DIPLOMA THESIS

Dosimetric evaluation of simultaneous integrated boost radiation therapy for patients with tumor in head and neck region

Német Brigitta Tímea

Supervisor: Dr Pesznyák Csilla
associate professor
BME Nuclear Technic Institute
Departament of Nuclear Technic

BME

2019

Contents

MŰEGYETEM 1782

Diplomamunka feladat a Fizikus mesterképzési szak hallgatói számára

A hallgató neve: Német Brigitta Tímea	specializációja: Fizikus MSc - orvosi fizika
A záróvizsgát szervező tanszék neve: Nukleáris Technikai Intézet	

A témavezető neve: Dr. Pesznyák Csilla
- tanszéke: Nukleáris Technikai Intézet
- beosztása: egyetemi docens
- email címe: pesznyak@reak.bme.hu

A kidolgozandó feladat címe: Szimultán integrált boost besugárzási technika dozimetriai vizsgálata fej-nyak tumoros betegek esetén

A téma rövid leírása, a megoldandó legfontosabb feladatok felsorolása:

A szimultán integrált boost (SIB) besugárzási technika klinikai alkalmazása fej-nyak tumoros betegek esetén nagyon precíz, körült körültekintő munkát igényel. A klinikai gyakorlatban általában az intenzitás modulált forgó besugárzási technikát (IMAT) alkalmazzák, nagyon szigorú minőségbiztosítás mellett. Az IMAT során több mezőből történik a besugárzás, miközben a lineáris gyorsító gantry-je folyamatosan mozog. Optimalizáló eljárások segítségével tetszőleges számú szegmens (al-mező) hozható létre, melyek biztosítják a kívánt dóziseloszlást, ehhez inverz tervezési módszert használnak. A diplomamunka az Országos Onkológiai Intézetben kell elkészíteni, ahol a hallgató megtanulja a Varian Eclipse tervezőrendszer használatát. A diplomamunka célja, hogy a daganatos betegek esetén vizsgálja a besugárzási terv minőségi és dozimetriai paramétereit, és meghatározza a klinikai alkalmazhatóságának minőségi követelményeit. A hallgató feladatai:

1. Intenzitás modulált forgó besugárzástervezés megismerés, irodalomkutatás SIB besugárzás esetén

2. Fej-nyak régió SIB sugárterápiás tervének elkészítése RapidArc technikával.

3. Dózis-térfogat hisztogram elemzése és dozimetriai paraméterek kigyűjtése a céltérfogatról és védendő szervekről, az eredmények értékelése a homogenitás és konformitás indexek segítségével.

4. A RapidArc technika minőségellenőrzési, minőségbiztosítási protokolljának elkészítése SIB kezelések esetén.

5. A RapidArc technikával készült besugárzási tervek dozimetriai ellenőrzése és elemzése.

A záróvizsga kijelölt tételei:

Dátum: 02. 08. 2018

Hallgató aláírása:	Témavezető vagy tanszéki konzulens aláírása:	A témakiírását jóváhagyom (tanszékvezető aláírása):

Önállósági nyilatkozat

Alulírott Német Brigitta Tímea a Budapesti Műszaki és Gazdaságtudományi Egyetem Fizikus MSc szakos hallgatója kijelentem, hogy ezt a diplomamunkát meg nem engedett segédeszközök nélkül, önállóan, a témavezető irányításával készítettem, és csak a megadott forrásokat használtam fel.

Minden olyan részt, melyet szó szerint, vagy azonos értelemben, de átfogalmazva más forrásból vettem, a forrás megadásával jelöltem.

Budapest, 2019 június

Aláírás,

1 Objectives

The simultaneous integrated boost (SIB) technique used in clinical application in treatment of tumors in head and neck region requires a precise and prudent work. In clinical practice the intensity modulated arc therapy (IMAT) is used with very strict quality assurance. During IMAT the radiation is delivered from multiple fields while the gantry of the linear accelerator is in constant motion. Multiple segments could be made with the help of optimization processes, and invers planning technique is used to assure the desired dose distribution. The diploma theses should be made at The National Institute of Oncology (Budapest, Hungary), where the student learns the use of Varian Eclipse treatment planning system. The purpose of the thesis is to analyze the quality and dosimetry parameters in treatment plans of cancer patients, and to define the clinical applicability of the quality requirements.

The tasks of the student:

1. To learn about intensity modulated arc therapy, literature research in case of SIB irradiation.
2. To create treatment plans for head and neck region with SIB RapidArc technique.
3. To analyze the dose-volume histogram and to acquire dosimetric parameters for planning target volume and organs at risk, the results should be evaluated using homogeneity and conformity index.
4. To define a protocol for quality assurance and quality control in case of SIB RapidArc technique.
5. To verify and analyze the dosimetry of treatment plans created with RapidArc technique.

2 Introduction

In head and neck region are concentrated the basic physiologic functions such as nutrition, respiration, and communication, including speech. Tumors in this area can cause severe consequences, depending on their different locations. Mistakes during the therapy in this region could cause damage in the life quality of the patient [1]. Radiation-induced changes can be divided into two groups depending on their time of occurrence. Acute side effects are present during or immediately after treatment and late side effects need months or years to develop after the end of radiotherapy. The radiation dose, the irradiated field, the healing capacity of the exposed cells and other factors are related to the progression and no reversibility of these induced changes. One of the most common acute side effect experienced by the patients treated with radiotherapy for head and neck is mucositis. The cells in the epithelium lost their ability of renewal which causes mucosal atrophy and ulceration. This can cause pain and difficulties in swallowing and speech. Damage of the salivary glands can cause decrease in salivary flow rate. As a result patients experience oral dryness (xerostomia) causing burning sensation, cracked lips and increased susceptibility to oral infections [2].

2.1 Inverse treatment planning

In 1982 Brahme et al [3] published for the first time about a mathematical problem which is related to the inverse treatment planning. The beam intensity profile was calculated for a doughnut shaped target volume with a circular structure at the center, using some simplifying assumptions. The group from Karolinska Institute in Stockholm, succeeded to calculate a point irradiation density, by defining a point irradiation distribution. The optimal dose distribution was decomposed into small point distributions. The deconvolution concept had a good potential to solve some inverse planning problems for clinical uses, but eventually was never used in clinical practice [4].

A few years later, in 1988, Yair Censor developed a feasibility search method. The purpose of this method was to find a plan that could satisfy specific constrains, like upper or lower dose limits in different organs. This method had some properties that are used in today's inverse planning systems. For example, the dose influence matrix, which pre-calculates the dose contribution from each beam element to each volume element [4].

The inverse problem had no exact mathematical solution, because in reality there is no chance to deliver all prescribed dose only to the target volume and no dose to the surrounding healthy tissues and organs at risk. The best achievable plan is as close as possible to the ideal plan, but is still feasible. An optimization method of simulated annealing was introduced, which basically simulated the technical process of annealing a metal. This method has a big advantage of escaping local minimum while searching for a global optimum [4].

Even if this method has some imperfections, and there are much faster algorithms, the simulated annealing has been implemented in the Peacock TPS and was used for making the first treatment plan based on IMRT technique in 1994 [4].

An optimization formula was developed by Thomas Bortfeld for the inverse planning problem using fast gradient methods. The code was rewritten by Konrad Preiser, and the program KonRad was born in 1997. The main goal of this upgrade was creating a dynamic and interactive planning system support for IMRT [4].

As treatment plans were made with IMRT technique, it started to make clear for the users that inverse planning based on simple dose objectives and constrains did not presented good results in case of lung treatments. Another approach was to use physical dose-volume limits for healthy lung tissue instead of pure dose limits. The most recent developments regarding inverse planning algorithms are focused on representation of the clinical prescription and objectives. The result of this approach is that the final treatment plan is not just a mathematically optimal result but from a clinical point of view is the most advantageous plan too [4].

2.2 Hardware development for IMRT

The physical parts of the LINAC and the calculation and optimization algorithms of the TPS software were not developed in the same time. While the first algorithms for invers treatment planning were available from early 1980s, the physical conditions delivering the plans were nonexistent. The LINAC should have been able to produce an intense narrow photon pencil beam that can be magnetically scanned across a target. An easier solution was represented by a beam that could mechanically scan the target, for example tomotherapy. A mechanical binary intensity modulator was implemented as part of the tomotherapy, which delivered rotational IMRT beams in 1993 [4].

2.2.1 Development of the tomotherapy

The IMRT delivering technique in slices is known as tomotherapy. The whole concept of the binary modulator was first proposed by Swerdlooff in 1988. The result of this concept was the patent for the multivane intensity-modulating collimator (MIMiC) being held by the University of Wisconsin Alumni Research Foundation and licensed to NOMOS who first made it for practical use in 1992 [5].

In 1992 was firstly used a NOMOS MIMiC machine for tomotherapy along with its associated treatment planning system (TPS) PEACOCKPLAN, today known as CORVUS®. The new device was presented at ASTRO in Calgary and at a 3D radiotherapy meeting at the WHO in Geneva, that year. The design of the MIMiC was made in such a way that it could be attached to any LINAC. The idea behind the MIMiC was to be able to irradiate narrow slices of the patient at any time by rotating a slit collimator through a series of gantry angles. The modulation was provided by varying the dwell time of the attenuating elements in the slit. From the (TPS) was created a floppy disk to control the variation of the dwells through an onboard rotating computer. For the verification process the sequences were recorded and the machine monitored the gantry angles independently [5]. The MIMiC is still widely used in the USA nowadays.

The University of Wisconsin developed the spiral tomotherapy machine. This machine also used a MIMiC-like collimator to deliver a single slit of variable modulation with the variation controlled by the dwell time of the vanes. A primary difference was in the number of vanes, instead of a double set of 20, this MIMiC had a single set of 64 vanes. As the patient went longitudinally and slowly through the beam, the gantry was rotated more than once continuously. The dose modulation was achieved in the superior-inferior direction by choosing different fan-beam thicknesses (FTB). The pitch factor was the couch movement per rotation in units of the FTB. For carefully chosen values an advantageous overlapping occurred between adjacent helical rotations. The fundamentals of the device were announced the same year as for the other tomotherapy machine, but the first clinical deliveries were ten years later, in 2002. The Wisconsin tomotherapy device could be used to deliver simple radiotherapy treatment plans as well as complex IMRTs. Due to the lack of the flattening filter, the open beam had a higher intensity at the center of the beam and decreasing intensity toward the ends, which required a modulation for pseudo flattening the beam [5].

Comparatively with the number of the MIMiCs and other machines capable to deliver IMRT, there are very few of these machines.

In 2000, Gallant and Schreiner developed a tomotherapy machine using ^{60}Co sources. Multiple ^{60}Co sources were placed in a ring gantry and an optimization algorithm determined which beam to turn on, when and the amount of time to be open in order to deliver the established dose distribution. Next year, Schreiner has discussed the practical potential for IMRT with the machine and tested his theory on a phantom with a 1 cm^2 ^{60}Co pencil beam. The modulation was done in two ways: either by turning the ^{60}Co unit on and off as the phantom was stepped through the beam, or by varying the velocity of the moving phantom. Finally, a treatment plan generated with the MDS Nordion Theraplan Plus TPS was delivered successfully to the phantom. The measurements and the simulation agreed to 2%. During the years other experiments were made, with different arrangements of the ^{60}Co sources, but there is no clinical application of such machine for IMRT delivering [5].

In 2001, Achterberg and Muller have developed a new multi-focal static tomotherapy system which incorporated an MLC and table movement. It was a conceptual study, made by using the Monte Carlo Beam code and the ADAC Pinnacle^3 TPS [5].

2.2.2 Development of MLC

The first commercial MLCs appeared in the mid-1980s. A collimator consists of a certain number of leaves made out of tungsten, that can be moved towards each other and thus creating a great variety of field shape. These field openings are generated in such way to conform with the projection of the tumor target volume [4].

There are three main manufacturers and distributors of commercial MLCs with specific parameters like 10 mm leaf width at isocenter. These manufacturers are: Elekta (Philips), Siemens and Varian. The main difference between them is coming from the construction of the gantry. The Elekta (Philips) MLC replaces the upper jaws, while the Siemens MLC replaces the lower jaws. The third type is from Varian, which is a tertiary add-on at the patient side. The Elekta and Varian MLCs have rounded leaf ends but move on a plane. The Siemens MLC has straight leaf ends and moves on the arc of a circle focused at the source [5].

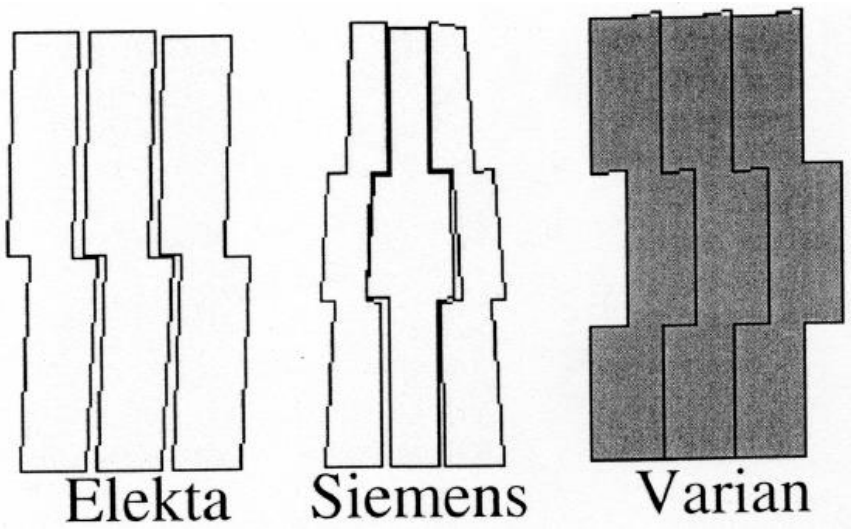


Fig. 1. A schematic diagram of the end-on view of various leaves [5]

Figure 1. shows the differences in leaf design that affect intra- and inter-leaf leakage for the three main manufacturers. In "Contemporary IMRT: Developing Physics and Clinical Implementation" book [5], the author presents the key observations regarding those three MLC types, as follows:

- the smallest collimator scattering is produced by the Elekta MLC
- the sharpest penumbra is generated by the Varian MLC
- the smallest radiation leakage is achieved by Siemens collimators
- the deepest tongue-and-groove underdose is induced by Elekta MLC
- and the largest stepped-edge effect for a 45º edge is made by Varian MLC [5].

All those differences in constructional design and positions of the MLC are sources of the differences occurring in terms of performance.

In early 1990s MLCs began to be commercially available. Originally it was created for shaping the radiation beam in 3D conformal radiotherapy, but lately the MLCs are used for delivering IMRT in different modes.

.

1. Step-and-shoot mode.

At the same time while the dynamic mode was developed, other groups like Art Boyer and his colleagues from MD Anderson Cancer Center in Huston were working on delivering

IMRT as a succession of discrete field settings like segments with a small fluence. Later this mode was named step-and-shoot, because the beam was off while the MLC leaves moved to their next position [4], or multiple static fields technique.

2. Dynamic mode.

In this mode the mechanical parts move while the beam is on. To produce a wedge-shape dose distribution, one leaf is left stationary and the opposite leaf is moving towards the stationary one, while the beam is on. Starting with a definite opening shape of the radiation field and then narrowing the field dynamically can create various shapes of intensity peaks [4].

In 1992, Convery and Rosenbloom [6], from the Royal Marsden Hospital, published a new approach regarding intensity profiles produced by MLCs. In one direction the intensity at any point was proportional with the difference between the time when the edge of the right leaf crossed the point and started the irradiation, and the time when the left leaf crossed that same point and stopped the irradiation. It means that the leaf motion trajectories should be constructed in such way that the time difference equals the desired intensity. Because there are more trajectories which fulfill the constrain, the most optimal is the one that delivers the intensity profile in the shortest time [4].

Improvements for the approach described above had been developed by three independent groups (the Karolinska group in Stockholm, the MSKCC group in New York and the DKFZ group in Heidelberg) in the following couple of years. The best solution was obtained when the left leaf shaped the positive part of the intensity slope and the right leaf took care of the negative part of the slope. These groups introduced in their models factors dealing with transmission through the leaves, the penumbra effects and others [4]

In practice the biggest problem was the leakage radiation, head scattering and some limitations of the MLCs construction. The users dealing with this type of radiation delivering mode tried to decrease the number of monitor units delivered, or the total number of segments, which led to reduce the overall treatment time.

3 Methods

3.1 Patient positioning and immobilization

The head and neck area contains many organs at risk. It is imperative that these organs get as low dose as possible and for the 95% of the tumor volume to be treated with at least 95% of the prescribed dose. Positioning and immobilization protocols assure the reproducibility of the patient for each treatment session, and the mentioned criteria could be fulfilled.

At the National Institute of Oncology in Budapest, the protocol for positioning a person with a head and neck tumor requires a head rest and a thermoplastic mask. A head rest is positioned on the bed of the computer tomography (CT), which serves the patient comfort and acts as a primary positioning device. They are specially designed to fit snugly under the patient's head and minimize the movement during the treatment. These head rests need to be the same during the whole treatment, so the treatment can be reproduced for each fraction. Some examples of these kind of head rests can be seen on Figure 2.

Fig. 2. Head rests used for patient positioning [7]

The evolution of technology and more complex and accurate treatments, raised the need for better positioning devices, or additional accessories for immobilization. For this purpose a thermoplastic mask is used for head and neck areas. The mask is heated up and then molded to the patient's contour. It is fixed to the CT table and later, to the treatment table or to a plastic plate that lies under the patient. The main role of the mask is to prevent movement inter and intra treatment fractions. There are multiple types of masks on the market and it is up to the clinic to decide which one to use. At the National Institute of Oncology in Budapest, where the

treatment plans were made for this work, they do not use masks with mouth-piece or bite-block for tongue and chin immobilization. These masks are uncomfortable for the patients experiencing early side effects of the treatment as mouth dryness and they are not providing considerable better results for immobilization. Figures 3. and 4. presents a mask and a plastic plate.

Fig. 3. Thermoplastic mask for head and neck [8]

Fig. 4. Plastic plate for the thermoplastic mask [8]

Each mask is individual for each patient and can be used for one whole treatment but for a later reirradiation they need a new one. On the exterior side of the mask are drawn the markers for laser positioning. The mask and the plate need to be compatible with each other, so the treatment can be reproduced with high accuracy.

If a mask does not fit properly, it can cause more damage than benefits for the patients. This error can be a result of weight loss of the patient or tumor shrinking. In this situation a new mask is required

3.2 CT simulation

Dedicated CT scanners are use in radiotherapy. A CT simulator consists of a large bore CT scanner with a wide opening, room lasers, and very important, a flat table top for a better match with the table from the radiotherapy treatment machines.

The simulation begins by placing the patient on the CT simulator table in the treatment position for verification. Target structures and organs of interest can be outlined directly on the CT images using tools in the virtual simulation software connected to the CT scanners. To simulate the treatment, digitally reconstructed radiographs (DRR) and beam's eye view (BEV) are used. The treatment beam geometry and shielding is carried out taking into account the target position and critical organs location [7].

Digitally reconstructed radiographies (DRR's) turn out to be essential in the planning and verification of radio-therapy treatments. These images are used in radiotherapy planning in order to mark out the area to be radiated. In a later stage, at the beginning of each radiation session, several DRR's are compared with portal images which are acquired at the moment. BEVs are projections of the treatment beam axes, field limits and outlined structures through the patient on to the corresponding DRRs, resulting in a synthetic representation of a simulation radiograph [7]. In figure 5. and 6. are shown a digitally reconstructed image and a beam eye view's of one of the patients with head and neck tumor.

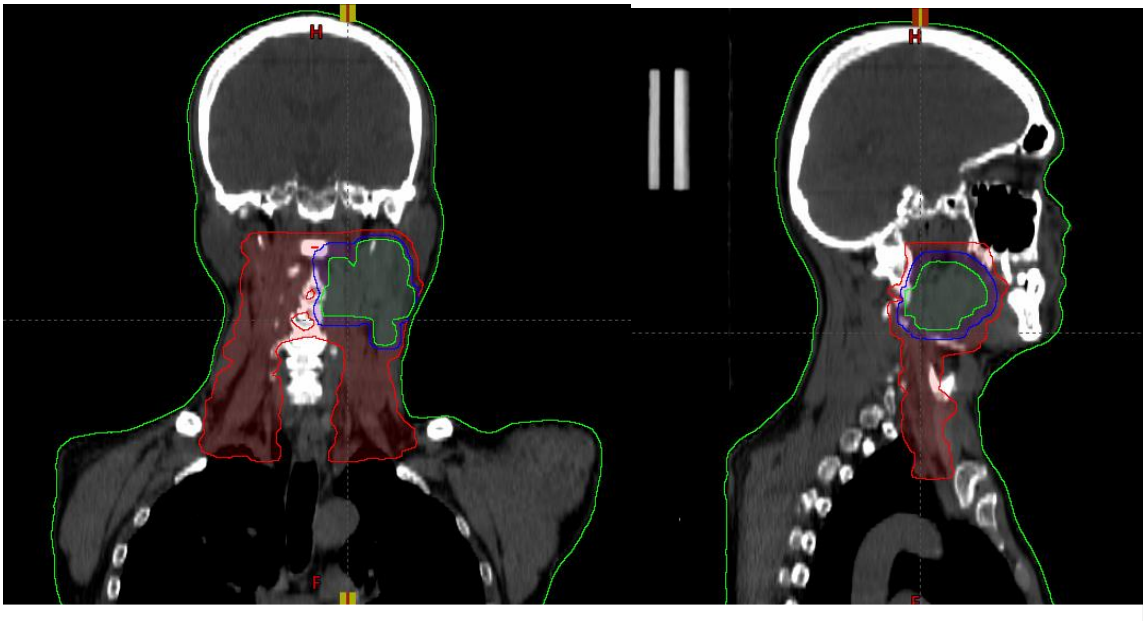


Fig. 5. DRR of one of the subject of the present work

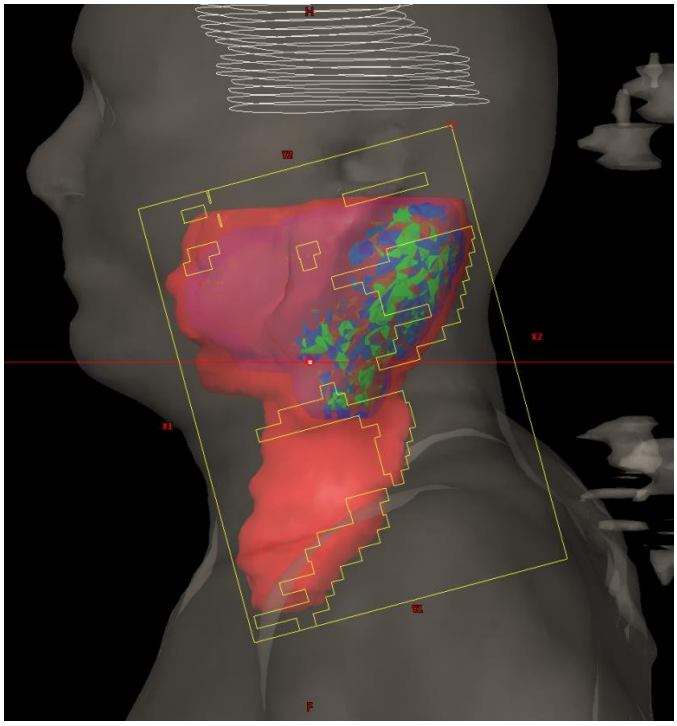


Fig. 6. BEV of one of the treatment plan made for the present work

For head and neck tumors, the CT scans are made from the top of the head to the clavicle or lower depending on the tumor position. The slices are 0.5 cm thick.

3.3 Target volumes and organs at risk

International Commission on Radiation Units and Measurements (ICRU) defined several volumes related to both tumor and normal tissues during the years. These definitions can be found in reports No 50, 62, 71, 78 and 83. Delineation of these volumes is a compulsory process before the planning process, and they also have a very important part after the planning process, in reports. The absorbed dose cannot be prescribed, recorded and reported without defining the target volumes and volumes of normal tissue at risk [9].

There are two very important volumes that need to be defined before the beginning of treatment planning. These volumes are: gross tumor volume (GTV) and clinical target volume CTV. During the process of treatment planning other volumes should be defined as: planning target volume (PTV) and organs at risk (OAR). As a result of treatment planning the last volumes that can be defined are the treated volume (TV) and the irradiated volume (IV) [10]. Figure 7. represents a graphical illustration of the defined volumes.

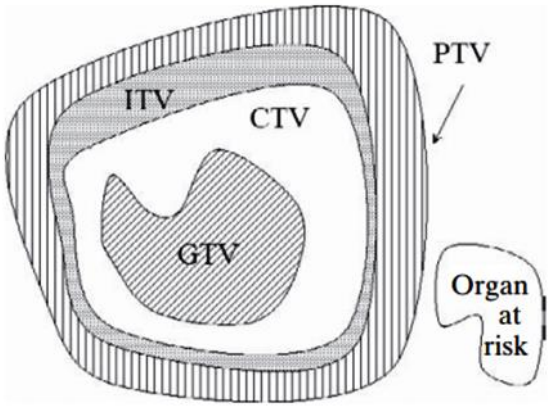


Fig. 7. Graphical illustration of the defined volumes based on ICRU reports [7].

- GTV

"*The gross tumor volume is the gross palpable or visible/demonstrable extent and location of malignant growth*" [10]. This volume may consist of primary tumor or other metastases, basically is corresponds to those parts of the malignant growth where the tumor cell density is the largest. This volume can be determined by different diagnostic methods such as clinical examinations and/or various imaging techniques. There are some reasons to define and report the GTV in an accurate and complete way. First of all, it is required for establishing

the staging of the tumor. Secondly, an adequate absorbed dose must be delivered to the whole volume to obtain the best local tumor control possible. Another reason is regarding the evaluation of the regression of the GTV; based on the results a redefinition of the CTV and PTV might be needed. Finally, changes of the volume size during the treatment might be predictive of the treatment outcome [9], [10].

- CTV

"The CTV is a volume of tissue that contains a demonstrable GTV and/or subclinical malignant disease with a certain probability of occurrence considered relevant for the therapy" [9]. The subclinical malignant disease is referring to the microscopic tumor spread at the boundary of the GTV, the possible regional infiltration into lymphatic nodes and the potential metastatic involvement of other organs. The delineation of the CTV is based on anatomic-topographic and biological considerations, without considering the movement of the tissues or technical factors. This volume in external beam therapy has to be irradiated to a specified dose according to a specified dose-time pattern. If different doses are prescribed, different CTVs should be defined. For example, a case like this is the boost therapy, where the high-dose volume is located inside the low-dose volume [9], [10].

- ITV

The internal target volume was firstly defined in the ICRU Report 62. It is the sum of the CTV and an internal margin (IM). The IM represents the margin that must be added to the CTV to compensate the expected physiologic movements and variation in size, shape and position of the CTV during the therapy. The ITV is basically an optional tool for helping to define the next volume, the PTV [9], [11].

- PTV

"The Planning Target Volume is a geometrical concept and it is defined to select appropriate beam sizes, and beam arrangements, taking into consideration, the net effect of all the possible geometrical variations, in order to ensure that the prescribed dose is actually absorbed in the CTV" [10]. A fixed coordinate system links the PTV to the beams. This volume is used for dose planning and for dose specifications. The dose distribution of the PTV has to

representative of the CTV dose. It is very important that the PTV is a geometrical concept used for treatment planning, and it is not representing a defined tissue or tissue border. The PTV surrounds the CTV with a margin that take into account the internal and the setup uncertainties, converted into margins [9], [10].

- TV

"The Treated volume is the volume enclosed by an isodose surface, selected and specified by the radiation oncologist as being appropriate to achieve the purpose of treatment" [10]. This volume was defined because of the limitations of the treatment techniques. The ideal situation would be to deliver dose only to the PTV, but because this is not achievable, it lead to the definition of the treated volume. It is expected that TV to be larger than the PTV, otherwise the tumor control is reduced and the plan needs to be reevaluated [10].

- IV

"The Irradiated volume is that tissue volume which receives a dose that is considered significant in relation to normal tissue tolerance" [10]. This volume depends on the treatment technique used [10].

- OAR

"Organs at risk are normal tissues whose radiation sensitivity my significantly influence treatment planning and/or prescribed dose" [10]. It is important to consider movements and uncertainties while defining this volume just like in PTV case. The ICRU in Report 50 divide the OARs into 3 different classes by how they react to radiation lesions. When defining an organ at risk it usually depends on the location of the CTV [10].

Ten patients with head and neck tumors were selected for the present work. In all patients, three target volumes were identified according to the ICRU guidelines presented above. The primary tumor and the clinically and/or radiobiologically involved nodes were treated with the highest dose of 70Gy. Areas macroscopically not involved by the disease, but considered at high risk of subclinical disease received 60Gy, and nodal regions with a low risk

of being pathologically involved received 54Gy. In case of the conventional three-step sequential technique (CONV) the same fraction dose with 2 Gy was prescribed for 35 fractions to each PTV, and in case of SIB the prescription for PTVs was 54 Gy, 60 Gy and 70 Gy in 30 fractions. The CTVs were expanded evenly by 5mm to obtain the PTV for each one. If the PTV exceed the body contour of the patient or was too close to it, 3mm were contracted of the PTV to allow the TPS to calculate accurately in the build-up region. The OARs for each patient contoured were: spinal cord, brainstem, right and left parotid glands, but other organs like: brachial plexus, cochlea left and right, esophagus, eyes, larynx, lens, mandible, optic chiasm, optic nerves, oral cavity, temporal lobes were also analyzed at the end.

The dose constrains regarding PTV coverage and the OARs were adapted from the IAEA guidelines and they are presented in Tabled 1.

Table 1. Dose constrains for PTV and OARs in head and neck region

Structure	Volume (%)	Dose (Gy)
PTV70	98	> 63
	95	>66.5
	50	=70
	2	<74.9
PTV60	98	>54
	95	>57
	50	60-62
PTV54	98	>48.6
	95	>51.3
	50	54-56
Spinal cord	2	<45
Brainstem	2	<50
Parotid L	mean	<24
Parotid R	mean	as low as possible

Figure 8. presents one of the ten patients PTVs. The red contour is the volume receiving 54Gy named PTV54, the volume contoured with green is PTV60 receiving 60Gy and finally the blue contour corresponds to the PTV70 receiving 70Gy. This is how PTVs look after the

expansions of the CTVs. At some points it can be seen they exceed the body contour of the patient, and this is why they need to be cropped.

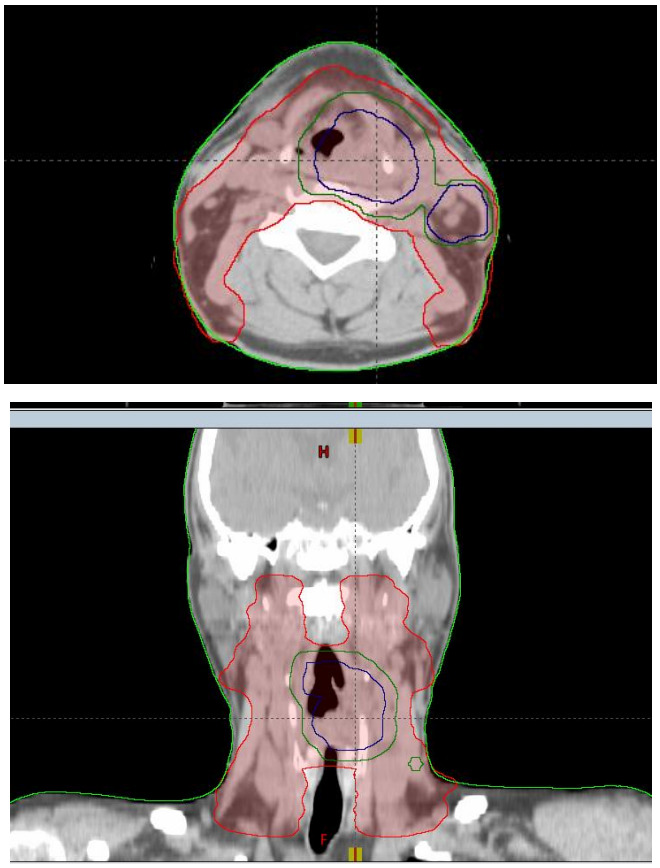


Fig. 8. Contours of the three PTVs for one of the ten patients

3.4 Treatment plans

For the 10 patients, two types of plan were made. The first was the conventional three-step sequential technique (CONV), where the dose was delivered in 3 steps and the dose sum of all the three plans was evaluated. Every step was made with 2 full arcs around the PTV. The second type was the SIB, where the doses for all three PTVs were delivered using only 2 arcs.

The collimation was chosen between 20°-30° depending on the anatomy of the patient and the position of the tumor. Using opposing collimation, the interleaf leakage percentage was reduced. The first arc was rotating clockwise between 181°-179° and the second was rotating counter clockwise between 179°-181°.

The treatment plans were made using Varian Eclipse™ and the dose was calculated using AAA v11.0.31 algorithm. A new isocenter was made for each PTV and it was placed in

the centre of the volume. The photon energy used was 6MV. The plans were assigned to Varian TrueBeam accelerator machine. The technical specifications of the LINAC are presented in Table 2.

Table 2. Technical specifications of Varian TrueBeam linear accelerator

Specification	Value
Rotating accuracy of the gantry	≤ 0,3°
Rotating domain of the gantry	± 185° from vertical
Rotating speed of the gantry	between 0-1 RPM
Number of MLCs	120
MLC's width in the middle	5 mm
MLC's width elsewhere	10 mm
MLC position accuracy	± 1 mm
MLC interleaf leakage	< 3%
Maximum speed of MLCs	0 - 2,5 cm/s

The most complex part of the treatment planning was establishing the optimizing parameters used for the optimizing algorithms, along with their relative weight factor. No set of parameters will always provide good results in dose distribution. The individual anatomy of each person and each localization made the establishment of the basic parameters a real challenge. After obtaining a general set of parameters, the optimization process started for each plan, or each step. The optimizing parameters used as the base for SIB plans are presented in Table 3.

A general step in optimization was cropping parts of the OARs that are included in the PTV volume. This was necessary to keep the dose of the healthy parts as low as possible, while the prescribed dose is delivered to the PTV. Such organs were for example the parotid glands or the oral cavity. Regarding the normal tissues, there is a build in option in the Eclipse™ system, named 'normal tissue objective' where one can pre-establish parameters to take in consideration while the optimizing process. Such parameters are: the start dose, the distance from target border, the fall-off the dose and the end dose. During the optimization process different combinations of these parameters were used for different plans or steps for obtaining the best possible results.

’Monitor units objective’ can also be used in optimization process. Delivering a lot of monitor units during the treatment sessions can lead to a higher scattered dose. In IMRT techniques the total monitor units (MU) and the prescribed dose are not linearly connected. The speed of the gantry or the speed of the leaves could cause major variations in total MU delivered. The results for the present work were obtained using normal tissue objective instead of monitor units objective.[12]

Table 3. Basic set of optimizing parameters used for SIB plans

structure	constrain	volume (%)	dose (cGy)	weight factor
54-60	upper	0	5400	350
	upper	50	5400	260
	lower	100	5380	420
	lower gEUD		5950	300
	upper gEUD		5000	250
60-70	upper	0	6060	330
	upper	50	6000	220
	lower	100	5980	400
	lower gEUD		6550	290
	upper gEUD		5500	200
PTV70	upper	0	7070	310
	lower	100	6930	350
	lower gEUD		7200	250
PTV60	upper	0	7070	250
PTV54	upper	0	7070	250
Brainstem	upper	0	4000	150
	upper gEUD		3100	180
spinal cord	upper	0	4100	300
	upper	30	3700	190
	upper	60	2924	180
left parotid	upper	50	800	200
	mean		1400	200
	upper gEUD		2000	150
right parotid	upper	15.2	1600	180
	mean		1600	150

The TPS is working with an objective function which is defined in equation 1.

$$F_{ob,j} = \sum_i (d_i - p)^2 \quad (1)$$

d_i is the calculated dose in a point i after j iterations, p is the planned dose. The objective function is the sum over the squared differences between calculated and prescribed doses for all points i in a structure.

A penalty is introduced for those cases when the dose at point i is above or below the objective, as presented in equation 2.

$$\begin{cases} \theta_k = 1, if\ k-th\ objective\ is\ vilated \\ 0, otherwise \end{cases} \quad (2)$$

As it can be seen in Table 3, each objective has a weight factor, which set the priority for that objective relative to the other objectives. Introducing the penalty and the weight factor in equation 1 and summarizing over all objectives, we obtain equation 3.

$$F_{ob,j}(K) = \sum_K \sum_i \theta_k * w_k * (d_i - p)^2 \quad (3)$$

As a final step, the best dose that can be obtain is by minimizing the objective function, equation 4.

$$\frac{\partial F_{ob,j}}{\partial j} = 0 \quad (4)$$

In the CONV case, the optimization process consisted of prescribing the dose for the actual PTV and establishing the dose constrains for the OARs. When the normal tissue objective was not enough for obtaining a very conformal dose distribution, other auxiliary volumes were defined to help the optimization process. Such an example can be seen in Figure 9. By establishing a dose constrain for the pink contour in Figure 9., the TPS was able to lower the dose between the two parts of the PTV. The difference in dose distribution generated by using or not using the auxiliary contoured volume for further constrains during the optimization process is shown in Figure 10.

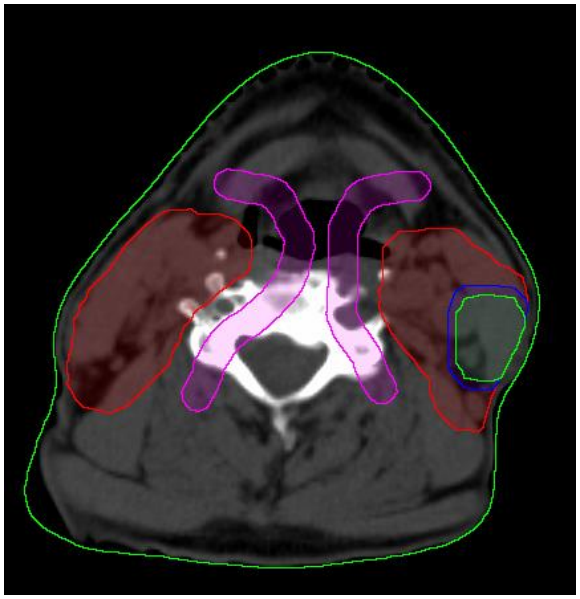


Fig. 9. Auxiliary volume contoured (pink) for the optimization process

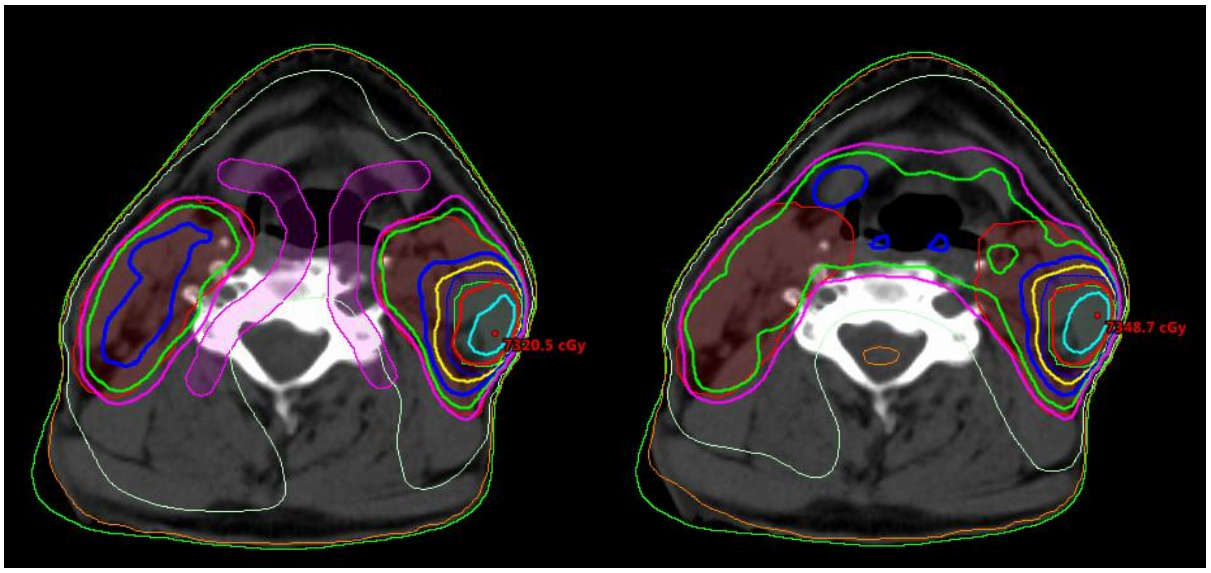


Fig. 10. Difference in dose distribution due to using the auxiliary contoured volume

Before starting the optimization process in case of SIB, two new volumes were defined. It was important to introduce in the optimization process the part of the PTV54 which is not included in PTV60. This volume was called ’54-60’ and that was the volume which received 54Gy. The other volume defined was the part of the PTV60 which is not included in PTV70, named ’60-70’. This volume received 60Gy. During the optimization process those volumes had special constrains that helped reaching the desired dose distribution. The contraction was

made with a certain margin where the actually delivered dose could have a fall-off. This margin was 3mm. Figure 11. presents the new volume, 54-60, in respect with the other PTVs. The 54-60 volume is marked with light green. It can be seen that there are parts of the PTV54 which are not included in 54-60 volume, this is the result of the 3mm margin; in the red zones the dose could not escalade from 60Gy to 54Gy.

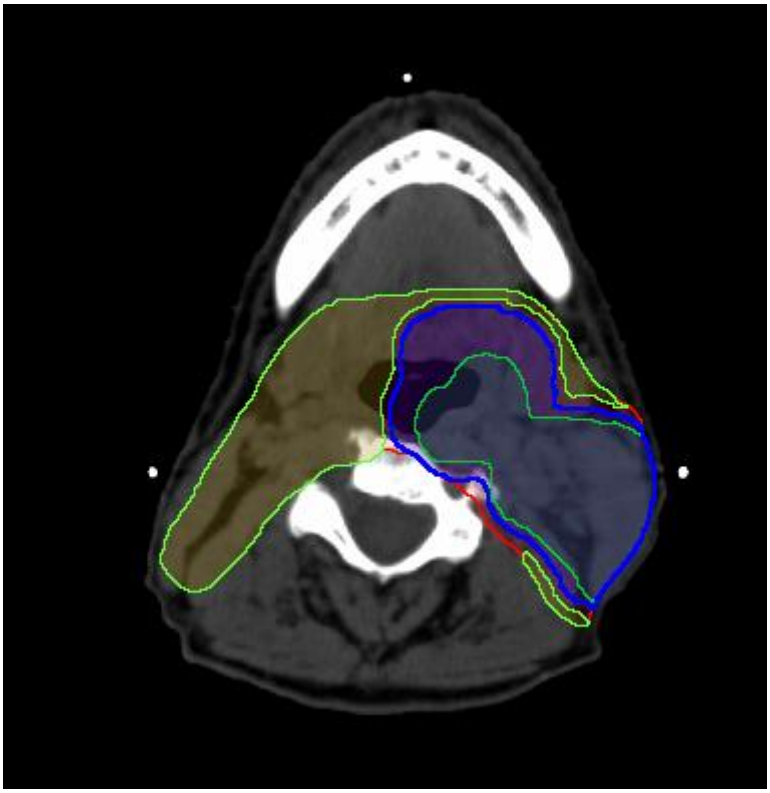


Fig. 11. Illustration of the new volume, 54-60 (light green), used for SIB plan

In other terms the optimization for SIB was similar to the CONV treatment planning process.

Even if there is a possibility to modify the parameters during the optimization algorithm several iterations were needed to obtain the desired dose distribution in respect with the dose constrains. Figure 12. and Figure 13. present the dose distribution obtained after the last iteration for CONV plan sum and SIB technique.

In the CONV case the isodose line corresponding to 60Gy and 57Gy follows the shape of the PTV54 and in case of SIB those lines are only extended to the margin of PTV60. Another example is the isodose line for 66.5Gy which covers a bigger volume than the actually PTV70 in case of CONV technique.

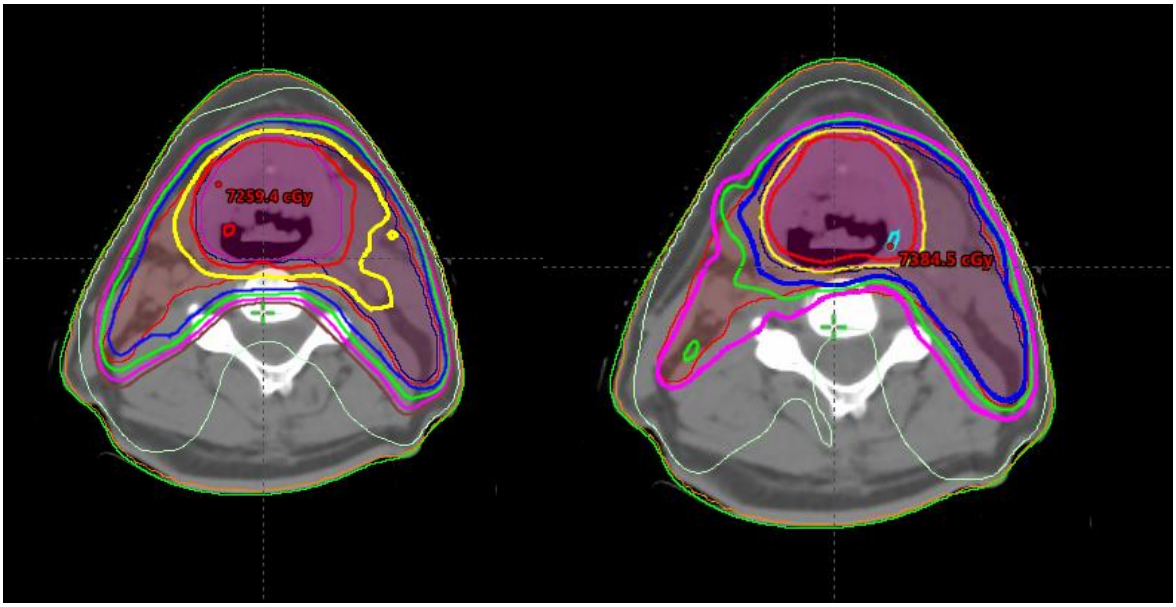


Fig. 12. Dose distribution in axial plane for CONV plan (left) and SIB plan (right).

Relation between colors and isodose line values: red-70Gy, yellow-66.5Gy, blue-60Gy, green-57Gy, purple-54Gy, brown-51Gy

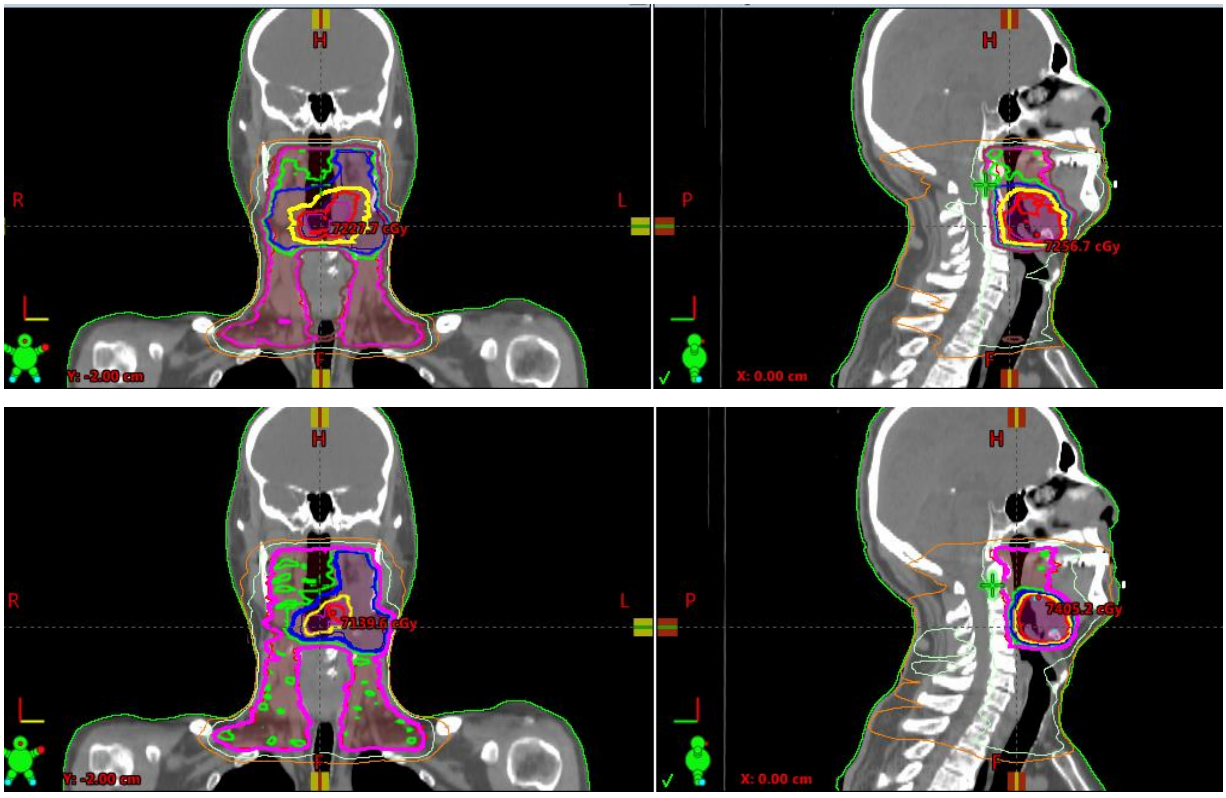


Fig. 13. Dose distribution in transversal and sagittal planes for CONV plan (up) and SIB plan (down)

3.4 Parameters for plan evaluation

The main tool for plans evaluation is the dose-volume histogram (DVH). The DVH represents a frequency distribution of dose values within a defined volume that may be the PTV itself or a specific organ in the vicinity of the PTV. Rather than displaying the frequency, DVHs are usually displayed in the form of 'per cent volume of total volume' on the ordinate against the dose on the abscissa [7]. Figure 14. shows the DHV from both of the CONV plan sum (lines with squares) and the SIB plan (lines with triangles) for one of the 10 patients.

Exact data regarding the volume of the PTVs and the dose received were collected with a plug-in for the Eclipse™ system. The obtained results were compared for the two different techniques and also verified if the plans correspond to the international guidelines. These parameters are presented in the Results chapter of the present work.

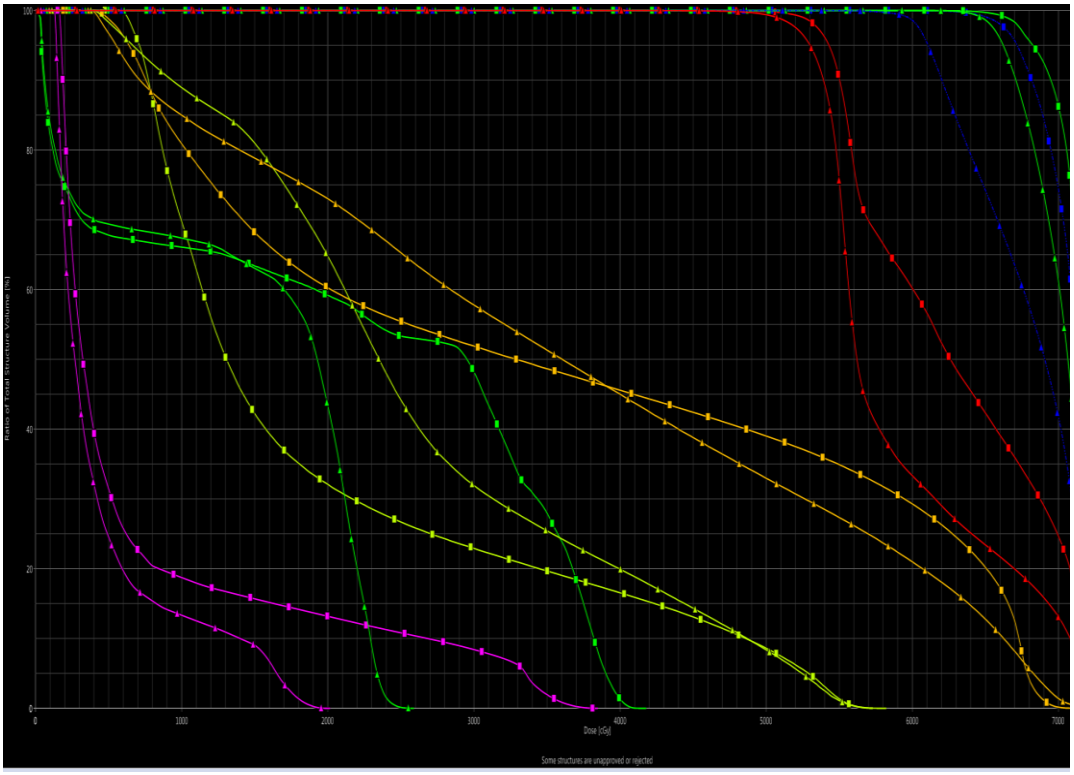


Fig. 14. DVH containing organs at risk and parts of PTVs for SIB plan and CONV plan sum. *The general color code for head and neck region is the following: purple for brainstem, yellow and orange for parotids, green for spinal. The PTVs are on the right hand side of the DVH with red for PTV54, blue for PTV60 and green for PTV70.*

Two indices are defined to help evaluate and improve a plan. These indices are the homogeneity and conformity index.

a. Homogeneity index

It is very important that the dose inside a target volume to be homogenous. The ICRU in Report 83 define the homogeneity index with the equation 5 [9].

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (5)$$

A dose is considered homogeneous if the difference between the minimum dose within the target volume and the maximum dose within the same volume reported to the average dose is close to zero. In real treatment plans this is not possible but values very close to zero can be achieved. For the SIB plans the dose is delivered to each PTVs at the same time. Because the target volumes are inside each other there is no possibility to calculate an accurate value for HI for the PTV54 and the PTV60. The HI was evaluated for the PTV70 for the SIB plans and for comparison the PTV70 from the plan sums made with CONV technique.

Using the plug-in for the Eclipse™ TPS, the values required were read out: the dose delivered to the 2% of the target volume (maximum dose), the dose delivered for the 98% of the volume (minimum dose) and the dose delivered to half of the volume (average dose).

b. Conformity index

The degree of dose conformity of the treated volume to the PTV is measured with the conformity index (CI). The CI is defined with equation 6, based on Khayaiwong P. et al "Dosimetric Comparison between Simultaneous Integrated Boost and Sequential Intensity-Modulated Radiotherapy Techniques in Nasopharyngeal Carcinoma" [13].

$$CI = \frac{PTV_{95\%}}{V_{95\%}} \quad (6)$$

Where $PTV_{95\%}$ is the volume inside the PTV receiving at least the 95% of the prescribed dose and the $V_{95\%}$is the total volume receiving the same dose. Ideally, the value of the CI would be 1, the whole target volume would receive the prescribed dose and the normal tissue would not be affected with such a high dose, but the dose escalation cannot be so steep, so the real value of the CI will never be exactly 1.

Using the same plug-in as before, these values were obtained and the CI was calculated for PTV70 for every plan.

4 Results

4.1 Target Volume

The IAEA guidelines for the target volume set 3 or 4 constrains, as presented in Table 1, in the previous chapter. It is imperative for the 98% and 95% of the PTV70 to receive more than 90%, and respectively 95% of the dose. It can be seen in Figure 15., both techniques are acceptable; the dose limits are satisfied. The results in case of the CONV technique are higher, than in SIB technique. This could be due to the sum of 3 plans, and because the dose fall-off is not as steep as in case of SIB technique.

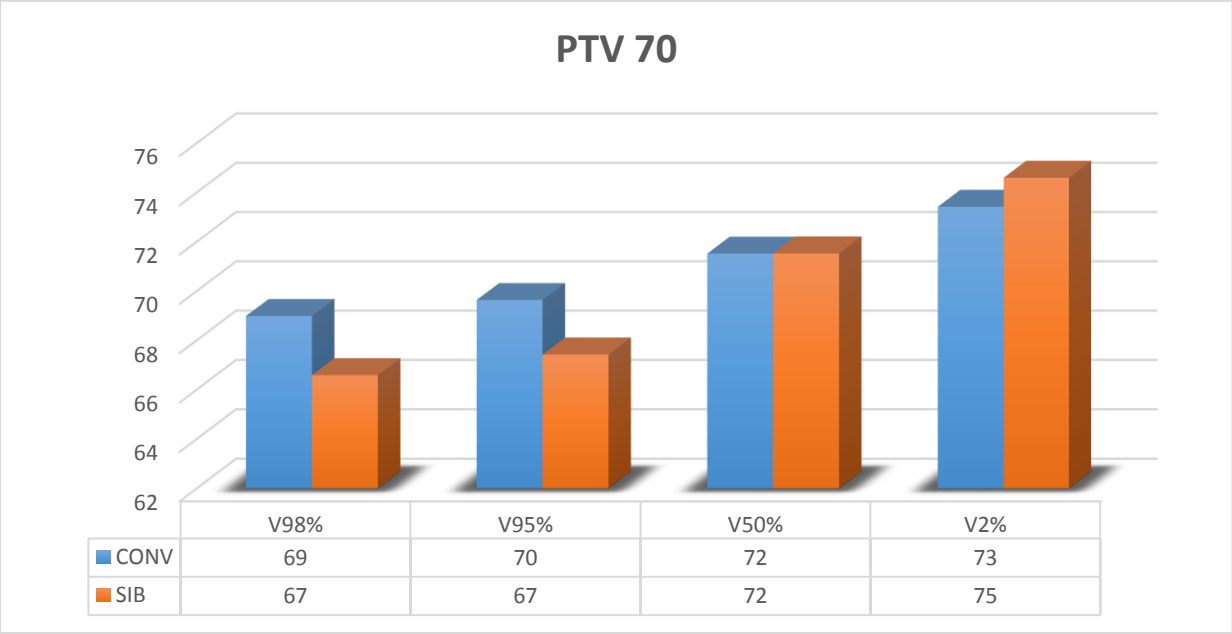


Fig. 15. Comparison between conventional and SIB technique in terms of dose coverage for PTV70

The results of the PTV60 are similar to the PTV70 results. Lower doses are achievable with SIB technique, which decreases the probability of developing side effects. The results for PTV60 in both cases can be seen in Figure 16.

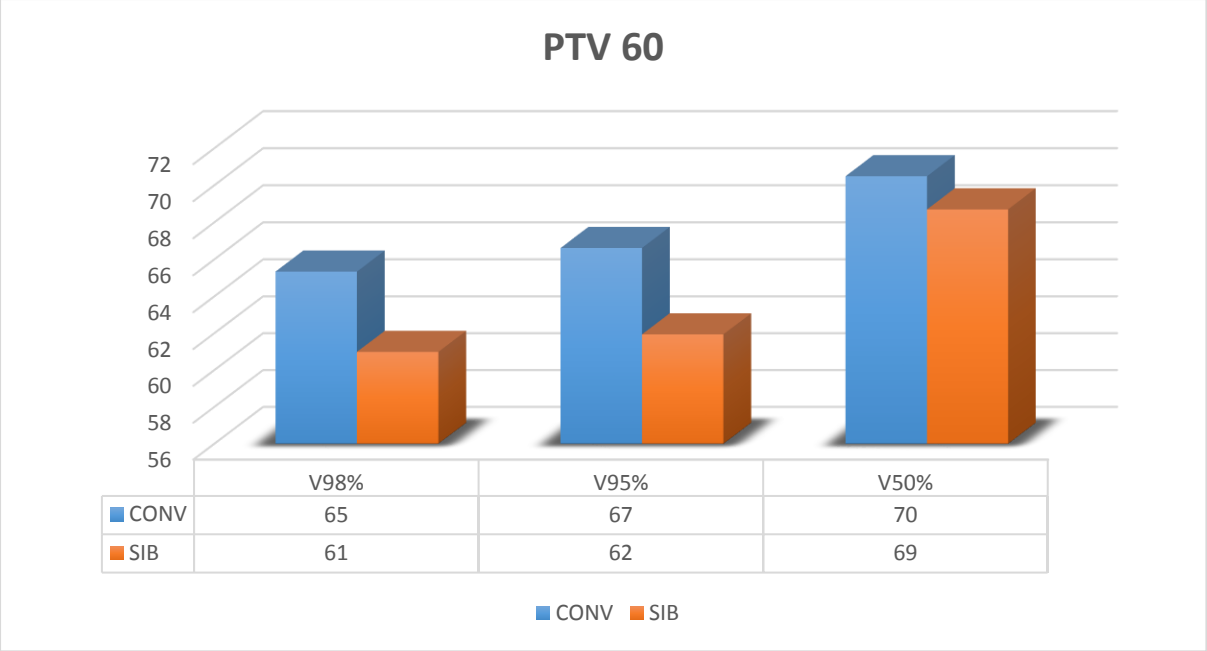


Fig. 16. Comparison between conventional and SIB technique in terms of dose coverage for PTV60

The PTV54 contained the elective nodes. As in the previous cases the plans made with SIB technique present lower doses, but the difference is not as big as it is for PTV60 and PTV70. This is a validation, that in case of CONV technique the higher doses are a result of the plan sums. Each step has a little bit higher doses, which in the end lead to a much higher dose. If one takes into account all 3 steps at once, the results are lower doses.

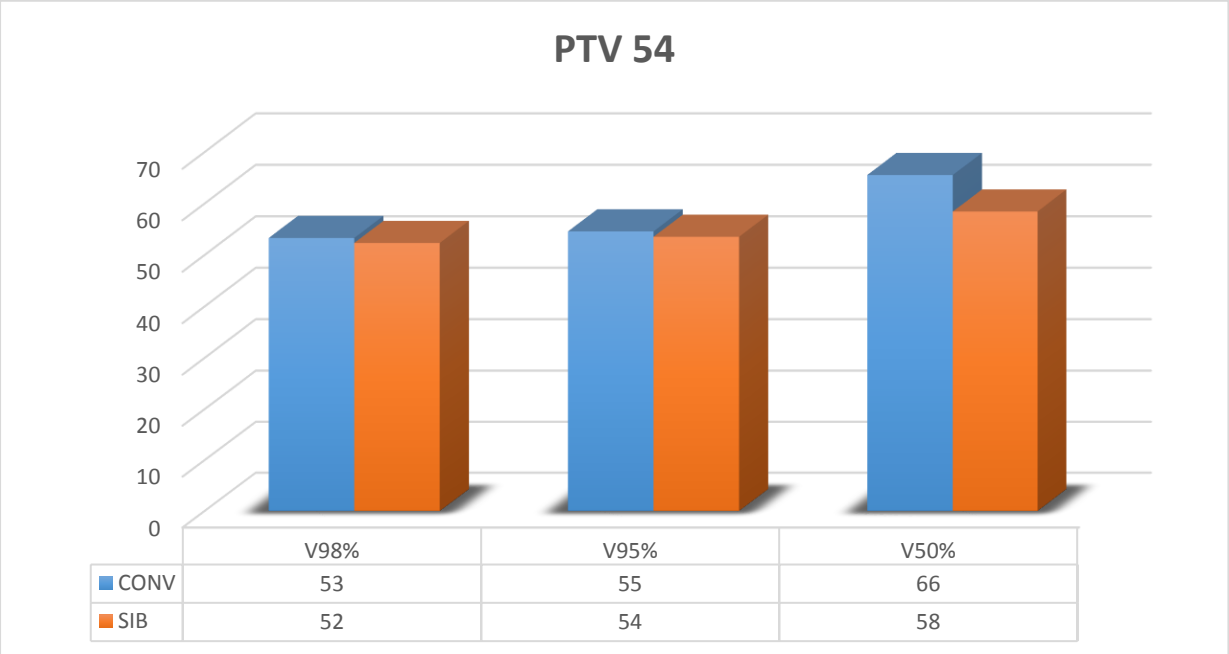
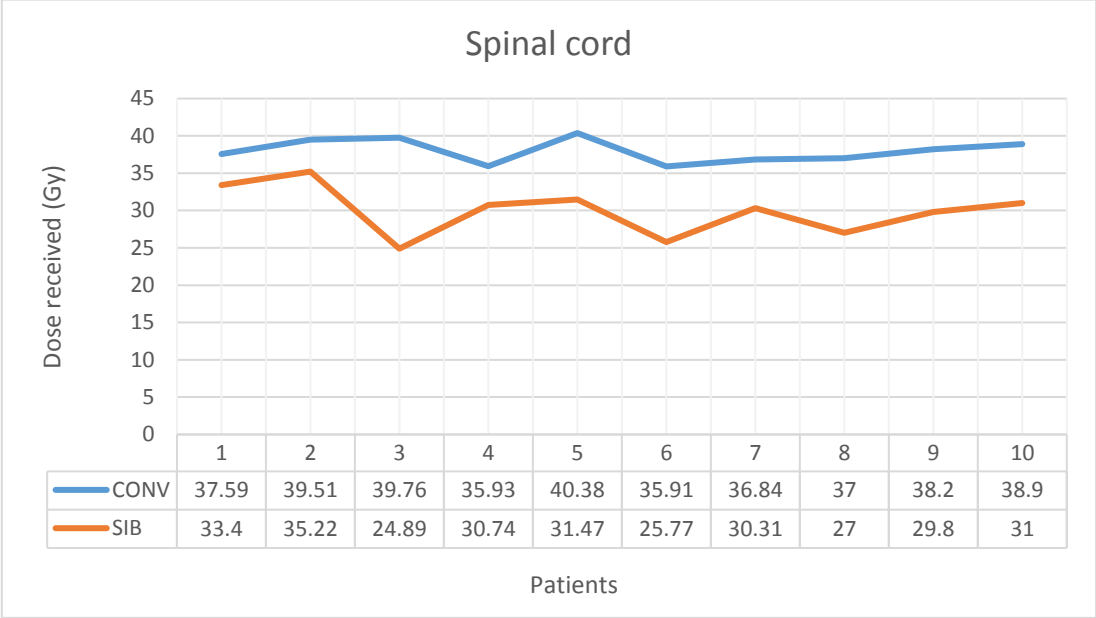


Fig. 17. Comparison between conventional and SIB technique in terms of dose coverage for PTV60

4.2 Organs at risk

The IAEA gives dose constrains only for spinal cord, brainstem and the left and right parotid. For the present work these organs represent the primary organs at risk. After the plans were finalized, the doses of other organs were also checked. These organs were considered secondary organs at risk.

The spinal cord was one of the most important organ from the head and neck region. A dose higher than 45Gy can raise significantly the risk of a fracture that can lead to paralysis. The Figure 18. presents the values of maximum doses of the spinal cord for each patient. The lowest dose was 24.9Gy with SIB and 35.9Gy with CONV technique. The maximum dose with CONV technique was 40.4Gy and 35.2Gy with SIB. The dose constrains suggested by the IAEA can be achieved with both techniques but the doses with SIB are significantly lower.



	1	2	3	4	5	6	7	8	9	10
CONV	37.59	39.51	39.76	35.93	40.38	35.91	36.84	37	38.2	38.9
SIB	33.4	35.22	24.89	30.74	31.47	25.77	30.31	27	29.8	31

Fig. 18. Comparison between conventional and SIB technique in terms of dose limits for spinal cord

The dose constrain for the brainstem was lower than for the spinal cord, but the same optimization parameter was used for both of them because it was imperative that the dose at the junction of the spinal cord and the brainstem to be as low as possible.

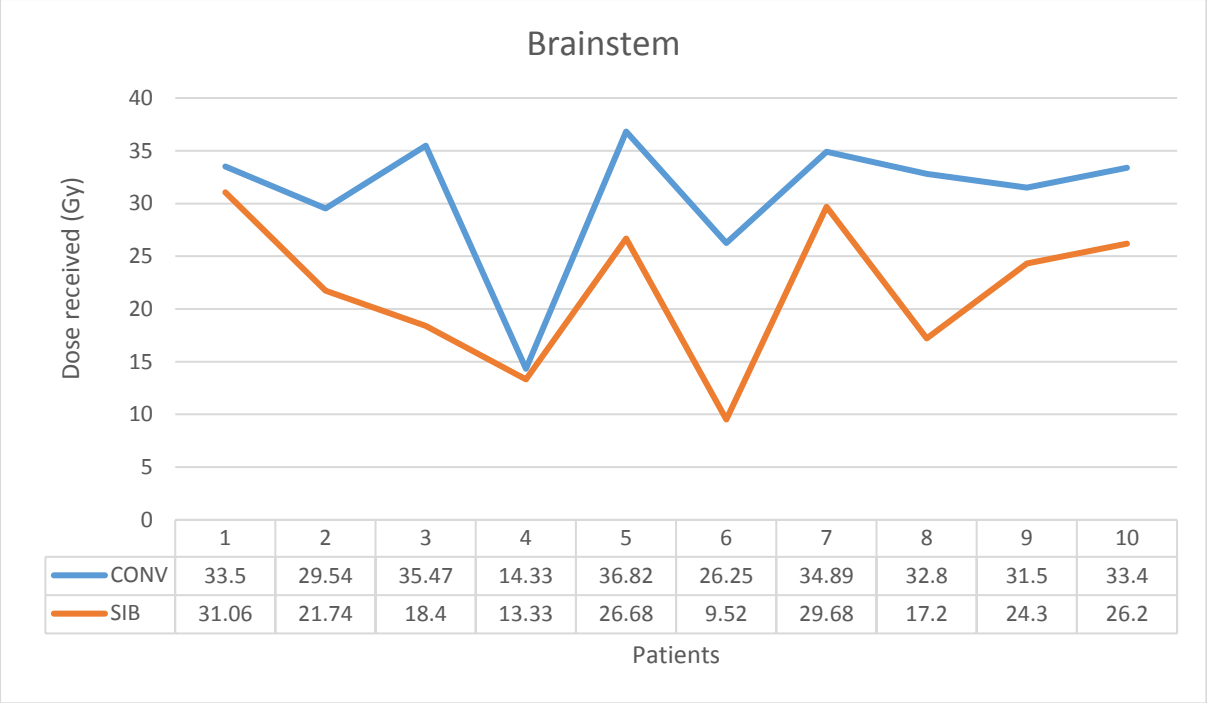


Fig. 19. Comparison between conventional and SIB technique in terms of dose limits for brainstem

The highest dose for the brainstem was 36.8 Gy in CONV case and 31Gy in SIB. The lowest dose was 14.3Gy in CONV case and 9.5Gy in SIB case. Figure 19. presents the values of maximum doses of the brainstem for each patient The big differences between the highest and lowest dose could be explained with the individual anatomy of the patients and the unique position of the tumors. The position of the PTV60 and PTV70 had a great influence on the individual results of the organs at risk. The dose constrains for the brainstem are kept but with SIB lower doses are achievable.

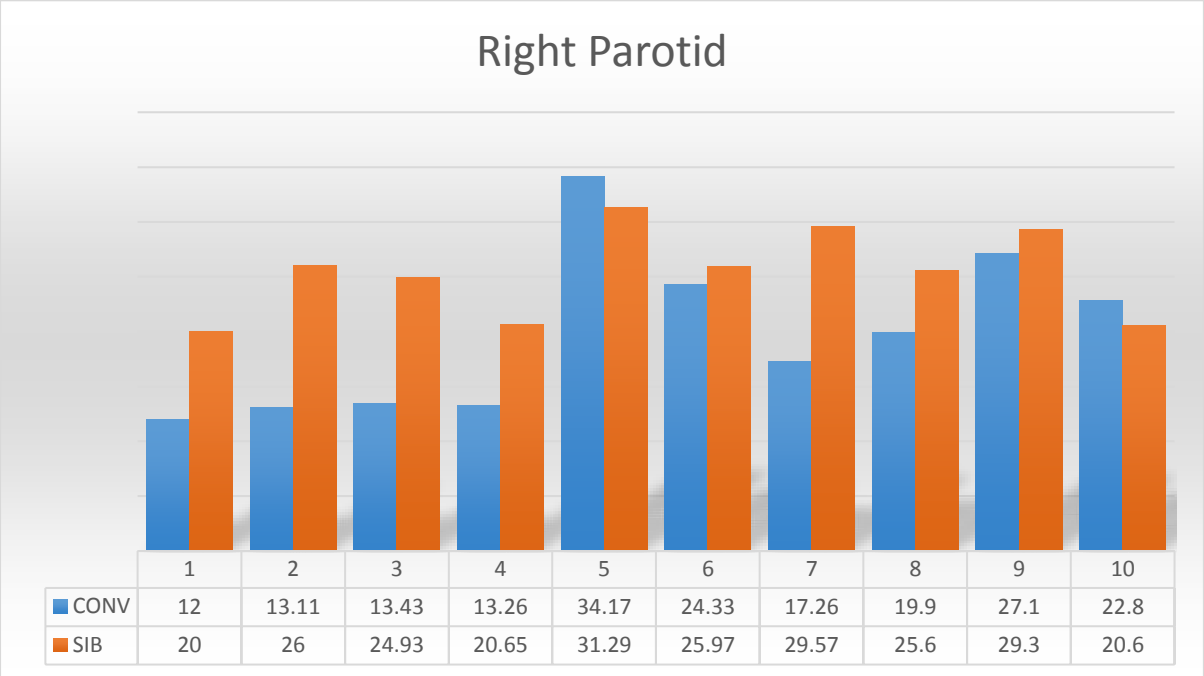
The parotid glands were part of the PTV60 or PTV70 in many cases. A too strong optimization parameter would keep the mean dose of the parotid beyond the dose constrain, but it would lead to an under dosage of the target volume. The main purpose was to destroy the tumor, the dose constrains for parotids could not always be kept.

	1	2	3	4	5	6	7	8	9	10
CONV	15	9.43	35.48	13.27	29.99	23.89	34.08	19.8	25.2	27.3
SIB	25	11	38.3	17.01	33.47	27.27	34.78	22.4	28.3	27.5

Fig. 20. Comparison between conventional and SIB technique in terms of dose limits for left parotid

The average of the mean doses for the left parotid glands is presented in Figure 20. for CONV and SIB technique. The red line in the figure represents the dose limit set at 24Gy as it is suggested by IAEA. It can be seen that both techniques have struggle keeping the dose beyond that limit but it can be concluded that lower doses can be achieved with CONV technique.

The average of the mean doses for the right parotid glands is presented in Figure 21.



	1	2	3	4	5	6	7	8	9	10
CONV	12	13.11	13.43	13.26	34.17	24.33	17.26	19.9	27.1	22.8
SIB	20	26	24.93	20.65	31.29	25.97	29.57	25.6	29.3	20.6

Fig. 21. Comparison between conventional and SIB technique in terms of dose limits for right parotid

The average of the mean doses of the left and right parotids for the 10 patients with the two techniques.

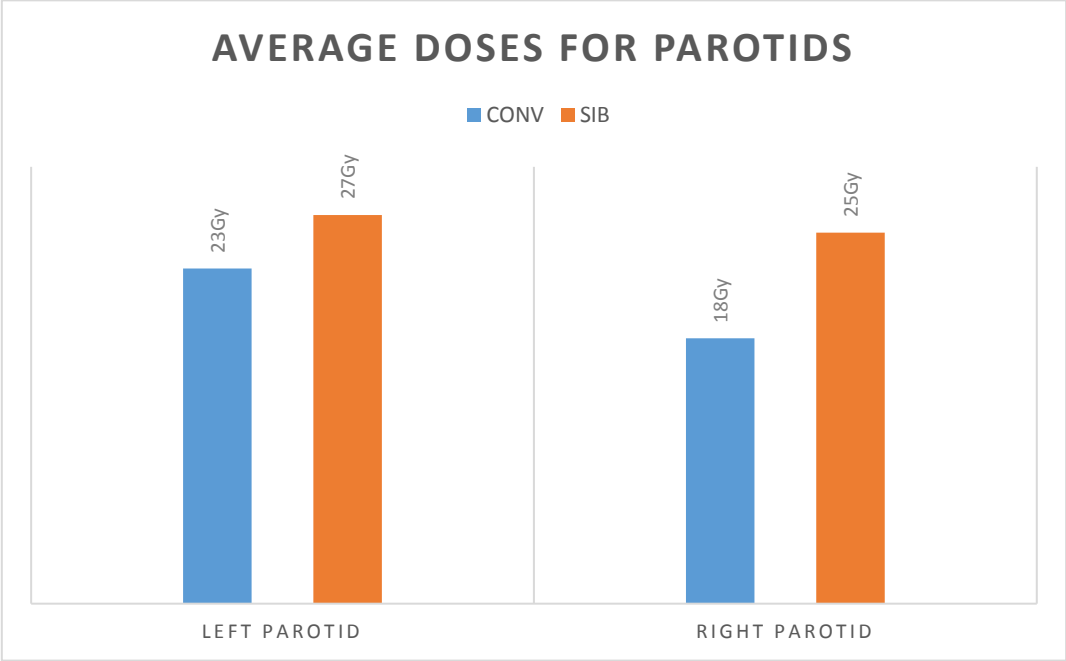
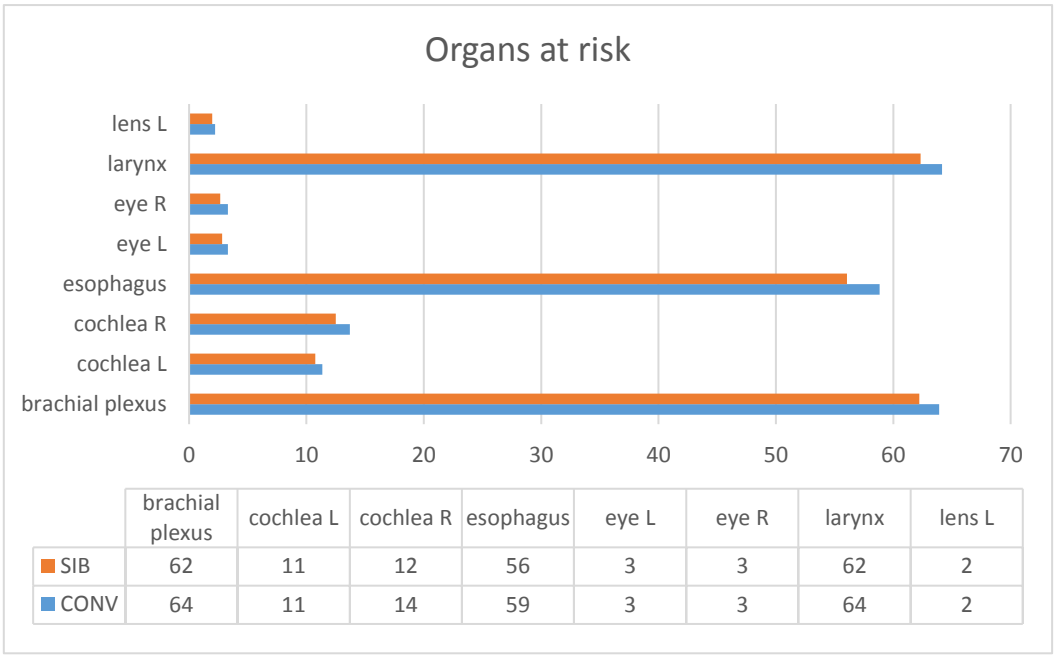


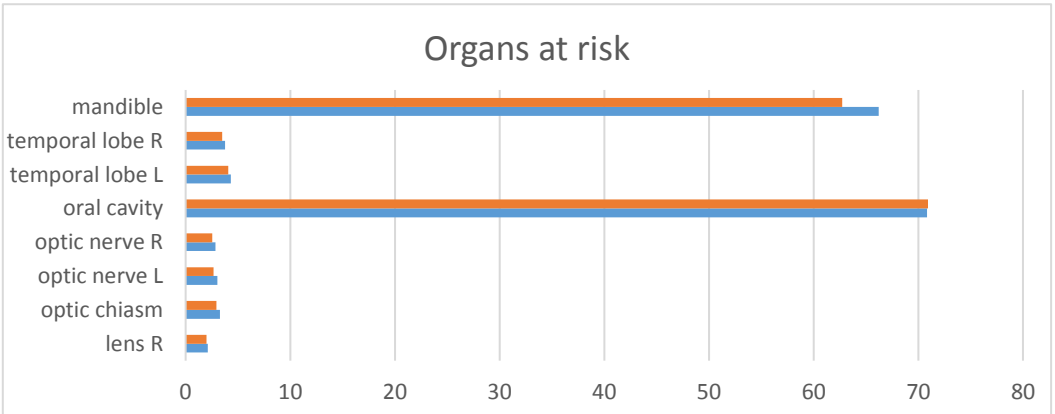
Fig. 22. Average of mean doses for left and right parotid glands

SIB technique is very useful for protecting organs at risk which are far from the target volume. CONV technique gives better results in case of organs which are very close or even part of the target volume.

The results of other organs at risk are presented in Figure 23. For these organs there is almost no difference in the absorbed dose. If there is still a difference, then it shows better results in case of SIB than for CONV technique.



	brachial plexus	cochlea L	cochlea R	esophagus	eye L	eye R	larynx	lens L
SIB	62	11	12	56	3	3	62	2
CONV	64	11	14	59	3	3	64	2



	lens R	optic chiasm	optic nerve L	optic nerve R	oral cavity	temporal lobe L	temporal lobe R	mandible
SIB	2	3	3	3	71	4	4	63
CONV	2	3	3	3	71	4	4	66

Fig. 23. Comparison between CONV and SIB technique in terms of absorbed dose for other organs at risk in the head and neck region

4.3 Indexes for plan evaluation

The most common indexes for plan evaluation are the conformity index and the homogeneity index. Their definitions are presented in the Methods section.

In case of the CI, the average value for plans made with CONV technique was 0.47, and for SIB was 0.88. This means that with SIB the obtained plans are more conformal. The prescribed dose is concentrated into the tumor volume and only a small part of it absorbed by the healthy tissue around the tumor volume.

The HI showed a better result for CONV-RA (0.005), than for SIB-RA (0.078). This big difference and worse result for SIB is due to the fact that the PTV70 in most of the cases was made of two different volumes contoured as one, and the normal tissue between them had lower dose. The dose distribution is following the shape of the 2 volumes and in between is a lower dose. The Figure 24. is very intuitive and gives an excellent visual representation of the CI and HI. In the left part the PTV70 is with red, PTV60 with green and the yellow part is for PTV54. In the other 2 pictures the scale of the dose is from 54Gy (green) up to 70Gy (red).

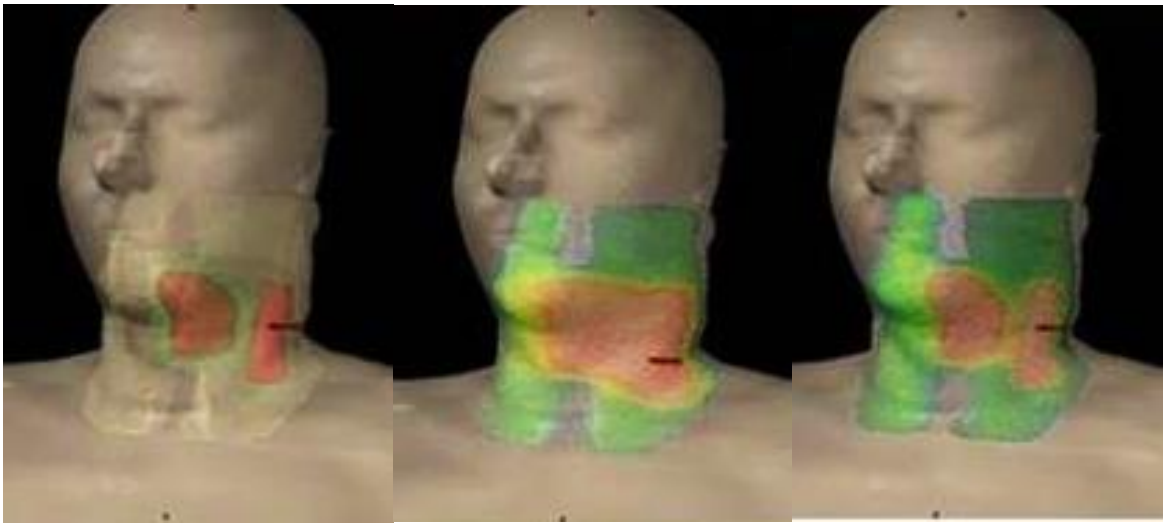
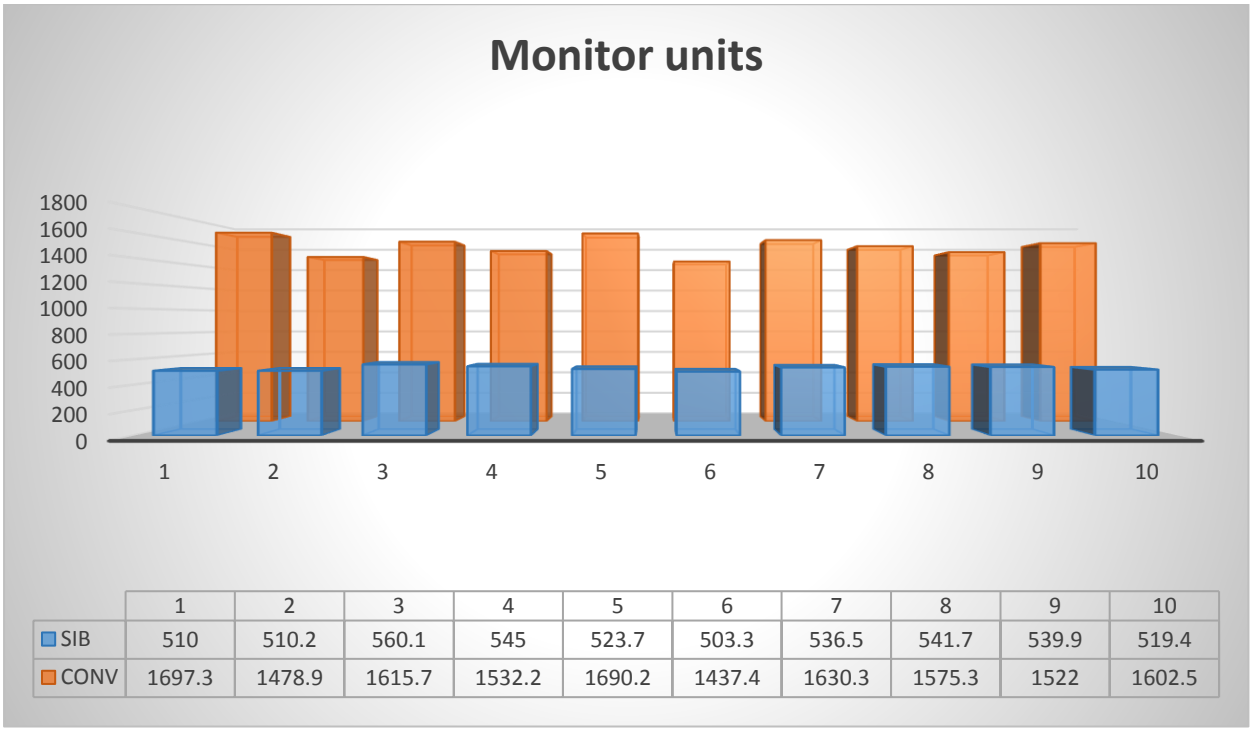


Fig. 24. The anatomy of the H&N tumor for one of the patients (left), 3 steps RapidArc IMRT plan-sum dose distribution (middle), SIB IMRT dose distribution (right).

4.4 Monitor units

A plan could be analyzed based on the MUs delivered. A low number of MUs can lead to decrease the plan quality and can compromise the target dose coverage, while a high number of MUs means that the plan is over modulated. The over modulation can be caused by the large number of small fields or segments created for dose delivery. An over modulated plan has high CI but the dose profile presents big differences between the maximum and minimum doses. Actually delivering an over modulated plan cannot be reproduced from one fraction to another, this is why the MUs are kept around a normal average number for treatment plans [12].

The MU for the 10 selected patients for the present work are presented in Figure 25.



	1	2	3	4	5	6	7	8	9	10
SIB	510	510.2	560.1	545	523.7	503.3	536.5	541.7	539.9	519.4
CONV	1697.3	1478.9	1615.7	1532.2	1690.2	1437.4	1630.3	1575.3	1522	1602.5

Fig. 25. Monitor units obtained for the plans with SIB and CONV technique

SIB technique uses only two arcs to deliver the prescribed dose. It can decrease the scattered radiation, and the total number of MUs by 30%.

5 Protocol for quality assurance and quality control

The SIB technique is not used as daily basics for head-and-neck technique, high level of quality assurance and quality control is demanded. Quality assurance (QA) is a comparison between the delivered dose to a phantom with the two dimensional dose distribution calculated by the TPS. The dose can be verified with films, portal dosimetry, 2D ion chamber array matrix, etc. For comparison between measured and calculated dose distribution ESTRO and AAMP suggest to use gamma analysis.

Gamma index is an essential tool which ensures the accuracy of applied plans and its potential to detect drawbacks in intended planar distribution. Usually the guidelines give criteria for two parameters: the dose difference and distance to agreement. The distance to agreement parameter represents a distance between the reference point and the closest data point in the compared dose distribution that has the same dose. This parameter is very useful especially in high dose gradient regions. A test is considered successful only if both parameters pass standard criteria given in the guidelines. Gamma score is measuring of how good a plan is, giving the percentage of dose points that satisfy the acceptance criteria [14].

To be able to perform QA for a patient, the whole plan should be copied, containing the field's configuration and dose parameters for a phantom and so the dose calculation could be made in one of the phantom's plane. The calculated doses are arranged in matrixes taking into account the positions of the detectors. This recalculated dose distribution is later compared with the initial plan by gamma index. The schematic representation of QA workflow is presented in Figure 26.

If the QA is performed with electronic portal imaging device (EPID), there is no need for a phantom. This two type of set ups for verification plans can be chosen from the TPS. The present work shows the results obtained using EPID for QA.

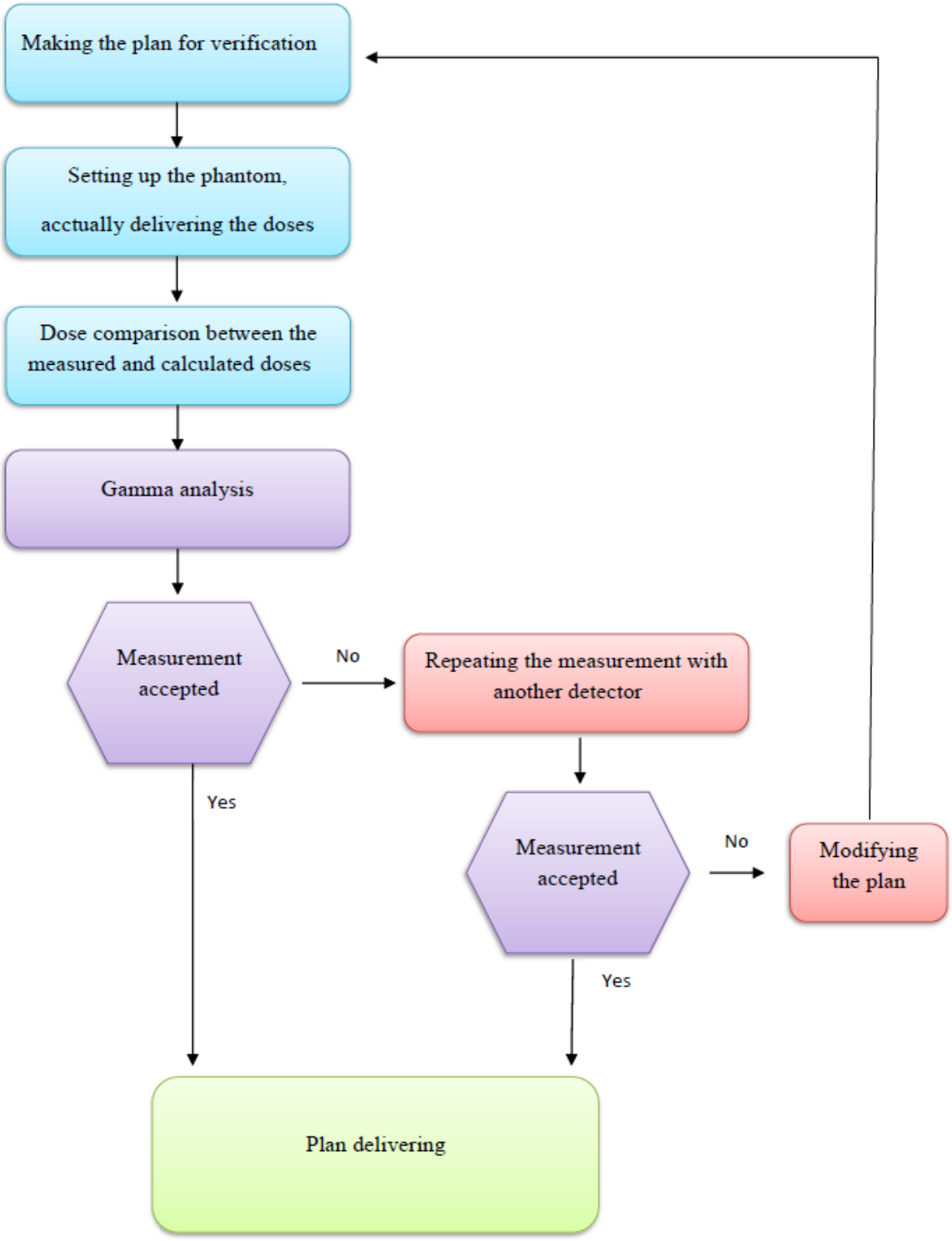


Fig. 26. Schematic representation of QA workflow.

When the verification plan is ready in the TPS it can be reached from the LINAC system as they are both part of the ARIA system. The measurement with EPID is easier because there is no need for setting up a phantom; the dose is just delivered from the LINAC to the detector.

While performing the gamma analysis the passing criteria is 95% match between calculated and delivered dose distribution. If the match is 95% or better the measurement is accepted and the plan can be delivered for the patient. In other case, if there is a mismatch bigger than 5% the measurement have to be repeated with another detector. The new results are evaluated with the same criteria. If the 95% is reached, the plan can be delivered to patient if not, the plan has to be modified and reevaluated. The circuit is repeated until the plan is considered suitable and safe to deliver in clinic.

The following criteria, presented in Figure 27, are used for evaluation, as they are suggested by national and international organizations:

- dose difference – 3% of reference value
- distance to agreement – 3mm
- improved gamma evaluation instead and local gamma evaluation
- threshold – 5%

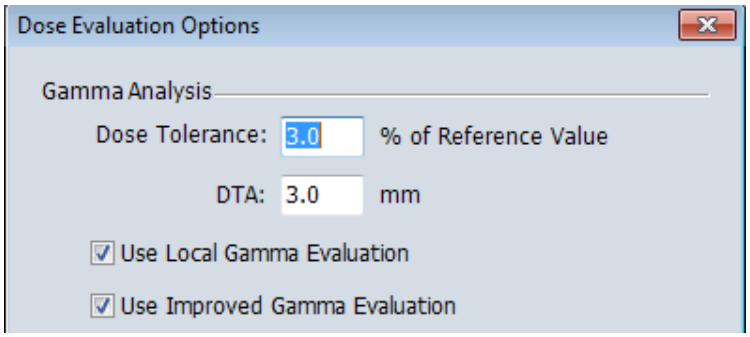


Fig. 27. Dose evaluation options used for gamma analysis

Calculated and measured fluence maps were compared using portal dosimetry analysis module incorporated in Varian software. The measurements were done on Varian TrueBeam accelerator machine. All plans meet the passing criteria. On average the plans made with SIB technique had lower gamma score (96%) than the plans made with CONV technique (97% for I step, 98% for II step and 98.5% for III step). Figure 28., Figure 29., presents the obtained results for CONV technique and SIB respectively.

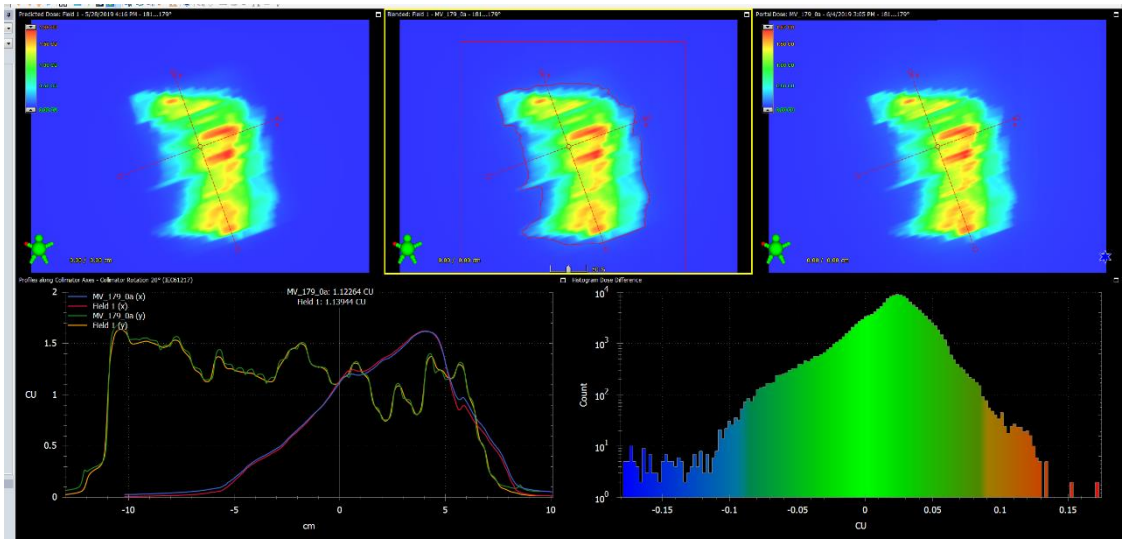


Fig. 28. Result of gamma analysis for the first arc from I step CONV plan.

In the first square, from upper left corner, is the predicted dose. In the upper right corner is the calculated dose distribution. The result of the measurement is presented in the upper middle part. In the lower part of the image are presented the differences obtained between the two doses. In the left hand side is presented the dose differences in terms of dose profile and on the right hand side the differences are showed in terms of dose volume histogram.

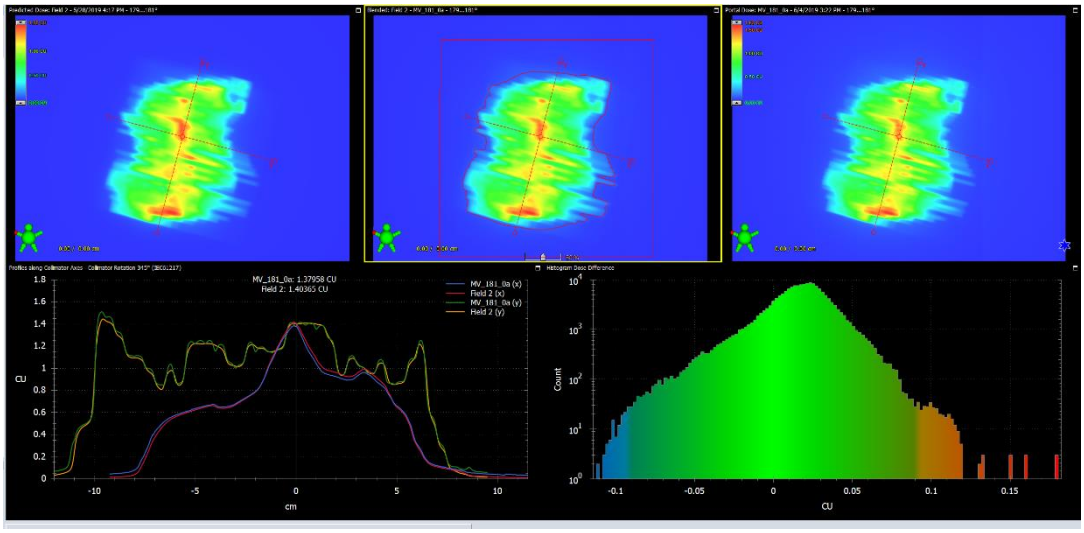


Fig. 29. Result of gamma analysis for the second arc from SIB plan

6 Discussion

Simultaneous integrated boost radiation therapy for patients with tumor in head and neck region provides many advantages allowing higher doses to the target volume with optimal distribution and sparing of organs at risk. Franceschini et al. [15] used two different fractionations for SIB one up to 70Gy and one up to 60Gy to review toxicity and outcomes in patients with head and neck cancer. They obtained in average higher doses than mines. This may be a result of using different protocols and guidelines. The average maximum in their study for the spinal cord and brainstem were 44Gy and 50,6Gy, while I could keep those values under 30Gy for spinal cord and 21Gy for brainstem. Their study did present better results in case of cochlea and larynx but it is due to the position of the tumor.

Cilla et al [16] analyzed the potential of VMAT to reduce the risk of swallowing problems after curative chemotherapy. They created an original standard plan not using objectives for swallowing organs. A second plan was developed from the first by adding special objectives to protect the swallowing organs. The dose of spinal cord and brainstem was similar to Franceschini et al [15] study, higher than my results, but no change when added more objectives. While the absorbed dose for the lens was unchanged and similar with my results, the doses for eyes were slightly higher in their study.

Treatment planning for external beam therapy could be very challenging, especially in case of head and neck region. As it can be already seen from the two other studies before, the result of planning process is strongly dependent of the skills of the individual planner and the institutional criteria, strategies or protocols applied to a plan. The need of consistency in treatment planning lead Fogliata et at [17] to develop processes and algorithms for automatization and harmonization. In their study they analyzed results of treatment plans my by RapidPlan DVH estimation model. During the optimization process only the objectives for PTVs were given, for the rests of the organs they were generated. Significantly lower doses were obtained for every OAR. Even if their results for brainstem and spinal cord are comparable with my results, for other organs like parotid glands, oral cavity and larynx they obtained higher sparing.

Since the beginning of VMAT it was a big question how many arcs are optimal to use. For the present work the treatment plans were made using 2 arcs in both cases SIB and CONV. Tol et al [18] made a study regarding the effect of increased number of arcs in radiotherapy. They used two, four, six and eight full arcs. The increased number of arcs resulted better homogeneity for the dose and improved OAR sparing. They showed the largest absolute gain

when increasing from two arcs to four arcs. In general, it shows 2Gy reduction in OARs sparing. Of course, those positives parts, come along with increased delivery time and increased MU. In the first case, the risk of movement during the treatment session is doubled, and in the second case the risk of radiation induced secondary malignancies increases. This is way, I choose to use 2 arcs and generally in clinics 2 arcs are used.

Brachytherapy with or without external radiotherapy can be a very useful treatment method due to really high doses delivered in small areas, very conformably. Akiyama at al [19] made a comparative study between image guided high dose rate brachytherapy and VMAT SIB techniques, in terms of conformity of dose distribution to PTV and doses to OARs. They obtained low doses for OARs in both cases. The VMAT planning protocol was different than the brachytherapy protocol. Akiyama at al used a set up for a total dose of 70Gy in external therapy but for brachytherapy after 70Gy other 20Gy were planned as boost. In the end, V95 was better with VMAT (98,4%) which is higher than the average for my plans (V95 is 96%). Both techniques provide good target coverage but with brachytherapy the OARs can be better protected, but it is necessary to be made long term follow ups and involve more patients.

The results could also be compared with tomotherapy. Stromberger et al [20] reported equivalent coverage regarding the PTV in both cases. Regarding my work, V95 for PTV70 in case of SIB was 67Gy and for them 66,3Gy. V95 for PTV60 was 62Gy in my plans and 58,1Gy in Stromberger's study. For the last target volume, PTV54 I obtained 54Gy for V95 and they obtained 52Gy for the same target volume. In case of tomotherapy the results were slightly higher. Stromberger et al report better homogeneity for tomotherapy and better conformity for VMAT SIB. Those results are similar to mine results, because I found better homogeneity value for CONV technique and better conformity for VMAT SIB [20].

In the same year the same team, Stromberger et al [21], made another comparative study. This time the results of VMAT SIB plans were compared with sequential technique. Our results meet their conclusion, which is validating my results. Stromberger et al found that SIB technique has higher conformity index and it is less over dosing technique, since the doses for sequential technique were higher than for SIB. Their final conclusion was that SIB might cause less acute and late toxicities, but further studies are required.

All plans from the present work were made for Varian TrueBeam accelerator machine. The MLC leaf's width in the middle is 5mm and outside the middle part is 10mm, as it was presented in previous chapters. Lafond et al [22] made a study for dosimetric investigation the

impact of MLC leaf width in VMAT. Lafond used Elekta MLCi2 and Beam Modulator machines, one with 10mm leaf width and the other 4mm width. They found out that results for Beam Modulator machine, which has smaller leaf's width, can decrease the delivered dose for OARs. On the other hand, the MU for this machine was 50% higher than for MLCi2. In terms of conformity index with wider leaf could obtain better results but for homogeneity the narrower leaf had better result. The final result is important in terms of OARs sparing, because in other cases the difference was insignificant. It is recommended to use narrower leaf for treating head and neck cancer with SIB technique.

Accurate 3D dosimetry is essential in modern radiotherapy techniques such as VMAT SIB. A very important part of radiation delivery is the quality assurance process. Rehman et al [23] observed the results obtained with thermoluminescent detectors (TLD), Gafchromic EBT films and Presage. For the present work I have done the QA for the 10 plans with EPID. It was observed that when the QA is performed with TLD or films detector most of the plans failed, but for Presage they passed. This is why it is very important what kind of dosimeters are use and also what protocols are made for the QA. TLD usually measure less dose than it is calculated.

7 Conclusion

Our work presents the dosimetric evaluation of simultaneous integrated boost radiation therapy for patients with tumour in head and neck region.

Based on our results we can conclude that the same tumor dose coverage can be achieved using SIB-RA as with CONV with a shorter overall treatment time and with better CI. With SIB-RA the average maximum doses for the spinal cord and the brainstem can be lowered, and the dose of the parotid glands can increase. Regarding the organs of interest in the H&N area, lower exposure can be performed using SIB-RA technique.

The SIB-RA is an advance radiotherapy technique, it was essential to perform a high level quality assurance and quality control protocol for the treatment plans. The passing gamma score was always higher than 95%.

Simultaneous integrated boost radiation therapy for patients with tumor in head and neck region could be a good alternative instead of CONV technique. Further investigations and more studies on a larger patient group are required for more precise results.

Bibliography

[1]. Marcu L, Toma-Dasu, I., Dasu, A., Mercke, C. Radiotherapy and Clinical Radiobiology of Head and Neck Cancer2018.

[2]. Tolentino EdS, Centurion BS, Ferreira LHC, Souza APd, Damante JH, Rubira-Bullen IRF. Oral adverse effects of head and neck radiotherapy: literature review and suggestion of a clinical oral care guideline for irradiated patients. Journal of applied oral science: revista FOB. 2011;19(5):448-54.

[3]. Brahme A, Roos, J., & Lax, I. Solution of an integral equation encountered in rotation therapy. . Physics in medicine and biology1982.

[4]. Thomas B. IMRT: a review and preview. Physics in Medicine & Biology. 2006;51(13):R363.

[5]. Webb S, Tripathi S. Contemporary IMRT: Developing Physics and Clinical Implementation2005.

[6]. Convery DJ, Rosenbloom ME. The generation of intensity-modulated fields for conformal radiotherapy by dynamic collimation. Physics in Medicine and Biology. 1992;37(6):1359-74.

[7]. Podgorsak EB. RADIATION ONCOLOGY PHYSICS: A HANDBOOK FOR TEACHERS AND STUDENTS: INTERNATIONAL ATOMIC ENERGY AGENCY

VIENNA; 2005.

[8]. Civco Radiotherapy [Available from: https://civcort.com/ro/thermoplastic/types-imrt-reinforced-style-27-thermoplastics/types-imrt-reinforced-sytle-27-thermoplastics-T7.htm.

[9]. Report 83. Journal of the International Commission on Radiation Units and Measurements. 2016;10(1):NP-NP.

[10]. Landberg T, Chavaudra J, Dobbs J, Hanks G, Johansson KA, Möller T, et al. Report 50. Journal of the International Commission on Radiation Units and Measurements. 2016;os26(1):NP-NP.

[11]. Landberg T, Chavaudra J, Dobbs J, Gerard JP, Hanks G, Horiot JC, et al. Report 62. Journal of the International Commission on Radiation Units and Measurements. 2016;os32(1):NP-NP.

[12]. Jiménez-Puertas S, Sánchez-Artuñedo D, Hermida-López M. Assessment of the Monitor Unit Objective tool for VMAT in the Eclipse treatment planning system. Reports of practical oncology and radiotherapy: journal of Greatpoland Cancer Center in Poznan and Polish Society of Radiation Oncology. 2018;23(2):121-5.

[13]. Khayaiwong P, Tungboonduangjit, P., Suriyapee, S., Boonkitticharoen, V., Oonsiri, S., Sanghangthum, T., & Oonsiri, P. Dosimetric Comparison between Simultaneous Integrated Boost and Sequential Intensity-Modulated Radiotherapy Techniques in Nasopharyngeal Carcinoma. 2012.

[14]. Maria A, Atia A, Khalid I, Quratul ain S, Farah A, Saeed Ahmad B. Interpretation of Gamma Index for Quality Assurance of Simultaneously Integrated Boost (SIB) IMRT Plans for Head and Neck Carcinoma. Polish Journal of Medical Physics and Engineering. 2017;23(4):93-7.

[15]. Franceschini D, Paiar F, Meattini I, Agresti B, Pasquetti EM, Greto D, et al. Simultaneous integrated boost–intensity-modulated radiotherapy in head and neck cancer. The Laryngoscope. 2013;123(12):E97-E103.

[16]. Cilla S, Deodato F, Macchia G, Digesù C, Ianiro A, Piermattei A, et al. Volumetric modulated arc therapy (VMAT) and simultaneous integrated boost in head-and-neck cancer: is there a place for critical swallowing structures dose sparing? The British journal of radiology. 2016;89(1059):20150764-.

[17]. Fogliata A, Reggiori G, Stravato A, Lobefalo F, Franzese C, Franceschini D, et al. RapidPlan head and neck model: the objectives and possible clinical benefit. Radiation oncology (London, England). 2017;12(1):73-.

[18]. Tol JP, Dahele M, Slotman BJ, Verbakel WFAR. Increasing the number of arcs improves head and neck volumetric modulated arc therapy plans. Acta Oncologica. 2015;54(2):283-7.

[19]. Akiyama H, Pesznyák C, Béla D, Ferenczi Ö, Major T, Polgár C, et al. Image guided high-dose-rate brachytherapy versus volumetric modulated arc therapy for head and neck cancer: A comparative analysis of dosimetry for target volume and organs at risk. Radiology and oncology. 2018;52(4):461-7.

[20]. Stromberger C, Wlodarczyk W, Marnitz S, Jamil B, Budach V, Raguse J-D, et al. Simultaneous Integrated Boost (SIB): RapidArc and Tomotherapy Plan Comparison for Unilateral and Bilateral Neck Irradiation2015. 2991-7 p.

[21]. Stromberger C, Ghadjar P, Marnitz S, Thieme A, Jahn U, Raguse J-D, et al. Comparative treatment planning study on sequential vs. simultaneous integrated boost in head and neck cancer patients : Differences in dose distributions and potential implications for clinical practice2015.

[22]. Lafond C, Chajon E, Devillers A, Louvel G, Toublanc S, Olivier M, et al. Impact of MLC leaf width on volumetric-modulated arc therapy planning for head and neck cancers. Journal of applied clinical medical physics. 2013;14(6):4074-.

[23]. Rehman J, Isa M, Ahmad N, Noor ul Huda Khan Asghar HM, Gilani ZA, Chow JCL, et al. Quality assurance of volumetric-modulated arc therapy head and neck cancer treatment using PRESAGE® dosimeter. Journal of Radiotherapy in Practice. 2018;17(4):441-6.