Only through a better understanding of how high doses of ionizing radiation act, clinicians will know exactly what we do, allowing us in the future to refine our treatments.

Radiosensitivity is the susceptibility of cells (tissues and organs) to be damaged and inactivated by ionizing radiation. To compare the radiosensitivity of different types of cells, we can use parameters directly read on the cell survival curve as the surviving fraction at 2 Gy (SF2) or parameters derived from mathematical models. The linear-quadratic (LQ) formalism is the most commonly used tool to compare fractionation sensitivity. The model is based on the assumption that cell

death is due to DNA strand breaks. However, studies have shown that the LQ model overestimates cell killing at high single doses because it predicts a survival curve that continuously bends downward whereas the experimental data are consistent with a constant slope at high doses. Therefore, there is concern that LQ model does not accurately predict tumor cell response at the higher doses per fraction used in SRS. In fact, there is a controversy about the limitations of the LQ model for predicting the biological effectiveness of SRS. Proponents of the use of the model argue that it is a mechanistic, biologically based model related to single and double-strand DNA breaks; it has sufficiently few parameters to be practical; it has well-documented predictive properties for fractionation/dose-rate effects in the laboratory and it is reasonably well validated, experimentally and theoretically, up to about 10 Gy/fraction and would be reasonable for use up to about 18 Gy per fraction. However, other authors believe that the use of the LQ model is inappropriate because much of the data used to generate the model are obtained in vitro at doses well below those used in SRS and does not consider the impact of radiation on cells other than the tumor cells (for example, the indirect tumor cell death caused by vascular damage); it does not accurately explain the observed clinical data and ignore the impact of radioresistant subpopulations of cells [17].

The LQ model remains widely used today with one of its most common applications being the calculation of the biological effective dose (BED). The BED formulation can be extended to determine a dose/fractionation regimen with equivalent efficacy (or biological effect). As discussed in detail above, the LQ model has a firm grounding in classical radiobiology in that it describes the generation of chromosome rearrangements that lead to a mitotic catastrophe-type cell death at least within the range of conventional fractionation. Clinically, the LQ model has underestimated the biological effect of higher doses, which appears at odds with a simple application of the LQ equation. A partial explanation may reflect the fact that the LQ model does not properly reflect the tumor complexity and the heterogeneity of cell types within the tumor and does not consider tissue-level effects (e.g., stromal and vascular interactions). Also, it does not consider other potentially important

mechanisms of cell death, other than mitotic catastrophe (e.g., ceramide-mediated apoptosis of endothelial cells).

Nowadays, there are several radiobiology models, which are used in radiotherapy [18-25]. With such purposes we found some results for Linear-Quadratic (LQ) model [18], Linear-Quadratic-Linear (LQL) model [19], Universal Survival Curve (USC) model [20], Padé Linear Quadratic (PLQ) model [21] and Linear-Quadratic-Cubic (LQC) model.

Table 1.2_Radiobiology model and their equations.

Model	**Parameters**	**Equation**
LQ model	α, β	$\ln(S_F) = -\alpha D - \beta D^2$
LQL model	α, β, D_t	$\ln(S_F) = -\alpha D - \beta D^2$, $D \leq D_t$ $\ln(S_F) = -(\alpha D_t - \beta D_t^2 + \gamma(D - D_t))$, $D \geq D_t$ $D_t = \frac{2D_q}{1-\alpha D_0}$
USC model	α, β, D_q, D_0, D_t	$\ln(S_F) = -\alpha D - \beta D^2$, $D \leq D_t$ $\ln(S_F) = -\frac{D}{D_0} + \frac{D_q}{D_0}$, $D \geq D_t$ $D_t = \frac{2D_q}{1-\alpha D_0}$
PLQ model	α, β, γ	$\ln(S_F) = \frac{-\alpha D - \beta D^2}{1+\gamma D}$
LQC model	α, β, γ	$\ln(S_F) = -\alpha D - \beta D^2 + \gamma D^3$

The USC proposed by Park et al. is a hybrid model. The LQ component for the linear and shoulder portions of the survival curve is maintained when the classical LQ model provides a good approximation to clinical or experimental data. However, for larger doses beyond the shoulder region where a linear component is expected to dominate, the historic multitarget model is used. In this particular model, dose D_T, is the transition point at which the linear component of the multitarget

model is tangential to the curved component of the LQ component. Thus, at doses of D_T or below, the curve is identical to the LQ curve, and at doses of D_T or greater, it approximates the multitarget model.

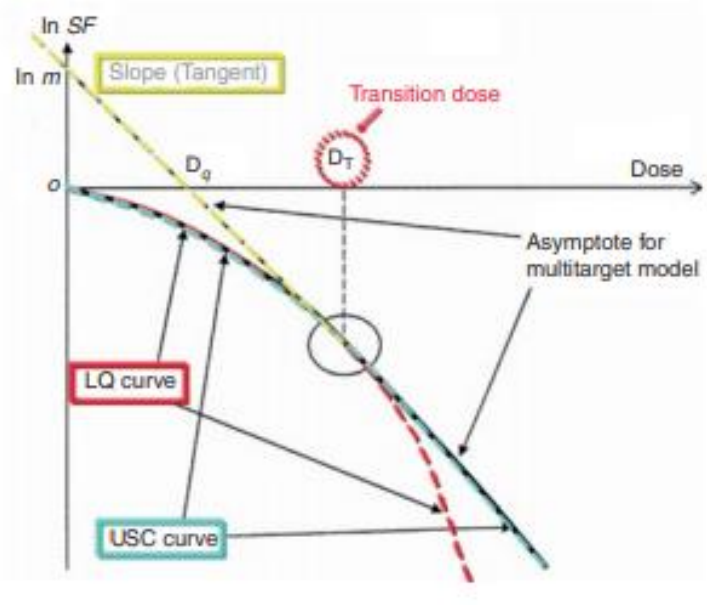

Figure 1.14_The USC model (cyan dashed line) is a hybrid between the LQ model (red dashed line)

The LQ-L model proposed by Astrahan was intended as a more manageable model than the USC and avoided the somewhat arbitrary fusion of the LQ and the multitarget principles. Whereas in the USC model various parameters had to be extrapolated and involved multiple mathematical manipulations, the LQ-L model eliminated the multitarget aspect and simply specified the loge cell kill per Gy in the final linear portion of the survival curve, where dose DT was the start of the linear portion. This composite approach also introduced an additional factor, γ, which represents the loge cell kill per Gy in the final linear portion of the survival curve (in the high-dose region). Additional mathematical calculations are therefore required to solve for γ in order to estimate the BED.

Table 1.3_BED calculation

Model	Parameters	BED calculation
LQ model	α, β	$BED_{LQ} = nd\,(1 + \frac{d}{\alpha/\beta})$
USC model	α, β, Dq, D_0, D_t	$BED_{USC} = n\,d\,(1 + \frac{d}{\alpha/\beta})$, $d < D_t$
		$BED_{USC} = \frac{1}{\alpha D_0}(n\,d - nDq)$, $d \geq D_t$
LQ-L model	α, β, D_t	$BED_{LQL} = n\,d\,(1 + \frac{d}{\alpha/\beta})$, $d < D_t$
		$BED_{LQL} = nD_t\,(1 + \frac{D_t}{\alpha/\beta}) + n\,(\frac{\alpha+2\beta D_t}{\alpha})(d - D_t)$, $d \geq D_t$

The PLQ, USC and LQL models have the fewest drawbacks at all doses. The extrapolation numbers and final slopes of these models are dose independent. The PLQ, USC and LQL models have the fewest drawbacks at all doses. The extrapolation numbers and final slopes of these models are dose independent. Final slopes and extrapolation numbers are independent of dose. And we can mark this as an advantage over the LQ model. Therefore, we can conclude that PLQ, USC and LQL models are theoretically justified. These models can replace other models for clinical applications at high doses. [26].

1.5 Quality Assurance

The quality assurance (QA) of dose distributions presents a challenging problem: dose distributions present 3D data and there are many ways in which the expected dose can differ from the delivered dose. the goal of analysis is to find gross deviations from clinically acceptable treatment plans with one simple to calculate metric. There are two main deviations which can occur in radiotherapy: inaccuracy of dose (i.e. the dose is some percentage different than the expected value) and positioning inaccuracies (i.e. the dose distribution is misaligned). Positioning accuracy is very important as un-irradiated tumor tissue will significantly decrease the efficacy of the treatment. Similarly, dose inaccuracies can manifest unexpected toxicities for structures which are close to their limits, and lower the probability of disease-free survival if the tumor is under-dosed. Low et. al. developed a method that tries to explicitly account for these types of errors, and it is called the gamma pass metric. In this method ideal accuracy specifications, such as the dose value accuracy and positioning accuracy, are specified. In the original publication, an

accuracy of 3 %, 3mm in the dose value and position were used respectively. Modern SRS treatment QA uses 2%, 2 mm or 2 %, 1 mm as positional accuracy is of greater importance when tight margins are used.

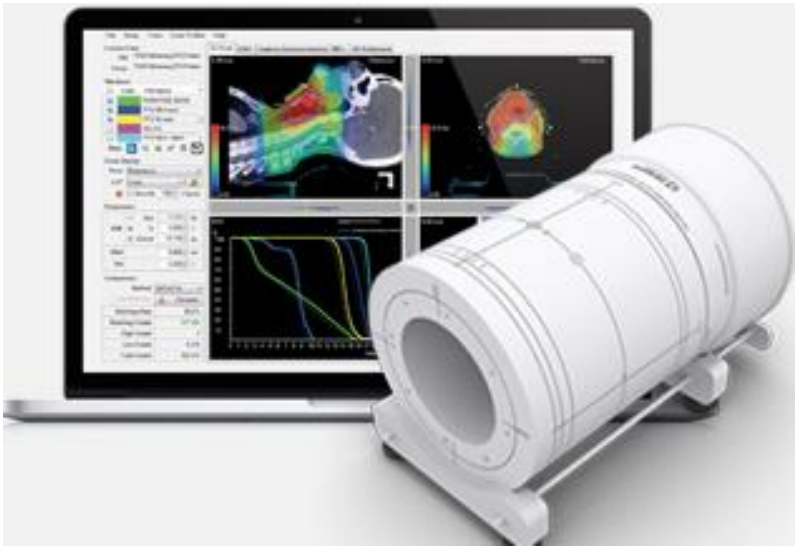

Figure 1.15_ArcCHECK detectors

ArcCHECK is the only true 4D array specifically designed for QA of today's modern rotational deliveries. At its heart are over 1300 SunPoint® Diode Detectors providing consistent and highly sensitive measurements for all gantry angles, with no additional hardware required. Independent absolute dose measurements enable the gold standard for stringent and efficient patient plan and machine QA testing.

Phantoms are ideally shaped like a patient. The cylindrical design of ArcCHECK intentionally simulates patient geometry to better match reality. ArcCHECK detectors are always positioned opposite the beam depending on what angle the gantry has. The detector does not change its geometry relative to the BEV. On the contrary, if a two-dimensional array is irradiated at an angle, then the geometry turns it into one-dimensional. The ArcCHECK detector can measure gantry angle, absolute dose and measurement time. The measured data can be transferred to a visualization system or TPS [27].

Chapter 2: Research project

Brain metastases (a secondary malignant growth) affect up to one-third of patients with cancer. A viable treatment strategy for brain metastasis is stereotactic radiosurgery (SRS) which is the delivery of high intensity, focused radiation to targets within the brain. However, in radiotherapy, the radiation needs to travel through healthy tissue before it can deposit energy in the cancerous tissue. This creates a challenging optimization problem: creating treatments which minimize the radiation exposure of normal tissue while delivering a sufficient amount of radiation to control the disease. As linear accelerators (linacs) are the most accessible SRS delivery devices used worldwide, this thesis focuses on linac-based SRS treatments.

2.1 Patients selection and contouring

The research study was carried out on at the Tomsk Regional Oncology Center. There were considered and selected two patients who had brain tumors and had been treating in Tomsk Oncology Center. All treatment plans were simulated using the Monaco treatment planning system v5.11 (Elekta Instrument AB, Stockholm) on the Elekta Synergy linac with photon beam energy equal to 6 MV.

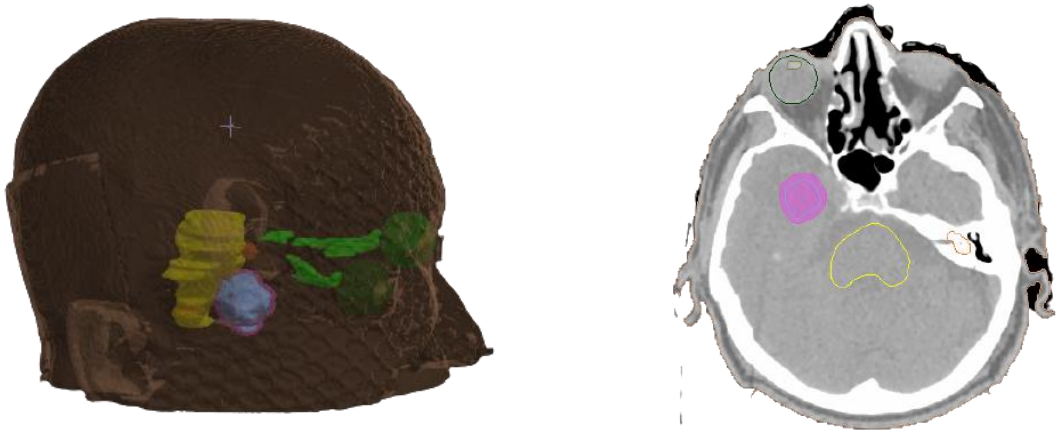

Figure 2.1_Patient 1’s tumor localization (3D and transverse view).

Figure 2.2_Patient 2's tumor localization (3D and transverse view).

Treatment planning for all patients was based on high-resolution computed tomography (CT) and magnetic resonance imaging (MRI). During CT scan and treatment, patients were fixated with the help of an individually fitted thermoplastic mask. To conduct topometric preparation for all patients, a Toshiba Aquilion spiral scanner (Toshiba, Japan) with a cut thickness of 0.5 mm was used, a reconstruction index of 2.0 mm. DICOM data was sent to the contouring station MonacoSim.

Later, contouring of critical organs and tissues, targets was carried out, planned volumes of exposure were determined. The MRI was thoroughly coregistered and served as basis for target GTV and organs at risk delineation. Considering the availability of intrafractional tracking and motion compensation, a safety margin of 3 mm was added to the GTV by isotropic expansion to create the planning target volume. Based on the obtained computed tomographic scans, a three-dimensional patient model was built.

Table 2.1_Patients' and tumor characteristics.

Patients'	Number of metastases	Total tumor volume, cm^3
Patient 1's	1	9,441
Patient 2's	2	5,418

Patient 1 (figure 2.1) had one tumor with PTV 9,441 cm^3. Patient 2 (figure 2.2) had two tumors with PTV1 2,656 cm^3 and PTV2 2,762 cm^3. In table 2.1 is presented patients' and tumor characteristics.

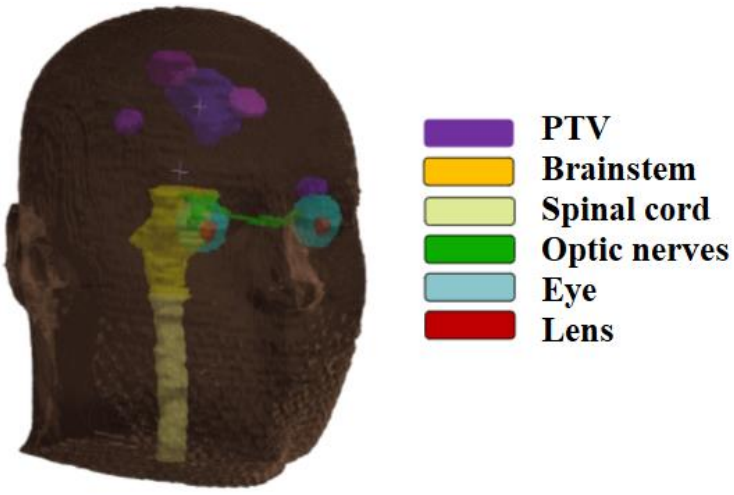

Figure 2.3_Contouring for both PTV and OARs

Dose prescription was done according to metastasis size and in compliance with current guidelines. All patients had given 18 Gy dose in one fraction. Such dose had been taken because our patients' tumors were in diameter 2-3 cm.

Table 2.2_Brain Dose Guidelines.

Brain metastasis	
Lesion diameter ≤2 cm	20–24 Gy
Diameter >2 cm but ≤3 cm	18 Gy
Diameter >3 cm but ≤4 cm	15–16 Gy

Dose constraints for OAR, specifically brain stem and optical tract were observed according to QUANTEC, TG101 data and literature recommendations. Treatment plans were designed according to guidance's and regulations for evaluation limits to organs at risk. In table 2.3 is presented limits which were must had been done.

SRS treatment of brain should be conformal in high and in intermediate doses to not alloy spread dose to normal tissue of brain. The toxicities of SRS brain tumors associate with V12, this is volume of brain which got dose equal to 12Gy.

Table 2.3_Limits for organ at risk

Organs	Limits
Brain	12 Gy to <10 cc
Brainstem	Max dose <15 Gy 10 Gy to <0,5 cc
Cochlea	Max dose <9 Gy
Optic nerves	Max dose <10 Gy 8 Gy to <0,2 cc
Optic chiasm	15 Gy to <0,2 Gy
Lenses	Max dose <12 Gy
Eyeball	Max dose <12 Gy

2.2 SRS planning: technical parameters

The VMAT plan optimization is generally divided into two steps: the first step is to optimize the ideal fluence map according to the constraint function and the second is to convert the optimized fluences into a deliverable sequence with MLC shapes and gantry positions. Planning relevant parameters (gantry angle interval, number of arcs, arc length, etc.) in the treatment planning system (TPS) affects the optimization of the plan and therefore influences its quality.

Monaco TPS uses sequencer for VMAT. The Monaco TPS optimizes the VMAT plan using the increment of gantry (IGA) parameter. The IG value divides the planned arc of VMAT into equal sectors. The number of sectors, which play the role in the leaf movement. In each sector, MLC leaves only move unidirectionally and may generate many CPs. While the first stage in on working, the fluence is

reordering along with sectors by sequencer. The leaves move between sectors, i.e. the leaves in the left edge in one sector move to the right field edge as the gantry rotates. The leaf edges arrive at the field edge at the beginning of the next sector where they change the direction. MLC completes round trips in different sectors successively until the end of treatment.

In common, if use a large IGA creates few sectors and its turn they can produce poor quality plans and increase treatment time, the same time if use a too small IGA it will give more sectors and may increase the quality of the plan.

For example, the 360° full-arc VMAT plan is divided into nine equal sector regions when the value of IG is 45° (figure 2.4).

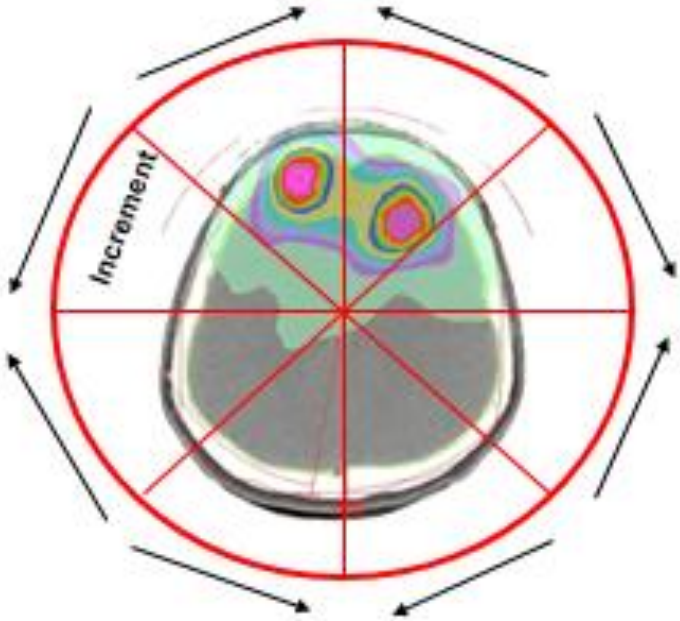

Figure 2.4_Increment of gantry

A starting value of 30 generally works well, lowering to 20 for more complex volumes. Lowering the sweep sequencer allows time for the MLC to move and modulate to accommodate the complex target. All our plans we planned in Monaco TPS for different IGA such as 15°, 20°, 30° and 40°.

The number of arcs or the number of sectors, which we use for planning can affect on the quality of that plan. It has been reported that multiple-arc plans had advantage in quality compared to single-arc plans. In our research, we changed

number of arcs between 1 to 4 for all patients, VMAT plans we generated using single isocenter.

The collimator angle is a very important parameter to gain a better dosimetric efficiency since it determines the optimization of freedom to shape a desired dose distribution and doses to normal organs could be controlled by blocking the organs properly. Current technology could not rotate the collimator during beam delivery. Collimator angle is selected individually for each patient; thus it is difficult to say recommendation which angle is better to set. Gantry angle is also selected individually and here also we can't say any recommendation. But we always use one full arc as basic and then we can set another arcs based on which organs we need to safe.

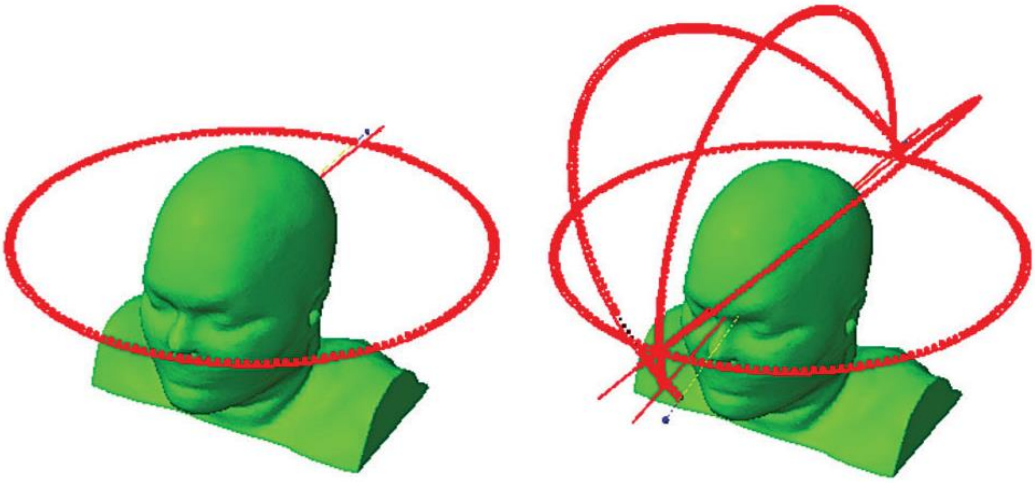

Figure 2.5_Single and multiple-arc plans

Non-coplanar radiotherapy uses a number of fixed or rotating radiation beams that do not share the same geometric plane relative to the patient. This reduces the beam overlap away from the tumor. Linear accelerators achieve this by rotating the recumbent patient around the isocentre on a treatment couch to a different position for each beam orientation. Couch angle we set 0°-360° to view influence of non-coplanar arcs.

The important role in the creation size and shape of the segments is taken by minimum segment width (MSW). In this study 3 VMAT plans, 0.5 cm MSW, 1.0

cm MSW, and 1.5 cm MSW, were generated, but other parameters and cost functions remained constant.

This study explores the influence of different technical parameters on VMAT treatment plans for brain tumor to identify the optimal technical parameters to improve the quality and delivery efficiency of clinical treatment plans. For the VMAT planning, the user should determine parameters such as gantry start angle, rotation direction, arc length, gantry spacing, number of arcs, and collimator angles. Next listed technical parameters (table 2.4) were changed and influence of them were looked through.

Table 2.4_Technical parameters TPS.

Technical parameters	Area
Segment width	0,5; 1; 1,5
Increment	15°, 20°, 30°, 40°
Arcs number	1 - 5
Collimator angle	0° - 360°
Gantry angle	0° - 360°
Couch angle	0° - 180°

For all patients we designed VMAT plans using the Monaco TPS and they were delivered by the Elekta Synergy linac with X ray beam energy equal 6 MV. And all these VMAT plans we planned with the next calculation properties: Grid spacing we taken as 3 mm, and Monte Carlo variance we selected as 0.8 %. Monte Carlo algorithm was selected for second stage dose calculation as a secondary algorithm and that is a final dose calculation. The dose was calculated not to the water but to the medium. For all plans was applied heterogeneity correction.

Table 2.5_Planning parameters used in TPS

Photon energy	6 MV
Delivery technique	VMAT
Grid Spacing	0.3 cm
Statistical Uncertainty	0.8 %
Algorithm	Monte Carlo

2.3 SRS planning: inverse planning; cost function

Monaco treatment planning system utilizes biological properties of the tissue and physical effects of radiation. This system has 3 biological constraints: Serial, Parallel and Target EUD, and 6 physical constraints: overdose DVH, quadratic overdose, target penalty, under dose DVH, quadratic under dose and maximum dose. So user has an option to set the cell sensitivity of the tumor in target EUD. The OAR can be set depending on the properties of the tissue, either serial or parallel cnstraints.

Target Penalty - defines dose and minimum volume coverage of tumor. We use two target objectives (Target EUD or Target Penalty) in prescription. Maximum Dose – control hotspots, very rigid constraint. Quadratic overdose- defines maximum dose but less rigid than “maximum dose”. Serial biological cost function is the preferred constraint for serial OARs.

Radiotherapy cost functions are created to convey the desires of the treatment planner to the optimization software. For all PTVs, plans aim to achieve 98% of PTV was covered with the 98% of prescription dose and an over-dosage of 110% of the prescription dose was allowed to 2% volume of the PTV. For all patients, we generated VMAT plans with different technical parameters (Table 2.4.), and other parameters and cost functions remained constant. The cost functions are presented below in Table 2.6.

Table 2.6_The cost functions of VMAT planning for brain tumor.

ROIs	Cost function	Parameter	Iso constraint
GTV	Target penalty	98 %	18 Gy
	Target EUD	0,25	18 Gy
	Quadratic overdose	19,5 Gy	0,1
PTV	Target penalty	98 %	17,8 Gy
	Quadratic overdose	19,4 Gy	0,1
Chiasma	Serial	k=18	8 Gy
	Maximum dose	NA	8 Gy
Brainstem	Maximum dose	NA	15 Gy
	Serial	k=18	10 Gy
Eye Left	Maximum dose	NA	7 Gy
Eye Right	Maximum dose	NA	7 Gy
Lens	Maximum dose	NA	7 Gy
Optic nerves	Serial	k=18	8 Gy
Patient	Serial	k=15	12 Gy

2.4 SRS planning: evaluation indices

There are many quantitative methods by which radiotherapy treatment plans are analyzed. Furthermore, there are different ways to represent the same information with little standardization. This can sometimes make the process of

treatment plan evaluation difficult. This section will focus on the definition of the dose metrics which are used in this work. For all plans were built Dose Volume Histogram (DVH) and calculated doses.

Based on DVH's data we evaluated metrics which describe quality of SRS, such as Homogeneity Index (HI), Conformity Index (CI), Paddick Conformity Index (PCI), and two Gradient indexes. All results by two patients are presented in APPENDIX A, APPENDIX B, APPENDIX C.

2.5 SRS planning: results

The objective of this study was to analyze the influence of the number of arcs on brain tumor volumetric modulated arc therapy plan. In this study, we analyzed all cases using single and multiply arc VMAT plans. In SRS, the number of beam directions that may be used from a conventional linac is more limited because of the location of the target and the risk of collision between the gantry and the patient's body or the treatment couch. Coplanar beam arrangements are faster and simpler to set up, but this requires all of the dose fall off to occur in a single, axial plane. Non-coplanar radiotherapy uses a number of fixed or rotating radiation beams that do not share the same geometric plane relative to the patient. This reduces the beam overlap away from the tumor. Conventional C-arm linear accelerators (linacs) achieve this by rotating the recumbent patient around the isocentre on a treatment couch to a different position for each beam orientation. These techniques often deliver higher fractional doses and require highly conformal, sharp dose gradients outside the planning target volume (PTV) to minimize dose to adjacent normal tissue.

Quality comparisons included evaluating the CI, HI, TC, mean doses and maximum doses to the PTV, as well as the dose-volume index of the OARs, MUs. The Volume of OAR receiving max dose was analyzed. The volume of normal tissue brain receiving greater than 12 Gy was compared.

Gantry, collimator and couch angles were selected individually according to target and OARs volumes.

First patient received next parameters:

The coplanar plan we made of two coplanar arcs. The first was from 190° and go long to 170°. The second arc began at 90° and continued till 240°. The couch angle for coplanar plans we setted at 0°. Collimator angle adjusted adhere tumor target and risk organs.

The non-coplanar plan was made by two coplanar arcs and one non-coplanar arc. The first was from 190° and go long to 170°. The second arc began at 90° and continued till 240°. The third arc began from 235° till 350°. The couch angle for coplanar plans we setted at 0°, for non-coplanar arcs 90° Collimator angle adjusted adhere tumor target and risk organs. MSW was 1cm and increment value was 30, 30 and 20.

Table 2.7_PTV dosimetric results of the coplanar and non-coplanar VMAT plans (Patient 1).

Parameter	Coplanar	Non coplanar
TC (98%)	99,95	99,97
Dmean	19,020	19,049
Dmax	20,118	20,008
CI	1,197	1,213
HI	0,079	0,078
PCI	1,223	1,234
GIlow	3,975	3,126
GIhigh	3,294	2,983
MUs	2814,19	3147,77
V12 brain, cc	11,929	10,034

Both techniques achieved the planning objectives in tumor coverage 98 % of tumor volume received ≥ 98%of the dose, Dmax not more than 110 % of the dose (not >2% of PTV). We found that the V12 Gy of non-coplanar VMAT plan was smaller than coplanar VMAT (6 %). Our study showed that the GIlow in

coplanar plan 3,975 and in non-coplanar 3,126, respectively. Our study showed that the GIhigh in coplanar plan 3,294 and in non-coplanar 2,983, respectively.

CI = 1 corresponds to the ideal dose coverage of the target; CI >1 indicates that the irradiated volume exceeds the target volume and covers part of the healthy tissue; and CI <1 indicates that the target volume is not fully radiated. CI= 1.2 is good.

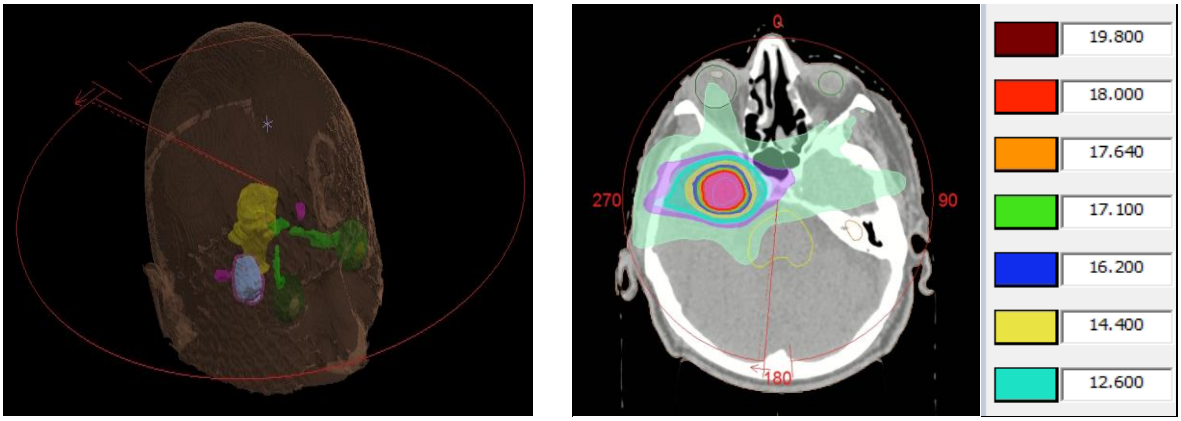

Figure 2.6_Patient 1's treatment coplanar plan (3D and transverse view).

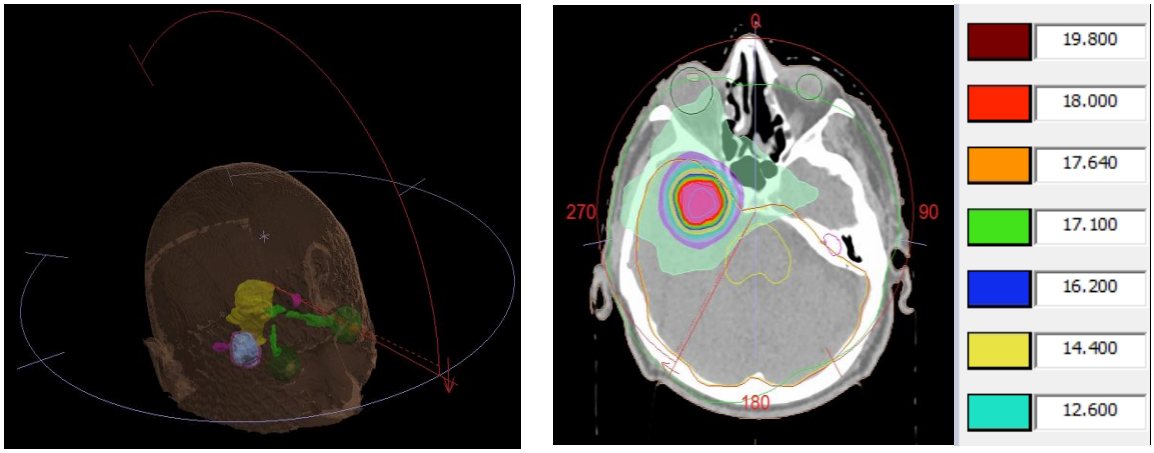

Figure 2.7_ Patient 1's treatment non coplanar plan (3D and transverse view).

Second patient had been setted up next parameters:

The coplanar plan we made of two coplanar arcs. The first was from 190° and go long to 170°. The second arc began at 100° and continued till 260°. The couch angle for coplanar plans we setted at 0°. Collimator angle adjusted adhere tumor target and risk organs.

The non-coplanar plan was made by two coplanar arcs and one non-coplanar arc. The first was from 190° and go long to 170°. The second arc began at 100° and continued till 260°. The third arc began from 220° till 360°. The couch angle for coplanar plans we setted at 0°, for non-coplanar arcs 90° Collimator angle adjusted adhere tumor target and risk organs. MSW was 1cm and increment value was 30, 30 and 20.

Table 2.8_PTV dosimetric results of the coplanar and non-coplanar VMAT plans (Patient 2).

Parameter	Coplanar	Non coplanar
TC (98%)	95,52	98,16
Dmean	18,818	18,905
Dmax	19,998	20,014
CI	1,170	1,176
HI	0,167	0,134
PCI	1,344	1,320
GIlow	2,391	2,228
GIhigh	5,502	4,901
MUs	3739,73	3458,82
V12 brain, cc	38,891	27,249

Non coplanar techniques achieved the planning objectives in tumor coverage 98 % of tumor volume received ≥ 98%of the dose, Dmax not more than 110 % of the dose (not >2% of PTV). We found that the V12 Gy of non-coplanar VMAT plan was smaller than coplanar VMAT (30 %). Our study showed that the GIlow in coplanar plan 2,391 and in non-coplanar 2,228, respectively. Our study showed that the GIhigh in coplanar plan 5,502 and in non-coplanar 4,901, respectively.

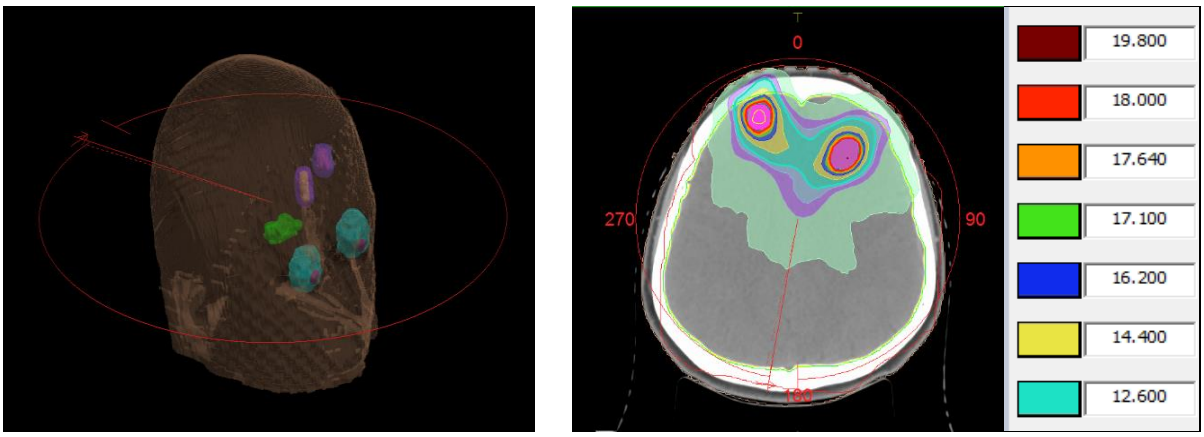

Figure 2.8_Patient 2's treatment coplanar plan (3D and transverse view).

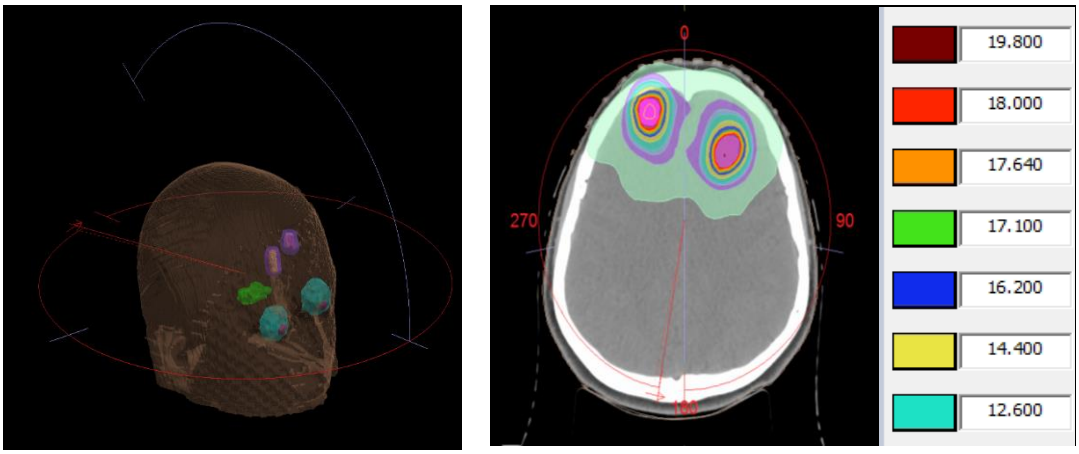

Figure 2.9_Patient 2's treatment non coplanar plan (3D and transverse view).

We found that the V12 Gy of non-coplanar VMAT plan was smaller than coplanar VMAT for both single and multiple lesion cases. Non coplanar beams can make the dose falloff more uniform in all directions, and reduce integral dose to the patient, but may make patient setup more difficult and time-consuming. In addition, couch rotation tends to be the least accurate motion in many linacs, and may introduce additional uncertainty in patient setup unless this is carefully checked.

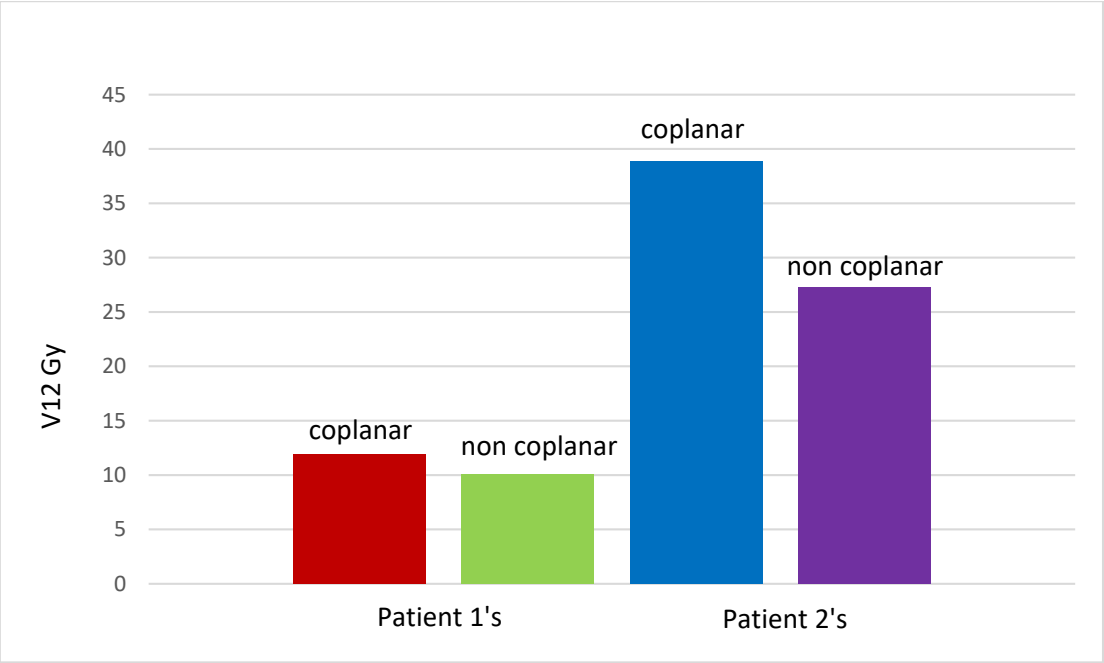

Figure 2.10_The volume of brain receiving 12 Gy in coplanar and non-coplanar treatment plan

The objective of this study was to analyze the influence of the increment of gantry angle on brain tumor volumetric modulated arc therapy plan. Volumetric modulated arc therapy (VMAT) plans were done with different increment of gantry angle like 15°, 20°, 30° and 40°. The remaining parameters were similar for all the plans. Quality comparisons included evaluating the HI, CI, TC, maximum doses, and mean doses to the PTV, as well as the dose-volume index of the OARs.The Volume of OAR receiving max dose was analyzed. The volume of normal tissue brain receiving greater than 12 Gy was compared. All plans met our dosimetric criteria.

There were no statistical significance differences were observed between VMAT 15, VMAT 20, VMAT 30 and VMAT 40 plans in dosimetric parameter of PTV such as D98%, D110%. VMAT 30 and VMAT 20 had superior HI and CI with good conformity. We analyzed the volume of brain normal tissue receiving doses ≥12 Gy between plans. The volume of normal tissue receiving ≥12 Gy was high in higher IGA that is VMAT 40.

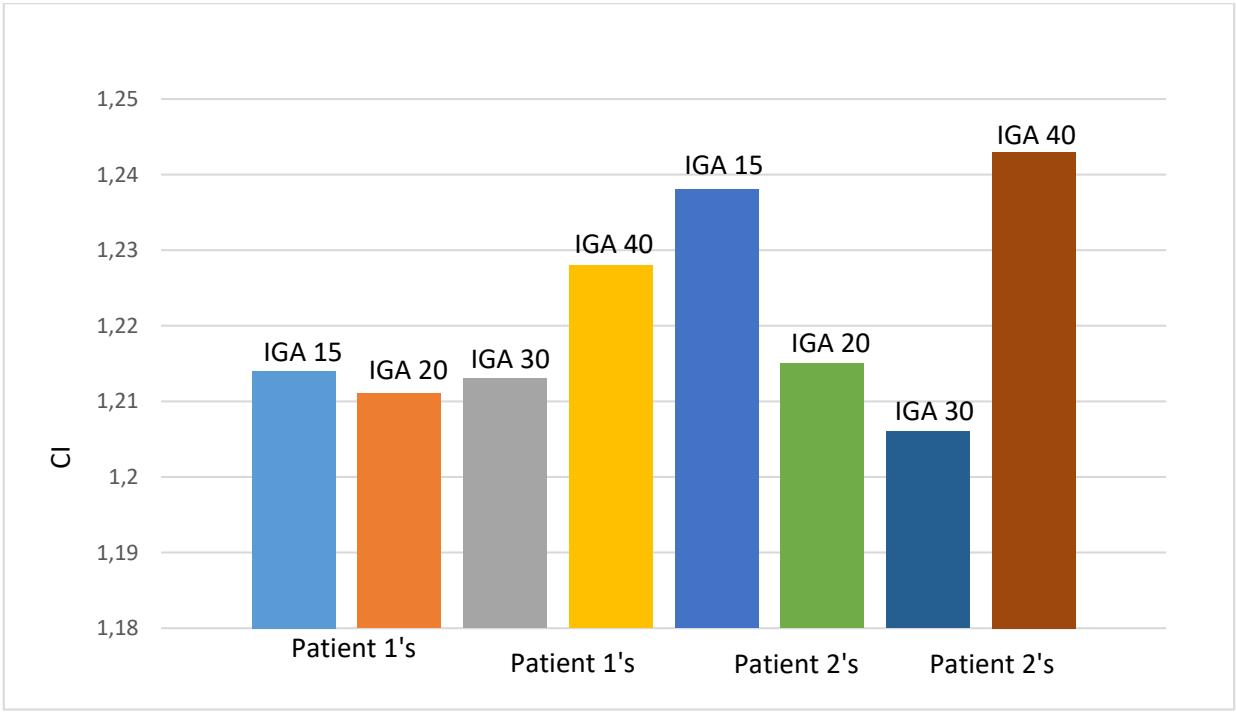

Figure 2.11_The volume of CI of the VMAT plans used to treat brain tumor patients devised using for different IGA.

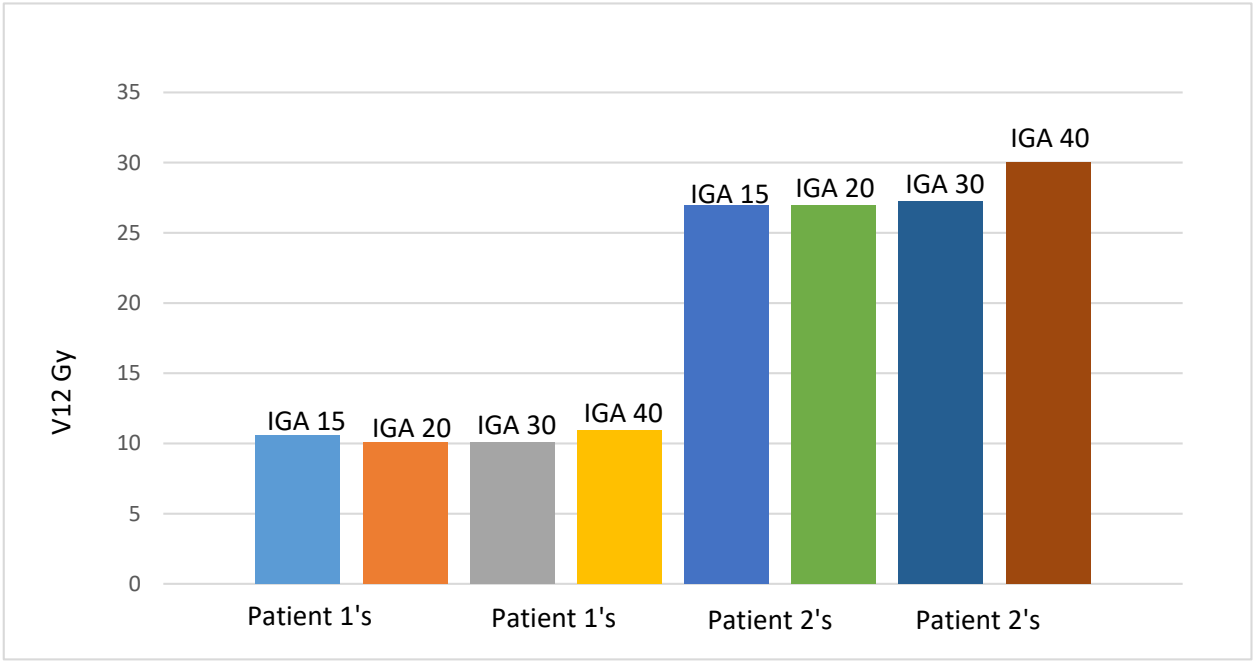

Figure 2.12_The volume of CI of the VMAT plans used to treat brain tumor patients devised using for different IGA.

As we already mentioned it, minimum segment width has an important role in creation and forming optimized apertures. And these segments may sometimes lead to the poor verification.

In this work we created three VMAT plans with different value of minimum segment width and that are 0.5, 1 and 1.5 and other parameters were constant. All plans were created in Monaco TPS.

The target doses of the VMAT plans are presented in Table 2.9. The maximum and mean PTV doses haven't showed markedly different values among these three plans. The target dose coverage of the plan using an MSW of 0.5 cm was higher than that of the plan using an MSW of 1.0 cm, which in turn was better than that of the plan using an MSW of 1.5 cm.

Table 2.9_PTV dosimetric results of the VMAT plans used to treat 2 brain tumor patients devised using three different MSWs.

Patients'	Parameter	0.5 cm MSW	1.0 cm MSW	1.5 cm MSW
Patient 1	TC (98%)	100	99,9	99,77
	Dmean	18,962	19,035	18,985
	Dmax	19,834	19,935	20,051
	CI	1,213	1,211	1,198
	HI	0,0074	0,082	0,0089
Patient 2	TC (98%)	98,16	98	91,31
	Dmean	18,851	18,966	18,605
	Dmax	19,998	19,990	20,324
	CI	1,190	1,261	1,034
	HI	0,034	0,123	0,182

OAR dose results are shown in Appendix. No significant differences were detected among to these three types of VMAT plans in terms of doses to the remaining OAR. The DVH results with these three plans in the Patient 1 with typical brain tumor are shown in Figure 2.12 -13.

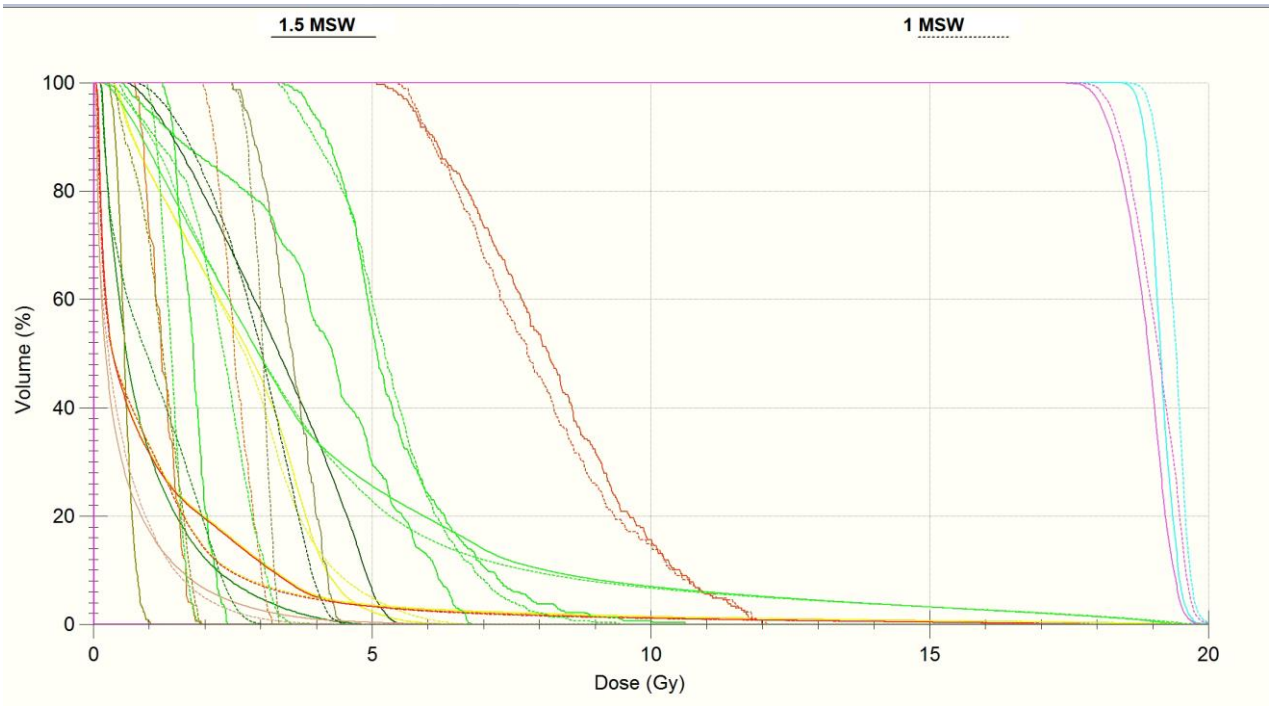

Figure 2.13_The DVH of 3 VMAT plans with different MSW (MSWs 1; 1.5) for a typical brain tumor

Using gamma analysis, we could achieve the quantitative analysis of distribution of dose, that was achieved by comparing the planned dose distribution and measured dose. The computed and measured doses were analyzed by ArcCHECK detector. The dose which was measured with higher MSW showed to us better agreement with the calculated dose. Thus we can come out to that if we increase MSW and its decrease VMAT complexity, so therapeutic efficiency may be improved too. Table 2.10 shows the reliability results of the gamma analysis. Parameters used for verification was 5%, 1mm and lower threshold 20%.

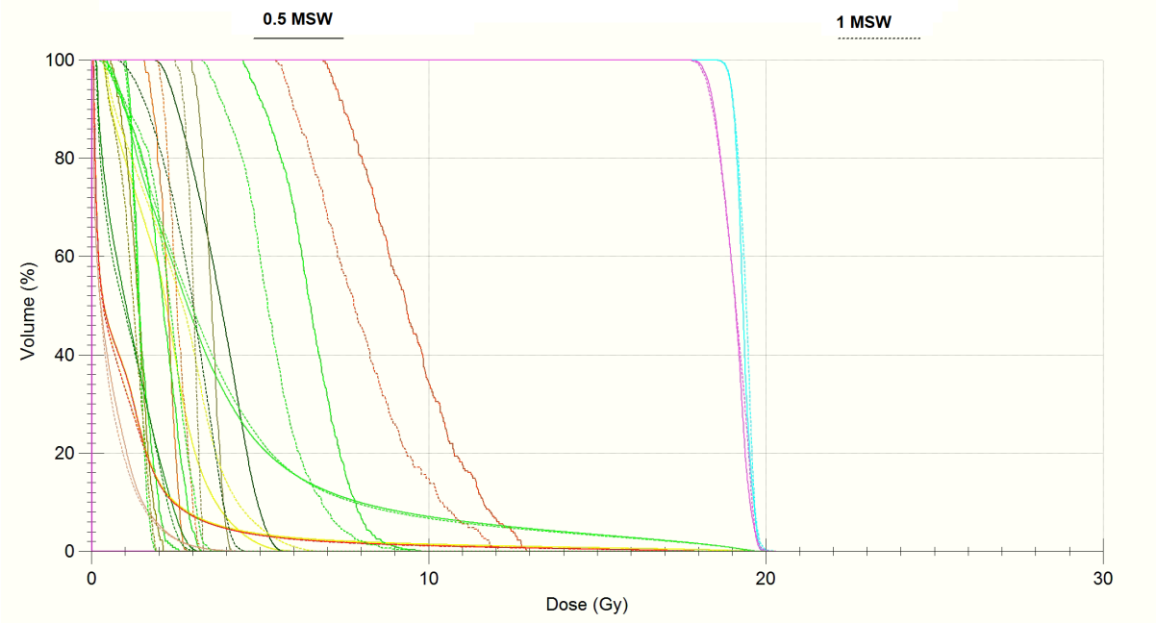

Figure 2.14_ The DVH of 3 VMAT plans with different MSW (MSWs 1; 1.5) for a typical brain tumor

Table 2.10_ Results of the gamma analysis.

Parameter	0.5 cm MSW	1.0 cm MSW	1.5 cm MSW
Patient 1			
Total Points	251	208	96
Passed	234	204	94
Failed	17	4	2
% Passed	93.2	98.1	97.9
Patient 2			
Total Points	278	215	105
Passed	255	211	101
Failed	23	4	4
% Passed	91,7	98.1	96,2

According to our results VMAT plans with MSW of 1.0 cm show a clear advantage in terms of a trade-off between plan quality and delivery efficiency for brain tumor.

The objective of this study was to analyze the influence of the technical parameters (number of arcs, increment, gantry angle, collimator angle, couch angle, minimum segment widths) on brain tumor VMAT plan. And in this study, we analyzed all cases using single and multiply arc VMAT plans and we defined optimal technical parameters for each patient. Table 2.11 -13 shows optimal technical parameters VMAT plan for each patients.

Table 2.11_Optimal technical parameters VMAT plan (Patient 1).

Segment width	1	1	1
Increment	30	20	20
MLC angle	50	0	250
Gantry angle	190	90	235
Couch angle	0	0	90
Arc length	350	210	105

Table 2.12_Optimal technical parameters VMAT plan (Patient 2).

Segment width	1	1	1	1
Increment	30	20	20	20
MLC angle	50	0	300	300
Gantry angle	210	100	220	220
Couch angle	0	0	60	290
Arc length	300	200	140	140

Table 2.13_ Dosimetric results of the VMAT plans

Patients’	Indices					
	HI	CI	PCI	GIlow	GIhigh	MUs
Patient 1	0,082	1,211	1,235	3,025	2,917	3116,16
Patient 2	0,114	1,208	1,257	2,372	4,410	3458,52

Table 2.14_PTV dosimetric results of the VMAT plans

Patients'	PTV				
	Dmin	Dmax	Dmean	V98%	V110%
Patient 1	17,395	19,935	19,035	99,9	0,31
Patient 2	16,640	19,897	18,906	98,75	0,09

Table 2.15_OAR dosimetric results of the VMAT plans

Patients'	OAR						
	Brain V12	Brainstem Dmax	Eyeball Dmax	Lenses Dmax	Optic chiasm Dmax	Optic nerves Dmax	Cochlea Dmax
Patient 1	10,034	6,547	4,032	1,906	2,199	9,181	9,037
	Brain V12	Eyeball L Dmax	Eyeball R Dmax	Lenses L Dmax	Lenses R Dmax	Optic chiasm Dmax	
Patient 2	27,886	1,395	1,139	0,346	0,405	2,363	

2.6 SRS planning: radiobiology evaluation treatment plans

The applicability of the linear quadratic (LQ) model to local control (LC) modeling after hypofractionated radiotherapy to treat brain cancer is highly debated. This study aims to compare the outcomes predicted by the LQ model with those predicted by two other radiobiological models in SRS for brain tumor.

Table 2.16_Model parameters used in this work (taken from Karlsson et al 1997, Malaise et al 1986, Stenerlöw et al 1994).

Parameters	Normal Brain Tissue	Tumor
α/β ratio (Gy)	2.47	8.31
α (Gy^{-1})	0.07	0.241
β (Gy^{-2})	0.03	0.029
s	0.94	-
γ	1.44	2.5
D_{50} (Gy)	6.70	10.31
D_0 (Gy)	-	1.44
D_q (Gy)	-	2.5
D_t (Gy)	-	7.66

A 1×18 Gy fraction regime was prescribed in the study; 1×18 Gy represents 18 Gy treated in 1 fraction. The importance of the two variables, treatment time and dose, can only be evaluated appropriately using the concept of biologically effective dose (BED) where the impact of the changes in treatment time can be taken into account for the different doses prescribed. The physical dose of the tumor was first converted to the BED.

Table 2.17_LQ model (Patient 1).

Structures	D, Gy	Value	α/β, Gy	BED_{LQ}, Gy
PTV	Dmax	19,935	8,31	69,610
	Dmean	19,035		64,326
Brainstem	Dmax	6,547	2,47	27,978
Brain	V12	12	2,47	120

Table 2.18_USC model and LQ-L model (Patient 1).

Structures	D, Gy	Value	α, Gy	D_q, Gy	D_0, Gy	D_t, Gy	BED_{USC}, Gy	BED_{LQ-L}, Gy
PTV	Dmax	19,935	0,241	2,5	1,44	7,66	50,239	49,625
	Dmean	19,035					47,646	47,060

Table 2.19_LQ model (Patient 2).

Structures	D, Gy	Value	α/β, Gy	BED_{LQ}, Gy
PTV	Dmax	19,935	8,31	69,610
	Dmean	19,035		64,326
Brainstem	Dmax	6,547	2,47	27,978
Brain	V12	12	2,47	120

Table 2.20_USC model and LQ-L model (Patient 2).

Structures	D, Gy	Value	α, Gy	D_q, Gy	D_0, Gy	D_t, Gy	BED_{USC}, Gy	BED_{LQ-L}, Gy
PTV	Dmax	19,897	0,241	2,5	1,44	7,66	50,130	49,511
	Dmean	18,906					47,274	46,693

There are many studies which have shown that the Linear-Quadratic (LQ) model is inappropriate to describe high dose per fraction effects in stereotactic high-dose radiotherapy. However, studies have shown that the LQ model overestimates

cell killing at high single doses because it predicts a survival curve that continuously bends downward whereas the experimental data are consistent with a constant slope at high doses.

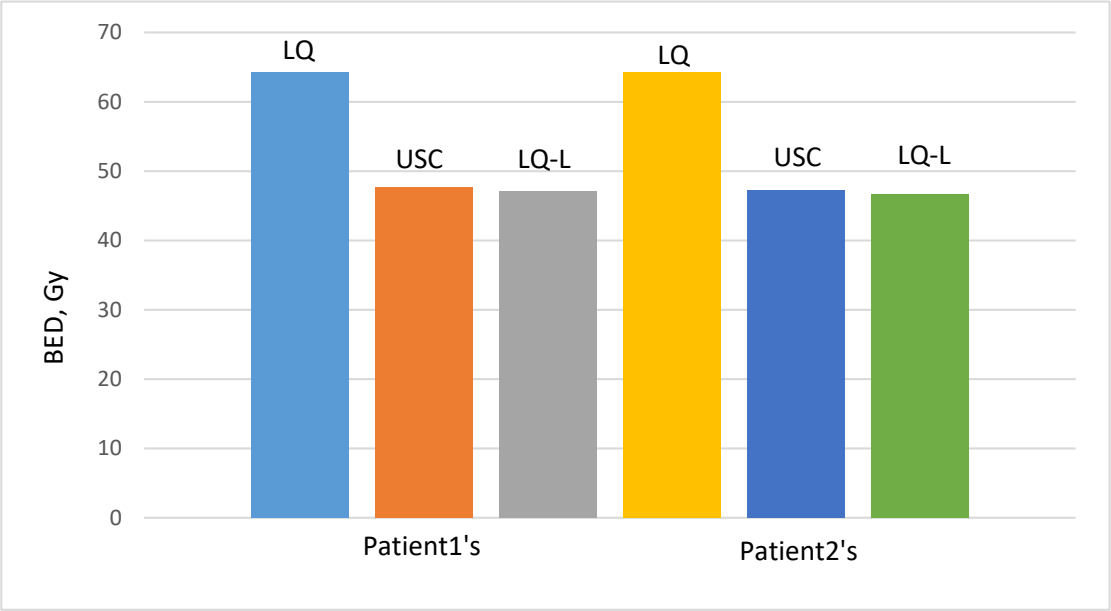

Figure 2.15_BED values of different models

2.7 Conclusion

Within this study, were designed dosimetric plans for stereotactic radiosurgery brain tumors on treatment planning system Monaco. Evaluation of all plans were cared adhere recommendation and protocols to predict radiation damages and pick up optimal dose distributions for each patient. 3D dosimetric evaluation were prepared using DVH for targets and OAR. And since DVH couldn't show us spatial details of dose distribution, we evaluated metrics describe quality of SRS, such as HI, CI, GI. For each patient we designed serial plans with different technical parameters. All plans were designed using inverse planning method.

In extracranial SRS/SRS, the number of beam directions that may be used from a conventional linac is more limited because of the location of the target and the risk of collision between the gantry and the patient's body or the treatment couch. Coplanar beam arrangements are faster and simpler to set up, but this requires all of the dose falloff to occur in a single, axial plane. Non-coplanar beams can make the

dose falloff more uniform in all directions, and reduce integral dose to the patient, but may make patient setup more difficult and time-consuming.

If we use a large IGA it may create few sectors and which can produce low quality plans, and increase treatment time, otherwise if we use a too small IGA it will give us more sectors and they can increase the quality of the plan. VMAT30 and VMAT20 had superior HI and CI with good conformity. The volume of normal tissue receiving ≥12 Gy was high in higher IGA that is VMAT 40.

Also for all plans we generated QA plans on ArcCHECK phantom, with constant geometry and monitor units for each beam. Various values of increment supplies well covering of a target. Low values of increment increased dose to the target. Rising increment from 0,5 to 1 could increase effectiveness and certainness of plans at 7 per cent by gamma index. According to our results VMAT plans with MSW of 1.0 cm show a clear advantage in terms of a trade-off between plan quality and delivery efficiency for brain tumor.

The objective of this study was to analyze the influence of the technical parameters (number of arcs, increment, gantry angle, collimator angle, couch angle, minimum segment widths) on brain tumor volumetric modulated arc therapy plan. In this study, we analyzed all cases using single and multiply arc VMAT plans and we defined optimal technical parameters for each patient.

Our studies have shown that the LQ model overestimates cell killing at high single doses because it predicts a survival curve that continuously bends downward whereas the experimental data are consistent with a constant slope at high doses.

Stereotactic radiosurgery, typically administered in a single session, is widely employed to safely, efficiently, and effectively treat small intracranial lesions. However, for large lesions or those in close proximity to critical structures, it can be difficult to obtain an acceptable balance of tumor control while avoiding damage to normal tissue when single-fraction SRS is utilized.

Chapter 3. Financial management, resource efficiency and resource saving

In this chapter we will discuss about financial part of project such as resource efficiency and resource saving and as well financial costs regarding of our project. To identify all strength and weakness, opportunities and threats related to our project we use SWOT-analysis, this will help us with our purpose and will give us an idea how we can work with each of our characteristics. For 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. Final assessment of the technical decision on particular criteria and in general case, made based on calculation of the resource efficiency indicator.

We should carefully come to this stage to prevent our research to vain. In this stage we need intently look through target market and segmentation and thus we could estimate our potential buyers. But firstly we need know the cost of our project.

This research is performed in Tomsk Regional Oncology Center using proper equipment such as linear accelerator Elekta Synergy, planning system Monaco and others.

3.1 Pre-research analysis

1) Competitiveness analysis of technical solution

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

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

In this work we analyze comparison of machines which could operate SRS brain tumors and they are: linear accelerator (C_1), gamma knife (C_2) and proton therapy (C_3). All methods are evaluated using five points scale, where 1 is the

weakest position and 5 is the strongest one. Evaluation map we present in table 3.1. Analysis of competitive technical solutions is determined by the formula:

$$C = \sum P_i \cdot W_i, \qquad (3.1)$$

C - the competitiveness of research or a competitor;

W_i– criterion weight;

P_i – point of i-th criteria.

Table 3.1_Evaluation card for comparison of competitive technical solutions

Evaluation criteria	Criterion weight	Points			Competitiveness		
		P1	P2	P3	C_1	C_2	C_3
Technical criteria for evaluating resource efficiency							
1. Energy efficiency	0.05	5	5	3	0.25	0.25	0.15
2. Functional capacity	0.05	4	3	3	0.20	0.15	0.15
3. Ease of operation	0.15	4	5	4	0.60	0.75	0.60
4. Reliability of results	0.20	4	5	4	0.80	1.00	0.80
5. Patient radiation load	0.05	4	4	4	0.20	0.20	0.20
6. Labour-intensiveness	0.20	5	4	3	1.00	0.80	0.60
Economic criteria for performance evaluation							
1. Widely accepted method	0.05	5	3	3	0.25	0.15	0.15
2. Competitive ability	0.05	4	5	3	0.20	0.25	0.15
3. Expected life-cycle	0.05	5	5	5	0.25	0.25	0.25
Total	1.00				3.75	3.8	3.05

There are no doubts that reliability of the results is most important in designing a treatment plan. We must be strong confident that our results are strongly lie in criteria that it must to be in. And any correction to the way to improve our results and decrease errors in treatment planning must be high greet.

To achieve that purpose we should give for designing a treatment plan a while time and intensively and the same time carefully work on it. And also we shouldn't forget about resource saving and make our work with less consumption of resource. Just with this way we can make a correction in design a treatment plan which might be unique and interest in finance side for investors.

Though GammaKnife shows better results in correction of uncertainties which could be in motion of patient but nonetheless linear accelerator has more function of capacity.

2) SWOT analysis

SWOT is a complex analysis solution with the greatest competitiveness. SWOT stands for Strength, Weakness, Opportunities and Threats and it has several stages.

The first stage is looking for strengths and weaknesses, opportunities and threats which may come out in its external environment and describing them. Here strengths are competitive side of our project. Weaknesses are some kind of limitations which mess us up to reach our goals. Opportunities are any situations which could appear in environment and make pour project more competitive. Threats are any objectionable situations which could distract or threat competiveness or the project.

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 help to identify what strategic changes are necessary.

The summative matrix of SWOT analysis is presented in Table 3.2.

Table 3.2_The summative matrix of SWOT analysis

	Strengths of the research project: S1. Deliver dose more precisely S2. Much effectively using equipment	Weaknesses of the research project: W1. Deficiency of data W2. Shortage of equipment
Opportunities: O1. Can use the equipment of the Tomsk Oncology Center O2. Reduction of a patient delivered dose	Strategy which based on strengths and opportunities: 1) Effectively use SRS treatment delivery 2) Reduction dose to normal tissue	Strategy which based on weaknesses and opportunities: 1) Opportunity to work at employer equipment for searching data

		2) Reduction of a patient delivered dose would increase quality of clinic
Threats: T1. Lack of appropriate data T2. Threat of external beam injury	Strategy which based on strengths and threats: 1) Using high technology equipment could increase financing 2) High quality treatment might increase financing	Strategy which based on weaknesses and threats: 1) High quality of treatment would rise financing of clinic 2) Using equipment more effectively will increase employee's education

SWOT analysis matrix can help us to view strong and weak sides of our project and correct it immediately according to our purposes. As for our work we see that advantages prevail over disadvantages.

3.2 Project initiation

The initiation process group consists of processes that are performed to define a new project or a new phase of an existing one. As part of the initiation processes, the initial goals and content are determined, and the initial financial resources are recorded.

1) The goals and results of the project

In this section we give information about the project stakeholders (table 3.3) and the hierarchy of the project aims, and the criteria for achieving them (table 3.4).

Table 3.3_Stakeholders of the project

Project stakeholders	Stakeholders expectation
Division of nuclear fuel cycle, PTU	Influence of the technical parameters of SRS brain tumors on radiobiologic and dosimetric evaluation
Tomsk Oncology Clinic	

Table 3.4_Purposes and results of the project

Purpose of the project:	To search influence of the technical parameters of Stereotactic Radiosurgery on dosimetric and radiobiologic evaluation to set the best configuration
Expected results of the project:	Clear information about how technical parameters of linear accelerator effect

	on dosimetric and radiobiologic evaluation of SRS brain tumors
Criteria for accepted of the project results:	Fully done work with all clear information adhered with explanations and analytically predicted
Requirements for the project results:	- Project's calculated results should have as lower errors as it could have - Results should have adhered explanation - All results have to be analyzed and chosen the best one - Project must be done it time

2) The organization structure if the project

In this section we talk who were included in the working group of the project, the roles of each participant in the project and the functions performed by each of the participant and their labor cost in the project (table 3.5).

Table 3.5_Working group of the project

№	Participant	Role in the project	Functions	Labor time, hours
1	E.S. Sukhikh, PhD, Chief of Medical Physicist of Tomsk Regional Oncology Center	Scientific advisor	Controlling the project	60
2	Ya. N. Sutygina, Medical Physicist of Tomsk Regional Oncology Center	Project assistant	Consulting the project	222
3	I. R. Sagov, master student TPU	Project executor	Performing the project	438
Total				720

3.3 Project limitations

Project limitations are all factors that can be as a restriction on the degree of freedom of the project team members.

Table 3.6_Project limitations

Factors	Limitations / Assumptions

Project’s budget	
Source of financing	National Research Tomsk Polytechnic University
Project timeline	March 2021 – June 2021
Date of approval of plan of project	15.03.2021
Completion date	06.06.2021

3.4 Planning of scientific and technical project management

The planning process group consists of the processes that are carried out to determine the overall content of the work, clarify the goals, and develop the sequence of actions required to achieve these goals.

The next step of planning a science project is build a project timeline (table 3.7) and a Gantt Chart (table 3.8).

Table 3.7_Project timeline

№	Job title	Duration, working days	Start date	Date of completion	Participants
1	Developing technical specification	4	15.03.21	19.03.21	Scientific advisor
2	Selection of research direction	2	20.03.21	22.03.21	Scientific advisor
3	Searching and selection materials of the topic	10	23.03.21	01.04.21	Student
4	Scheduling activities of the project	3	02.04.21	05.04.21	Assistant, student
5	Obtaining results	34	06.04.21	09.05.21	Assistant, student
6	Preforming calculation	7	10.05.21	16.05.21	Student
7	Analyzing results	7	17.05.21	23.05.21	Student

8	Verification results	4	24.05.21	28.05.21	Scientific advisor, student
9	Preparing for submitting	9	29.05.21	06.06.21	Student

For calculation working hours for each participant, we took 6-hour working day and we come out that for scientific advisor working hours is 60, for assistant is 222 hours and for student is 438 hours.

Further we build a Gantt chart. 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 3.8_Gantt chart

№	Activities	Participants	T_c, days	Duration of the project											
				March			April			May			June		
				1	2	3	1	2	3	1	2	3	1	2	3
1	Developing technical specification	Scientific advisor	4												
2	Selection of research direction	Scientific advisor	2												
3	Searching and selection materials of the topic	Student	10												
4	Scheduling activities of the project	Assistant, student	2												
5	Obtaining results	Assistant, student	34												
6	Preforming calculation	Student	7												
7	Analyzing results	Student	7												

8	Verification results	Scientific advisor, student	4												
9	Preparing for submitting	Student	9												

3.5 Scientific and technical research budget

When planning the budget of scientific research, it should be ensured that all types of planned expenditures necessary for its implementation are fully and reliably reflected. In the process of forming the budget, the planned costs are grouped according to the items presented in the table 3.9.

Table 3.9_Grouping costs by sections

Sections						
Raw material, products and goods costs	Special equipment costs	Basic salary	Additional salary	Social security pays	Overheads	Total planned costs
613863	6900	134122	13411	40640	43659	852595

I. Raw materials, purchased products and semi-finished goods (net of waste)

This section includes the cost of all types of materials, components and semi-finished products which are necessary to perform work.

The cost of materials is calculated according to the nowadays reliable prices (table 3.10). The value of materials cost include additionally transportation and procurement cost (3-5% of the price).

Table 3.10_Raw materials, components and purchased semi-finished goods

Name of position	Brand, size	Quantity (units, amount)	Price per unit (rubles)	Sum (rubles)
Linac	Elekta Synergy	1	182000000	182000000
Phantom	ArcCHECK	1	6000000	6000000
			Total cost for materials	188000000

Total transportation and purchasing cost (3-5%)	7520000
Total cost per article, C_m	195520000

The calculation of materials cost may be carried out next:

$$C_m = (1 + k_T) \times \sum_{i=1}^{m} P_i \times N_{consi}, \quad (3.2)$$

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.

As Linac and Phantom have been already bought here would be appropriate to calculate of depreciation of equipment. Depreciation we can find using next formula:

$$A = \frac{H_A * C * T_0}{365 * 100\%}, \quad (3.3)$$

where A – depreciation charges, rubles,

C – cost equipment, rubles,

$H_A = \frac{100}{T_{ex}}$ – annual depreciation,

T_{ex} – life expectation (30 years for Linac, 15 years for Phantom),

T_0 – time of use equipment (34 days).

Table 3.11_Depreciation charges

Name of equipment	Amount	C, rub.	H_A, %	T_0, days	A, rub.
Linac	1	182000000	3.4	34	576416
Phantom	1	6000000	6.7	34	37447
Total					613863

II. Special equipment for scientific experiment

This section includes all the costs associated with the purchase of special equipment (instruments, control and measuring equipment, stands, devices and mechanisms) necessary for carrying out work on a specific topic. The cost of materials is calculated according to the nowadays reliable prices (table 3.12).

Table 3.12_Costs calculation for specific equipment

Name of equipment	Quantity, units	Price per unit, rubles	Total cost for position, rubles
Thermoplastic mask	2	3450	6900

The value in table 3.12 have been calculated being count costs for transportation and installation and it constituted 15% of original cost or 450 rubles per thermoplastic mask.

III. Basic salary

This section includes the basic salary of scientific and engineering workers, workers of model workshops and experimental production facilities directly involved in the performance of work on this topic. The amount of salary expenses is determined based on the labor intensity of the work performed and the current system of remuneration. The basic salary includes a bonus paid monthly from the salary fund (the amount is determined by the Regulations on Remuneration of Labor).

This point 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 labor intensity of the work performed and the current salary system

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

$$S_b = S_a \times T_w, \quad (3.4)$$

where S_b – basic salary per participant;

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

The average daily salary is calculated by the formula:

$$S_d = \frac{S_m \times M}{F_v}, \quad (3.5)$$

где 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, 5 days per week;

F_v– valid annual fund of working time of scientific and technical personnel (198 days).

Table 3.13_The valid annual fund of working time

Working time indicator	
Calendar number of days	365
The number of non-working days - Weekends - Holidays	 104 14
Loss of working time - Vacation - Sick absence	 49 0
The valid annual fund of working time	198

Monthly salary is calculated by formula:

$$S_{month} = S_{base} \times (k_{premium} + k_{bonus}) \times k_{reg}, \quad (3.6)$$

where S_{base} – base salary, rubles;

$k_{premium}$ – premium rate;

k_{bonus} – bonus rate;

k_{reg} – regional rate (for Tomsk region is equal 1.3).

Table 3.14_Calculation of the basic salary

Performers	S_{base}, rubles	$k_{premium}$	k_{bonus}	k_{reg}	S_{month}, rubles	W_d, rubles	T_p, work days	W_{base}, rubles

Research advisor	35000	1	1	1.3	45500	2068	10	20680
Assistant	17310				22503	1022	37	37814
Project executor	17310				22503	1022	74	75628
Total								134122

IV. Additional salary

This section includes the amount of payments stipulated by the legislation on labor, 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:

$$W_{add} = k_{extra} \times W_{base}, \quad (3.7)$$

where W_{add} – additional salary, rubles;

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

W_{base} – base salary, rubles.

Table 3.15_Salary of scientific research project performers

Salary	Research advisor	Assistant	Project executor
Basic salary	20680	37814	75628
Additional salary	2068	3781	7562
Total payments	22748	41595	83190

V. Social security pays (labor tax)

Social security pays (so-called labor 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:

$$P_{social} = k_b(W_{base} + W_{add}), \quad (3.8)$$

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 - 27.1%.

Table 3.16_Labor tax

	Research advisor	Assistant	Project executor
Coefficient of deductions	0.3	0.271	
Salary, rubles	22748	41595	83190
Labor tax, rubles	6824	11272	22544

VI. Overhead cost

This section includes 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 basic and additional salary of employees.

Overhead is calculated according to the formula:

$$C_{ov} = k_{ov} \times (W_{base} + W_{add}), \quad (3.9)$$

where k_{ov} – overhead rate.

Table 3.17_Overhead cost

	Research advisor	Assistant	Project executor
Overhead rate	0.3		
Salary, rubles	22748	41595	83190
Overhead, rubles	6824	12478	24957

3.6 Determination of resource, financial, budgeting, social and economic efficiency of research

The effectiveness of a scientific resource-saving project includes social efficiency, economic and budgetary efficiency. Public efficiency indicators take into account the socio-economic consequences of the implementation of an investment project for society as a whole, including the direct results and costs of the project, as well as costs and benefits in related sectors of the economy, environmental, social and other non-economic effects.

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

Integral financial indicator is determined in the formula:

$$I_f^p = \frac{F_{pi}}{F_{max}}, \qquad (3.10)$$

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

F_{pi} – price for *i*-th variant of execution;

F_{max} – maximum cost of execution of a research project (including analogs).

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

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

$$I_m^a = \sum_{i=1}^{n} a_i b_i^a, \quad I_m^p = \sum_{i=1}^{n} a_i b_i^p \qquad (3.11)$$

where I_m^a is an integral indicator of resource efficiency of options;

a_i – the weight coefficient of the i-th parameter;

b_i^a, b_i^p – the score of the i-th parameter for the analog and development, set by an expert method on the selected rating scale;

n – the number of comparison parameters.

Calculated the integral resource efficiency indicator in the form of a table, an example of which is given below.

The integral efficiency indicator is calculated in the form of table and presented below (table 3.18). As analog we considered research SRS on GammaKnife.

Table 3.18_Comparative evaluation of the characteristics of the project execution options

Criteria	Parameter weight factor	Points		Integral resource efficiency indicator	
		Project	Analog	Project	Analog
1. Energy efficiency	0.05	5	5	0.25	0.25
2. Functional capacity	0.05	4	3	0.2	0.15
3. Ease of operation	0.15	4	5	0.6	0.75
4. Reliability of results	0.20	4	5	0.8	1
5. Patient radiation load	0.05	4	4	0.2	0.2
6. Labor-intensiveness	0.20	5	4	1	0.8
Economic criteria for performance evaluation					
1. Widely accepted method	0.05	5	3	0.25	0.15
2. Competitive ability	0.05	4	5	0.2	0.25
3. Price	0.05	5	4	0.25	0.2
Total	1.00			3.75	3.6

An integral efficiency indicator of the scientific research project (I_{fin}^{p}) and of the analog (I_{fin}^{a}) are determined according to the formula of the integral basis of the financial integral resource efficiency:

$$I_{fin}^{p} = \frac{I_{m}^{p}}{I_{f}^{p}}, \quad I_{fin}^{a} = \frac{I_{m}^{a}}{I_{f}^{a}} \tag{3.12}$$

Comparison of the integral indicator of the efficiency of the current project and analogs will determine the comparative efficiency the project. Comparative project efficiency:

$$E_{av} = \frac{I_{fin}^{p}}{I_{fin}^{a}}, \tag{3.13}$$

where E_{av} – is the comparative project efficiency;

I_{fin}^{p} – integral indicator of project;

I_{fin}^{a} – integral indicator of analog.

Comparative project efficiency presented below.

Table 3.19_Comparative project efficiency

№	Indicator	Project	Analog
1	Integral financial indicator	0.510	0.489
2	Integral resource efficiency indicator	3.750	3.60
3	Integral efficiency indicator	7.353	7.347
4	Comparative project efficiency	1.0008	

Have compared the values of indicators of the project and the analog we can state that the project is more competitive than analog though not much but whatever.

3.7 Conclusion

In this chapter we have considered the main part of financial management, resource efficiency and resource saving**.**

Competitiveness analysis of technical solution showed that work is at good competitive and might be interest in finance side for investors. All results presented in table 1.

We saw that complex analysis solution SWOT could make possible to see all the strongest and the weakest sides of the project and also strategies to avoid or to solve no purpose expenses. There was designed the summative matrix of SWOT analysis (table 3.2).

All scientific and technical project management presented in the Gantt chart (table 3.8).

There was calculated scientific and technical research budget with all expenses, which in its turn come out as 852595 rubles (table 3.9).

Comparison our project with the analog showed us that our project has advantages under the analog though it not much (table 3.19).

Chapter 4. Social responsibility

4.1 Introduction

In this chapter we talk about social responsibility while designing Stereotactic Radiosurgery (SRS) treatment plan on linear accelerator.

What is stereotactic radiosurgery? First of all, is not surgery: there is no cutting, no serving and no anesthesia. This is actually precisely targeted radiation that is delivered much higher dose than traditional radiation therapy while sparing healthy tissue and organs near the body. This method of surgery uses for patient who cannot tolerate traditional surgery.

In this project we investigate two patients who were treated with SRS of brain tumors in Tomsk Regional Oncology Center. There were changed technical parameters, such as collimator angle, segment width, gantry angle, couch angle, quantity of arcs and semi-arcs.

4.2 Legal and organization items in providing safety

Nowadays one of the main ways to radical improvement of all prophylactic work referred to reduce Total Incidents Rate and occupational morbidity is the widespread implementation of an integrated Occupational Safety and Health management system. That means combining isolated activities into a single system of targeted actions at all levels and stages of the production process.

Occupational safety is a system of legislative, socio-economic, organizational, technological, hygienic and therapeutic and prophylactic measures and tools that ensure the safety, preservation of health and human performance in the work process [27].

According to the Labor Code of the Russian Federation, every employee has the right:

- to have a workplace that meets Occupational safety requirements;
- to have a compulsory social insurance against accidents at manufacturing and occupational diseases;

- to receive reliable information from the employer, relevant government bodies and public organizations on conditions and Occupational safety at the workplace, about the existing risk of damage to health, as well as measures to protect against harmful and (or) hazardous factors;
- to refuse carrying out work in case of danger to his life and health due to violation of Occupational safety requirements;
- be provided with personal and collective protective equipment in compliance with Occupational safety requirements at the expense of the employer;
- for training in safe work methods and techniques at the expense of the employer;
- for personal participation or participation through their representatives in consideration of issues related to ensuring safe working conditions in his workplace, and in the investigation of the accident with him at work or occupational disease;
- for extraordinary medical examination in accordance with medical recommendations with preservation of his place of work (position) and secondary earnings during the passage of the specified medical examination;
- for warranties and compensation established in accordance with this Code, collective agreement, agreement, local regulatory an act, an employment contract, if he is engaged in work with harmful and (or) hazardous working conditions.

The labor code of the Russian Federation states that normal working hours may not exceed 40 hours per week. The employer must keep track of the time worked by each employee.

Rules for labor protection and safety measures are introduced in order to prevent accidents, ensure safe working conditions for workers and are mandatory for workers, managers, engineers and technicians.

4.3 Basic ergonomic requirement for the correct location and arragment of researcher's workplace

The workplace when working with a PC should be at least 6 square meters. The legroom should correspond to the following parameters: the legroom height is at least 600 mm, the seat distance to the lower edge of the working surface is at least 150 mm, and the seat height is 420 mm. It is worth noting that the height of the table should depend on the growth of the operator.

The following requirements are also provided for the organization of the workplace of the PC user: The design of the working chair should ensure the maintenance of a rational working posture while working on the PC and allow the posture to be changed in order to reduce the static tension of the neck and shoulder muscles and back to prevent the development of fatigue.

The type of working chair should be selected taking into account the growth of the user, the nature and duration of work with the PC. The working chair should be lifting and swivel, adjustable in height and angle of inclination of the seat and back, as well as the distance of the back from the front edge of the seat, while the adjustment of each parameter should be independent, easy to carry out and have a secure fit.

4.4 Occupation safety

A dangerous factor or industrial hazard is a factor whose impact under certain conditions leads to trauma or other sudden, severe deterioration of health of the worker [27].

A harmful factor or industrial health hazard is a factor, the effect of which on a worker under certain conditions leads to a disease or a decrease in working capacity.

4.4.1 Analysis of harmful and dangerous factors that can create object of investigation

The object of investigation is stereotactic radiosurgery plans. Investigation was carried using Monaco system on PC, thus this object itself cannot cause harmful and dangerous factors.

4.4.2 Analysis of harmful and dangerous factors that can arise at workplace during investigation

The working conditions in the workplace are characterized by the presence of hazardous and harmful factors, which are classified by groups of elements: physical, chemical, biological, psychophysiological. The main elements of the production process that form dangerous and harmful factors are presented in table 4.1.

Table 4.1_Possible hazardous and harmful factors

Factors (GOST 12.0.003-2015)	Work stages			Legal documents
	Development	Manufacture	Exploitation	
Deviation of microclimate indicators	+	+	+	Sanitary rules 2.2.4.548–96. Hygienic requirements for the microclimate of industrial premises.
Excessive noise		+	+	Sanitary rules 2.2.4 / 2.1.8.562–96. Noise at workplaces, in premises of residential, public buildings and in the construction area.
Increased level of electromagnetic radiation	+	+	+	Sanitary rules 2.2.2 / 2.4.1340–03. Sanitary and epidemiological rules and regulations "Hygienic requirements for personal electronic computers and work organization."
Insufficient illumination of the working area		+	+	Sanitary rules 2.2.1 / 2.1.1.1278–03. Hygienic requirements for natural, artificial and combined lighting of residential and public buildings.
Abnormally high voltage value in the circuit, the closure which may occur through the human body	+	+	+	Sanitary rules GOST 12.1.038-82 SSBT. Electrical safety. Maximum permissible levels of touch voltages and currents.

Increased levels of ionizing radiation	+	+	+	Sanitary Rules 2.6.1. 2523 -0 9. Radiation Safety Standards (NRB-99/2009).

The following factors effect on person working on a computer:

- physical:
  - temperature and humidity;
  - noise;
  - static electricity;
  - electromagnetic field of low purity;
  - illumination;
  - presence of radiation;
- psychophysiological:
  - psychophysiological dangerous and harmful factors are divided into:
    - physical overload (static, dynamic);
    - mental stress (mental overstrain, monotony of work, emotional overload).

Deviation of microclimate indicators

The air of the working area (microclimate) is determined by the following parameters: temperature, relative humidity, air speed. The optimum and permissible values of the microclimate characteristics are established in accordance with [29] and are given in table 4.2.

Table 4.2_Optimal and permissible parameters of the microclimate

Period of the year	Temperature, C	Relative humidity,%	Speed of air movement, m/s
Cold and changing of seasons	23-25	40-60	0.1
Warm	23-25	40	0.1

Excessive noise

Noise and vibration worsen working conditions, have a harmful effect on the human body, namely, the organs of hearing and the whole body through the central nervous system. It results in weakened attention, deteriorated memory, decreased response, and increased number of errors in work. Noise can be generated by operating equipment, air conditioning units, daylight illuminating devices, as well as spread from the outside. When working on a PC, the noise level in the workplace should not exceed 50 dB.

Increased level of electromagnetic radiation

The screen and system blocks produce electromagnetic radiation. Its main part comes from the system unit and the video cable. According to [2], the intensity of the electromagnetic field at a distance of 50 cm around the screen along the electrical component should be no more than:

- in the frequency range 5 Hz - 2 kHz - 25 V / m;
- in the frequency range 2 kHz - 400 kHz - 2.5 V / m.

The magnetic flux density should be no more than:

- in the frequency range 5 Hz - 2 kHz - 250 nT;
- in the frequency range 2 kHz - 400 kHz - 25 nT.

Abnormally high voltage in the circuit

Depending on the conditions in the room, the risk of electric shock to a person increases or decreases. Do not operate the electronic device in conditions of high humidity (relative air humidity exceeds 75% for a long time), high temperature (more than 35 ° C), the presence of conductive dust, conductive floors and the possibility of simultaneous contact with metal components connected to the ground and the metal casing of electrical equipment. The operator works with electrical devices: a computer (display, system unit, etc.) and peripheral devices. There is a risk of electric shock in the following cases:

- with direct contact with current-carrying parts during computer repair;
- when touched by non-live parts that are under voltage (in case of violation of insulation of current-carrying parts of the computer);

– when touched with the floor, walls that are under voltage;
– short-circuited in high-voltage units: power supply and display unit.

Table 4.3_Upper limits for values of contact current and voltage

	Voltage, V	Current, mA
Alternate, 50 Hz	2	0.3
Alternate, 400 Hz	3	0.4
Direct	8	1.0

Insufficient illumination of the working area

Light sources can be both natural and artificial. The natural source of the light in the room is the sun, artificial light are lamps. With long work in low illumination conditions and in violation of other parameters of the illumination, visual perception decreases, myopia, eye disease develops, and headaches appear.

According to the standard, the illumination on the table surface in the area of the working document should be 300-500 lux. Lighting should not create glare on the surface of the monitor. Illumination of the monitor surface should not be more than 300 lux.

The brightness of the lamps of common light in the area with radiation angles from 50 to 90° should be no more than 200 cd/m, the protective angle of the lamps should be at least 40°. The safety factor for lamps of common light should be assumed to be 1.4. The ripple coefficient should not exceed 5%.

Increased levels of ionizing radiation

Ionizing radiation is radiation that could ionize molecules and atoms. This effect is widely used in energetics and industry. However, there is health hazard. In living tissue, this radiation could damage cells that result in two types of effects. Deterministic effects (harmful tissue reactions) due to exposure with high doses and stochastic effects due to DNA destruction and mutations (for example, induction of cancer).

To provide radiation safety with using sources of ionizing radiation one must use next principles:

a) keep individual radiation doses from all radiation sources not higher than permissible exposure;
b) forbid all activity with using radiation sources if profit is low than risk of possible hazard;
c) keep individual radiation doses from all radiation sources as low as possible.

There are two groups of people related to work with radiation: personnel, who works with ionizing radiation, and population.

Table 4.4_Limatation of dose for people who related with radiation

Quantity	Dose limits	
	personnel	population
Effective dose	20 mSv per year in average during 5 years, but not higher than 50 mSv per year	1 mSv per year in average during 5 years, but not higher than 5 mSv per year
Equivalent dose per year in eye's lens	150 mSv	15 mSv
Skin	500 mSv	50 mSv
Hands and feet	500 mSv	50 mSv

Effective dose for personnel must not exceed 1000 mSv for 50 years of working activity, and for population must not exceed 70 mSv for 70 years of life.

In addition, for women from personnel of age below 45 years there is limit of 1 mSv per month of equivalent dose on lower abdomen. During gestation and breast feeding women must not work with radiation sources.

For students older than 16, who uses radiation sources in study process or who is in rooms with increased level of ionizing radiation, dose limits are quarter part of dose limits of personnel.

4.4.3 Justification of measure to reduce the levels of exposure to hazardous and harmful factors on the research

Deviation of microclimate indicators

The measures for improving the air environment in the production room include: the correct organization of ventilation and air conditioning, heating of room. Ventilation can be realized naturally and mechanically. In the room, the following volumes of outside air must be delivered:

- at least 30 m ^{3} per hour per person for the volume of the room up to 20 m ^{3} per person;
- natural ventilation is allowed for the volume of the room more than 40 m ^{3} per person and if there is no emission of harmful substances.

The heating system must provide sufficient, constant and uniform heating of the air. Water heating should be used in rooms with increased requirements for clean air.

The parameters of the microclimate in the laboratory regulated by the central heating system, have the following values: humidity 40%, air speed 0.1 m / s, summer temperature 20-25 ° C, in winter 13-15 ° C. Natural ventilation is provided in the laboratory. Air enters and leaves through the cracks, windows, doors. The main disadvantage of such ventilation is that the fresh air enters the room without preliminary cleaning and heating.

Excessive noise

In research audiences, there are various kinds of noises that are generated by both internal and external noise sources. The internal sources of noise are working equipment, personal computer, printer, ventilation system, as well as computer equipment of other engineers in the audience. If the maximum permissible conditions are exceeded, it is sufficient to use sound-absorbing materials in the room (sound-absorbing wall and ceiling cladding, window curtains). To reduce the noise penetrating outside the premises, install seals around the perimeter of the doors and windows.

Increased level of electromagnetic radiation

There are the following ways to protect against EMF:

- increase the distance from the source (the screen should be at least 50 cm from the user);
- the use of pre-screen filters, special screens and other personal protective equipment.

When working with a computer, the ionizing radiation source is a display. Under the influence of ionizing radiation in the body, there may be a violation of normal blood coagulability, an increase in the fragility of blood vessels, a decrease in immunity, etc. The dose of irradiation at a distance of 20 cm to the display is 50 μrem / hr. According to the norms [2], the design of the computer should provide the power of the exposure dose of x-rays at any point at a distance of 0.05 m from the screen no more than 100 μR / h.

Fatigue of the organs of vision can be associated with both insufficient illumination and excessive illumination, as well as with the wrong direction of light.

Increased levels of ionizing radiation

In case of radiation accident, responsible personnel must take all measures to restore control of radiation sources and reduce to minimum radiation doses, number of irradiated persons, radioactive pollution of the environment, economic and social losses caused with radioactive pollution.

Radiation control is a main part of radiation safety and radiation protection. It is aimed at not exceeding the established basic dose limits and permissible levels of radiation, obtaining the necessary information to optimize protection and making decisions about interference in the case of radiation accidents, contamination of the environment and buildings with radionuclides.

The radiation control is control of:

- Radiation characteristics of radiation sources, pollution in air, liquid and solid wastes;

- Radiation factors developed with technological processes in working places and environment;
- Radiation factors of contaminated environment;
- Irradiation dose levels of personnel and population.

The main controlled parameters are:

- Annual effective and equivalent doses;
- Intake and body content of radionuclides;
- Volume or specific activity of radionuclides in air, water, food products, building materials and etc.;
- Radioactive contamination of skin, clothes, footwear, working places and etc.
- Dose and power of external irradiation;
- Particles and photons flux density.

Radiation protection office establish control levels of all controlled parameters in according to not exceed dose limits and keep dose levels as low as possible. In case of exceeding control levels radiation protection officers start investigation of exceed causes and take actions to eliminate this exceeding.

During planning and implementation of radiation safety precautions, taking any actions about radiation safety and analysis of effectiveness of mentioned action and precautions one must value radiation safety with next factors:

- characteristics of radioactive contamination of the environment;
- probability of radiation accidents and scale of accidents;
- degree of readiness to effective elimination of radiation accidents and its aftermathches;
- number of persons irradiated with doses higher than controlled limits of dose;
- analysis of actions for providing radiation safety, meeting requirements, rules, standards of radiation safety;
- analysis of irradiation doses obtained by groups of population from all ionizing radiation sources.

Abnormal high voltage value in the circuit

Measures to ensure the electrical safety of electrical installations:

- disconnection of voltage from live parts, on which or near to which work will be carried out, and taking measures to ensure the impossibility of applying voltage to the workplace;
- posting of posters indicating the place of work;
- electrical grounding of the housings of all installations through a neutral wire;
- coating of metal surfaces of tools with reliable insulation;
- inaccessibility of current-carrying parts of equipment (the conclusion in the case of electroporating elements, the conclusion in the body of current-carrying parts) [30].

Insufficient illumination of the working area

Desktops should be placed in such a way that the monitors are oriented sideways to the light openings, so that natural light falls mainly on the left.

Also, as a means of protection to minimize the impact of the factor, local lighting should be installed due to insufficient lighting, window openings should be equipped with adjustable devices such as blinds, curtains, external visors, etc.

4.5 Ecologic safety

4.5.1 Analysis of the impact of the research object on the environment

There are two groups of sources of ionizing radiation in medicine: radioactive substance or material (iodine, palladium, cesium or iridium for brachytherapy) and radiation-generating machines (linear accelerator or X-ray machine).

All radiation-generating machines are required to have a containment building in according to international requirements. The walls of containment buildings are several feet thick and made of concrete and therefore can stop the release of any radiation emitted by the machines into the environment.

4.5.2 Analysis of the environment impact of the research process

Process of investigation itself in the thesis do not have essential effect on environment. One of hazardous waste is fluorescent lamps. Mercury in fluorescent lamps is a hazardous substance and its improper disposal greatly poisons the environment.

Outdated devices goes to an enterprise that has the right to process wastes. It is possible to isolate precious metals with a purity in the range of 99.95–99.99% from computer components. A closed production cycle consists of the following stages: primary sorting of equipment; the allocation of precious, ferrous and non-ferrous metals and other materials; melting; refining and processing of metals. Thus, there is an effective disposal of computer devices.

4.5.3 Justification od environment protection measures

Pollution reduction is possible due to the improvement of devices that produces electricity, the use of more economical and efficient technologies, the use of new methods for generating electricity and the introduction of modern methods and methods for cleaning and neutralizing industrial waste. In addition, this problem should be solved by efficient and economical use of electricity by consumers themselves. This is the use of more economical devices, as well as efficient regimes of these devices. This also includes compliance with production discipline in the framework of the proper use of electricity.

Simple conclusion is that it is necessary to strive to reduce energy consumption, to develop and implement systems with low energy consumption. In modern computers, modes with reduced power consumption during long-term idle are widely used.

4.6 Safety in emergency

4.6.1 Analysis of probable emergencies that may occur at the workplace during research

The fire is the most probable emergency in our life. Possible causes of fire:

- malfunction of current-carrying parts of installations;

- work with open electrical equipment;
- short circuits in the power supply;
- non-compliance with fire safety regulations;
- presence of combustible components: documents, doors, tables, cable insulation, etc.

Activities on fire prevention are divided into: organizational, technical, operational and regime.

4.6.2 Substantiation of measures for the prevention of emergencies and the development of procedures in case of emergencies

Organizational measures provide for correct operation of equipment, proper maintenance of buildings and territories, fire instruction for workers and employees, training of production personnel for fire safety rules, issuing instructions, posters, and the existence of an evacuation plan.

The technical measures include compliance with fire regulations, norms for the design of buildings, the installation of electrical wires and equipment, heating, ventilation, lighting, the correct placement of equipment.

The regime measures include the establishment of rules for the organization of work, and compliance with fire-fighting measures. To prevent fire from short circuits, overloads, etc., the following fire safety rules must be observed:

- elimination of the formation of a flammable environment (sealing equipment, control of the air, working and emergency ventilation);
- use in the construction and decoration of buildings of non-combustible or difficultly combustible materials;
- the correct operation of the equipment (proper inclusion of equipment in the electrical supply network, monitoring of heating equipment);
- correct maintenance of buildings and territories (exclusion of the source of ignition - prevention of spontaneous combustion of substances, restriction of fire works);
- training of production personnel in fire safety rules;

- the publication of instructions, posters, the existence of an evacuation plan;
- compliance with fire regulations, norms in the design of buildings, in the organization of electrical wires and equipment, heating, ventilation, lighting;
- the correct placement of equipment;
- well-time preventive inspection, repair and testing of equipment.
- In the case of an emergency, it is necessary to:
- inform the management (duty officer);
- call the Emergency Service or the Ministry of Emergency Situations - tel. 112;
- take measures to eliminate the accident in accordance with the instructions.

4.7 Conclusion

In this section about social responsibility the hazardous and harmful factors were revealed. All necessary safety measures and precaution to minimize probability of accidents and traumas during investigation are given.

Possible negative effect on environment were given in compact form describing main ecological problem of radiation-generating machines using in medicine.

It could be stated that with respect to all regulations and standards, investigation itself and object of investigation do not pose special risks to personnel, other equipment and environment.

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APPENDIX A

Table A.1_Ttechnical parameters of Patient 1

№		Beam 1	Beam 2	Beam 3
1	Segment width	1		
	Increment	30		
	MLC angle	0		
	Gantry angle	190		
	Couch angle	0		
	Arc length	350		
2	Segment width	1		
	Increment	30		
	MLC angle	0		
	Gantry angle	210		
	Couch angle	0		
	Arc length	300		
3	Segment width	1	1	
	Increment	30	30	
	MLC angle	50	0	
	Gantry angle	190	90	
	Couch angle	0	0	
	Arc length	350	210	
4	Segment width	1	1	1
	Increment	30	30	30
	MLC angle	50	0	250
	Gantry angle	190	90	235
	Couch angle	0	0	90
	Arc length	350	210	105
5	Segment width	1	1	1
	Increment	40	40	40
	MLC angle	50	0	250
	Gantry angle	190	90	235
	Couch angle	0	0	90
	Arc length	350	210	105

6	Segment width	1	1	1
	Increment	15	15	15
	MLC angle	50	0	250
	Gantry angle	190	90	235
	Couch angle	0	0	90
	Arc length	350	210	105
7	Segment width	1	1	1
	Increment	30	20	20
	MLC angle	50	0	250
	Gantry angle	190	90	235
	Couch angle	0	0	90
	Arc length	350	210	105
8	Segment width	0,5	0,5	0,5
	Increment	30	20	20
	MLC angle	50	0	250
	Gantry angle	190	90	235
	Couch angle	0	0	90
	Arc length	350	210	105
9	Segment width	1,5	1,5	1,5
	Increment	30	20	20
	MLC angle	50	0	250
	Gantry angle	190	90	235
	Couch angle	0	0	90
	Arc length	350	210	105

Table A.2_ Results of influence of technical parameters of Patient 1

№	Indices					
	HI	CI	PCI	GIlow	GIhigh	MUs
1	0,097	1,142	1,230	3,112	3,807	2814,19
2	0,086	1,214	1,237	3,990	3,433	2917,20
3	0,079	1,197	1,223	3,975	3,294	2956,77
4	0,078	1,213	1,234	3,126	2,983	3147,77

5	0,078	1,228	1,244	3,172	3,025	3216,11
6	0,087	1,214	1,256	2,998	2,845	3109,74
7	0,082	1,211	1,235	3,025	2,917	3116,16
8	0,074	1,213	1,232	3,114	3,046	2948,58
9	0,089	1,198	1,230	3,021	3,208	3737,98

Table A.3_ PTV dosimetric results of the VMAT plans used to treat patient 1 devised using different technical parameters.

№	PTV				
	Dmin	Dmax	Dmean	V98%	V110%
1	16,839	20,118	18,969	99,27	0,57
2	17,645	20,098	19,071	100	1,04
3	17,503	20,118	19,020	99,95	0,1
4	17,557	20,008	19,049	99,97	0,63
5	17,664	19,865	19,043	100	0,06
6	17,425	20,142	19,2	99,95	1,07
7	17,395	19,935	19,035	99,9	0,31
8	17,657	19,834	18,962	100	0,01
9	17,446	20,051	18,985	99,77	1,38

Table A.4_ OAR dosimetric results of the VMAT plans used to treat patient 1 devised using different technical parameters.

№	OAR						
	Brain V12	Brainstem Dmax	Eyeball Dmax	Lenses Dmax	Optic chiasm Dmax	Optic nerves Dmax	Cochlea Dmax
1	12,881	7,405	5,474	4,223	1,464	7,869	9,545

2	12,934	7,494	7,526	4,719	1,829	8,280	11,964
3	11,929	7,490	6,495	4,286	1,713	9,595	11,048
4	10,034	7,073	5,270	3,206	2,167	9,210	11,053
5	10,908	6,788	4,998	2,817	2,043	10,013	11,163
6	10,544	6,503	4,903	3,027	2,038	9,263	11,099
7	10,034	6,547	4,032	1,906	2,199	9,181	9,037
8	10,659	6,933	5,592	3,503	1,667	10,137	11,204
9	11,456	7,263	5,983	3,436	2,245	9,974	10,593

APPENDIX B

Table B.1_ Technical parameters of Patient 2

№		Beam 1	Beam 2	Beam 3	Beam 4
1	Segment width	1			
	Increment	30			
	MLC angle	0			
	Gantry angle	190			
	Couch angle	0			
	Arc length	350			
2	Segment width	1			
	Increment	30			
	MLC angle	0			
	Gantry angle	190			
	Couch angle	0			
	Arc length	350			
	Max number of arcs	2			
3	Segment width	1			
	Increment	30			
	MLC angle	0			
	Gantry angle	210			
	Couch angle	0			
	Arc length	300			
	Max number of arcs	2			
4	Segment width	1	1		
	Increment	30	30		
	MLC angle	50	0		
	Gantry angle	190	100		
	Couch angle	0	0		
	Arc length	350	200		
5	Segment width	1	1	1	
	Increment	30	30	30	
	MLC angle	50	0	300	
	Gantry angle	190	100	220	

	Couch angle	0	0	90	
	Arc length	350	200	140	
6	Segment width	1	1	1	
	Increment	40	40	40	
	MLC angle	50	0	300	
	Gantry angle	190	100	220	
	Couch angle	0	0	90	
	Arc length	350	200	140	
7	Segment width	1	1	1	
	Increment	15	15	15	
	MLC angle	50	0	300	
	Gantry angle	210	100	220	
	Couch angle	0	0	90	
	Arc length	300	200	140	
8	Segment width	1	1	1	
	Increment	30	20	20	
	MLC angle	50	0	300	
	Gantry angle	190	100	220	
	Couch angle	0	0	90	
	Arc length	350	200	140	
9	Segment width	0,5	0,5	0,5	
	Increment	30	20	20	
	MLC angle	50	0	300	
	Gantry angle	210	100	220	
	Couch angle	0	0	90	
	Arc length	300	200	140	
10	Segment width	1,5	1,5	1,5	
	Increment	30	20	20	
	MLC angle	50	0	300	
	Gantry angle	210	100	220	
	Couch angle	0	0	90	
	Arc length	300	200	140	
11	Segment width	1	1	1	1
	Increment	30	20	20	20

	MLC angle	50	0	300	300
	Gantry angle	210	100	220	220
	Couch angle	0	0	60	290
	Arc length	300	200	140	140

Table B.2_ Results of influence of technical parameters of Patient 2

№	Indices					
	HI	CI	PCI	GIlow	GIhigh	MUs
1	0,176	1,131	1,333	2,252	5,343	3739,73
2	0,200	1,116	1,319	2,460	5,923	4371,12
3	0,201	1,183	1,377	2,461	5,860	4095,04
4	0,167	1,170	1,344	2,391	5,502	3504,79
5	0,134	1,176	1,320	2,228	4,901	4054,53
6	0,144	1,243	1,402	2,480	4,881	4373,04
7	0,142	1,238	1,399	2,439	4,460	3802,66
8	0,123	1,215	1,329	2,430	4,813	3786,09
9	0,034	1,190	1,356	2,729	4,207	4006,08
10	0,182	1,034	1,496	2,256	6,021	4430,77
11	0,114	1,208	1,257	2,372	4,410	3458,52

Table B.3_ PTV dosimetric results of the VMAT plans used to treat patient 2 devised using different technical parameters.

№	PTV				
	Dmin	Dmax	Dmean	D98%	D110%
1	14,776	20,148	18,706	95,38	0,84
2	15,223	20,160	18,710	95	0,80
3	14,687	19,991	18,719	95,32	0,32
4	15,056	19,998	18,818	95,52	0,87

5	16,184	20,014	18,905	98,16	0,73
6	16,155	19,927	18,916	96,67	0,45
7	16,237	20,123	18,924	97,23	0,91
8	16,437	19,990	18,966	98	0,95
9	16,214	19,998	18,851	98,16	1,13
10	14,783	20,324	18,605	91,31	3,20
11	16,640	19,897	18,906	98,75	0,09

Table B.4_ OAR dosimetric results of the VMAT plans used to treat patient 2 devised using different technical parameters.

№		OAR				
	Brain V12	Eyeball L Dmax	Eyeball R Dmax	Lenses L Dmax	Lenses R Dmax	Optic chiasm Dmax
1	42,151	2,22	2,281	1,273	1,084	1,210
2	36,411	2,207	2,287	1,279	1,089	1,236
3	37,537	2,232	2,289	1,283	1,0820	1,218
4	38,891	2,265	2,209	1,296	1,106	1,265
5	27,249	1,922	2,203	1,138	1,074	1,113
6	29,981	2,204	2,322	1,068	1,401	0,777
7	26,926	1,508	2,129	0,939	0,973	1,475
8	29,939	1,456	2,023	0,623	1,307	1,405
9	26,039	1,751	2,475	1,026	1,216	1,751
10	47,257	1,294	2,278	0,147	1,145	1,317
11	27,886	1,395	1,139	0,346	0,405	2,363

APPENDIX C

ArcCHECK QA of Dose Distribution

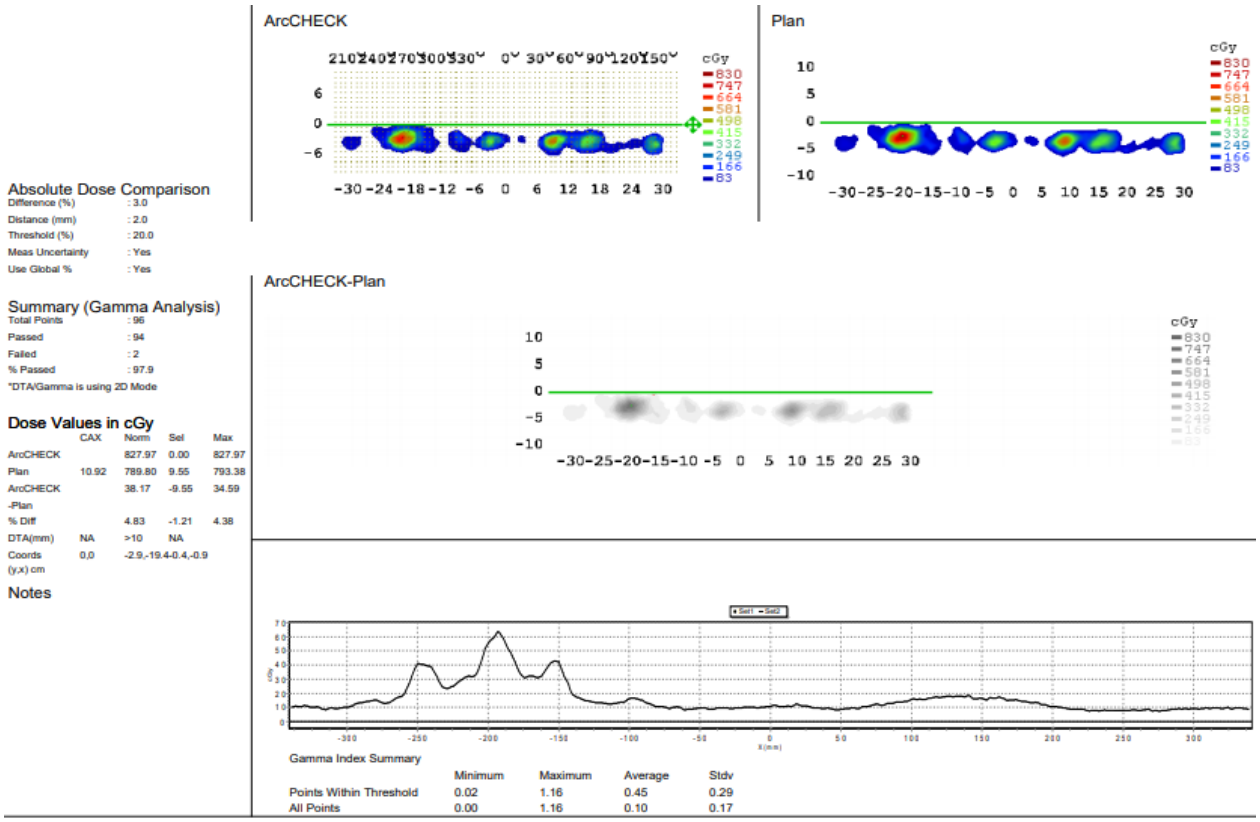

Figure D.1_ ArcCHECK QA of Dose Distribution (MSW 1.5 cm)

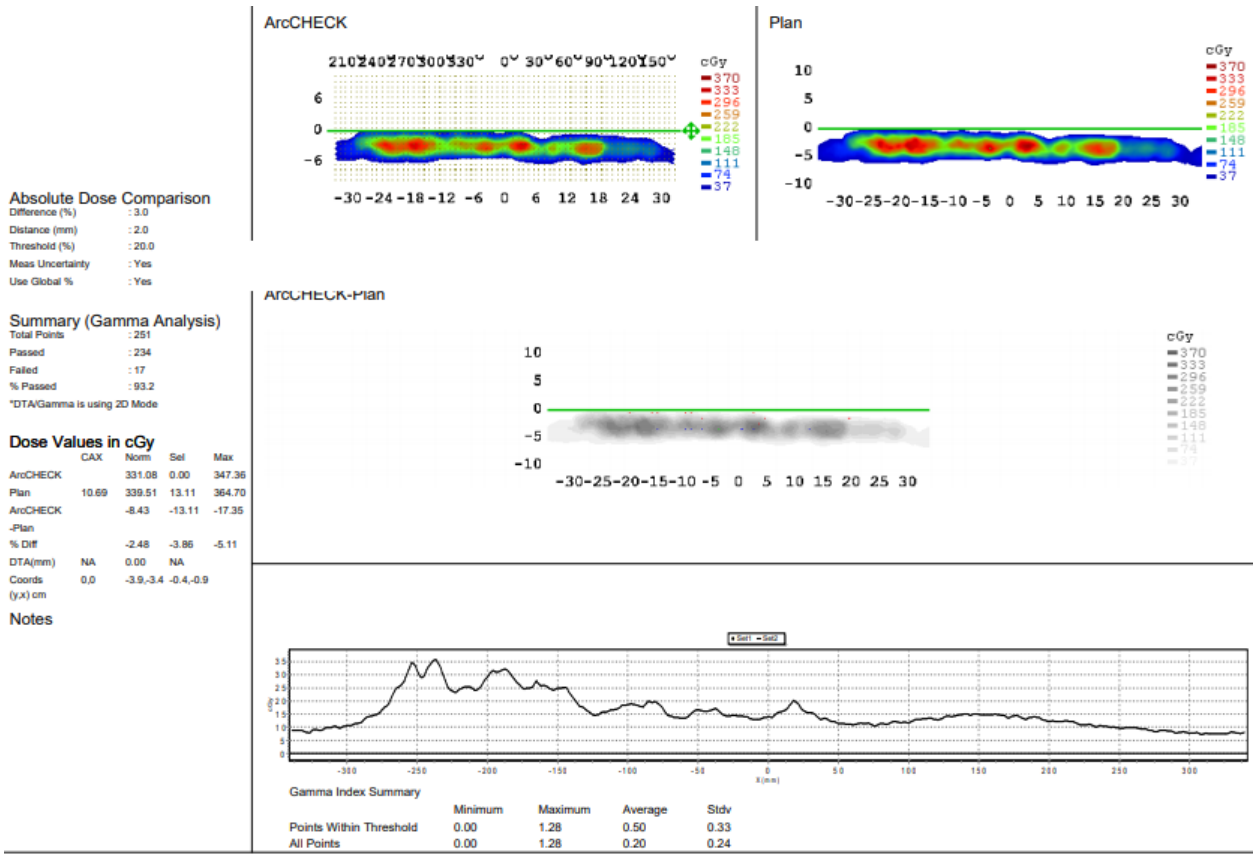

Figure D.2_ ArcCHECK QA of Dose Distribution (MSW 0.5 cm)

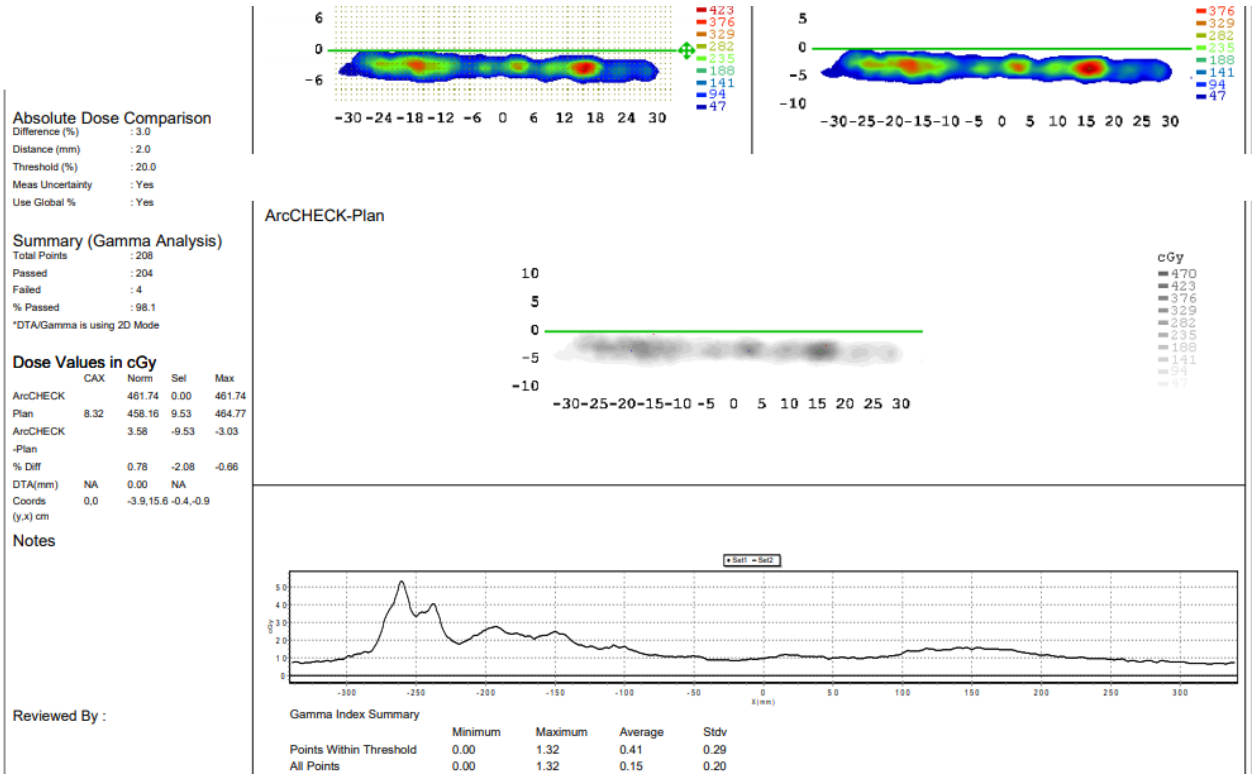

Figure D.3_ ArcCHECK QA of Dose Distribution (MSW 1 cm)