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First steps towards improving teletherapy inverse planning of the Boldrini Infant Center using external solvers

Campinas
16/06/2023

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First steps towards improving teletherapy inverse planning of the Boldrini Infant Center using external solvers[1]

Report presented to the Institute of Mathematics, Statistics and Scientific Computing as part of the requirements for obtaining credits in the supervised extension project course, under the guidance of Prof. Aurelio Ribeiro Leite de Oliveira.

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[1] This project was supported by the CNPQ.

Abstract

Teletherapy is a cancer treatment that uses ionizing radiation to extinguish tumour cells. These ionizing particles are delivered via a linear accelerator (*LINAC*), an instrument that rotates around the patient distributing radiation at every feasible angle. The treatment's goal is to use the smallest dose required to eliminate cancerous tissue while sparing healthy organs. To accomplish this, there is a planning phase before the proper treatment, where medical physicists decide how the *LINAC* is supposed to operate, aiming to achieve an optimal dosage distribution. The plan is elaborated in a treatment planning system (*TPS*) software, so the instructions can be sent to the *LINAC*. One of the features that some *TPS* offer is inverse planning. This tool is constituted by optimization algorithms that look for optimal treatment plans. Sadly, *TPS* licenses are expensive, and most hospitals can not afford updates on them regularly.

Fortunately, some inverse planning features can be implemented outside of the in-house *TPS* of the hospital, and these are relatively simple to create when compared to an entire *TPS*. This way, the hospital can make use of state-of-the-art teletherapy inverse planning algorithms to drastically improve treatment quality and speed at almost zero cost. For that reason, and also aiming to strengthen the relationship between researchers in exact sciences and hospitals, the purpose of this project is to discuss the compatibility of the staff, technology available, clinical practice and the *TPS* of the Boldrini Infant Center radiotherapy sector to external solvers, as well as the methodology to implement those solvers and its possible positive outcomes, based on the author's visits at the hospital during the last years. Ultimately, leading to the first steps required towards an improvement of the teletherapy inverse planning practice at Boldrini using external solvers.

It was concluded that their workflow is already pretty optimized. However, additional features like beam angle optimization for step-and-shot, as well as *VMAT* and *IMAT* trajectories, would surely refine their angle choices. Also, an external feature to deal with online adaptive planning would make the most out of a cone beam *CT* used only for positioning purposes. Finally, from the academic perspective, the Bodrini Infant Center also disposes of a welcoming staff and a great environment fro researchers from Unicamp.

Contents

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Acronyms

BAC Beam Angle Configuration. 23

BAO Beam Angle Optimization. 14

BEV Beams's Eye View. 14

CBCT Cone Beam CT. 22

CERR Computational Environment for Radiological Research. 26

CT Computational Tomography. 12

CTV Clinical Target Volume. 13

DAO Direct Aperture Optimization. 16

DDM Dose Deposition Matrix. 20

FMO Fluence Map Optimization. 14

GTV Gross Tumor Volume. 13

GUI Graphical User Interface. 24

IGRT Image Guided Radiation Therapy. 22

IMAT Intensity Modulated Arc Therapy. 16

IMRT Intensity Modulared Radiation Therapy. 8

INCA National Institute of Cancer. 8

ITV Internal Target Volume. 13

LINAC Linear Accelerator. 8

LSO Leaf Sequencing Optimization. 9

MLC Multileaf Collimator. 11

MRI Magnetic Resonance Imaging. 14

NTCP Normal Tumor Control Proability. 16

OAR Organ At Risk. 13

PRV Planning Risk Volume. 13

PTV Planning Target Volume. 13

RT Radiotherapy. 8

SBRT Stereotactic Body Radiation Therapy. 22

SI International System of Units. 12

SUS Brazilian unified health system. 21

TCP Tumor Control Proability. 16

TPS Treatment Planning System. 8

VMAT Volumetric Intensity Modulated Arc Therapy. 16

1 Introduction

A global estimate showed that approximately 18 million new cases of cancer and 9.6 million cancer-related deaths occurred in the world in 2018 (Bray et al. [2018]). According to the National Institute of Cancer *INCA*, Brazil will have approximately 625,000 new cases for each year of the 2020 to 2022 triennium.[2] One of humanity's weapons to fight against this malady is the worldwide known cancer treatment called radiotherapy (*RT*), which emerged from the discovery of the *X-Ray* in 1895, giving rise to the first radiotherapy book, printed in 1904 (Freund [1904]). It comprises the usage of ionizing radiation to extinguish the tumor by making small ruptures in the *DNA* inside tumor cells which prevents their multiplying and leads them to death (Abshire and Lang [2018]). In the external beam radiation therapy context, called teletherapy as well, ionizing particles are delivered by a linear accelerator (*LINAC*), an instrument that rotates around the patient distributing a radiation dose at every feasible angle (Almeida [2012]). Even with the freedom to choose angles, most types of teletherapy do not reach all parts of the body, which means they are not helpful in treating cancer that has spread through the patient. However, more than half of people with cancer are treated with radiation because of its versatility in being used either alone or in combination with other treatments. Nowadays, this procedure has been used to cure or shrink early-stage tumors, prevent tumor recurrence, treat symptoms caused by advanced cases, and treat cancer that has recurred.

But not all that glitter is gold. Radiation is well known to raise the risk of getting cancer, and this is one of the possible side effects that oncologists have to think about when they weigh the benefits and risks for each patient. These risks back in the emergence of teletherapy treatments were incredibly higher than that of contemporary ones. Their major cause was that older treatment plans often either delivered too little radiation dose to the *PTV* (Planning Target Volume), too much radiation dose to the *PRT* (Planning risk volume) or both. Thus, what is at stake as regard treatment plans is the patient's quality of life against the probability of the eradication of their disease (Romeijn et al. [2006]).

A revolution started in the late 1990s when a brand new type of treatment emerged: the *IMRT* (Intensity Modulated Radiation Therapy); capable of creating non-uniform fluxes to improve dose distribution (Bortfeld [2012]). In light of this sophistication, the treatments' planning phase began to draw more attention not just from physicians, medical physicists and radiologists, but also from engineers and mathematicians (Webb [2003]). The planning phase's major goal is to decide how the linear accelerator is supposed to deliver radiation at each angle to achieve an optimal dosage distribution. Not coincidentally, "optimal dose distribution" alludes to an optimization problem; which is, of course, what this subject is all about. In clinical practice, the optimization algorithms can be found in moderns *TPS* (treatment planning system). These are software, in general, created by the linear accelerator's manufacturers or by other companies focused on solutions in medical physics to assist medical physicists with treatment planning.

Therefore, in *RT* planning, the linear accelerator and the *TPS* are the two main properties which define the treatment planning quality. Unfortunately, both the linear accelerator's prices and *TPS*'s licenses are particularly expensive, so very few hospitals have *RT* treatment available, and when they do, most probably the linear accelerator or the *TPS* is outdated. In addition, it is not quite viable for a hospital to build its own *TPS* from scratch since too many features are required for a functional *TPS*. Luckily, there are important features for *IMRT* that are relatively easy to implement, apart from the *TPS* internal code, which the user could simply take the external's routine output and use as input in the commercial *TPS*. Those features are local solvers for the three main optimization problems within *IMRT* that compose the

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[2] Source: `https://www.inca.gov.br/estimativa/introducao`

planning method called *inverse planning*: the Beam Angle Optimization (*BAO*), Fluence Map Optimization (*FMO*), and the Leaf Sequencing Optimization (*LSO*). Most recent examples of these practices are the *ECHO*[3] framework (Zarepisheh et al. [2022]) and the *Nymph* [4] algorithm (Gorissen [2022]). Such local solvers do not require refined visual interfaces nor integration with any commercial *TPS*. Accordingly, research projects for undergraduate and graduate students can be created to develop on these software and make use of state-of-the-art *RT* planning optimization algorithms to drastically improve treatment's quality and speed with almost zero cost. Even though the idea sounds inviting, it is not a trivial task to determine whether a *RT* sector as a whole is compatible with a local solver or not. Once the piece of software is at the hospital's disposal, the solvers must match with the *RT* sector's capability of dealing with the new tool. For that reason, and also aiming to strengthen the relationship between researchers in exact sciences and hospitals, this project's goal is to discuss the compatibility of the staff, technology available, clinical practice and *TPS* of the Boldrini Infant Center radiotherapy sector to external solvers, as well as the methodology to implement those solvers and its possible positive outcomes, based on the author's visits at the hospital during the last years; ultimately leading to the first steps required towards an improvement of the radiotherapy inverse planning practice of Boldrini using external solvers.

An explanation of how the monograph is organized as follows. Section 2 covers the basic radiotherapy planning concepts, while section 3 gives an overview of the analyzed hospital. In section 4, the methodology of how the hospital's information was gathered study is presented, followed by the discussion of the hospital's state and the conclusion in sections 5 and 6, respectively.

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[3] https://masoudzp.github.io/

[4] https://3142.nl/nymph/

2 Radiotherapy planning background

2.1 Radiation therapy classification

It is surprisingly easy to mix up the different types of radiotherapy. The very first step into this topic is to understand which of them this report is about.

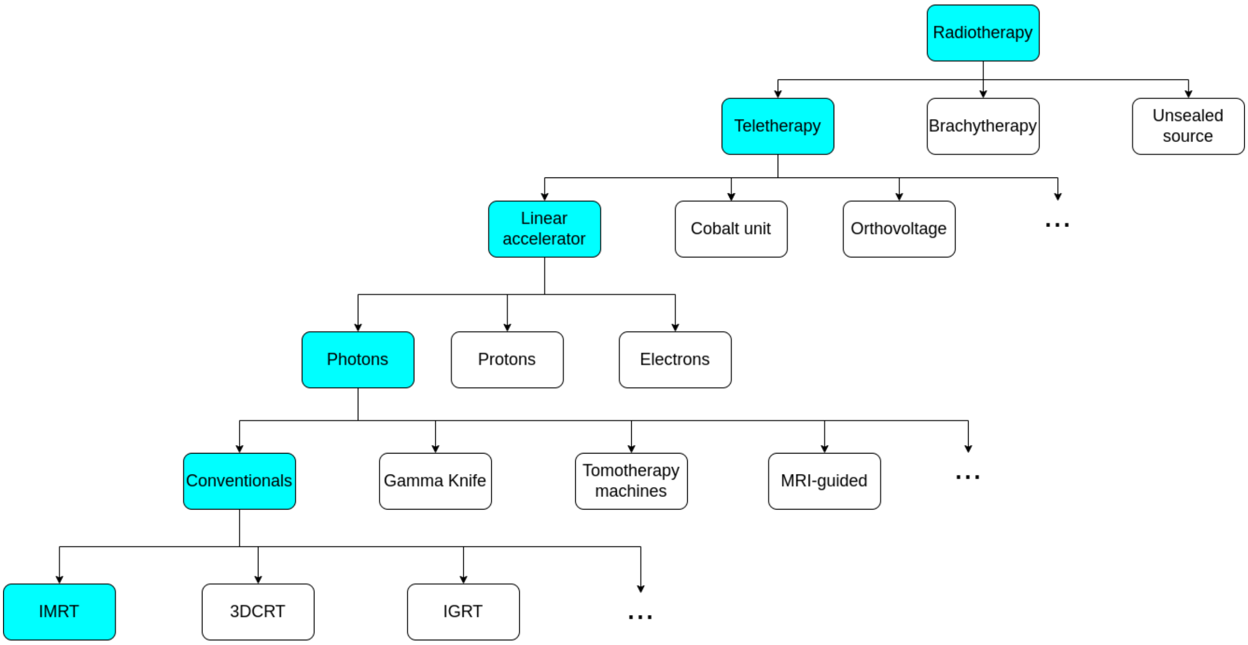


Figure 1: Tree diagram of radiation therapy classifications.

As highlighted in figure 1, this project is concerned with the teletherapy field, where radiation is generated and delivered from the outside of the patient (Almeida [2012]). An example of a different approach is brachytherapy, from the Greek “brachys”, meaning “short distance”, where the source of radiation is encapsulated and inserted in the patient at or near the tumor, temporarily or permanently (Guinot et al. [2017]). In contrast, the unsealed radiation therapy delivers radiation via an injection into the bloodstream, the use of body cavities, or by swallowing it (Volkert and Hoffman [1999]).

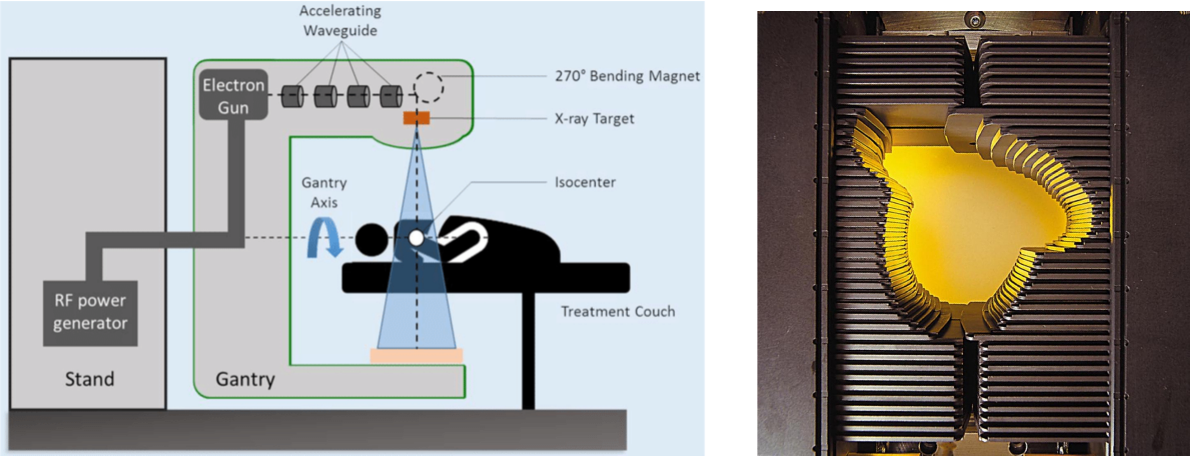
To perform better treatments then, many different machines used in teletherapy were created in the last decades. The one studied in this project, the most popular kind nowadays, is the linear accelerator. However, one can also find in older treatment stations some equipments for superficial radiation therapy that uses low energy *X-rays*, or those for cobalt therapy, which uses cobalt-60 isotopes, among other types of equipment.

Because of its versatility, a linear accelerator may have different shapes and sizes that consequently change its application. For instance, *Gamma Knife* is a very precise robot used in radio surgeries (Lindquist [1995]), and thomotherapy machines are very similar to *CT* scanners albeit with a built-in binary *MLC* (Mackie et al. [1999]). For the sake of the project, the most conventional type is supposed, represented in the figure 2a.

Finally, given the wide range of ways to deliver the radiation dose to the patient, which will be discussed later in the text, the optimization models in question investigates the *IMRT* approach, as mentioned in the introduction.

2.2 Linear accelerator

The main equipment for most teletherapy treatments is the linear accelerator. Even though there are different brands on the market, its components common to all different types are represented in the schematic figure 2a[5], followed by a brief description.



(a) Components of a typical linear accelerator.

(b) Example of a large *MLC*.

Figure 2: Linear accelerator components and *MLC* example.

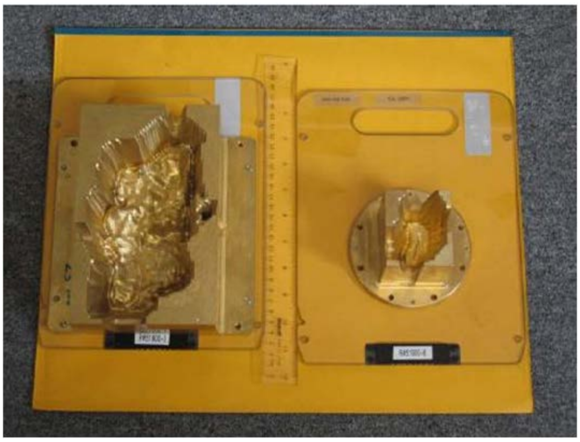


Figure 3: Example of compensator blocks.

This is an isocentric tool; the gantry can make a complete turnaround on its axis, which allows the dose to be irradiated from any direction and to be intercepted at a fixed point in space, the isocenter [6]. The treatment table, or treatment couch, where the patient gets partially immobilized, moves forwards and backwards, away from or towards the gantry, and rotates in the horizontal plane around its vertical axis.

Below the region called "X-ray Target" it is located the collimator, which collimates the beams, changing their format. Older collimators used compensator blocks to adress the change in the fluences format, as showed in figure 3 [7]. Today, the most efficient one is the Multileaf Collimator (*MLC*), shown in the figure 2b[8]. Its leaves can move in static (step-and-shoot)

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[5] Image taken from the article (Jumeau et al. [2020])

[6] A more precise definition of isocenter can be found at (Zhang et al. [2015])

[7] Image taken from the book (Almeida [2012])

[8] Image taken from the article (Baatar et al. [2018])

or dynamic fashion, in order to establish an ideal field format on each static angle or on the gantry‘s arc of movement; more about it is discussed in section 2.5. As was mentioned earlier, a binary *MLC* can extend a blade completely or not extend it at all. On the other hand, a standard *MLC* can extend its blades for all along its length.

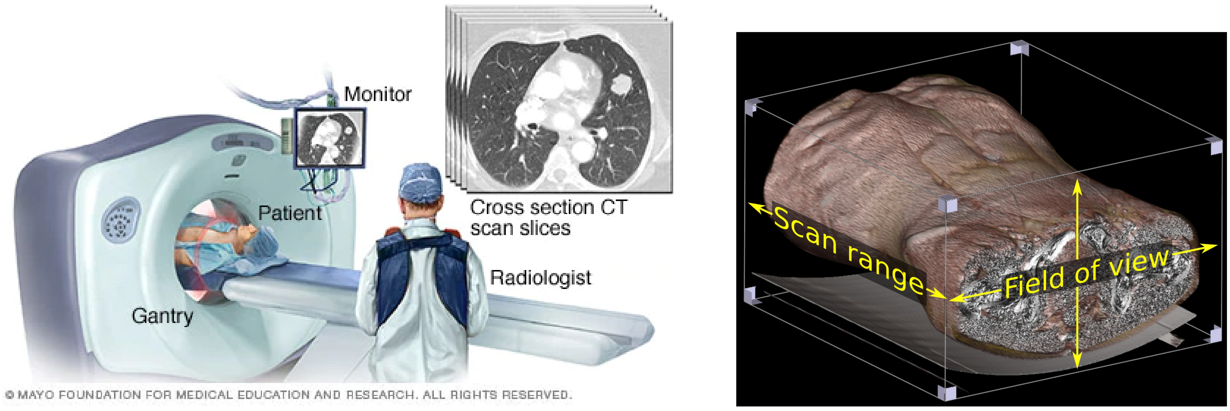
Essentially, *IMRT* is a *RT* technique that uses the *MLC* to create non-uniform radiation fluences, which are delivered to the patient from any position of the treatment beam, in order to improve dose distribution.

2.3 Computational Tomography

Once a patient is diagnosed with cancer and referred for *RT* treatment, the oncologist commonly orders a tomography (or a *MRI*), also known as *CT* scan, of the treatment region, in order to prescribe the amount of ionizing radiation dose for each treatment region measured in gray (Gy), where gray is a unit of ionizing radiation dose in the *SI*. It is defined as the absorption of one joule of radiation energy per kilogram of matter (Bureau international des poids et measures et al. [1977]).

A tomography is nothing more than a collection of radiological images, known as slices, in one of the three possible patient planes; sagittal, coronal and transverse; [9] represented in figure 4a[10], which can later be computationally collected to build a three-dimensional structure of the treatment region, as shown in the figure 4b[11], allowing for a more precise visualization of the organs which enables doctors and medical physicists to make better decisions.

In addition, a treatment planning based in an X-Ray instead of a *CT* scan may be useful in emergency situations. This practice is generally called as 2D planning.



(a) Illustration of a *CT scan* in the transversal plane.

(b) Three dimensional reconstruction of an abdomen and pelvis *CT* scan.

Figure 4: Tomography execution and 3D reconstruction.

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[9] The number of slices can vary as the *CT* scan machine changes. *TROTS* database, for instance, has *CT* scans with different numbers of slices for each case.

[10] Image taken from the website: https://www.mayoclinic.org/tests-procedures/ct-scan/multimedia/ct-scan-slices/img-20008348

[11] Image taken from the article (Haggstrom [2014])

2.4 Treatment volumes

With the *CT* scan, oncologists make the delineation of the treatment volumes before prescribing any radiation dose. The classification of these structures is displayed in the figure 5[12], followed by their description.

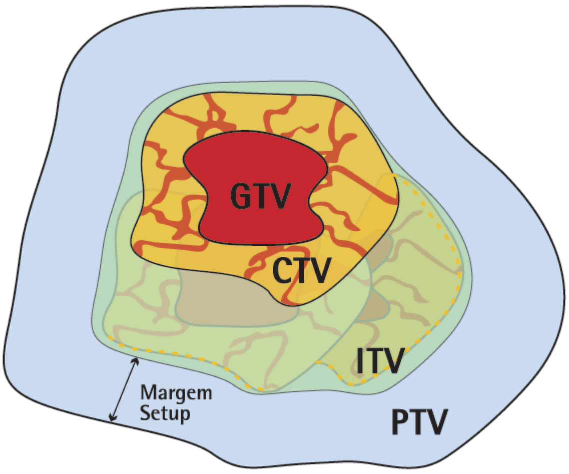

Figure 5: Treatment volumes classification.

- *GTV*, or "Gross Tumor Volume": tangible or visible volume of the disease.
- *CTV*, or "Clinical Target Volume": volume of tissue that contains *CTV* or subclinical disease not grossly visible, but with a certain probability of occurrence considered relevant for treatment.
- *ITV*, or "Internal Target Volume": defined as the *CTV* plus a margin that includes uncertainties in the size, shape and position of the *CTV* relative to anatomical landmarks (i.e., bladder filling, breathing movements, etc). This is called the inner margin.
- *PTV*, or "Planning Target Volume": the dose distribution format that must ensure with a clinically acceptable probability that the entire *CTV* has received the prescribed dose, considering geometric uncertainties such as organ movement and patient positioning on the table.
- *PRV*, or "Planning Risk Volume": similar to the previous one, refers to the dose distribution format that must ensure with clinically acceptable probability that all *OAR*'s (Organ At Risk) receive less than the prescribed dose limit, considering the same uncertainties.

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[12] Image taken from the book (Almeida [2012])

2.5 Planning

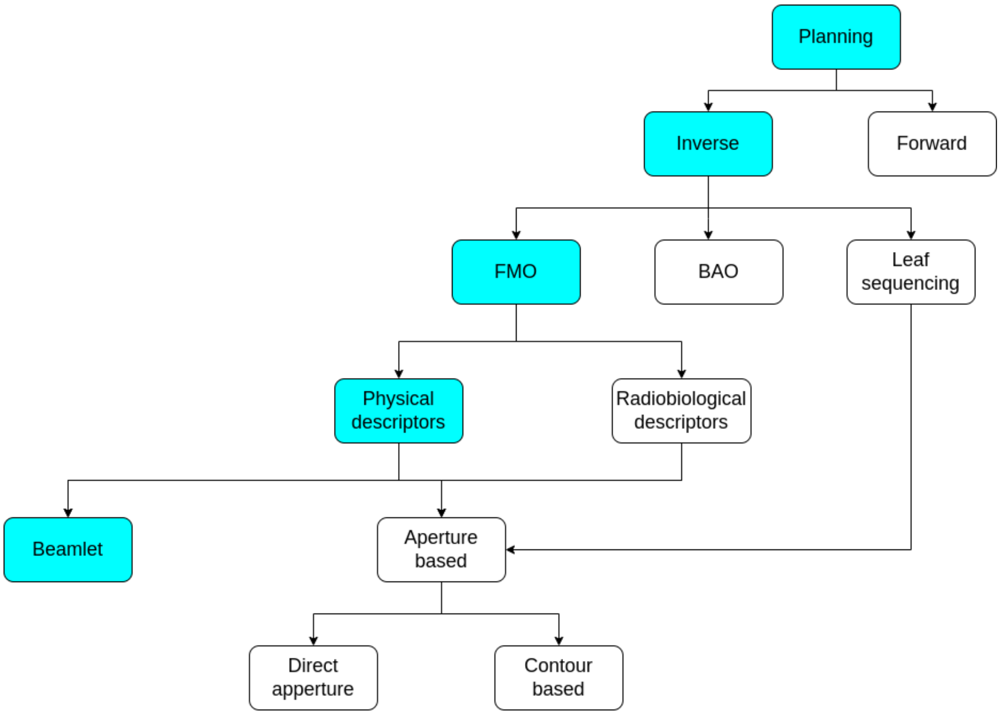

Figure 6: Radiotherapy planning categories.

In light of what has been told, this project is about the planning phase of the teletherapy to which the linear accelerator used must have a *MLC* and its dose delivery based on *IMRT*. It may seem a lot, though it is still not enough to properly define the project's context. There is not only one exclusive way to approach the planning phase, and its details are discussed in this section. Figure 6 introduces them.

It is worth explaining that, inherent to any kind of planning, the medical physicist has to decide beforehand the energy of the linear accelerator, the isocenter's spatial location, the patient's position on the treatment couch, etc. These aspects are not discussed deeply in the project.

2.5.1 Forward vs Inverse

Forward planning is a manual process of choosing the open field formats based on the Beams's Eye View (*BEV*) (Khan et al. [2021]), and their weights for each previously selected treatment angle. Then, given a first incidence, subfields that radiate part of the target are added in order to decrease hot spots (spots with excessive dose), complement the dose in uncovered regions or protect some *OAR* that is in that direction. These steps are presented in figure 7[13].

However, in cases with irregularly shaped *PTV*, concavities, or multiple *OAR*'s, the use of inverse planning is essential. While forward planning depends entirely on the operator, inverse planning incorporates the piece of software mentioned in the section 1 to automatically solve one or all the three subproblems of dose delivery: the beam angle optimization (*BAO*) problem, the fluence map optimization problem (*FMO*), and the leaf sequencing problem. The *BAO* problem aims to find the optimal angle treatments given the patient's tomography or *MRI*, together with the dose prescriptions to each structure. Similarly, the *FMO* intends to compute the optimal fluences for each chosen angle in *BAO*. Lastly, the optimal fluences calculated in

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[13] Image adapted from the book (Almeida [2012])

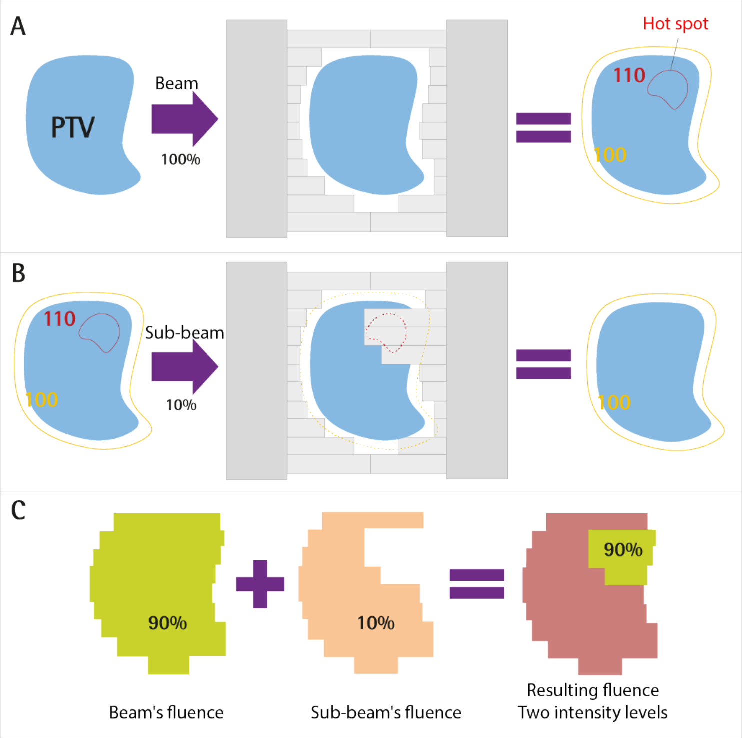
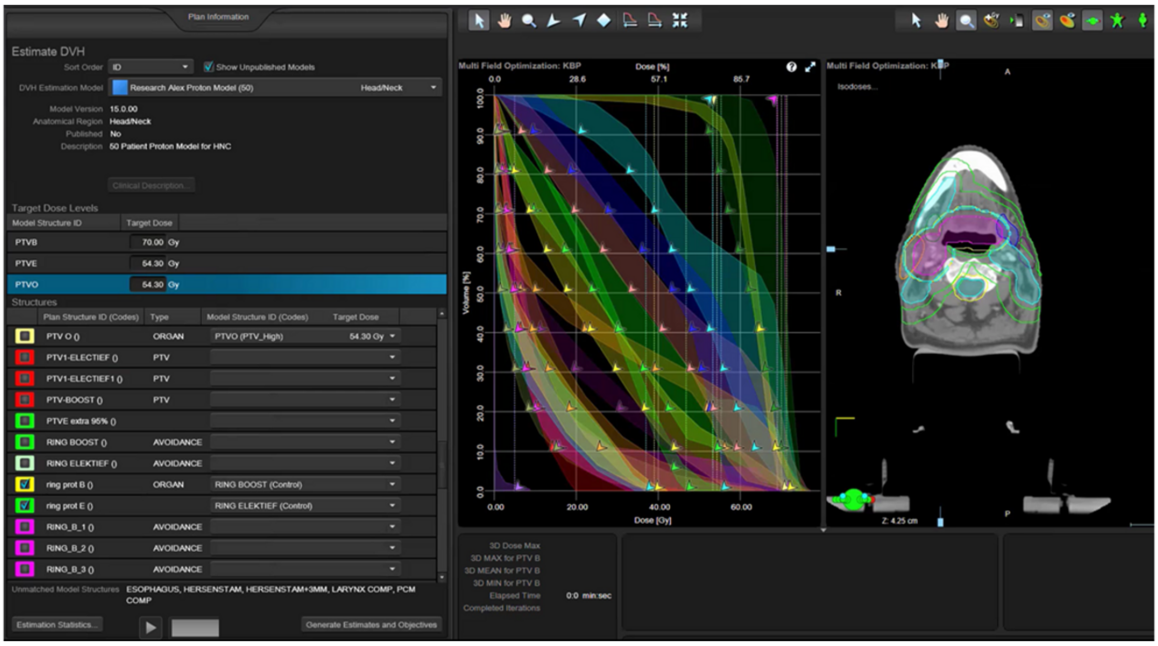


Figure 7: Example of a forward planning approach.

the *FMO* problem are decomposed into *MLC*'s segments in the leaves sequencing optimization process. A detailed explanation of the last two problems is given in sections 2.5.3 and 2.6.

It is worth noticing that, be in forward or inverse planning, the planning is entirely carried out in a *TPS*. An example of its interface is showed in the figure 8.



Estimate DVH

Sort Order: ID
☑ Show Unpublished Models
DVH Estimation Model: Research Alex Proton Model (50) Head/Neck
Model Version: 15.0.00
Anatomical Region: Head/Neck
Published: No
Description: 50 Patient Proton Model for HNC

Target Dose Levels

Model Structure ID	Target Dose
PTVB	70.00 Gy
PTVE	54.30 Gy
PTVO	54.30 Gy

Structures

	Plan Structure ID (Codes)	Type	Model Structure ID (Codes)	Target Dose
☐	PTV O ()	ORGAN	PTVO (PTV_High)	54.30 Gy
☐	PTV1-ELECTIEF ()	PTV		
☐	PTV1-ELECTIEF1 ()	PTV		
☐	PTV-BOOST ()	PTV		
☐	PTVE extra 95% ()			
☐	RING BOOST ()	AVOIDANCE		
☐	RING ELEKTIEF ()	AVOIDANCE		
☑	ring prot B ()	ORGAN	RING BOOST (Control)	
☑	ring prot E ()		RING ELEKTIEF (Control)	
☐	RING_B_1 ()	AVOIDANCE		
☐	RING_B_2 ()	AVOIDANCE		
☐	RING_B_3 ()	AVOIDANCE		

Unmatched Model Structures: ESOPHAGUS, HERSENSTAM, HERSENSTAM+3MM, LARYNX COMP, PCM COMP

3D Dose Max
3D MAX for PTV B
3D MEAN for PTV B
3D MIN for PTV B
Elapsed Time: 0:0 min:sec
Completed Iterations

Figure 8: Varian's *TPS* example called *Eclipse*

2.5.2 Physical vs radiobiological descriptors

The *FMO* is an optimization problem with no trivial formulation for the objective function. There are countless ways of modeling the relation between the radiation fluences and the patient's body.

Physical descriptors are composed simply of the dose prescriptions given by the oncologist and the tumor dose uniformity level (Almeida [2012]). A very known example showed in (Crooks and Xing [2002]) is the least-squares formulation, where the goal is to minimize the 2-norm of the difference between the prescribed dose, and the dose from the ideal fluence. The linear model approached in this project is classified as a physical descriptor as well. Radiobiological descriptors, on the other hand, consider the dose prescriptions in addition with biological parameters of tumor type and normal critical tissues for the calculation of tumor control probability (*TCP*) and normal tissue complication probability (*NTCP*) (Mesbahi et al. [2019]).

Regardless of how the flowchart represents the distinction between these two, there are formulations that, in fact, incorporate physical and radiobiological descriptors (Dirscherl et al. [2009]), aiming to preserve both qualities.

2.5.3 Beamlet vs Aperture based optimization

Beamlet and aperture based optimization are different approaches when canculating the ideal fluence map.

The figure 9[14] summarizes the difference between the two methods. In the beamlet approach, the collimator is discretized in "beamlets", and the intensity administered by each of them is determined by the time the respective *MLC* blade allows radiation to pass through. Then, the optimization model must calculate the optimal intensity (or weight) for each beamlet at every treatment angle. This is how this project's model works.

On an opposite construction, when using aperture based optimization, the collimator is not discretized in beamlets. The planning process is based on a small pre-set of apertures (*MLC* configurations) per beam direction. The optimization is then limited to calculating the optimal weights of these pre-defined openings (which can, for example, be derived from the patient's anatomy), or the simultaneous optimization of the shapes and weights of the openings. The former approach is called Contour-Based Aperture Optimization, while the latter is called Direct Aperture Optimization (*DAO*). Direct aperture optimization is more often applied in intensity modulated arc therapy (*IMAT*) and volumetric intensity modulated arc therapy (*VMAT*) (Bortfeld [2012]).

One of the main advantages of aperture optimization compared to beamlet-based optimization is that many problems that are related to blades sequencing can be avoided. Since the approach deals with the apertures directly, there is no need for leaf sequencing afterwards. In addition, established fields comprise a few segments per beam, which are similar to conventional fields and, therefore, easier to verify.

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[14] Image adapted from the book (Almeida [2012])

2.6 Leaf sequencing problem

Once the *FMO* problem is solved, the *MLC* has the incumbency of performing the dose delivery based on the ideal fluences.

Because the linear accelerator's power is constant during treatment, it is only possible to create fluences of constant intensity. Because of that, each ideal fluence is constituted by the sum of many constant fluences. Now, remember that each beamlet intensity or weight is related to the amount of time this beamlet is going to be opened, allowing radiation to pass through. Then, the *MLC* has to create a set of movements that will correspond to the time of exposure of each beamlet. The image 10 represents how this process happens with a simple example. The numbers 5, 10 and 15 represent different intensities for the beamlets painted in yellow, orange, and red, respectively.

Having said that, one must be beware this example. It does not mean that the linear accelerator can only create beams with intensity of value 5. By "constant", the authors only mean that every beamlet of the aperture in question has to have the same intensity. In other words, since the intensity is just related to the amount of time the aperture is going to be opened, the linear accelerator can create constant fluences with different intensities than 5 by just letting it open more or less time. In the same example, to create a constant fluence with intensity of value 10 on every beamlet, the machine just needs to let the *MLC* open twice the time it was needed on the constant fluence of value 5.

Also, the set of movements for each ideal fluence is not unique. Given a non-trivial ideal fluence, there are many ways of creating and ordering the *MLC* movements in order to deliver the same total dose, and the figure 10 just represents one possible solution.

The problem of finding the optimal set of movements for the *MLC* is not accomplished by this project once its interests rely just on calculating the ideal fluence.

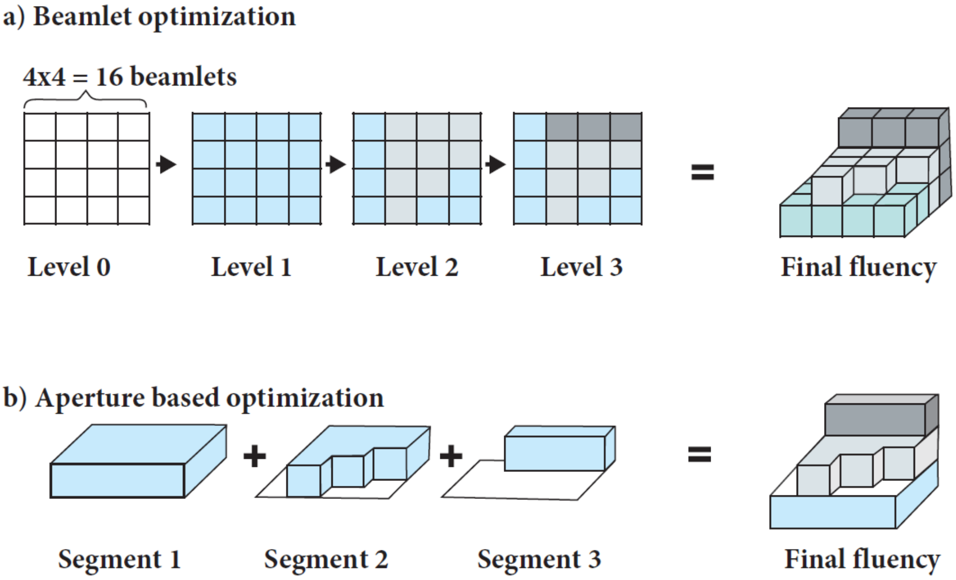

Figure 9: Beamlet vs aperture optimization.

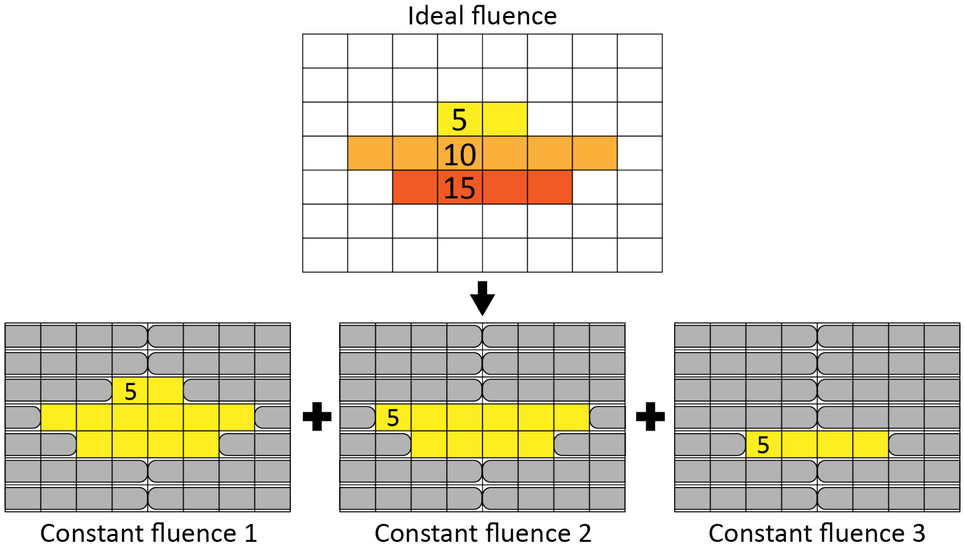

Figure 10: *MLC* sequencing of an ideal fluence example.

2.7 Planning overview

To finish the planning section, an overview of the entire process, supposing a step and shoot philosophy, is given in the figure 11[15], and a list of different methods of *IMRT* is presented in the table 1, adapted from the article (Grégoire and Mackie [2011]), as well as a comparison between different methods is presented in the image 12.

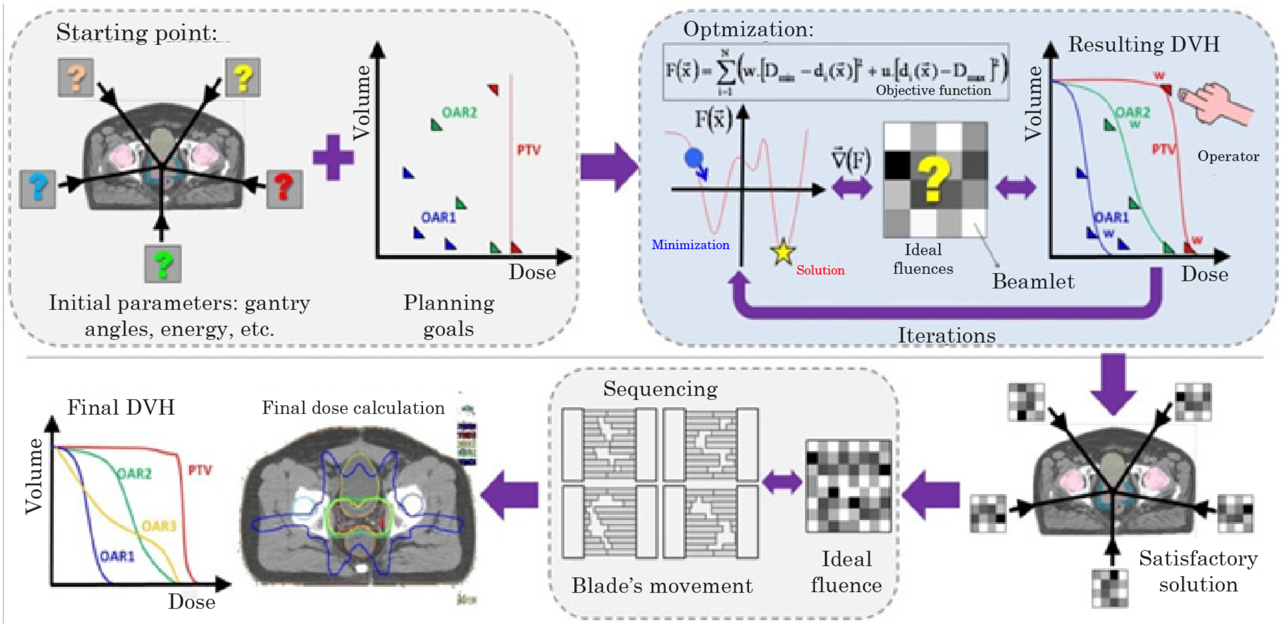

Figure 11: Step and shot planning overview

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[15] Image adapted from the book (Almeida [2012])

Type of method	Intensity modulation method	Preferred optimization approach
Compensator blocks	A beam filter designed to provide a patient-specific intensity pattern designed by an optimization procedure	Optimized beamlets
Segmental *MLC* (step and shoot)	Multiple *MLC* segments delivered from each treatment direction	Direct-aperture optimization
Dynamic *MLC* (sliding window)	Blades slide across the field at different rates	Optimized beamlets
Intensity modulated arc therapy (*IMAT*)	Blades slide across the field at different rates	Direct-aperture optimization
Volumetric modulated arc therapy (*VMAT*)	*MLC* blades move while the gantry rotates with variable speed.	Direct-aperture optimization

Table 1: Preferred optimization approaches for each *IMRT* method.

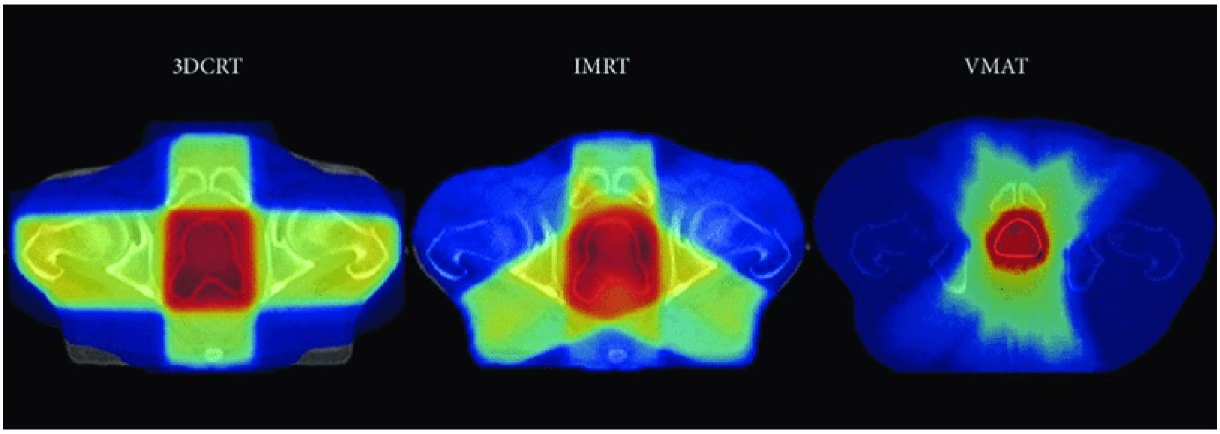

Figure 12: A comparision between *3DGRT*, *IMRT* and *VMAT* techniques.

2.8 *DDM* matrix

One very particular but important concept for one of the discussions later on in this text is the definition of Dose Deposition Matrix (*DDM*) or pencil-beam matrix. This matrix is the basis of any optimization model regarding inverse *RT* planning.

Consider the discretization of the tomography's three-dimensional reconstruction in voxels. Following the scheme shown in the figure 13, the matrix construction begins with the onset of the radiation beam, in orange, in the collimator's direction. As previously mentioned, the *MLC* can reshape the beam format, which is discretized in pixels called beamlets. The green structures represent the *PRV*, the red ones represent the *PTV*, and the grey ones are regular tissue.

Let a_{ij} be the dose attenuation coefficient of the i-th voxel with the j-th beamlet, as shown in figure 13. The decision variable x_j, called pencil-beam, is a weight that relates to the amount of time the associated beamlet is opened, allowing radiation to pass through. The total dosage received by the i-th voxel of the structure is given by the linear relationship $d_i = \sum_j a_{ij}x_j$. This equation means the longer a beamlet lets radiation pass through, the greater the radiation intensity through it and the greater the radiation delivered to the patient.

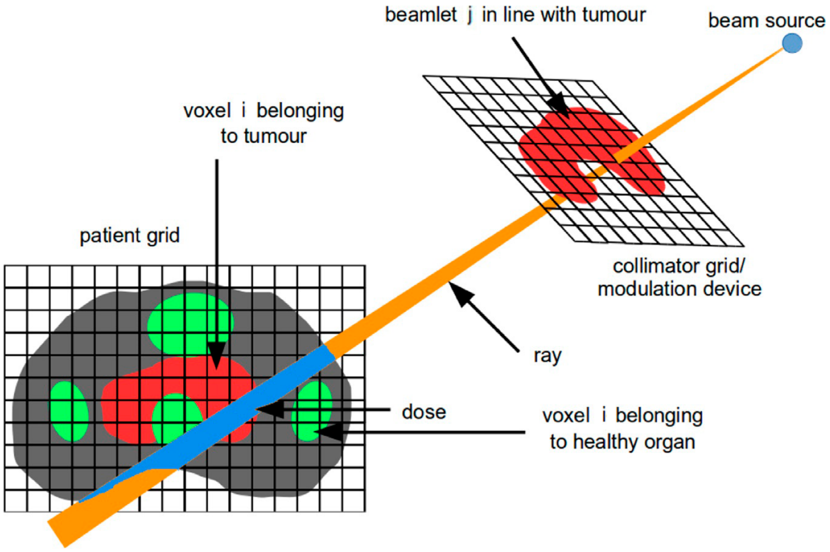

Figure 13: Patient and collimator discretizations for the pencil-beam matrix.

3 The hospital

The Boldrini Infant Center was founded in 1978 as an ambulatory by the Lady's Club from Campinas. Afterwards, the hospital was built exclusively with donations from companies and the community and was opened on May 24, 1986.

The hospital is a philanthropic institution specialized in pediatric oncology and hematology, being a national and South American reference center in those areas. The *RT* sector, however, is separated from the main building and also accepts adults. On average, 20% of their patients are the children from the hospital, and 80% come from the unified health system (*SUS*). [16]

The hospital takes place next to the Unicamp's campus in Barão Geraldo; just a 20-minute walk from the *IMECC*.

Figure 14: The Boldrini hospital.

4 Methodology and discussion

The information gathered to produce this report comes from the author's visits to the hospital since February 2020 and meetings with Guilherme Giacomini, one of the medical physicists at the *RT* sector responsible for treatment planning. Despite that, to filter the information and address the hospital's adaptability to external solvers, a set of questions were precisely created.

In the next section, the questions are presented, each followed by its answer and discussion.

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[16] The information and image was taken from the website https://www.boldrini.org.br/

5 Discussion

5.1 Technology available

- **What *LINAC*s and *TPS*s are available?**

  As discussed in section 1, the *LINAC* and *TPS* used during the treatment highly affect the treatment planning quality. Modern *LINAC*s offers (*IGRT*) (like Electronic portal imaging and Cone beam *CT*) (Chen et al. [2009]), more *MLC* leaves, more movement and isocentric precision, etc. While the latest *TPS*s has more accurate dose computations, advanced features for inverse planning, freedom to perform treatments as *VMAT*, *IMAT*, among others.

  In the Boldrini's *RT* sector, two *LINAC*s are available: a *Varian Clinac 6EX*, alongside with the *TPS Eclipse* 15.1 and a *MLC* with 120 leaves, and an *Elekta Synergy*, with its *TPS Monaco* 5.11 and a *MLC* with 160 leaves.

  The *Elekta Synergy* is the newest one, capable of performing *IGRT* with Cone Beam *CT* (*CBCT*) showed in figure 15 [17], and its *TPS* allow treatments like *VMAT* and *IMAT*, whereas the *Varian Clinac 6EX*, that is the older one, does not have any inbuilt *IGRT* feature, and its *TPS* is limited to conventional *IMRT*. Both the *CBCT* from the *Elekta Synergt* and the portal imaging from the *Varian Clinac 6EX* are routinely used.

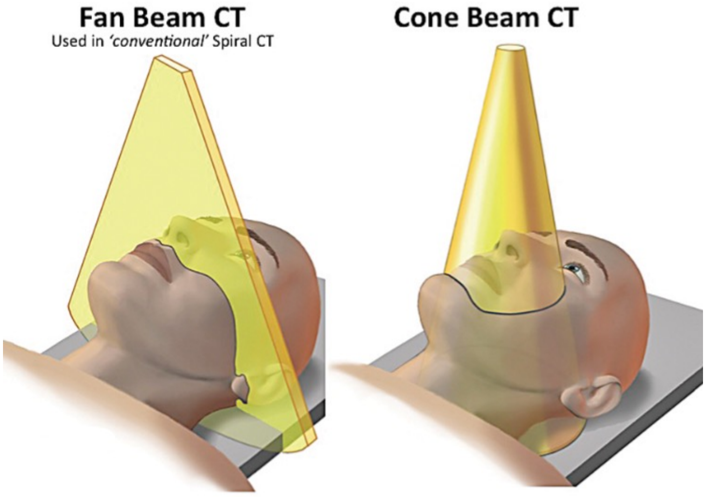

Figure 15: Conventional *CT* scan vs *CBCT*

  Even though the *LINACS* have their differences, the *Eclipse* and *Monaco TPS* are pretty recent and have many inverse planning features, making the most out of each *LINAC*, and most probably will continue to be used for many years. Therefore, updating the external solvers during this time would not be necessary. In addition, both *LINAC*s perform (*SBRT*) (El Naqa et al. [2018]), and the *Elekta Synergy* has an electron beam alongside the photon one, making superficial treatments possible with compensator blocks. Notice that inverse planning is generally not required for superficial treatments.

  That being said, since the *CBCT* is currently used only for positioning purposes and not for online adaptive planning (Lim-Reinders et al. [2017]), a positive intervention would be to create an external software with this feature, aiming to use as much information from

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[17] Image taken from the website
https://raiosxis.com/a-diferenca-entre-tomografia-fan-beam-e-cone-beam

the *CBCT* as possible to adapt the plan to the current patient's geometry. In the same philosophy, it is also possible to create online adaptive plannings using portal imaging from the *Varian LINAC*, but since the portal image contains much less information than the *CBCT*, the online plannings quality would be questionable.

- **How many computers are available for the treatment planning?**

  The machines available for the treatment planning play a crucial role in the adequate functioning of the *TPS* and the external solver. Luckly, Boldrini has a *RT* sector with four dedicated machines, all running *Windows* as the operational system, for the treatment planning:

  - Two machines with an Xeon 4110 and 32Gb of RAM running *Eclipse*;
  - Two machines with an Xeon 6132 and 128Gb of RAM running *Monaco*.

  The amount of *RAM* of both machines is more than enough for the inverse problems and dose computations to be performed without any complications, and the powerful processors are just making it faster. However, even with such processors, in some cases, the medical physicists have to let the computer run for hours, or even at night, to get the result the next morning due to the complexity of the computations in extreme situations. In fact, the Monte Carlo simulations made to compute the final deposited dose commonly require an enormous computational time (Andreo [2018]) as well as some exceptional inverse planning problems. Nevertheless, the average cases of *FMO*, *LSO* converge within minutes; only *BAO* may take a few minutes more.

  Ultimately, the infrastructure is perfect for regular computations and more complex ones, both using the external solvers and the in-house *TPS*.

- **Does the treatment couch also rotate?**

  Yes, it does. This feature allows medical physicists to create non-coplanar treatment plans. Differently than the *FMO* problem, there are many protocols for Beam Angle Configuration (*BAC*) choice because of the relatively similar geometry between patients from the same cancer cases. Therefore, some *TPS*s do not incorporate *BAO*, and this is the case for the Boldrini's version of *Eclipse* and *Monaco*. Indeed, the protocol usage might be enough for simple cases to acquire satisfactory treatment plans. On the other hand, when a bigger number of angles are necessary, or when a *IMAT* or *VMAT* is going to be performed, given the many degrees of freedom the couch and the *LINAC* have, the choice for the optimal *BAC* without *BAO* becomes nearly impossible for a human. The figure 16[18] exemplifies it.

  For that reason, and recalling that the Boldrini's *RT* sector already has efficient *FMO* and *LSO* solvers in their *TPS*s, an external solver for the *BAO* problem in step-and-shot treatments, as well as *IMAT* and *VMAT*, would be one of the most beneficial interventions for the hospital.

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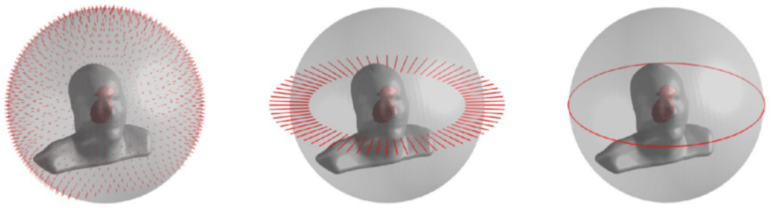
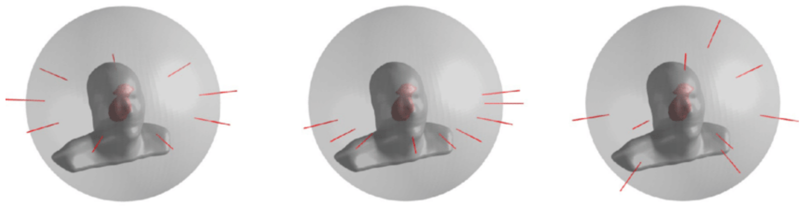
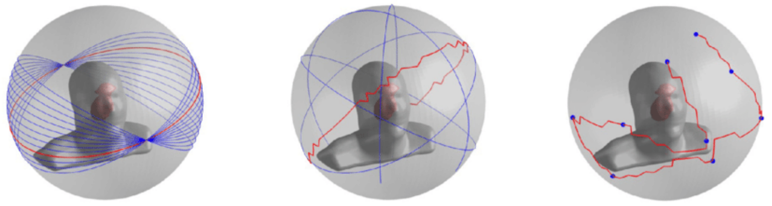
[18] Image taken from the article (Smyth et al. [2019])



(a) 4π (b) 2π (c) VMAT



(d) sns (e) BAO sns (f) NC BAO sns



(g) NC C VMAT (h) NC GC VMAT (i) NC BAO VMAT

Figure 16: Different *BAC* choices

5.2 Staff

- **How many medical physicists are available for the treatment planning?**

  There are four medical physicists available, including Guilherme. Since there are also four computers available, this is the perfect scenario for treatment planning once they do not need to share machines.

- **Does the staff have experience with inverse radiotherapy planning?**

  Yes, they do. All four of them have years of experience with inverse planning. Especially, Guilherme also has some computational skills, which substantially facilitate the dialogue with him and the rest of the staff.

- **How receptive would the staff be to an external solver?**

  Their biggest concerns are:

  - The software has to be user-friendly;
  - It should not disorganize the current planning workflow;
  - It has to be easy to setup.

  Since the external solver just offers a stand-alone feature, it does not require complex *GUI*; only the necessary to change the optimizer parameters. About the workflow, the solver is only intended to be optional while planning a treatment, and not required. For instance, when facing any difficulty, they may want to use the external solver to compare its solution with the in-house *TPS*, or utilize any feature that their *TPS* does not offer. Lastly, the solver's setup will depend mostly on the programming language used to create it. Most preferably, languages like *Python*, *Julia*, and *C* should be used due to their performance and free usage, rather than *MATLAB* and others that may require a paid license.

5.3 Clinical practice

- **How much time an "easy", "moderate", and "hard" treatment plans commonly take?**

  - Easy: 10 to 20 minutes;
  - Moderate: 1 to 2 hours;
  - Hard: 1 to 3 days.

  In easy cases, forward planning is sufficient and inverse planning is unnecessary. Therefore, the time difference between easy and moderate cases comes from the required iterations with the *TPS* inverse planning tools once these are plans where the forward approach would not provide satisfactory dose delivery. That being said, a hard case is when the treatment goals can not be achieved, so a dialogue with the patient's oncologist is required. Once these professionals are not easily available and many meets may be required, the planning phase can take several days until the treatment goals are met.

  In conclusion, it is also worth noticing that this is a common problem among treatment stations rather than a particular aspect of Boldrini. Thus, the time required for most iterations of inverse planning tools in hard cases is minimal compared to this logistic problem.

- **Does the demand require more curative or palliative treatments?**

  The *RT* sector and the hospital as a whole receive 80% of your patients from the *SUS*, and only 20% from the own hospital. Then, the majority of the treatments are curative rather than palliative.

  One must be aware that curative treatments are generally harder to plan than palliative ones since curative treatments require an ablative dose to the *PTV*. Therefore, the *RT* sector as a whole has to be able to create feasible ablative plans. Luckily, Boldrini has all the infrastructure needed for that, along with an experienced staff to create the plans.

- **Does the usage of 2D planning is a common practice?**

  Only in emergency cases, when the patient has to be treated as fast as possible.

  Therefore, most treatments performed are planned using a *CT* scan, where the inverse planning tools are more useful. They can also be adapted to 2D plans. Nevertheless, the use of inverse planning tools in emergency cases might not be the optimal workflow the hospital would adopt.

5.4 *TPS*

- **Does it is possible to export the *DDM* matrices from the *TPS*?**

  As far as Guilherme is concerned, it is not possible. A direct consequence is that for the external solver to work, it would be required to generate the *DDM* matrices outside of the *TPS*, to work as an input for the external solver. The most used software for that is *CERR* (Deasy et al. [2003]).

  Fortunately, *CERR* is easy to use, and the only additional step for the medical physicists to take, rather than generating the matrices, would be to put those files in the same folder the solver is located.

- **Does the *TPS* allow the manual change of the ideal fluences?**

  Yes, *Eclipse* and *Monaco* allow. This is important for *FMO* external solvers, once the fluences should be changed directly on the *TPS* to match the solution given by the solver. However, changing these fluences one by one would take too much time. Maybe an approach with *DAO* should be more interesting, or even finding a way to copy and paste the solution from the external solver to the *TPS*.

- **Does the *TPS* offer any inverse planning feature?**

  Both *Eclipse* and *Monaco* offers *FMO* and *LSO*, but not *BAO*, as already mentioned in the third question.

5.5 Additional information

- **4D *CT* scan for moving *PTV*.**

  For cases where the *PTV* position oscillates with the respiratory or peristaltic movements, a 4D *CT* scan is performed to track the entire *LINAC* trajectory within a cycle and then treat this whole area. Both *Eclipse* and *Monaco* have specific features to deal with 4D planning, so an external solver would not be necessary in those situations.

6 Conclusions

This project discussed how the current clinical practice and infrastructure of the Boldrini Infant Center's *RT* sector would be compatible with external solvers for inverse *RT* planning. It was concluded that their workflow is already pretty optimized, but there is room for improvement. First, since their *TPS* does not include *BAO*, a *BAO* external solver for step-and-shot as well as *VMAT* and *IMAT* trajectories would surely refine their *BAC* choices. Also, the *CTCB* in the *Elekta* is currently being used only for positioning corrections; therefore, an external feature for online adaptive *RT* could be created in order to make the most out of the *CTCB* feature.

From an academic perspective, the Bodrini Infant Center also disposes a great environment for research. Doubtlessly, the staff welcomes researchers for testing state-of-the-art algorithms to compare with their in-house *TPS*; as long as the criteria of the section 5.3 are met.

Ultimately, the work also aims to inspire new researchers to work with *RT* planning, and for those who are willing to, encourages the pursuit of effective dialogue with oncologists and medical physicists, focusing on humility and empathy to elaborate on the basic knowledge of what happens in treatment stations. As is well put by David Sheppard:

> *It is our hope that the community of optimization experts will be able to offer further insights that will improve our ability to solve these difficult problems.*

7 Supplementary information

- Boldrini infant center's website `https://www.boldrini.org.br/`;
- You can ask for a *Monaco* demo for free on the following link `https://www.elekta.com/products/radiation-therapy/monaco/`

8 Acknowledgments

I would like to express my deepest appreciation to Guilherme Giacomini and the team of medical physicists at Centro Infantil Boldrini, who guided me on my very first steps studying radiotherapy planning and who let me visit the treatment stations throughout the years.

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