

## Mémoire

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*Master Thesis*

RapidPlan Implementation with gEUD for prostate  
cancer

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*Radiotherapy department CHU Namur*

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Master en sciences physique à orientation  
spécialisée en radiophysique médicale

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PALEM-TORRACO Eduardo

# Abstract

A radiotherapy department uses radiation to kill cancerous cells of the patient.

Planification treatment is a big part of the work for a physicist in a radiotherapy department. The goal is to achieve an acceptable coverage of the target while sparing normal tissues. There are different strategies to achieve the goal, but they are dependant on the physicist experience. All the strategies are iterative process that are time consuming.

New software and algorithm are based on the the Knowledge Based Planning, that aims to make the process more efficient and less reliable on the physicist experience.

Varian has developed his version of this algorithm, RapidPlan. It is an algorithm that uses machine learning to try and predict an achievable dose from the patient anatomy.

In this thesis I implemented RapidPlan for the prostate cancer treated with VMAT with double dose level that follows the prescription 66Gy - 50Gy. I used gEUD objectives for the implementation, as they were shown to be a powerful tool to achieve an acceptable planification.

I created "\_in" and "\_out" structure on the OAR to use with the gEUD, as it has been proven of their efficacy when combined with gEUD objectives. For now the use of double gEUD for RapidPlan is still not advised, as it will still need some manual tuning after the use of RapidPlan. Thus the use of a single gEUD with one or more objectives gives better results.

The use of "\_in" and "\_out" structure are proven to be useful in lessening the hotspots and the usage of a closed loop strategies to help having a better final model.

The RapidPlan model created for VMAT can also be used for IMRT treatments, even if they are rarer. In the case of a IMRT planification needed, the RapidPlan model can still be used.



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# Chapter 1

## Introduction

### 1.1 Radiotherapy

Radiotherapy is a technique used for killing malignant cells exploiting ionising radiation. It can be used alone as a curative treatment or as a part of an adjuvant therapy. It is most generally used against cancerous tumours. In this case the purpose of the ionising radiation is to damage the DNA of the tumour which will lead to its cellular death.

Ionising radiation are radiation that can be in form of electromagnetic waves ( $\gamma$ -rays or X-rays) or particles (protons, neutrons,  $\beta$ -particles,  $\alpha$  – *particles* or heavy nuclei) that have enough energy to ionise atoms or molecules, directly or indirectly, by detaching one or more electrons from them [1]. There is not a fixed energy threshold to distinguish between ionising and non-ionising radiation because the ionisation energy changes for each atom or molecule.

#### 1.1.1 Historical context

One can say that the history of radiotherapy started in 1895 with the discovery of X-Rays by the German physicist Wilhelm Conrad Röntgen. Soon after the discovery of X-Rays there were some early experiments which proved that exposure to X-Rays could produce negative effects on the area of interest [2].

On the 29th January 1896, the first cancer treatment using X-Rays was done [3]. We had to wait until to 1902 to have the first proposal for the first type of dosimetry. This dosimetry was done with a salt-mixture that when it was exposed to X-Rays it would change colour from yellow to green [4]. In 1928, after the first Association of International Radiology conference, the use of ionisation chamber was widely adopted [5].

Up until the 1950s, there was not a real treatment planning. As a matter of fact radiotherapy was based on low energy with low penetration power. It was only when the first mega-voltage systems based on  $^{60}\text{Co}$   $\gamma$ -rays was introduced that started the first radiotherapy

period.

At the time the treatment planning was only based on basics radio-graphic images. In 1972, CT images started to be used for the treatment planning, that was not much more complex than plans done with basics radio-graphic images.

In 1982, a Swedish medical physicist introduced Intensity Modulated Radiation Therapy. The IMRT was able to be created thanks to the change of the shape of the collimator with a multi-leaf collimator (MLC). The first machine with this technique was commercialised in 1992.[6-7]

Due to the introduction of the MLC, new techniques could be born.

Since then, radiotherapy has advanced a lot and was more focused on 3D patient-based dosimetry.

### 1.1.2 Basics Radiotherapy

There are different kinds of radiotherapy : external beam radiotherapy and internal radiotherapy (Brachytherapy). In this thesis, I will focus on external beam radiotherapy with beam of photons of 6MV.

#### 1.1.2.1 Interaction of photons with matter

Photons can interact with atoms in different ways.

The can interact with : the whole atom, tightly bounded electrons, loosely bounded electrons, the nucleus

There are 3 main interactions for the photons :

- Photoelectric effect
- Compton scattering
- Pair production

We can see, on the fig.1.1, the dominant interaction considering the energy of the incident photon and the atomic number of the target material.

##### 1.1.2.1.1 Photoelectric effects

When photons have a sufficient energy to completely ionise an electron of the atomic shell it can undergo the photoelectric effect. The electron will completely absorb the photon energy, some of the energy will be used to break the binding between the electron and the nucleus and the rest will be transformed in kinetic energy for the ejected electron.

The probability of this interaction is proportional to :  $\frac{Z^3}{E^3}$  [8]

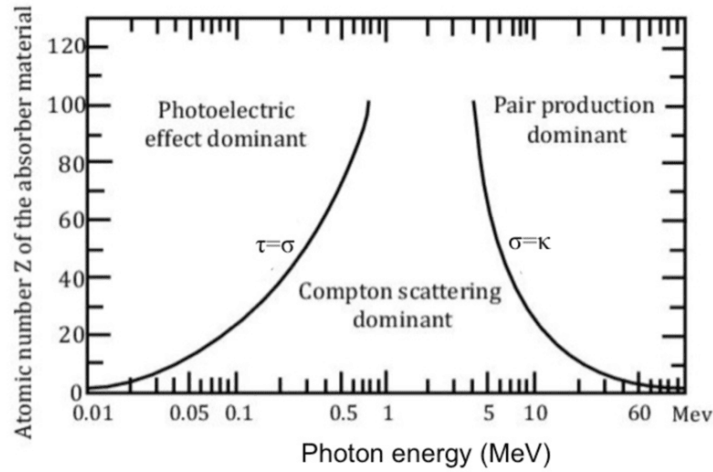


Figure 1.1: Probability of the photon interaction with matter considering the energy of the photons and the atomic number of the target material [10].

- $Z$  = Atomic number of the nucleus target
- $E$  = Energy of the incident photon

#### 1.1.2.1.2 Compton scattering

When photons have a higher energy than the binding energy of the electron, the photon could be scattered by the electrons without being absorbed and it could give some energy to the electron. As a result this will give us a photon with a lower energy than the incident one and a recoil electron.

Compton scattering depends a bit on the  $Z$  of the target material and it is the dominant interaction in human tissues between photon energy of 30keV and 30MeV.[8]

The probability of this interaction is :  $\frac{1}{E}$ . [10]

#### 1.1.2.1.3 Pair production

Above the threshold of 1.022MeV, photons can interact with the electromagnetic nuclear field of the target nucleus. The photon can disappear and become an electron-positron pair. The pair will share the energy of the photon to create the mass and kinetic energy.

Those pair will loose their kinetic energy by interacting with the matter around them. The electron will be absorbed into the electric shell of an atom and the positron will be annihilated with an electron creating 2 photons with an energy of 511keV [8].

The probability of this interaction is proportional to :  $Z \times \ln(E)$  [10]

#### 1.1.2.2 Creation of the photon beam

They can be generated via an accelerator or by a radioactive material. In this case, it will engendered using a linear accelerator. [8-9]

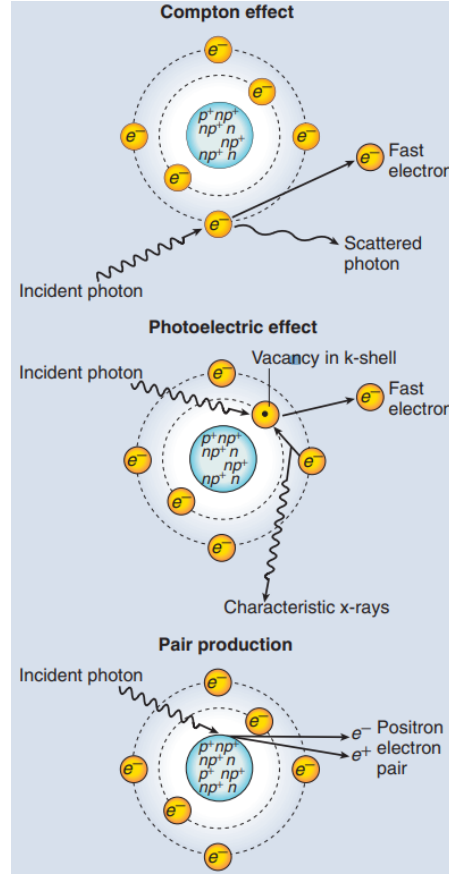


Figure 1.2: 3 main interactions of photons with matter. Photoelectric effect for low energy photons. High energy photons for Compton scattering. Higher energy photon for pair production.

We can define the energy of the EM radiation by linking it to the frequency of the electromagnetic wave :

$$E = h \times \nu$$

- $h$  = Plank constant :  $6.62607015 \times 10^{-34} \text{ m}^2 \text{ kg s}^{-1}$
- $\nu$  = Frequency of the electromagnetic wave [ $s^{-1}$ ]

As already stated above, the photons beam is generated using a linear accelerator, which will use an EM field to accelerate a beam of electrons up to the treatment energy. Afterwards with the use of electromagnets, the electron beam will be deviated and will strike a target that will generate a beam of photons. The photon beam will then pass through a flattening filter to ensure an homogeneous beam before it goes towards the patient [9].

On fig.1.3., we can see the sketch on how the photon beam is created after that the electron beam hit the target.

Most external radiotherapy machines are isocentrics, which means that the machine's head will rotate around an axis that passes between the isocenter and the centre of rotation of the machine. The isocenter is the cross point between the axis of rotation of the gantry, the collimator

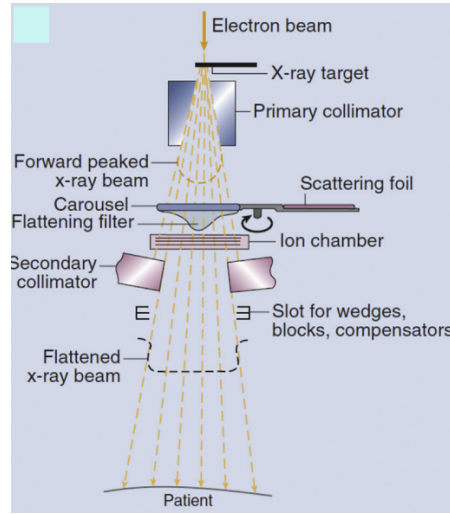


Figure 1.3: Schematising of the electron beam hitting the target and creating the photon beam. The primary collimator will shape the beam size. The flattening filter will create an homogeneous dose field. The ionisation chamber will check the dose at the exit of the machine's head. The secondary collimator will allow us an even accurate beam shape [9].

and the couch. This type of machine will allow us precise calculation between the patient position and the treatment head position. The treatment head can rotate around the isocenter because of the gantry. We can see on fig.1.4 a sketch of the isocenter. This point is at the convergence of the 3 axis of rotation of the radiotherapy machine : the gantry, the collimator and the couch [9].

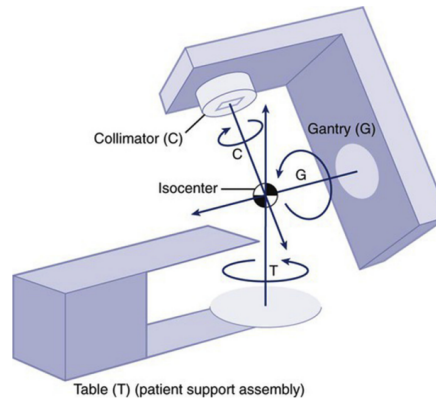


Figure 1.4: Schematising of the isocenter of gantry for an external radiotherapy machine [9].

### 1.1.3 Practical basics of radiotherapy in hospital

When a patient comes for a radiotherapy treatment, he must undergo some steps before getting the treatment delivery.

The classical procedure is listed as follow and will be explained more carefully in the next paragraphs.

1. Simulation
2. Target volume delineation
3. Treatment planning
4. Treatment delivery

#### **1.1.3.1 Simulation**

The patient will first go through a simulation. After the simulation, the initial treatment will be generally delivered a few days later. This step serve different purposes.

It allows to generate a reproducible setup: the patient can be in the same position for each treatment session with the help of immobilisation devices. As a matter of fact, uncertainty in patient position will lead to uncertainty in the delivery of the dose.

Simulation will also allow to take a CT scan of the area of interest. By doing so it is possible to identify target volumes and normal tissue. It is also possible to plan and calculate the needed dose. [9]

#### **1.1.3.2 Target volume delineation**

The radiotherapist will use the CT-scan taken at the simulation and will delineate not only the target volume but also the normal tissue of the patient. This is done on the CT-scan, but the delineation can be done with other types of imaging (MRI, PET-scan, SPECT) that could aid to have a better definition of the tumour volume. [9]

The structure delineated follow the ICRU Nomenclature :

- GTV : Gross Target Volume
- CTV : Clinical Target Volume
- ITV : Internal Target Volume
- PTV : Planning Target Volume
- OAR : Organ at risk

##### **1.1.3.2.1 Gross Target Volume**

The Gross Target Volume is the gross demonstrable extent of the tumour. The delineation can be done if the tumour is visible and big enough. In some cases, like for a post-operation radiotherapy, the GTV may not be possible to delineate. [11]

**1.1.3.2.2 Clinical Target Volume**

The Clinical Target Volume is formed by of the GTV and the tissues whereas it is a presumed tumour. The delineation of the CTV supposes that there are no tumour cells outside the volume. [11]

**1.1.3.2.3 Internal Target Volume**

The Internal Target Volume is recommended by the ICRU 62. The volume includes the CTV with an internal margin to compensate for the internal physiological movements. [11]

**1.1.3.2.4 Planning Target Volume**

The Planning Target Volume is formed by the CTV with an internal margin and a setup margin. Internal margin are the same one as the ITV and the setup margin are created for the setup uncertainties.[11]

This margin can be calculated using the Van Herk Formula [12] :

$$M_{PTV-CTV} = \alpha\Sigma + \beta\sigma - \beta\sigma_p$$

- $\Sigma$  = Systematic errors
- $\alpha$  = Coefficient for the systematic errors for the coverage of a certain percentage of the patients
- $\sigma$  = Random errors
- $\beta$  = Coefficient for the systematic errors for the coverage of a certain percentage of planning volume
- $\sigma_p$  = Random errors due to the beam penumbra

**1.1.3.2.5 Organ At Risk**

The Organ At Risk are the healthy organs situated near the target volume which are susceptible to being irradiated.

There could be added a margin for an organ at high risk, and so creating another volume : Planning Organ At Risk. The added margin would follow the same setup as the PTV. [11]

**1.1.3.2.6 Treated Volume**

The treated volume is the volume that is covered by the isodose of prescription. Therefore the treated volume is generally a bit larger than the PTV. [11]

**1.1.3.2.7 Irradiated volume**

The volume receiving a significant dose is called the irradiated volume. This volume is always larger than the treated volume and than the PTV. This depends on the technique used.[11]

We can see the different volume in fig.1.5.

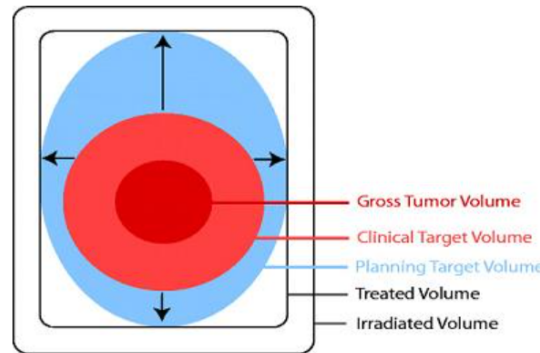


Figure 1.5: Schematising of the margins of the planning volume [11].

### 1.1.3.3 Treatment planning

After delineating the volume, the radiotherapist prescribes the desired dose coverage and the OAR constraints. This doing is called the clinical goal. And it may differ for each case.

Finally the medical physicist or the assistant will use a treatment planning system. This treatment planning consists in optimising a treatment plan that would meet the goals set by the radiotherapist.

The physicist and dosimetrist can select different types of treatment to achieve the goals. The target for the physicist is to get a better sparing of the healthy tissues while still having an acceptable covering dose for the PTV. [9]

This part will be explained with more detail in the next section.

### 1.1.3.4 Treatment delivery

The treatment will be delivered to the patient in the same position as the simulation. The RTTs are in charge to deliver this treatment.

## 1.2 Dosimetry

As said before, in this section, the treatment planning will be explained with more details.

### 1.2.1 Basics Dosimetry

Before going further with the explanations I would like to define some basics concepts.

### 1.2.1.1 Dose

There are two way to measure the dose : the absolute dose and the relative dose.

The relative dose is the ratio between 2 doses. It can be used to assert a certain factor or parameter. The relative dose can also be used as a ratio of two different doses that are measured or simulated with different parameters.

The absolute dose is the value of the measured or calculated dose.

In radiotherapy when we speak about dose, we talk about the absorbed dose which is a quantity of the energy deposited in the matter by ionising radiation per unit mass. The unit we are talking about is the Gray [Gy]. This is used for every kind of ionising radiation [13].

$$D = \frac{d\epsilon}{dm} \quad [Gy] = J \, Kg^{-1}$$

- $d\epsilon$  = Mean energy absorbed by the medium from ionising radiation
- $dm$  = Mass of the medium having absorbed the energy from the ionising radiation

### 1.2.1.2 Percentage depth dose curve

The percentage depth dose curve (PDD) relates the absorbed dose given to a medium by a radiation beam to the depth of the beam. The curve is normalised at the  $d_{max}$  at 100% as we can see on fig.1.6. [17]

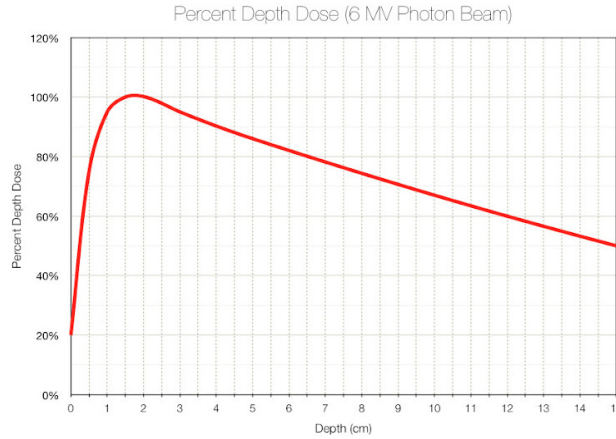


Figure 1.6: Example of a PDD curve for a 6X beam with a field size of  $10 \times 10 \text{ cm}^2$  .[18]

As we can see on fig.1.6, there is a build-up region when the beam enter a material. This build-up is due to the fact that most electrons liberated by the 6MV beam have energies between 1 to 2 MeV up to 6MeV, and electrons with those energies travels around 1-2cm, which explain the build-up region. After the peak, it will start to fall-off due to the losing of energy.

### 1.2.1.3 Monitor Units

A monitor unit, is a measure for the output belonging to each machine. [21]  
At the CHU Namur, for the 6MV photon beam, they calibrated the machines in order to have  $100\text{UM} = 0.798\text{Gy}$  when measuring the dose at DSP90 and 10cm depth in a water phantom. They calibrated the machines as such, for having  $100\text{UM} = 1\text{Gy}$  at the peak of the PDD curve.

### 1.2.1.4 Dose Volume Histogram

The DVH can be defined as an histogram that relates the dose given into the relative volume of a structure [14]. While planning, we can use the Dose Volume Histogram to see the dose given to the PTV or one or more OAR. The DVH is really helpful for comparing easily doses from different planifications or to analyse quickly the quality of a planification. The DVH is not the only tool for analysing the quality, but it can be a fast and useful tool for this task. As we can see on fig.1.7 there is an example of DVH.

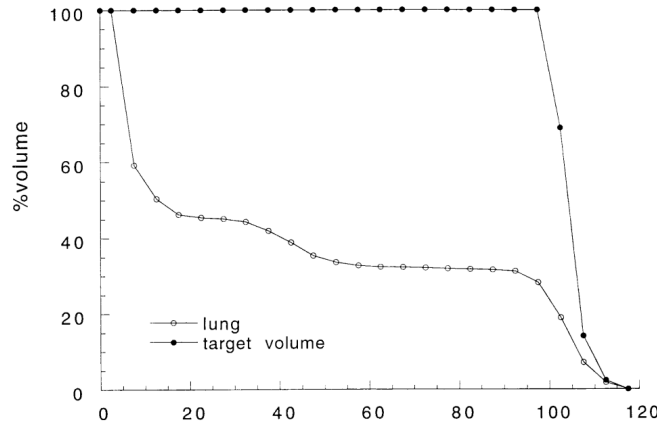


Figure 1.7: DVH of the PTV and lung of a planned plan [15].

### 1.2.1.5 Isodose

The isodose is defined as the line in which all points who belong to the line have the same dose.

In all cases, the line reattaches to itself, and we know on account of its definition that all the points inside the isodose have a higher dose than the specified value.

As we can see on fig.1.8 where the isodose 95% prescription cover the whole of the target volume.

### 1.2.1.6 Fluence

The fluence is defined as the total number of particles crossing over a surface of unit section at a certain distance of the source of ionising radiation.[16]

The dose delivered at a certain point will also be related to the fluence and the particle energy.



Figure 1.8: Example of the isodose D95% that covers the PTV, the green line is the isodose 95% of the prescribed dose and the red is the PTV.

### 1.2.2 Planification treatment

The TPS I used is Eclipse from Varian.

The goal of the planification treatment is to have an adequate coverage of the PTV while sparing the OAR.

In radiotherapy the most used technique for planification treatment is the inverse planning. There are 2 type of inverse planning :

- IMRT : Intensity - Modulated Radiation Therapy.

IMRT is a technique of radiotherapy planning that uses CT-scan to calculate the dose absorbed by the patient, as all the others techniques. This technique consists in using different beams at different angles with a modulated intensity and with a static gantry. The intensity modulation is done by the MLC and calculated by the treatment planning system following the objectives given by the physicist.

There are 2 type of IMRT : step and shoot and sliding window. The difference between the two is that step and shoot, wait for the leaf of the MLC to stop moving before irradiating and that the sliding window irradiate while the leaf of the MLC are moving.

- VMAT : Volumetric Modulated Arc Therapy.

VMAT is a more advanced technique than the IMRT. The treatment is delivered by different arcs rather than different beams. The gantry is moving during the beam period. The beam intensity is modulated in the same way as it was in the IMRT sliding window.

#### 1.2.2.1 Objectives function

In the inverse planning, the physicist adds the constraints on the different structures of the patient and the TPS calculates the optimised plan in accord to the constraints asked. The TPS create with the constraints a "cost function" that will be minimised by modulating the

fluence of the beams or arcs.

The cost function is : [20]

$$F_{obj} = \sum_{PTV} F_{PTV} + \sum_{OAR} F_{OAR} + F_{NTO}$$

- $F = \xi w(d_i - p)^2$ 
  - $w \equiv$  Linear function of priority of each objective
  - $\xi \equiv$ 
    - \* 1 if the objective is reached
    - \* 0 if the objective is not reached
  - $d_i \equiv$  The dose at the  $i_{th}$  iteration
  - $p \equiv$  the dose of the objective

There are different objectives that can be used and modified during the planning optimisation : Upper, Lower, Mean, Upper gEUD, Lower gEUD, Target gEUD, NTO.

#### 1.2.2.1.1 Upper

It is the maximum dose to a percentage volume of the structure. If the calculated dose is higher than the one asked by the function, then the upper function is reached. It is commonly used for putting limits to the OAR.

#### 1.2.2.1.2 Lower

It is the minimum dose to a percentage volume of the structure. If the calculated dose is lower than the one asked by the function, then the lower function is reached. It is commonly used on the PTV because that the volume is covered by the prescription dose.

#### 1.2.2.1.3 Mean

If the calculated mean dose of the whole structure is lower than the one asked by the function, then the mean function is reached.

#### 1.2.2.1.4 gEUD

The gEUD is defined as : [20]

$$gEUD = \left( \sum_i v_i D_i^a \right)^{\frac{1}{a}}$$

- $v_i =$  Fractional organ volume receiving a dose  $D_i$

- $a$  = Parameter describing the volume effect

The parameter  $a$  has been defined to be organ specific in the literature , but there are only a few studies that tried to estimate the  $a$  value for different organs. [20]

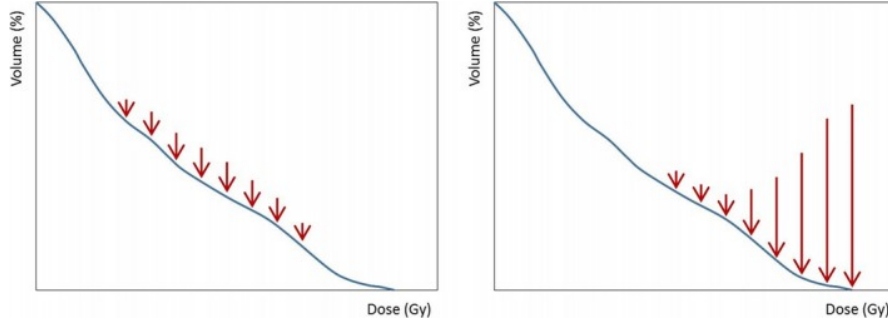


Figure 1.9: The schematising of the concept for the gEUD. The arrows indicate the strength applied to the DVH for different  $a$  value. On the left  $a = 1$ . On the right  $a > 10$ . [20]

The gEUD cost function is treated in the same way as the normal cost function. The main discrepancy is that the variation of doses become the difference of gEUD.

In Eclipse, there are 3 gEUD function, they are the same gEUD basic function that need to reach the equivalent uniform dose defined as the gEUD.

Nevertheless in order to have a better understanding, these functions are separated in 3 categories:

- Target gEUD :  $a \in [-40, -1]$  it is defined for the exact equivalent uniform dose value
- Lower gEUD :  $a \in [-40, -1]$  it is defined as the minimum equivalent uniform dose value
- Upper gEUD :  $a \in [1, 40]$  it is defined as the maximum equivalent uniform dose value

On fig.1.9. and fig.1.10. We can see the effect of the  $a$  on a OAR DVH and for a PTV DVH with a high  $a$ .

- $a \rightsquigarrow -\infty \Rightarrow \text{gEUD} \approx \text{Minimum dose}$
- $a = 1 \Rightarrow \text{gEUD} \approx \text{Mean}$
- $a \rightsquigarrow +\infty \Rightarrow \text{gEUD} \approx \text{Maximum dose}$

[20]

In a clinical study, we can see on fig.1.11 the influence of gEUD dosimetry for a whole rectum, cropped rectum and a 4mm cropped rectum.

The best dosimetry done with the gEUD were done with a cropped rectum at 4mm. And the influence of the " $a$ " were minimal. [20]

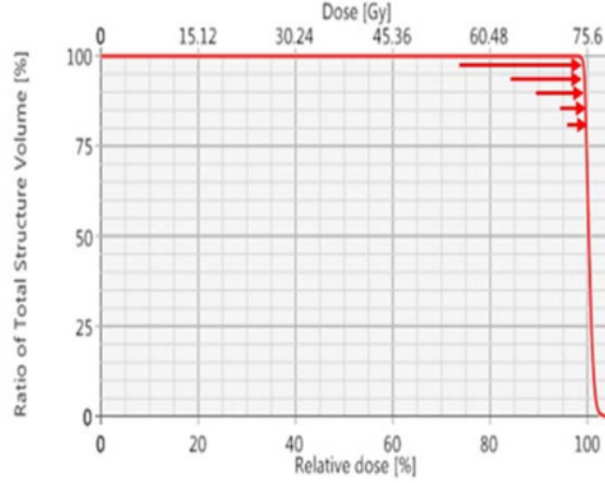


Figure 1.10: Example of a Target gEUD with a high  $a$ . [22]

In the same study, they looked at the DVH behaviour with different " $a$ " for different crop. And with increasing " $a$ " the usefulness of a cropped rectum become more and more prominent. That is normal, because the higher the " $a$ " the more the gEUD will work on the high doses of the DVH.

With low " $a$ " we can see that the use of a cropped 4mm rectum is less useful, even if we can still see that it lower the DVH at low doses. We can see those effects on fig.1.12. [20]

#### 1.2.2.1.5 NTO

Normal Tissue Objective is a spatially varying constraint in Eclipse used to limit the dose to healthy tissues by steepening the dose gradient at the PTV edges.

You can selected 2 NTO in Eclipse, they follow the same formula, but the automatic one changes its parameter following the planification, and the manual one is where the user changes the parameters [21].

$$F_{NTO}(x) = f_0^{-k(x-x_{start})} + f_\infty(1 - e^{-k(x-x_{start})}), \forall x \geq x_{start}$$

- $x_{start}$  = Distance from planning target volume
- $f_0$  = Start dose
- $f_\infty$  = End dose
- $k$  = Fall-off

## 1.3 Prostate Cancer

Prostate cancer is the second most frequent cancer found in men worldwide and the fifth cancer leading death worldwide.[22]

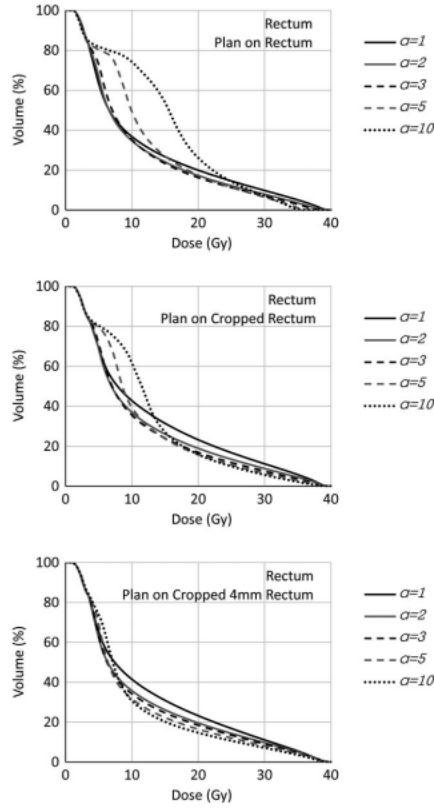


Figure 1.11: Whole rectum DVHs of prostate case for different gEUD  $\alpha$  value settings. Plans optimized on the whole rectum, OAR cropped by the target, OAR cropped 4 mm by the target. [20]

The prostate is a gland found only in males, it produces some fluids that are part of the semen. The prostate is situated below the bladder and behind the seminal vesicle. And finally there is the urethra that goes through the centre of the prostate. We can see a sketch of the prostate anatomy on fig.1.13.[23]

The prostate cancer, like all other cancer, begins when some cells start to grow out of control, ergo becoming tumoral cells. The vast majority of prostate cancer are adenocarcinoma, which is a cancer developed by the glands cells.

There are different treatments for the prostate cancer. These treatments will depend on the cancer stage, on the age and the health of the patient.

If the cancer stay internally at the prostate the treatments are: External radiotherapy, Brachytherapy, Cryosurgery, High-intensity focused ultrasounds and prostatectomy.

If the cancer becomes metastatic then hormonal therapy and chemotherapy are the common treatments employed.[24]

External beam radiotherapy, is one of the most important tools to cure localised prostate cancer because it is the common therapy for men with intermediate or high-risk of side-effects. [40-41]

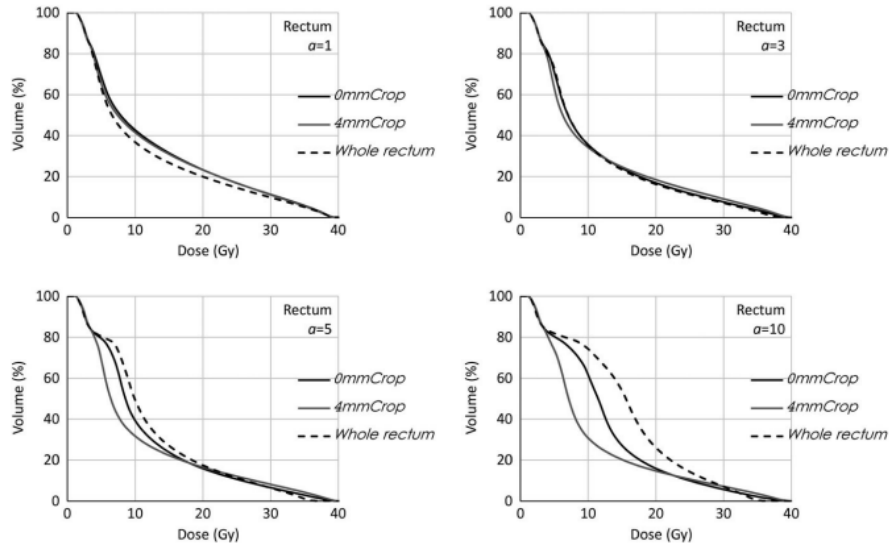


Figure 1.12: Whole rectum DVHs optimized on different OARs (whole OAR, cropped by the target, cropped 4 mm by the target). a gEUD parameter set to 1, 3, 5, 10. [20]

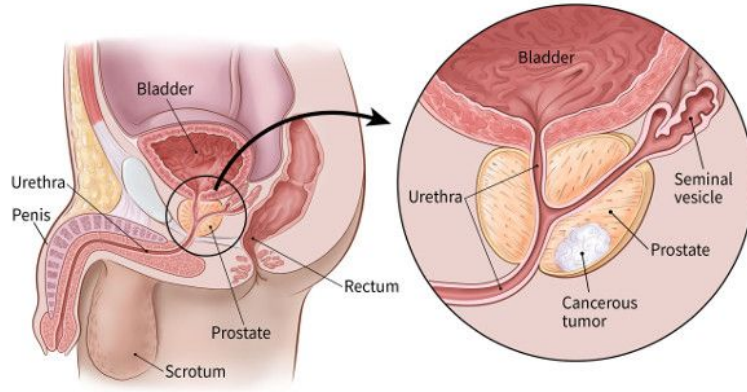


Figure 1.13: Schematising of the prostate site and how the cancer is developed in the prostate. [23]

### 1.3.1 Epidemiology in Europe

In Europe during 2020 the prostate cancer is the fourth most common cancer in Europe and it is the most common one among men. It is the third most deathly cancer in males as we can clearly see in fig.1.12.

The estimated number of new cancer in Europe in 2020 is of 148.1 cases per 100 000, with a cumulative risk of being diagnosed with prostate cancer before the age of 75 is 8.18% . The estimated new death of prostate cancer in Europe in 2020 is of 35.2 cases per 100 000, with a cumulative risk of dying of prostate cancer before the age of 75 is 0.97%.

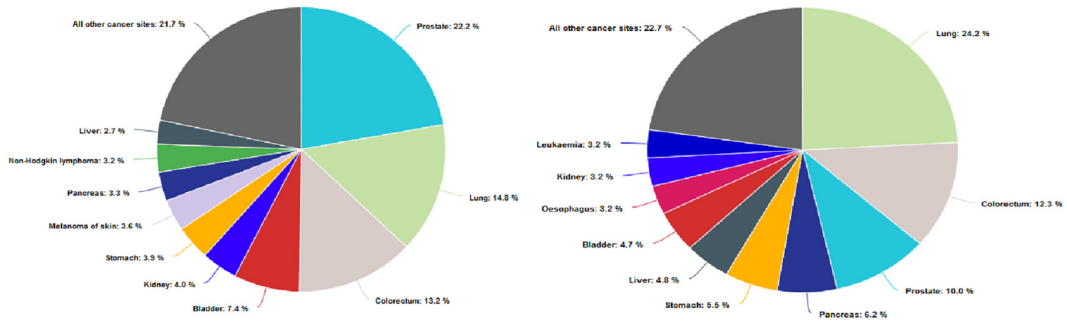


Figure 1.14: Incidence and mortality of prostate cancer in Europe in 2020.

## 1.4 RapidPlan

All planning strategies aim to cover the PTV with enough dose while sparing all the other healthy tissues even though it is difficult to assess the best possible trade-off between the healthy tissues and the PTV.

As stated before, IMRT and VMAT are inverse planning strategies, where the physicist needs to input parameter into the TPS to find the best possible solution of the planification.

This is an iterative process and it is time consuming and user-dependent. For a plan to be considered acceptable, it needs to check all the clinical goals set by the radiotherapist, but even if all the clinical goals are observed, it does not mean that the plan could be optimised even further. Thus this process is not perfect and could lead to sub-optimal plan and large variations of plan quality. [29-30]

This process is really dependent on the physicist abilities to plan and on his experience. To solve this problem, to simplify the process and to make it more faster, the "Knowledge Based Planning" was investigated. [25]

### 1.4.1 Knowledge Based Planning

KBP has two main functions : it can predict an achievable dosimetry for a new planning using prior knowledge and it can also help the physicist in the planification. [29-30-31]

The efficacy of the dose prediction is based on :

- Quality of the planning data inserted in the model
- Similarities between the old plan inserted in the model and the new plan
- The regression of the different structures inserted in the model

In this thesis, I will use the KBP RapidPlan engine from Varian Medical system, introduced in the Eclipse treatment planning system in the release 13.5.

RapidPlan uses old plans to create a new model for estimating the DVH and setting the best objectives on the OAR and PTV set in the model, in order to have the best planning. The predicted plan has a similar quality of those set. This solve the problem of consistencies between different plans and speed up the process.

RapidPlan uses a regression analysis to correlate the geometry of the OARs and the PTV with the DVH, by using a set of pre-planned plans.

## 1.4.2 RapidPlan estimation algorithm

### 1.4.2.1 Algorithm

An algorithm is a finite sequence of instruction, done by a computer, used to solve specifics problems or to perform computations. By making use of artificial intelligence, algorithms can perform automated deductions and to use the appropriate mathematical and logical test, following various path. [51]

An heuristic algorithm, is an algorithm used for solving problems when a classical method is too slow or when only an approximate answer is needed. It also does not guarantee correct or optimal results. The reason is that the algorithm will trade accuracy and precision for speed. It can be seen as a shortcut.

**1.4.2.1.1 RapidPlan Algorithm** RapidPlan is a Knowledge Base Planning, implemented in Varian Eclipse treatment planning system. Its primary objective was to improve planning time, plan quality and plan quality consistency. [30]

RapidPlan uses machine learning technique that is supervised by the user, in other words it is a supervised machine learning. It needs to be trained with at least 20 cases. During the utilisation of RapidPlan for a new planification, it provides its objectives according to the set of plans used in the model. [39]

### 1.4.2.2 Machine Learning

Machine learning uses algorithms that receives input data to predict output value. As more data is added to these algorithms, they will optimise and improve their performance, by developing "intelligence". Machine learning is a subset of artificial intelligence.

Artificial intelligence is a term used to describe a machine or, in this case, an algorithm that mimic and display "human skill" such as learning and problem solving.

"Machine learning is the study of computers algorithms that can improve automatically through experience and by the use of data" .

In this case, we will feed RapidPlan with prior existing treatment plans. Only then our machine learning task is to predict what DVH could achieve with its proper geometry due to the new treatment. We only need to insert the following input : beam, target and OAR geometry. After

a complex process, the algorithm gives us the output, which is the resulting plan.

The algorithm is based on heuristic principles. A heuristic technique is an approach of problem solving, learning or discovery that employs a convenient method. It is not guaranteed to be optimal or perfect, but sufficient enough for the time being. This principle is used in cases where finding a perfect solution is difficult and time consuming. That is why heuristic methods are used to speed up the process of finding a satisfactory solution.[28]

The algorithm will be useful only if the remaining level of uncertainty is acceptable and the estimation model is applicable to a large variety of cases.

### 1.4.2.3 DVH Estimation Algorithm

The DVH estimation models are trained with a set of plans, thanks to their structure set, dose and field geometry. It has 2 phases : extraction and training.

We will need to insert the extracted data, as mentioned for machine learning, into the algorithm and then we can train it. When fully trained, we can use the DVH estimation model with a DVH estimate, with upper and lower bound, and optimisation objectives for the planner. As we can see on figure 1.15.

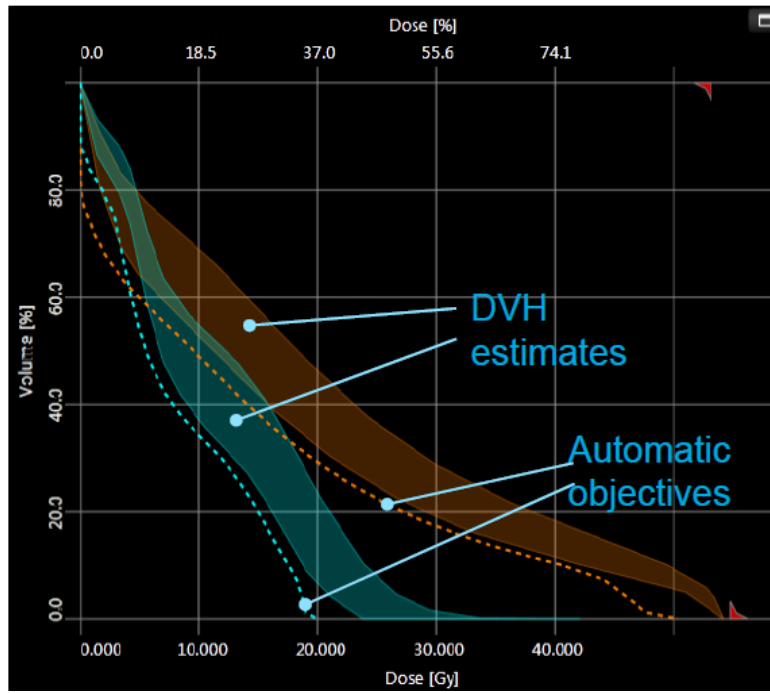


Figure 1.15: Example of a DVH estimate and the objectives set using RapidPlan. [28]

For different cases, we will need to feed the algorithm with different numbers of samples depending on the region of interest. Varian advises us with the following samples [28]:

- Diagnosis specific : between 20 and 30 plans
- General pelvic/abdomen region : between 30 and 50 plans

- General chest region : between 50 and 70 plans
- General H&N region : minimum 70 plans

In those basic principles, behind those numbers, the more the anatomy of a patient moves, the more cases you need. In general, our target are fairly similar in cases of pelvic/abdomen region and are almost the same in case of a specific diagnosis.

In this thesis, we will try to implement RapidPlan for diagnosis specific case. More information will be given in the following pages.

#### 1.4.2.3.1 Extraction Phase

The algorithm starts with the extraction phase, which is done individually for each plan.

Then we have the OAR partitioning and each OAR in a plan has a separate model. The OAR will be segmented based in on-field and target geometry, thus being partitioned in smaller sub-components. For the volume partition, it will use segment model with a 2.5mm of structure resolution.

The OAR will be partitioned at the start with in-field region and out-of-field region. For the in-field part, the dose will be greatly affected by the optimisation and the overlapping part with the PTV, which will have a dose level comparable to it. The geometric evaluation will be calculated for the whole structure : OAR volume, overlap (with PTV volume), out-of-field, and joint target volume. As we can see on fig.1.16 the out-of-field and in-field region [28].

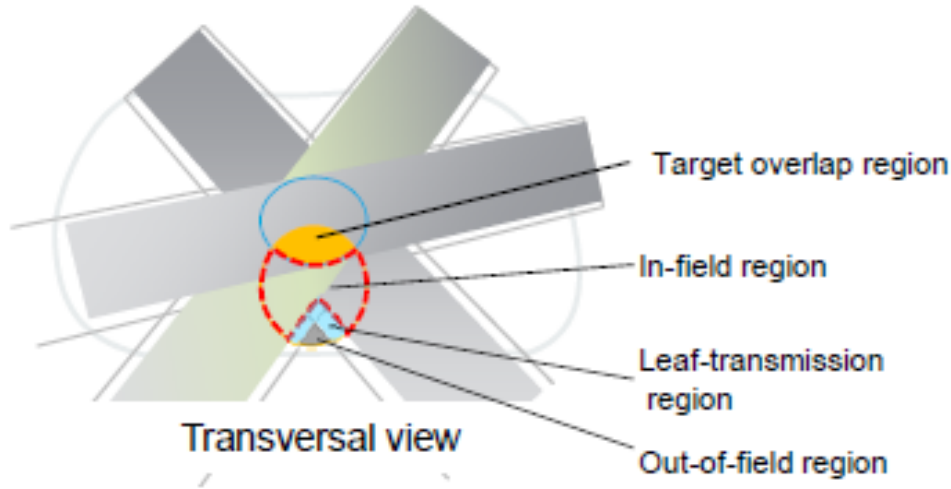


Figure 1.16: Schematisation of the partitioning done by RapidPlan algorithm for an IMRT planification. Where it segments the part of the target following the geometry of the beam [28].

For the partitioning of the OAR structures there is a different weight for each part of the structure during the optimisation :

- Out-of-field volume : will receive only the scattered dose.
- Leaf-transmission: the dose received in this area will not be strongly affected by the optimisation.

- In field : the dose received in this area will be the most affected affected by the optimisation.
- Overlap with the PTV : dose levels will be comparable to target distribution.

For the regression of each structure that has been used and trained, the algorithm needs at least 20 different plans where those structures are present. If the minimal number of structures present in the plans is not met, then the algorithm will only use their mean and standard deviation for the DVH estimation curves. The mean and the standard deviation need at least 2 data points. If even those minima are not met, then the model will not be trained for those structures. Thus a default model will be used.

There are 3 default models, that are used for a different geometry part of the structure :

- Default model overlap : all the overlap volume with the PTV will receive 100% of the prescribed dose.
- Default leaf-transmission model : all the leaf-transmission volume of the structure will receive 4% of the prescribed dose.
- Default out-of-field model : all the out-of-field volume of the structure will receive 0Gy.

We can see on fig 1.17. the part of the DVH affected by this reasoning. And that the DVH will be a sum of the various partitions of the structures.

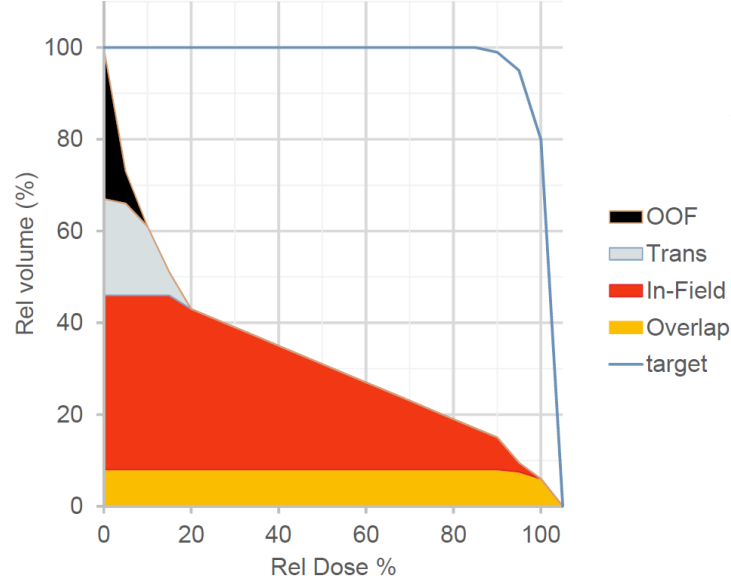


Figure 1.17: DVH extraction from a planification following a normal partition[28]

It starts from the overlap partition. This part of the DVH can not be optimised, as it is a volume part where we need to give the dose.

Next, the in-field partition is added to the cumulative DVH. This partition can be greatly affected by the optimisation, as a consequence we can try to reduce the dose as low as possible.

Afterwards, the leaf transmission partition is added. The dose in this volume is just received on

account of the geometry. The beam will not be blocked by the jaws, but only by the MLC. The dose in this partition cannot be really optimised by the reason of the geometry.

Finally the out-of-field region. This partition follows also the same principle as the others.

For evaluation of the geometry, the algorithm will take into account multiple target shapes and dose levels.

The expected behaviour is to try to spare normal tissue. Once the geometry has been set, RapidPlan will limit the dose to the distributions achievable. Hence the geometric "signature", that is the geometry of the beam and may be static (IMRT) or dynamic (VMAT), should be correlated to the planned dose.

Varian uses the "Geometry-based Expected Dose" or GED. The GED uses the distance from the voxel to the target surface per each target.

$$GED(i) \propto \sum_{f=1}^n \sum_{t=1}^m \delta_t \times \frac{e^{-\lambda h(i)}}{h(i)^2} \times C_{t,f,l}$$

Where :

- $\sum_{t=1}^m \delta_t$  : sum on the target dose levels.
- $\frac{e^{-\lambda h(i)}}{h(i)^2}$  : PDD where
  - $\lambda = \text{attenuation coefficient}$
  - $h(i) = \text{Source Target Distance.}$
- $C_{t,f,l}$  : tissue sparing coefficient for target t, calculated for field f, and fanline l (in field f)

In the fig.1.18 we can see the differences between the real dose slice and the GED for a 7 field IMRT planification.

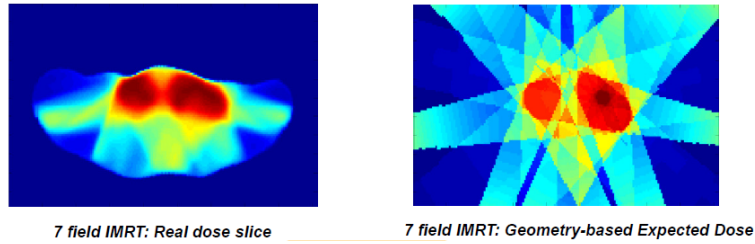


Figure 1.18: Difference between the real dose slice and GED in a 7 field IMRT. [28]

GED is a parameter used to characterise a given PTV, OAR and field geometry. It is calculated for all voxels in the data-set henceforth creating a GED-volume histogram.

As we can see in fig.1.19., voxel 1 and 2 are at roughly the same distance from the PTV, but voxel 1 is closer to the source than voxel 2. Because photons have attenuation in the tissues and they follow the inverse square from the source, the GED in voxel 1 is higher than the GED

in voxel 2. The  $h(i)$ , as mentioned before, is the source target distance, that can be split in the source skin distance, and the skin target distance :

$$e^{-\lambda \times h(i)} = e^{-\lambda \times (SSD + STD)} = e^{-\lambda \times SSD} + e^{-\lambda \times STD}$$

For the same line, we know that the SSD is constant, hence the GED is only due to the attenuation and the inverse square.

We can also add a rule; if the fanline does not intercept a PTV, the GEDs of all the voxels contained in that fanline are 0.

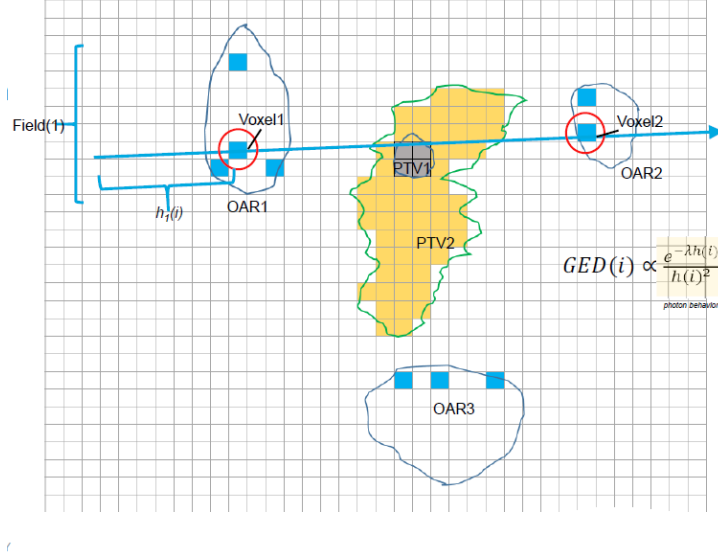


Figure 1.19: Influence of the PDD in the GED. [28]

In fig.1.20., we can see that voxel 2 and 4 are at the same distance from the source and they have the same PDD. But in this case, the fanline for voxel 2 passes through the PTV 1 and PTV 2, so it is expected to have a higher dose than the dose for the voxel where its fanline only passes through PTV 2. This is due to the fact that PTV 1 has a higher prescription dose compared to PTV 2, thus forcing to have a bigger fluence passing through PTV 1. thus we multiply the PDD by the target dose levels.

$$GED(i) \propto \sum_{t=1}^m \delta_t \times \frac{e^{-\lambda h(i)}}{h(i)^2}$$

As we can see in fig.1.21., voxel 5 and 6 have both similar distance from the source and target "skin". They both go through the same target, but voxel 5 intercepts a longer distance of the target than voxel 6. This propriety is characterised by including 2 additional factors that can be defined by 4 parameters:

- $C_{t,f,l}$  = tissue sparing coefficient for target t, field f and fanline l
- $d_{tl}$  = distance of fanline l travelling inside target t

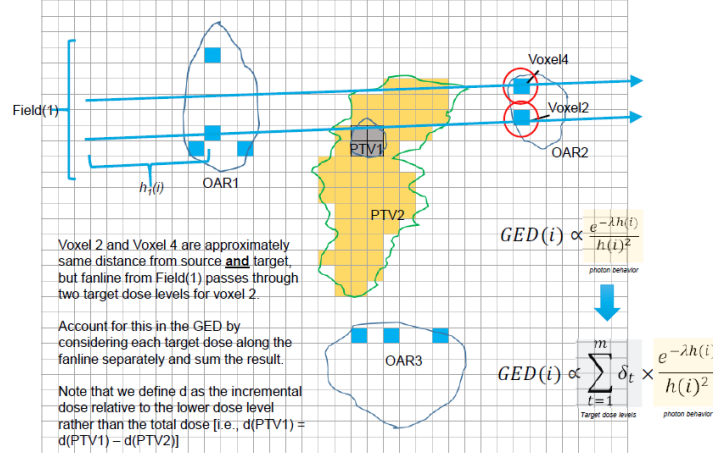


Figure 1.20: Influence on the GED for different dose level target, where dose PTV 1 is higher than dose PTV 2. [28]

- $G(d_{tl})$  = is a monotonically increasing function that describes the intensity differences between different fanlines in a single field
- $H_f$  = longest distance of any fanline in field  $f$  travelling inside the PTV

Hence, in the same field, different beamlets will need to be modulated in because of their trajectory into the PTV. If the beamlet passes through a bigger portion of the target, then its intensity will be higher than a beamlet that goes through a smaller portion. This characteristic is captured by the inter-field modulation factor  $G(d)$ , which is incorporated into the wider coefficient  $C_{t,f,l}$ . This coefficient is the summary of both  $H_f$  and  $G(d_{tl})$  [28].

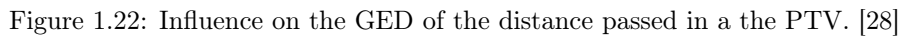
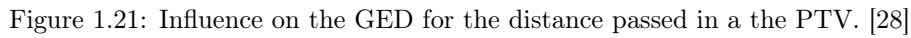
$$C_{t,f,l} = G(d_{tl}) \times H_f$$

$$GED(i) \propto \sum_{t=1}^m \delta_t \times \frac{e^{-\lambda h(i)}}{h(i)^2} \times C_{t,f,l}$$

Finally, in fig.1.222 we can see that the GED of a certain voxel can have a contribution from multiple fields. In conclusion, we need to sum for each trajectory intercepted by voxel  $i$ . [28]

$$GED(i) \propto \sum_{f=1}^n \sum_{t=1}^m \delta_t \times \frac{e^{-\lambda h(i)}}{h(i)^2} \times C_{t,f,l}$$

Once we calculate the GED for each voxel, we can determine the DVH of both the GED and the real dose for a given OAR. Then, the algorithm tries to find correlations between the 2 parameters. If a correlation can be found, then giving a new geometry, it could predict the achievable dose. [28]



Training is done for the entire set of plans. Each volume partition is trained separately. The algorithm calculates one model per region, and the sum of the different regions leads to a model for each OAR. Then there is the analysis of the differences between the GEDs and DVH, which can lead to the regression model.

To obtain the different PCA, you have to first subtract the mean DVH curve from all the DVH curves. Then, you have to subtract the PC1 (first partial component), which is the parameter that represents the majority of the volume left and so on until you can reconstruct the original histogram with less than 5% of error.

25

easily.

On fig.1.21. You can see the representation of the partial component analysis.

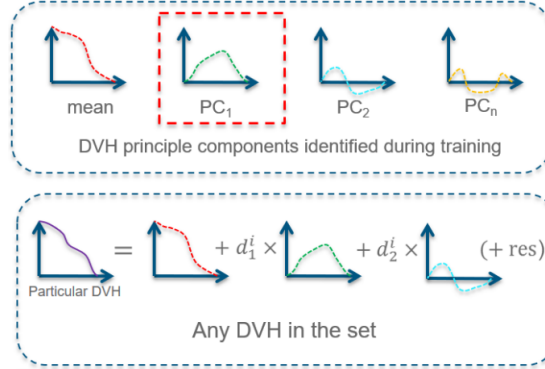


Figure 1.23: Example of a partial analysis component and the parametrization of a particular DVH. [28]

The regression model is calculated for the in-field region for each OAR per each DVH PCA. The algorithm uses the step-wise regression, which is an iterative process that will finally lead to convergence.

The first iteration is called "forward" and it adds input to the DVH PCA. The second one is called "backward", which subtracts the parameters to the first iteration until there are no more parameters to add or subtract. Basically, the regression model is equal to a set of coefficients that can be used to estimate the principal component score of the DVH from the geometry. The coefficient are what RapidPlan find to characterise a DVH for a new model.

Moreover there are built in control for the model configurations like the following : Cook's distance, Modified Z-metrics, Studentized Residual Metrics.

- Cook's distance : A parameter used to estimate the influence of a data point when performing a least-squares regression analysis
- Modified Z-metrics : The modified z-score that tells us how many standard deviations away a value is from the mean
- Studentized residual metrics : It is the quotient resulting from the division of a residual by an estimate of its standard deviation. It is used for the detection of outliers.

### 1.4.3 Literature for RapidPlan

Even if RapidPlan has been widely studied, unfortunately I could not find any paper that stated the optimisation objectives of their RapidPlan model. Consequently, before beginning the implementation process I experimented with some RapidPlan models and the gEUD, without quantifying the different models, thus I did not wrote in this paper those models, but just the finals one.

RapidPlan has already been widely studied in different treatment sites since its introductions. Those studies have already proven its usefulness in improving the quality of plans, cutting plan timing and enhancing inter-patient consistencies. Unfortunately, not a single paper quantified the improvements. [32-34-35-36-37-41]

RapidPlan has been proven to standardise the planning quality between planners with widely different experiences and between different centres. [36-37]

Even after the benefits of the implementation of RapidPlan have been widely proven, the use of RapidPlan is still not widely implemented, even if it is still growing. This is due to the lack of time for implementing it. Indeed, its implementation is a time consuming process and, as a matter of fact, a lot of centres do not have neither the time nor the manpower to do such a job.

This problem has been already tackled by some studies. One of the solutions was the introduction of a script-driven automated planning. But smaller centres may not rely on this approach due to the lack of older planification available during the same time span.[38]

The correlation quality between the structure's geometry and the DVH estimation is relative to the quality of the set in the RP model. It is also dependant on the consistent quality of the set model, on the regression of the predictive models and on the correlation between geometry model set and geometry of new plans. Consequently, a set with high quality plans with a relatively generalised geometry with enough consistency must be chosen. [32-33-34]

RapidPlan implementation is an iterative process and an heuristic method and as a consequence even if it is not as user dependant as the treatment planning it still is dependant on the constraints settled by the physicist [29]. But afterwards, it may lead to a better consistency between different plans.

The implementation of RapidPlan with a closed loop strategy has been proven effective by the literature. A closed loop strategies consists in creating a new RapidPlan model, model B, by feeding it with the plans optimised thanks to the precedent RapidPlan model A. [35-38]

But this technique must be applied with caution, because by doing too much iterations during the closed loop strategy it may lead to an overfitting of the structures used in the model.

The usage of the optimised plans for a new RapidPlan model will lead to a decrease in usefulness of our RapidPlan model and it will become less and less generalised model. And as a result, the plans will be more and more similar. [35-38]

Furthermore some studies have shown the feasibility of using a RapidPlan model, implemented with VMAT models, for IMRT planning, in the case of the same treatment site. This can be possible because a full-arc VMAT covers all possibilities for the field angles in IMRT. Plus the GED algorithm of RapidPlan is independent from the type of treatment.

The study has shown that a RapidPlan model trained with only VMAT planification will lead to an improved organ sparing both quality and consistency related to a manually optimised IMRT plan. However, Wu and al. still recommend a manual processing after the use of RapidPlan for a better tuning of the optimisation. [37]

A weak point in using RapidPlan with auto-generated priorities (priorities generated by RapidPlan), for the planification where the beam need to go trough an heterogeneous medium, is that it requires a manual modification to reach an acceptable dose homogeneity. In the meanwhile, acceptable planification were generated with fixed priorities for the prostate cancer planification.

Even though, the plans were clinically acceptable, it was demonstrated that an expert physicist could still improve the planification. Consequently, it is recommended by some papers that a manual optimisation should be done immediately upon the usage of RapidPlan.

A RapidPlan planification could still be optimised further, even so the usage of RapidPlan still reduced significantly planning time, thus still being useful. [42-43-44]

It also has been exposed that there is no statistical difference between having a RP model with or without geometric outliers. A geometric outlier is a treatment planification in the model set that differs vastly from the other models.

Statistically pulling out from a RP model the geometric outliers makes no change in the final planification. [45]

Finally, it has been observed that there are small changes going from a model set of 20 patients to a model set of 60 patient. The changes were minimal, but still useful. [46]

## Chapter 2

# Methods

### 2.1 RapidPlan Implementation

#### 2.1.1 Selection Process

We wanted to focus on the prostate treatment with 2 dose levels because they were the most used treatment for prostate cancer at CHU Namur.

At the CHU Namur, the prescription dose used for a prostate treatment with 2 dose levels (SIB : Single Integrated Boost) are :

- 70Gy/2Gy - 57.75Gy/1.65Gy : given in 35 fractions
- 66Gy/2.64Gy - 50Gy/2Gy : given in 25 fractions
- 66Gy/2Gy - 56.10Gy/1.7Gy : given in 33 fractions
- 60Gy/3Gy - 44Gy/2.2Gy : given in 20 fractions

The 2 dose levels are given simultaneously. The location of the dose levels will be explained in the following paragraph.

And their usage in the time spanning from October 2019 to October 2021 were :

Prescription Dose	Total number used	Percentage time used
70Gy/2Gy - 57.75Gy/1.65Gy	22	13.1 %
66Gy/2.64Gy - 50Gy/2Gy	100	59.52 %
66Gy/2Gy - 56.10Gy/1.7Gy	8	4.76 %
60Gy/3Gy - 44Gy/2.2Gy	38	22.62 %

Table 2.1: Statistic of the prescription dose usage.

As we can clearly see on table 2.1 the most used dose prescription, at the radiotherapy service of the CHU Namur, for prostate cancer with 2 dose levels was 66Gy/2.64Gy-50Gy/2Gy. It is a treatment given in 25 fractions.

Those 2 levels covers either :

66Gy/2.64Gy	50Gy/2Gy
Prostate	Seminal vescicle
Prostate + seminal Vescile	Prostate lymph node

Table 2.2: Placement of the dose levels

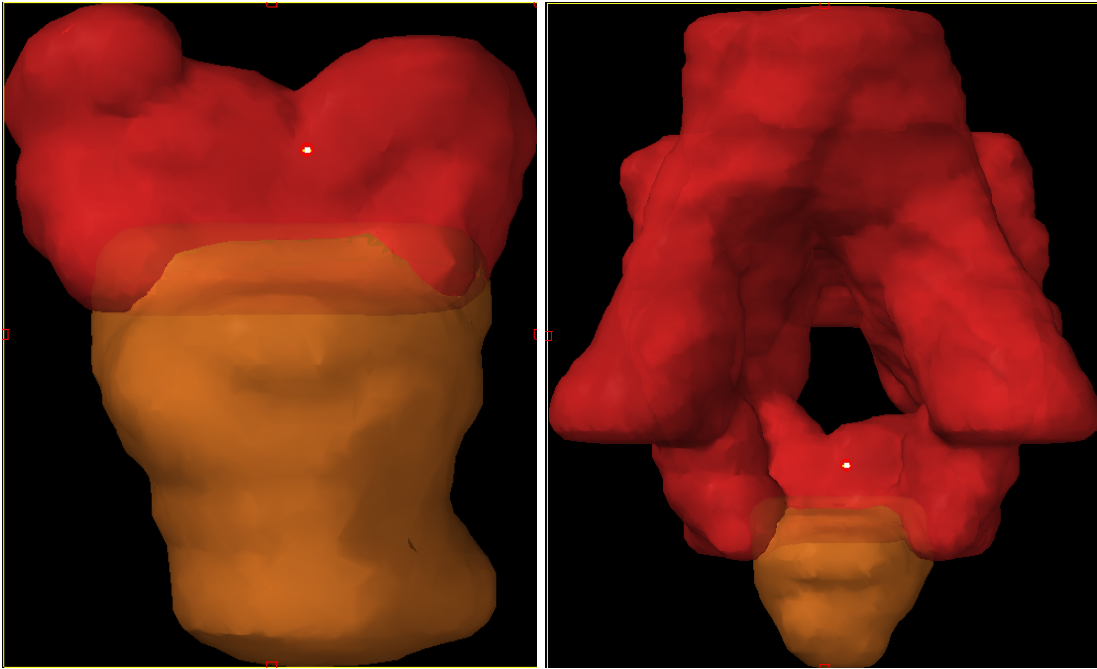


Figure 2.1: Exemple of the 2 PTV at 2 doses levels, the orange is PTV 66 Gy and the red one is the PTV 50 Gy. On the left, without lymph nodes. On the right with lymph nodes.

As we can guess on fig.2.1, there is a significant size difference between the two cases. For having the most generalised RapidPlan model I needed to insert in the model set an adequate number of both type of geometry. the model set was composed of :

	Numbers of plans
Total	56
With lymph nodes	23
Without lymph nodes	33

Table 2.3: Number of plans taken.

Even if Varian advise us to us at least 20 plans as previously said in the paragraph 1.4.3., the more plans you have in your model, the more improvements you have up until a limit. [46]

That is why I have chosen to have 56 plans, with both planification with lymph nodes and without lymph nodes. The proportion of the plans with and without lymph nodes taken into the model set was similar to the proportion of the plans with and without lymph nodes done in the 2 years span.

### 2.1.2 Structure set

For a better dosimetry, I created personalised structure on all the plans in the model set.

Because of the anatomy of the pelvic region and the marge to the cancerous volume (cfr 1.1.3.2.4), the overlapping of the PTV with the OAR is a common occurrence. Hence, there is a risk of conflicting optimisation objectives in the TPS; the avoidance of this occurrence is the reason that I created some personalised structures.

Moreover it was studied that for the use of gEUD during the optimisation for the pelvic treatment it was better fitted to use cropped structures with a 4mm crop from the PTV [21]. More details will follow in the upcoming section.

As follow, I not only created different structures for the implementation of RapidPlan but I also used some structures that were already present. The structure I both used and created, that will be explained in the following paragraph are :

- PTV\_High\_eval
- PTV\_Low\_eval
- PTV\_Low\_hotspot
- OAR\_in
- OAR\_out
- OAR

#### 2.1.2.1 PTV\_High\_eval

This is a structure normally used at the CHU Namur. This structure is the volume of the PTV that lies further than 5mm to the surface of the body.

Because of the build-up region that we have seen on the PDD for 6X photon (cfr 1.2.1.6) and because the dose calculation algorithm of Eclipse, trying to optimise for a dose level so close to the surface of the patient will lead to a dose hotspot deeper in it. This is not a standardised margin and it may vary in each radiotherapy centre.

The mathematical formula to express it is :

$$PTV\_High\_eval = PTV\_High \cap (Body - 5\vec{mm})$$

In this specific case, the `PTV_High_eval` always lies further than 5mm from the surface of the body, nevertheless I used this structure in case there was an exception where the prostate anatomy varied from a normal patient.

We can see it on fig.2.2. in orange.

### 2.1.2.2 PTV\_Low\_eval

This was also a structure already used at the CHU Namur. This structure is used because of the overlapping of the `PTV_High` and `PTV_Low`, due to the margin added. During the optimisation it is preferred to favour the High dose PTV.

We will also take the volume of the `PTV_Low` that lies 5mm from the body for the same reasons named before.

The mathematical formula to express it is :

$$PTV\_Low\_eval = (PTV\_Low \cap (Body - 5\vec{mm})) \not\subset PTV\_High\_eval$$

As for the `PTV_High_eval`, the `PTV_Low_eval` always lies further than 5mm from the surface of the body, but for the same reason, I preferred using this structure.

We can see it on fig.2.2. in red.

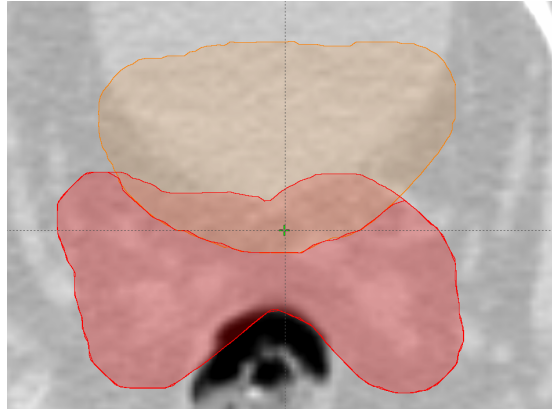


Figure 2.2: `PTV_6600_eval` and `PTV_5000_eval`, which are considered respectively as `PTV_High_eval` and `PTV_eval` in orange and red

### 2.1.2.3 PTV\_Low\_hotspot

This was a structure already used at the CHU Namur, it is the volume of the `PTV_Low_eval` that lies 8mm from the `PTV_High_eval`.

Because the `PTV_Low_eval` is close fitted to the `PTV_High_eval` and due to their different dose levels, it is impossible to put an optimisation objective to avoid hotspots. To bypass this

problem, we place the optimisation objective onto the  $PTV\_Low\_hotspot$ , which lies 8mm from the PTV. Leaving some space for a dose gradient to be optimised by the TPS.

The mathematical formula to express it is :

$$PTV\_Low\_hotspot = PTV\_Low\_eval - (PTV\_High\_eval + 8\vec{mm})$$

We can see it on fig.2.3. is the fraction of the  $PTV\_5000\_eval$ , in a slight darker red.

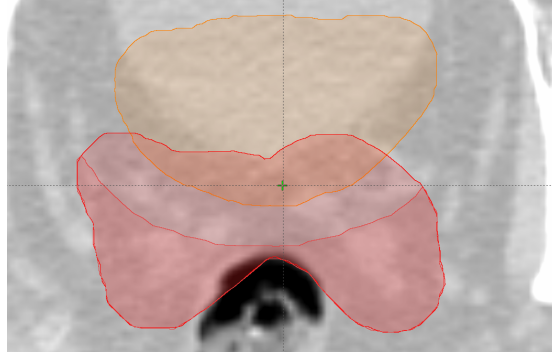


Figure 2.3:  $PTV\_5000\_hotspot$  in a darker red compared to the  $PTV\_6600\_eval$  in orange and  $PTV\_5000\_eval$  the combination of a lighter red and darker red.

#### 2.1.2.4 OAR\_in

Those structures were created for the implementation of RapidPlan. It is the volume of a OAR that overlaps with at least one of the two PTV.

As I already said, the planification treatment using gEUD improves when combined with cropped structure for the "in" and the "out" (cfrt 2.1.2), but it makes impossible to place optimisation objectives on the part of the OAR that overlaps with one of the two PTV stopping us from putting an upper objective to avoid hotspots.

The mathematical formula to express it is :

$$OAR\_in = OAR \cap (PTV\_Low\_eval + PTV\_High\_eval)$$

The OAR for which I created this structure are : rectum, anal canal, bladder, small bowel, sigmoid colon.

I wanted to do the same for the large bowel, but there was only one case where it overlapped with the PTV out of the 56 planification in the set model. Thus rendering impossible the training of the structure set by RapidPlan (cfrt 1.4.2).

We can see it on fig.2.4.

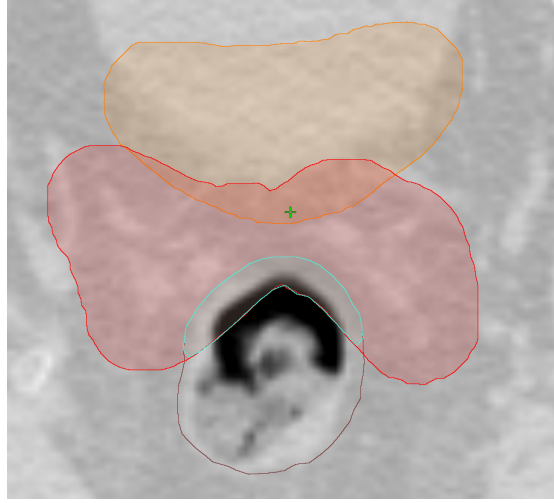


Figure 2.4: Rectum\_in in blue compared to the PTV\_5000\_eval in red and PTV\_6600\_eval in orange.

#### 2.1.2.5 OAR\_out

Those structures were created for the implementation of RapidPlan. It is the volume of a OAR that lies 4mm from both PTVs.

I created those structures because of the improved planification using gEUD with cropped OARs (cf 2.1.2).

The mathematical formula to express it is :

$$OAR_{out} = OAR - ((PTV_{Low\_eval} + PTV_{High\_eval})) + 4mm$$

The OAR for which I created this structure are the same named in the previous paragraph.

We can see an example for this structure it on fig.2.6.

#### 2.1.2.6 OAR

I only used only one OAR structure : large bowel. As I previously said, it only occurred once in the 56 plans that it was present as "BowelLarge\_in". In such a way, I preferred using the whole structure.

### 2.1.3 RapidPlan Implementation

The process advised by Varian for a model configuration such as the prostate model is the following, and will be explained in further details in the next paragraph [28]:

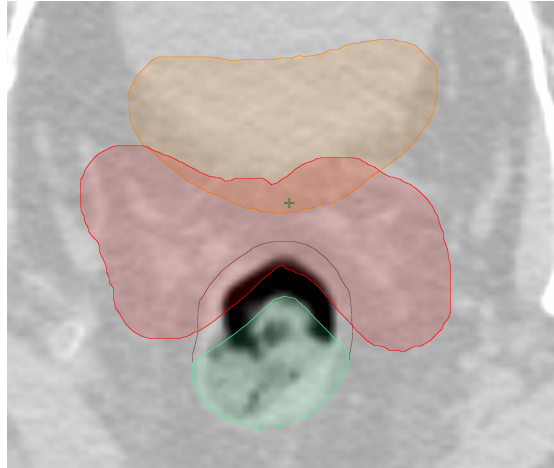


Figure 2.5: Rectum\_out in light green compared to the PTV\_5000\_eval in red and PTV\_6600\_eval in orange.

1. Define the scope and clinical goals of the model.
2. Add a DVH estimation model container and structures.
3. Add plans to the DVH Estimation Model.
4. Train the DVH estimation model.
5. Verify the results of model training : add Optimisation objectives.

[28]

### 2.1.3.1 Define the scope and clinical target of the model

As already told, the implementation of RapidPlan will be done for the prostate treatment and for a specific prescription for VMAT. The model obtained will be tested for another VMAT prescription and the same prescription for IMRT plans.

The clinical target is to achieve treatment plans that will reach all the clinical goal attached to the prescription. The created plans will have either the same quality or better than the plans in the model set.

The treatment plans will be preferred to reach the coverage of the 95% prescription isodose to 100% of the target volume, but I will consider acceptable if those plans could give us acceptable (acceptable planification are a subjective matter and depends on the patient anatomy hence they can not be fixed by some rules), they can plan that could be improved furthermore. This will still lead to a better time efficiency for the physicists.

Another implementation of RapidPlan found that the treatment plans created with RapidPlan could be optimised even further by a trained physicist. This will still give a better time efficiency due to the better starting point from the optimisation, instead of starting from a blank planification (Cfrt1.4.3).

### 2.1.3.2 Add a DVH estimation model container and structures

I started by creating a new model by creating all the structures mentioned in the previous paragraphs.

I followed the guidelines given by Varian.[28]  
I added the structures for the models as I wanted to generate some DVH estimations. Some structures in the model are not always present in the plans from the model set. The name of the structures and their ID were created to match automatically with the ID and names in the structure set.

The model contains several target structures, they are not automatically matched even if they have the same ID and structure name.

### 2.1.3.3 Add plans to the DVH estimation model

I remember to the reader that I used a total of 56 plans to insert into the model.

#### 2.1.3.3.1 General plan set guidelines

I tried to create the most general model possible one in this case. As a consequence, I placed all the plans on the model without considering the structure overlap, the size OAR and target and the numbers of arc.

But I still used the treatment plans with the same treatment technique (VMAT) and with the dose prescription.

Even though the minimum number for creating a model was 20, I decided to generate 56 plans in order to have a more generalised model (cf 1.4.2.2).

Even if RapidPlan allows to insert the same plan with a different planification, I always inserted different plans [28].

All the planification present in the set model were accepted for treatment even if some had some clinical goals that were not achieved. Because of the unique anatomy of the patient, the physicist and radiotherapist decided that it was impossible to achieve those goals.

### 2.1.3.4 Train the DVH estimation model

In the beginning, I inserted all the plans with all of the structures present in it and all the correct prescriptions (cf 2.1.3.2).

Then you can train the model, RapidPlan gives all the different DVH superposition and statistic about the planification.

### 2.1.4 Verification of the results of model training

The verification of the model training were accomplished by using the model analytic from Varian and using the statistical information given by RapidPlan.

Model Analytics is the first cloud-based application for knowledge guidance from Varian. When a DVH estimation model is uploaded into Model Analytics, it is automatically analysed and the results are given immediately.

This tool helps us by giving a guidance in the outlier identification.

We can see the processus on fig.2.6.

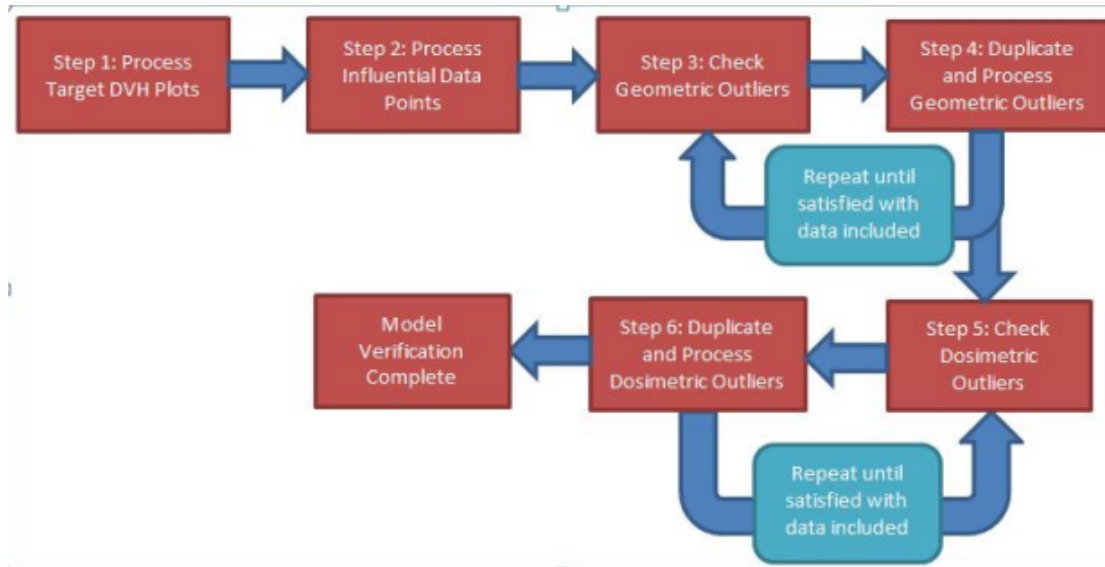


Figure 2.6: Schematising of the process for the verification of a RapidPlan Mode. [28]

1. Processing the target DVH by training the model
2. Processing the influential data points by training the model
3. Checking the geometric and dosimetric outliers with the tools implemented in RapidPlan : Cook's distance, etc...
4. Removing the most important geometric and dosimetric outliers
5. Repeat until satisfied and model verification complete

After the model is extracted and exported into Model Analytics, it will be analysed. Model analytics will follow two phases.

1. Individual outlier structures, from specified plans in the model set, are identified and will be advised to take them out of the model, and iterate again until an acceptable model will be achieved. This is at the discretion of the model planner.

2. Model Analytics will identifies the remaining structures that are significantly different from the rest of the model and will report any gaps in the data.

I also verified the model in RapidPlan by checking the Cook's distance then I removed the influential data points in the regression. I iterated this processus as many time as I needed to achieve a model that I was satisfied of.

I tried to achieve a  $R^2$  as close as possible to 1, but for the Rectum structures I never had more than 0.609 due to the variation of the anatomy from a patient to another. It was, then, impossible for it to give a better regression. This was also observed in other pelvic RapidPlan model. [28]

### 2.1.5 RapidPlan models

I have created 5 different models by iterating and comparing with the last model iteration. I will explain further the changes on each iteration .

In the first RapidPlan model I took the manually optimised plan and imported it in the set. But for the other, I compared every manually optimised one with the RapidPlan optimised one, then I put into the new models the best one between the manually optimised and the RapidPlan optimised.

#### 2.1.5.1 RapidPlan implementation models

I created the RapidPlan models in an iterative process, aiming to improve the plan quality with each iteration. When I started this process I didn't knew how many Rapidplan models I needed to achieve an acceptable quality. I finished by doing 5. The idea behind was to continue up until when a new model gave me worse results than the precedent model.

Rapidplan aim to achieve a minimum for the cost function (cfirt 1.2.2.1), and with this process for creating the model there is no way of knowing if the best model achieve an absolute minimum or a local minimum, but it was the most efficient way of creating the models due to the time constraints of the simulations for this thesis.

All the constraints and NTO for the models are in the annex 1.

**2.1.5.1.1 RP Model 1 : RP1** I placed fixed optimisation objectives on all the targets because it would give a better results for the pelvic treatment (cfirt 1.4.3).

For the OAR\_out, I put 2 gEUD with different value with generated dose to try to optimise on the whole DVH (Cfirt 1.2.2.1.4). I also set optimisation objectives on the 20Gy dose for trying to decrease the volume receiving it. And so reducing the low doses volume and having a bigger dose gradient around the target.

For the OAR\_in, I put an upper objective to avoid hotspots and in order to achieve the clinical goals sets by the radiotherapist.

I used a classic NTO, that would try to force the 95% isodose at 3mm from the target border.

I didn't put at 0mm from the target border in order to not shrink too much the 95% isodose around the PTVs.

**2.1.5.1.2 RP Model 2 : RP2** In this model I did not changed a lot of parameters : it was just a refining of the priorities and NTO with a change in the plans into the model set. I compared the 56 plans singularly MO vs RP1, and put into the model the best of each comparison. (cfrt 1.4.3)

The last big change was the changing of the plans set was the lowering of the lower objective for the PTV\_High\_eval, because of the conflict with the upper on the z\_Rectum\_in. In RP1 I set an upper on the z\_Rectum\_in that was lower than the lower set on the PTV\_High\_eval, thus giving a contradictory objective.

**2.1.5.1.3 RP Model 3 : RP3** In this model I again compared all of the 56 plans MO vs RP1 vs RP2 and I put into the model set the best one in it. (cfrt 1.4.3).

For the OAR\_out I replaced the double gEUD with a single gEUD and an upper on 1% volume of the structure to try having a better planification.

I lower and refined the priorities accordingly. The "Distance from target border" of the NTO was set to 0 for trying having a better conformity.

I also stopped using the "z\_BowelLarge\_out" and started using the "BowelLarge", because there was only one occurency where the two structures were different. (cfrt 2.1.2)

**2.1.5.1.4 RP Model 4 : RP4** In this model, I again compared separately each of the 56 planifications (MO vs RP1 vs RP2 vs RP3) and I chose the best for each one to put into the model set.

I removed the upper 0% from the PTV\_low\_eval and the z\_CanalAnal\_in, because I noticed they were not useful. I also added an upper 0% on the z\_ColonSigm\_in to avoid and decrease the hotspot for this structure. I also removed the upper 20Gy on the z\_Bladder\_out and z\_ColonSigm\_out because they were counter productive.

Finally I also refined the priorities and the NTO accordingly.

**2.1.5.1.5 RP Model 5 : RP5** As per usual, I compared separately each of the 56 planifications (MO vs RP1 vs RP2 vs RP3 vs RP4) and I chose the best for each to put into the model set.

I only changed the priorities of all the objectives to "Generated", as such RapidPlan will chose them accordingly.

**2.1.5.1.6 RP model with standard planifications : RP\_sp4** After comparing the first 5 models, I took the best of the 5 and created a model with the same objectives but the

planifications in the models where all the manual optimised one. I created this to confirm the hypothesis that putting new RapidPlan optimised models into it would get us a better model. (cfrt 2.1.3)

**2.1.5.1.7 RP Model without in and out : RP\_wo** After comparing the first 5 models, I took the best of the 5 and used its objectives to create a new model without the structures "\_in" and "\_out". The best of the 5 models was RP4, this will be explained furthermore in the next sections.

I didn't use any structure with the "\_in" and "\_out", but the entire structure. I put all the objectives that I previously used separated into the "\_in" and "\_out" into the full structure and I refined the objectives accordingly.

This model was created to assess if the use of the structures "\_in" and "\_out" were useful.

## 2.1.6 Test

I tested all the 5 model for the prescription : 66Gy/2.64Gy - 50Gy/2Gy

Then the best of the 5 model has been tested also for :

- VMAT 2/3 arcs : 70Gy/2Gy - 57.75Gy/1.65Gy
- VMAT 2/3 arcs : 60Gy/3Gy - 44Gy/2.2Gy
- IMRT 5 Beam : 66Gy/2.64Gy - 50Gy/2Gy
- IMRT 7 Beam : 66Gy/2.64Gy - 50Gy/2Gy

For the two IMRT test, I will test with two different beams geometry.

As we can see on fig.2.8. the 2 geometries are mirrored. The biggest impact on this is that IMRT A irradiates the target without irradiating directly the rectum and IMRT B irradiates the target while irradiating directly the rectum. This is the same principle for the IMRT 7 beams A and B as we can clearly see on fig. 2.9.

Following that, I chose to create 2 more models, to do some more tests.

One with the same structures and constraints that of the best model, but the plans in the set model were all the manually optimised plans.

The other one, was one without \_in and \_out structures where the constraints set for them were combined into the OAR.

Those 2 models were compared with the manually optimised plans and the best of the first 5 models. The comparison was done with the clinical goal : 66Gy/2.64Gy - 50Gy/2Gy.

## 2.2 Clinical constraints

The clinical constraints come from the protocol attached to the plan before the planification, the radiotherapist attaches the protocol to plan by his own discretion.

There are 2 type of constraints : volume constraints and dose constraint.

### 2.2.1 Volume Constraints

The volume constraint is noted as  $VxGy$  [% or  $cm^3$ ]. It is required that the volume of the isodose  $xGy$  is smaller than a certain percentage of the total volume of the OAR (%) or of a fixed volume (cc).

### 2.2.2 Dose constraints

The dose constraint is noted as  $Dx\%$  [Gy]. It is required that  $x\%$  volume of the PTV or OAR is irradiated to be more or less than the constraint (more for the PTV, less for the OAR) , or that the mean dose received by the volume to be less than a certain dose  $x$ .

### 2.2.3 Clinical prescription

As said above on 2.1.6, I will test following the clinical prescriptions also for different dose prescriptions.

#### 2.2.3.1 Clinical prescription 66Gy/2.64Gy - 50Gy/2Gy

The clinical constraints for the prescription : 66Gy/2.64Gy - 50Gy/2Gy, 70Gy/2Gy - 57.75Gy/1.65Gy, 0Gy/3Gy - 44Gy/2.2Gy are in the third annex.

## 2.3 Plan evaluation

On the planification I always normalised that 100% of the prescribed dose is given to 50% of the PTV\_High\_eval volume. This is a step always done, because the final goal for the PTV\_High\_eval is to be a perfect step function. This is clearly impossible due to the uncertainties, but to try and achieve the goal this step helps to normalise the DVH of the PTV\_High\_eval around 100% of the prescribed dose.

The models will be compared on all the clinical constraints from the clinical protocols for all the OARs and PTVs, and on 3 index for the PTVs. I took the average and standard deviation of the results of the clinical constraints and the 3 index for having a better assessment of the plan quality, but it is just a faster tool to show the results, the reality is that the results don't always follow a normal distribution, and for the OAR individual results depend heavily on the the patient geometry.

The 3 index, that will be explained in more details in the following sections are :

- CIP95, Conformity Index Paddick 95% isodose.
- CIP100, Conformity Index Paddick 100% isodose.
- HI , Uniformity Index.

### 2.3.1 Index

#### 2.3.1.1 Conformity Index Paddick

A conformity index is a formula to see how well the volume of a certain isodose conforms to the shape and size of a target volume. Because the conformation of a certain isodose to the shape and size of a target is related to the success of the irradiation, and accurate Conformity Index (CI) is needed to assest the quality of the planification.[47]

In the literature, different CI were compared and analysed. The two most used CI were [47] :

- $PITV$  (*Prescribed Isodose Treatment Volume*) =  $\frac{PIV}{TV}$ 
  - PIV = Volume prescribed isodose
  - TV = Target volume
- $RCI$  (*Raiation Conformity Index*) =  $\frac{V_{PIV}}{V_I}$ 
  - $V_{PIV}$  = target volume
  - $V_I$  = volume of the target volume covered by the prescription isodose

They are easy to calculate, but they have intrinsic flaws. For the PITV and RCI, a score of 1 should be a perfect score. If the score is greater than 1 it indicates over-treatment, if the score is lower than 1, it indicates under-treatment, and vice-versa for the RCI. Nonetheless, those are heavily criticised because they do not take into account the location of the PIV relative to the TV.

The PITV could score 1, whether the RCI conforms perfectly to the TV or not. We can see the process on fig.2.10.

For the RCI, a perfect score would be a score of 1, and it will never be higher than 1. Although the RCI would not gives us a false perfect score for radiation distribution far from the

target volume, it would give us a perfect score even if the isodose volume does not conform to the PTV, which leads to overtreatment. As we can see on fig 2.11. [47]

A new index was created, the Conformity Index Paddick (CIP). Which combines the two indexes.

$$CIP = \frac{TV_{PIV}}{TV} \times \frac{TV_{PIV}}{PIV} = \frac{TV_{PIV}^2}{TV \times PIV}$$

- $TV_{PIV}$  = volume of the target covered by the prescription isodose
- $PIV$  = volume of the target isodose
- $TV$  = target volume

A score of 1 is the perfect score for this index. It cannot be higher than 1.

As we can see on fig.2.12, the CIP gives us a better CI that can be used in a wider range of cases, while still giving us an easy understanding of the plan quality. Nevertheless, it still has intrinsic flaws, such as not taking into account the dose gradient around the target volume or the type of normal tissues.

In this case the CIP100 will always be near 50% because of the normalisation of 100% of the dose given to 50% of the PTV\_High\_eval volume.

### 2.3.1.2 Homogeneity Index

The Homogeneity Index (HI) is a tool used for analysing the dose uniformity in the target volume. Different formulas are used in the literature, but the most common used one is [48]:

$$HI = \frac{D2\% - D98\%}{DP}$$

- $D2\%$  = dose to 2% of the target volume, indicating the max dose
- $D98\%$  = dose to 98% of the target volume, indicating the min dose
- $DP$  = prescribed dose to the target volume

The reason behind the selection of the D2% and D98% is that the calculation of the dose maximum and minimum is sensitive to the calculation parameter. Furthermore, the high dose gradient in IMRT and VMAT could skew the minimum dose. A perfect score would be 0, the higher it gets the worse it becomes.

This index still had its limitation such as the multiple indexes proposed in the literature and their difficulties in their interpretation. Moreover, the limited information regarding the usefulness of having a planification with a lower HI compared to one with a higher HI. Even if some studies suggest that a better dose homogeneity (lower HI) will lead to a better OAR preservation. [49]

### 2.3.2 Plan

For all the models created with the clinical prescription 66Gy/2.64Gy - 50Gy/2G, I compared them with the MO plans and with the model created before. During the implementation I compared the 56 planifications of the model set.

For the 2 different clinical prescriptions I will compare the RP plans with the MO. I compared all the planifications done in the 2 years span.

20 planifications (11 with lymph nodes and 9 without lymph nodes) for the 60Gy prescription.

10 planifications (1 with lymph nodes and 9 without lymph nodes) for the 70Gy prescription.

For the IMRT vs VMAT, I will compare the 4 against the MO VMAT. I compared 20 planifications taken arbitrarily from the model set as to have a sample with the same proportion of planifications with and without lymph nodes. In total they were 20 planifications (12 without lymph nodes and 8 with lymph nodes).

#### 2.3.2.1 Kolmogorov-Smirnov test

For comparing the models, I will use the Kolmogorov-Smirnov test. Because the data were not always distributed following a normal distribution, I could not do a test-t Student. This is a statistical test that allows to compare two or more distributions that don't follow the normal distribution.

The Kolmogorov-Smirnov test determines if two distributions are statistically different or not, without making specific assumptions. I will use a p-value of 0.05 to determine if the distributions are statistically different or not.

I performed the Kolmogorov-Smirnov test following with an online tool [50] created by the company AAT Bioquest. This tool has been cited in 5 different publications.

### 2.3.3 Determining the better model

For determining the better model, I compared the different clinical goals and the 3 index defined in the previous sections.

Because this RapidPlan implementation is for a double target prescription, the 2 targets will be superposed, so that the usage of the CIP95 and CIP100 would be difficult to understand for the lower dose target, I only used them for the PTV\_High\_eval.

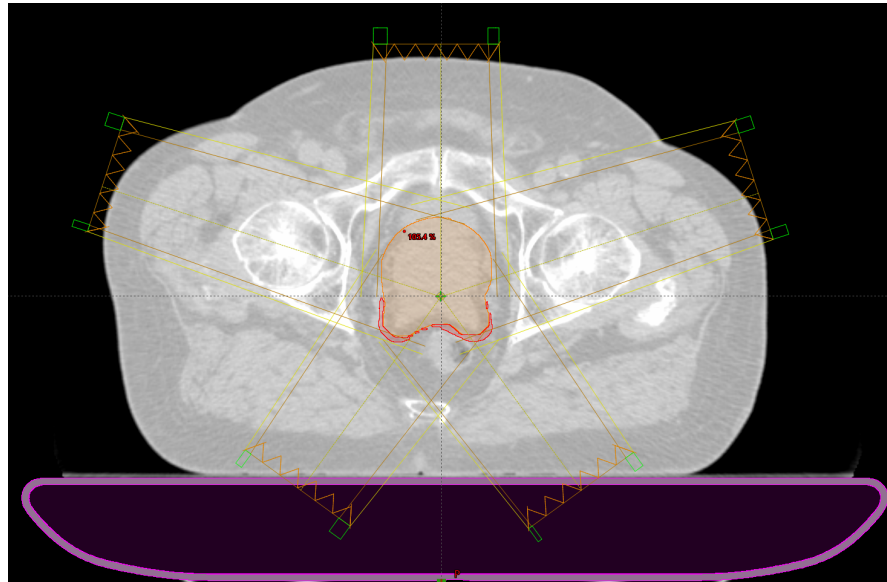
I used the HI for the PTV\_High\_eval and the PTV\_Low\_hotspot, I did not use it for the PTV\_Low\_eval because of its adjacency with the PTV\_High\_eval, thus we would have skewed results. Indeed, being up to the PTV\_High\_eval, the results would be skewed.

For determining if a model is better than another, I will compare if the coverage and conformity of the isodose is statistically different from one to another. If they are, then I will check if there are statistical differences in the clinical goals for the OAR and see if the one with

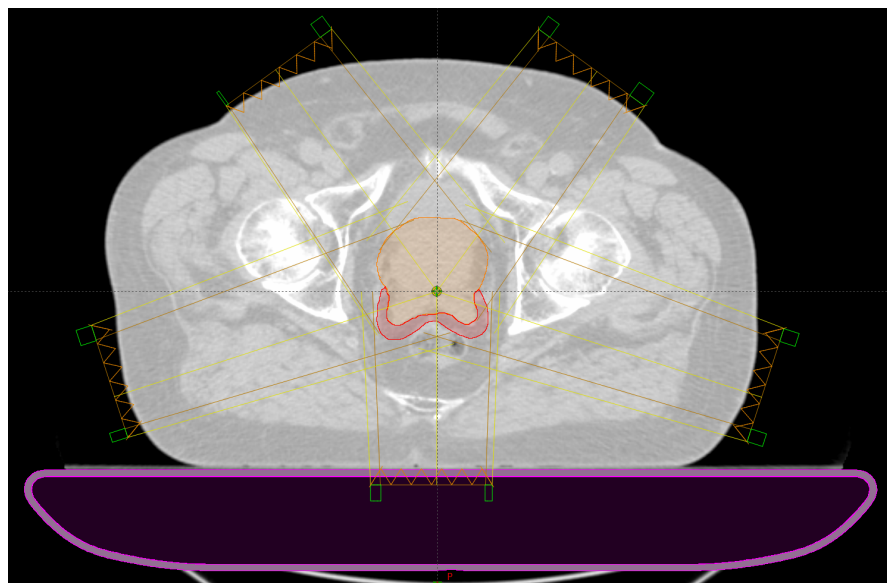
the better coverage and isodose has at least no statistical difference or better OAR sparing. If the OAR is worse on the model with the better coverage and conformity of the isodose, the model is worse.

For the comparison of model where there are no statistical differences for the coverage and conformity of the isodose, I will look if there are statistical differences for OAR sparing, if there are, then the one with the better OAR sparing is better, if there are not then the 2 models are statistically equal.

An important part is that the definition of "acceptable planification" is a subjective matter and there isn't an absolute consensus amongst physicist. For me, an acceptable planification is a planification that achieves all the clinical constraints while still having an adequate coverage of the isodose 95% prescription. An adequate coverage isn't defined because it depends on the geometry of the PTV, if the PTV is big enough to overlap with a bone structure, it will be accepted that the isodose don't cover that part of the PTV or if there are micro volume on the edge of the PTV aren't covered by the isodose it could still be accepted, because there are uncertainties on the dose calculation algorithm of the TPS.

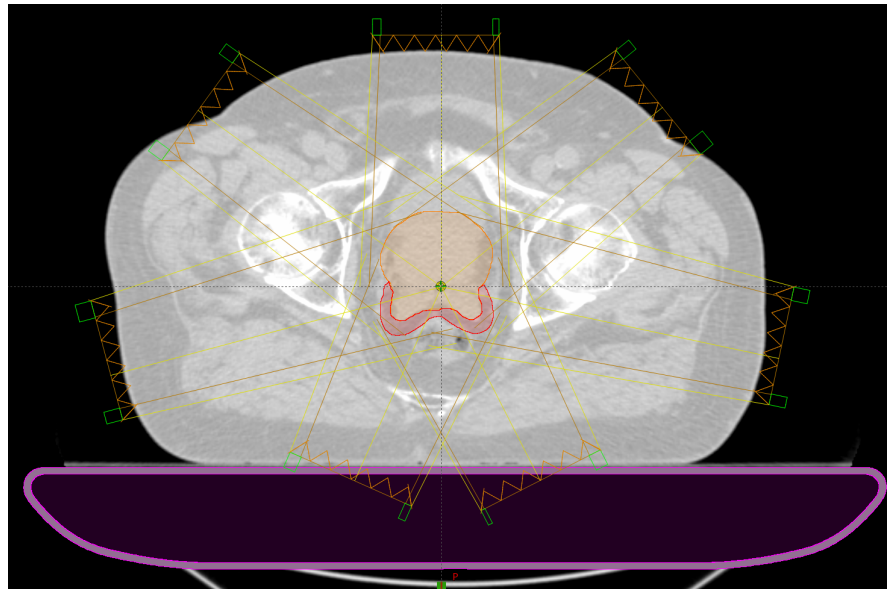


(a)

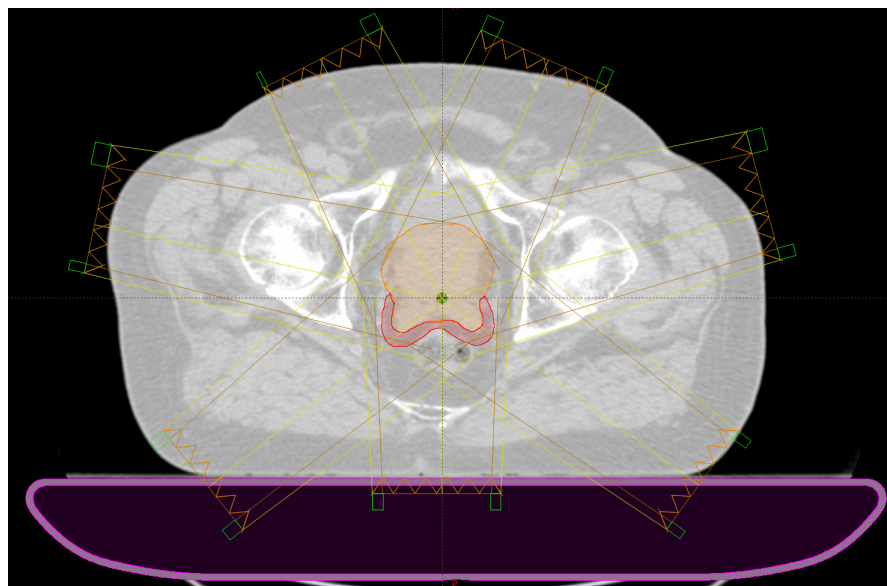


(b)

Figure 2.7: Image of the 2 geometries for IMRT : a) IMRT 5 A; b) IMRT 5 B



(a)



(b)

Figure 2.8: Image of the 2 geometries for IMRT : a) IMRT 7 A; b) IMRT 7 B

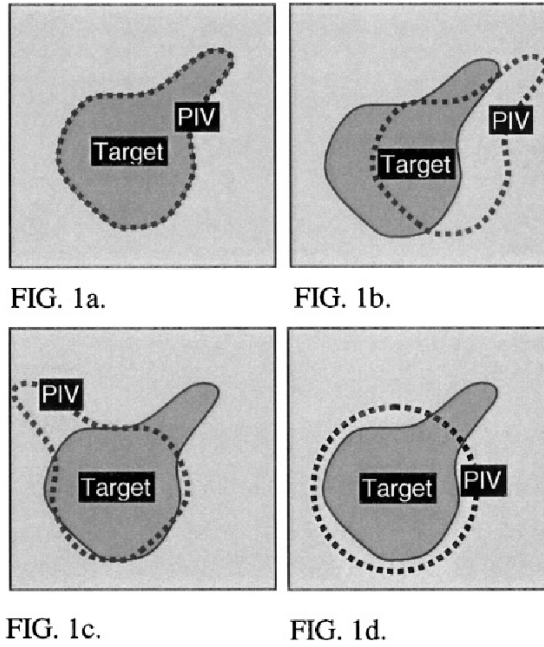


Figure 2.9: Cross-section of four different three-dimensional treatment plans using the PIV ration. The area shaded is the TV and the dashed line is the prescription isodose. The PIV of all 4 is one. [47]

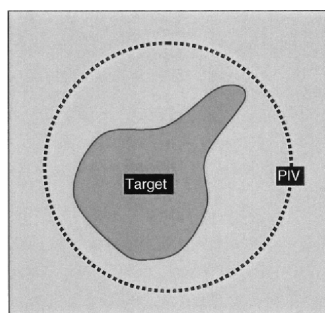


Figure 2.10: A non conformal dose plan that has a perfect RCI of 1. [47]






Isodose Plan	Parameters	PITV	$RCI_i$	Proposed Index
		$\frac{PIV}{TV}$	$\frac{TV_{PIV}}{TV}$	$\frac{TV_{PIV}^2}{TV \times PIV}$
1 	$TV = 5cm^3$ $TV_{PIV} = 5cm^3$ $PIV = 10cm^3$	2.00	<b>1.00</b>	0.50
2 	$TV = 5cm^3$ $TV_{PIV} = 3cm^3$ $PIV = 3cm^3$	0.60	0.60	0.60
3 	$TV = 5cm^3$ $TV_{PIV} = 4cm^3$ $PIV = 5cm^3$	<b>1.00</b>	0.80	0.64
4 	$TV = 5cm^3$ $TV_{PIV} = 3cm^3$ $PIV = 5cm^3$	<b>1.00</b>	0.60	0.36
5 	$TV = 5cm^3$ $TV_{PIV} = 5cm^3$ $PIV = 5cm^3$	1.00	1.00	1.00

Figure 2.11: Comparison of the 3 CI for various treatment plans. [47]

## Chapter 3

# Results

Now, I will talk about the results of the comparison between the model for each case. I will compare separately the 33 cases without lymph nodes and 23 cases with lymph nodes. In order to have a clear understanding if a model works better for one or another. The other comparison will be done with all these cases together.

In the second annex there will be all the graph of all the constraints for each comparison. I advise dearly to have them on the side for each comparison to have a better understanding, even if just with the tables should be enough to understand the differences.

### 3.1 Comparison between models

As stated above, I will compare separately the planification with lymph nodes and without lymph nodes.

I will start with the comparison between the 5 models to understand which one is better. I will compare for each PTV and OAR separately.

#### 3.1.1 Planning treatment without lymph nodes

##### 3.1.1.1 PTV\_6600\_eval

As we can clearly see from Table 3.1 and 3.2, the  $D_{95\%}$  is statistically lower, compared to the MO plans, for all the models with the only exception being RP4.

Unlike what it is said in the literature (cf 1.4.3), the hotspots in the PTV were not statistically different for any case, as the exception when comparing the model 2 and the model 3.

The HI were fairly similar for all cases, but the fact that the models gave more consistent results, it gave a statistical difference in some cases.

For the CIP100, we waited for a measure of around 0.5, and when it was the case, then the only

difference was the smaller standard deviation because of the more consistent plans.

As for the CIP95, we had more consistent results and also statistically higher, this is due to the better conformity of the isodose 95% because the  $D_{95\%}$  was statistically lower for all cases except for the model 4.

Between models, the biggest statistical difference was between model 4 and model 5, that is caused by the generated priorities.

Table 3.1: Mean and standard deviation of the model parameter for PTV\_6600\_eval

	MO	RP1	RP2	RP3	RP4	RP5
PTV_6600_eval						
D95% [Gy]	64.51 $\pm$ 0.42	64.09 $\pm$ 0.24	64.17 $\pm$ 0.15	64.11 $\pm$ 0.25	64.39 $\pm$ 0.13	63.87 $\pm$ 0.45
D0.1cc [Gy]	68.29 $\pm$ 0.60	68.00 $\pm$ 0.37	68.00 $\pm$ 0.42	68.36 $\pm$ 0.42	68.70 $\pm$ 0.50	68.14 $\pm$ 0.28
HI	0.051 $\pm$ 0.012	0.055 $\pm$ 0.007	0.054 $\pm$ 0.007	0.057 $\pm$ 0.007	0.071 $\pm$ 0.007	0.079 $\pm$ 0.011
CIP100	0.47 $\pm$ 0.11	0.49 $\pm$ 0.02	0.49 $\pm$ 0.01	0.49 $\pm$ 0.01	0.49 $\pm$ 0.01	0.50 $\pm$ 0.02
CIP95	0.86 $\pm$ 0.05	0.90 $\pm$ 0.03	0.90 $\pm$ 0.02	0.89 $\pm$ 0.02	0.89 $\pm$ 0.02	0.91 $\pm$ 0.01 height

Table 3.2: P-value of the comparison between models for PTV\_6600\_eval, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
PTV_6600_eval									
D95% [Gy]	0.01	< 0.01	0.13	< 0.01	< 0.01	0.06	< 0.01	< 0.01	< 0.01
D0.1cc [Gy]	0.12	0.10	0.98	0.65	< 0.01	0.06	0.05	0.29	< 0.01
HI	0.03	0.03	0.72	< 0.01	0.34	0.24	0.97	< 0.01	< 0.01
CIP 100	0.06	0.05	1.00	0.03	1.00	0.65	0.97	0.05	0.97
CIP 95	< 0.01	< 0.01	0.80	< 0.01	0.96	0.03	0.17	< 0.01	< 0.01

### 3.1.1.2 PTV\_5000\_hotspot and PTV\_5000\_eval

As we can clearly see on table 3.3 and 3.4, the RapidPlan optimised plan were more consistent with a smaller standard deviation. For the PTV\_5000\_eval and PTV\_5000\_hotspot we have different behaviours, the  $D_{95\%}$  is not statistically different for almost all cases, and between models we have some statistically differences.

Table 3.3: Mean and standard deviation for the model parameter of PTV\_5000\_eval and PTV\_5000\_hotspot

	MO	RP1	RP2	RP3	RP4	RP5
PTV_5000_hotspot						
D0.1cc [Gy]	52.39 $\pm$ 1.32	51.62 $\pm$ 0.44	51.56 $\pm$ 0.43	52.19 $\pm$ 0.55	51.87 $\pm$ 0.50	51.70 $\pm$ 0.47
HI	0.065 $\pm$ 0.019	0.047 $\pm$ 0.010	0.049 $\pm$ 0.011	0.060 $\pm$ 0.011	0.058 $\pm$ 0.011	0.057 $\pm$ 0.011
PTV_5000_eval						
D95% [Gy]	49.01 $\pm$ 0.40	49.35 $\pm$ 0.10	49.20 $\pm$ 0.11	49.25 $\pm$ 0.25	49.07 $\pm$ 0.12	48.97 $\pm$ 0.16

Table 3.4: P-value for model comparison PTV\_5000\_eval and PTV\_5000\_hotspot, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
PTV_5000_hotspot									
D0.1cc	< 0.01	< 0.01	0.88	0.17	< 0.01	0.23	0.03	0.01	0.29
HI	< 0.01	< 0.01	0.98	0.17	< 0.01	0.87	0.65	0.06	0.84
PTV_5000_eval									
D95%	< 0.01	< 0.01	< 0.01	0.04	< 0.01	0.24	0.09	0.01	0.01

### 3.1.1.3 Rectum

As we can understand tables 3.5 and 3.6, when comparing RP optimised with the Manually optimised plans, we have that the RP optimised plan to have a better rectum sparing for doses lower than 53Gy and the dose coverage across different doses. Furthermore, other than for the model 5, there were no differences on the hotspot dose. For the model 5, we have lower doses for each constraint the Rectum that are statistically significant.

Between models there were not many differences, sometimes the hotspots were statistically different. They were always on acceptable levels.

Table 3.5: Mean and standard deviation for the model parameter of Rectum

Rectum	MO	RP1	RP2	RP3	RP4	RP5
V62Gy [%]	11.85 $\pm$ 3.16	10.25 $\pm$ 3.33	9.96 $\pm$ 2.82	10.13 $\pm$ 2.88	10.18 $\pm$ 2.88	8.68 $\pm$ 2.43
V53Gy [%]	21.29 $\pm$ 5.29	18.17 $\pm$ 5.03	17.37 $\pm$ 4.42	17.62 $\pm$ 4.54	17.35 $\pm$ 4.42	15.98 $\pm$ 4.19
V44Gy [%]	35.33 $\pm$ 7.08	29.80 $\pm$ 7.01	28.44 $\pm$ 6.77	27.78 $\pm$ 6.75	27.28 $\pm$ 6.53	25.48 $\pm$ 6.40
V35Gy [%]	50.06 $\pm$ 9.17	42.69 $\pm$ 8.58	40.58 $\pm$ 8.81	38.34 $\pm$ 8.51	37.34 $\pm$ 8.34	34.74 $\pm$ 8.05
V27Gy [%]	63.43 $\pm$ 11.85	59.13 $\pm$ 9.61	55.67 $\pm$ 9.56	51.30 $\pm$ 9.47	49.44 $\pm$ 9.47	45.22 $\pm$ 9.33
D30% [Gy]	46.81 $\pm$ 5.49	43.17 $\pm$ 5.10	41.94 $\pm$ 5.12	41.13 $\pm$ 5.87	40.55 $\pm$ 6.01	38.62 $\pm$ 6.46
D25% [Gy]	49.92 $\pm$ 5.09	46.88 $\pm$ 4.78	45.83 $\pm$ 4.79	45.42 $\pm$ 5.45	44.94 $\pm$ 5.49	43.19 $\pm$ 5.90
D53% [Gy]	32.05 $\pm$ 7.45	29.20 $\pm$ 5.55	28.08 $\pm$ 5.12	26.20 $\pm$ 5.06	25.24 $\pm$ 5.20	22.97 $\pm$ 5.03
D0.1cc [Gy]	65.57 $\pm$ 0.40	65.49 $\pm$ 0.37	65.65 $\pm$ 0.42	65.28 $\pm$ 0.50	65.62 $\pm$ 0.35	65.33 $\pm$ 0.31

Table 3.6: P-value for comparison of model for Rectum, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Rectum									
V62Gy	0.15	0.17	0.92	0.29	1.00	0.41	1.00	0.01	0.29
V53Gy	0.07	0.10	0.90	0.17	1.00	0.10	1.00	0.01	0.65
V44Gy	0.01	0.01	0.69	0.01	0.97	0.01	1.00	0.01	0.45
V35Gy	0.01	0.01	0.47	0.01	0.85	0.01	0.97	0.01	0.65
V27Gy	0.02	0.01	0.22	0.01	0.17	0.01	0.85	0.01	0.29
D30%	0.01	0.01	0.78	0.01	0.65	0.01	0.97	0.01	0.45
D25%	0.01	0.01	0.75	0.01	0.97	0.01	1.00	0.01	0.45
D53%	0.01	0.01	0.21	0.01	0.29	0.01	0.84	0.01	0.17
D0.1cc	0.37	0.65	0.23	0.05	0.03	0.65	0.03	0.01	0.03

### 3.1.1.4 Anal canal

As we can see on table 3.7 and 3.8. There is not any statistical difference with the first 4 models, the only statistical difference was when comparing the RP model 5 and the manually optimised. Even without any statistical difference, we can still see a decrease in the mean dose for the anal canal. The absence of the statistical difference is probably due to the high standard deviation. This is due to the different anatomies of a patient.

Table 3.7: Mean and standard deviation for the model parameter of anal canal

Canal_Anal	MO	RP1	RP2	RP3	RP4	RP5
Dmean [Gy]	16.16 $\pm$ 7.94	13.57 $\pm$ 7.74	13.63 $\pm$ 7.60	13.29 $\pm$ 7.50	12.90 $\pm$ 7.52	11.63 $\pm$ 6.74

Table 3.8: P-value for comparison of model for anal canal, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Anal canal									
Dmean	0.01	0.01	0.01	0.04	0.05	0.24	0.10	0.01	0.01

### 3.1.1.5 Bladder

As we can see on table 3.9 and 3.10, the only statistical differences for the bladder clinical goal were for the model 4 where the hotspot was higher. For the model 5 we can see that the variance for the hotspot was the half of the other, which means that it gave more consistent planification for the bladder.

Between models there were only 4 statistical differences.

Table 3.9: Mean and standard deviation for the model parameter of bladder

Bladder	MO	RP1	RP2	RP3	RP4	RP5
V49Gy [%]	19.27 $\pm$ 9.86	17.89 $\pm$ 9.99	16.80 $\pm$ 9.10	16.77 $\pm$ 9.17	16.43 $\pm$ 8.96	15.50 $\pm$ 8.77
V62Gy [%]	10.31 $\pm$ 6.03	9.52 $\pm$ 5.97	9.12 $\pm$ 5.66	9.26 $\pm$ 5.75	9.31 $\pm$ 5.81	8.47 $\pm$ 5.46
D53% [Gy]	18.07 $\pm$ 12.93	17.04 $\pm$ 12.37	15.53 $\pm$ 10.96	14.41 $\pm$ 10.31	13.77 $\pm$ 9.88	12.58 $\pm$ 9.19
D0.1cc [Gy]	67.58 $\pm$ 0.52	67.45 $\pm$ 0.52	67.49 $\pm$ 0.56	67.68 $\pm$ 0.56	68.30 $\pm$ 0.64	67.30 $\pm$ 0.28

Table 3.10: P-value for comparison of bladder parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Bladder									
V49Gy	0.78	0.65	0.95	0.65	0.97	0.01	1.00	0.17	0.84
V62Gy	0.72	0.65	0.99	0.84	1.00	0.17	1.00	0.29	0.84
D53	0.76	0.45	0.87	0.45	0.97	0.84	1.00	0.10	0.97
D0.1cc	0.73	0.84	0.97	0.45	0.29	0.29	0.01	0.01	0.01

### 3.1.1.6 Sigmoid colon

For the sigmoid colon as we can see on table 3.11 and 3.12, there is not any statistical difference other than the  $V_{35Gy}$  when comparing MO and RP model 5. But even without the statistical differences we can see a slight decrease for all the RP model in almost all of the parameters, the absence of the statistical difference is due to the high standard deviation, which are caused by the big difference in patient anatomies.

Table 3.11: Mean and standard deviation for the model parameter of sigmoid colon

Colon_Sigmoid	MO	RP1	RP2	RP3	RP4	RP5
V62Gy [%]	$0.04 \pm 0.13$	$0.02 \pm 0.09$	$0.02 \pm 0.07$	$0.03 \pm 0.10$	$0.02 \pm 0.10$	$0.02 \pm 0.06$
V53Gy [%]	$0.13 \pm 0.44$	$0.11 \pm 0.36$	$0.08 \pm 0.27$	$0.10 \pm 0.35$	$0.09 \pm 0.33$	$0.08 \pm 0.29$
V44Gy [%]	$1.11 \pm 1.60$	$0.99 \pm 1.39$	$0.70 \pm 1.09$	$0.81 \pm 1.23$	$0.75 \pm 1.12$	$0.59 \pm 0.93$
V35Gy [%]	$2.71 \pm 3.53$	$2.22 \pm 2.81$	$1.67 \pm 2.23$	$1.83 \pm 2.36$	$1.72 \pm 2.20$	$1.29 \pm 1.68$
V27Gy [%]	$4.64 \pm 5.99$	$3.74 \pm 4.58$	$2.97 \pm 3.74$	$3.11 \pm 3.86$	$2.94 \pm 3.66$	$2.15 \pm 2.67$
D30% [Gy]	$6.16 \pm 4.57$	$5.33 \pm 3.22$	$5.23 \pm 3.00$	$5.12 \pm 2.84$	$5.05 \pm 2.75$	$4.58 \pm 2.35$
D25% [Gy]	$7.28 \pm 5.62$	$6.24 \pm 3.97$	$6.04 \pm 3.64$	$5.87 \pm 3.42$	$5.76 \pm 3.30$	$5.13 \pm 2.76$
D53% [Gy]	$3.57 \pm 2.25$	$3.29 \pm 1.89$	$3.31 \pm 1.85$	$3.30 \pm 1.84$	$3.27 \pm 1.80$	$3.05 \pm 1.63$
D0.1cc [Gy]	$33.68 \pm 20.82$	$33.03 \pm 21.70$	$30.98 \pm 21.39$	$31.55 \pm 21.72$	$31.63 \pm 21.63$	$30.42 \pm 21.52$

Table 3.12: P-value for comparison of colon sigmoid parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Sigmoid colon									
V62Gy [%]	1.00	0.97	1.00	1.00	1.00	1.00	1.00	0.33	1.00
V53Gy [%]	0.46	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.60
V44Gy [%]	0.88	0.35	0.76	0.52	0.85	0.57	0.98	0.35	0.93
V35Gy [%]	0.53	0.11	0.29	0.39	0.88	0.29	1.00	0.03	0.88
V27Gy [%]	0.94	0.42	0.46	0.40	0.96	0.40	0.97	0.10	0.59
D30% [Gy]	0.99	0.99	1.00	0.89	1.00	0.89	1.00	0.67	0.89
D25% [Gy]	0.99	0.90	0.99	0.89	1.00	0.89	1.00	0.45	0.89
D53% [Gy]	0.99	0.99	1.00	0.99	1.00	0.99	1.00	0.90	0.89
D0.1cc [Gy]	1.00	0.90	0.99	0.99	1.00	0.99	1.00	0.99	1.00

### 3.1.1.7 Bowel small

As we can see on table 3.13 and 3.14., there is not any statistical difference for the bowel small.

Table 3.13: Mean and standard deviation for the model parameter of small bowell

Bowel_Small	MO	RP1	RP2	RP3	RP4	RP5
V45Gy [cc]	$0.00 \pm 0.00$	$0.00 \pm 0.00$	$0.00 \pm 0.00$	$0.00 \pm 0.00$	$0.00 \pm 0.00$	$0.00 \pm 0.00$
D2% [Gy]	$3.18 \pm 2.23$	$2.95 \pm 1.78$	$3.05 \pm 1.71$	$2.93 \pm 1.70$	$3.04 \pm 1.77$	$2.86 \pm 1.60$
D0.1cc [Gy]	$5.18 \pm 4.14$	$4.86 \pm 3.58$	$4.79 \pm 3.71$	$4.44 \pm 3.14$	$4.58 \pm 3.33$	$4.33 \pm 2.93$

Table 3.14: P-value for comparison of small bowel parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Small bowel									
V45Gy [cc]	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
D2% [Gy]	1.00	1.00	0.99	0.99	0.99	1.00	1.00	1.00	0.98
D0.1cc [Gy]	0.95	1.00	0.95	0.99	1.00	0.95	0.99	0.97	1.00

### 3.1.2 Planning treatment with lymph nodes

#### 3.1.2.1 PTV\_6600\_eval

In table 3.15 and 3.16, we can assert that the  $D_{95\%}$  is statistically lower for all models, but the model 4 is the one that decreases the least, and is still within acceptable limits compared to the manually optimised plan.

The hotspot is statistically lower compared to the manually optimised for model 1 and 2, for the other models it is the same.

The homogeneity index was statistically higher for all the 5 models.

And for the CIP95 it was statistically higher for the 5 models too.

Another interesting feature is that the standard deviation of all parameters for the PTV\_6600\_eval were always smaller than the standard deviation for the manually optimised.

Table 3.15: Mean and standard deviation for the model parameter of PTV\_6600\_eval

PTV_6600_eval	MO	RP1	RP2	RP3	RP4	RP5
D95% [Gy]	64.70 $\pm$ 0.44	64.15 $\pm$ 0.27	64.15 $\pm$ 0.17	64.10 $\pm$ 0.23	64.45 $\pm$ 0.13	63.96 $\pm$ 0.33
D0.1cc [Gy]	68.13 $\pm$ 0.71	67.72 $\pm$ 0.24	67.73 $\pm$ 0.19	68.02 $\pm$ 0.26	68.24 $\pm$ 0.42	68.28 $\pm$ 0.33
HI	0.048 $\pm$ 0.016	0.053 $\pm$ 0.006	0.052 $\pm$ 0.005	0.054 $\pm$ 0.004	0.051 $\pm$ 0.005	0.06 $\pm$ 0.01
CIP 100	0.50 $\pm$ 0.05	0.50 $\pm$ 0.01	0.50 $\pm$ 0.009	0.50 $\pm$ 0.01	0.50 $\pm$ 0.01	0.50 $\pm$ 0.01
CIP 95	0.84 $\pm$ 0.07	0.90 $\pm$ 0.02	0.90 $\pm$ 0.021	0.89 $\pm$ 0.03	0.88 $\pm$ 0.02	0.90 $\pm$ 0.02

Table 3.16: P-value for comparison of PTV\_6600\_eval parameter, in green the p-value lower than 0.05

PTV_6600_eval	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
D95% [Gy]	< 0.01	< 0.01	0.13	< 0.01	< 0.01	0.06	< 0.01	< 0.01	< 0.01
D0.1cc [Gy]	0.12	0.10	0.98	0.65	< 0.01	0.06	0.05	0.29	< 0.01
HI	0.03	0.03	0.72	< 0.01	0.34	0.24	0.97	< 0.01	< 0.01
CIP 100	0.06	0.05	1.00	0.03	1.00	0.65	0.97	0.05	0.97
CIP 95	< 0.01	< 0.01	0.81	< 0.01	0.97	0.03	0.17	< 0.01	< 0.01

#### 3.1.2.2 PTV\_5000\_hotspot and PTV\_5000\_eval

We can see in table 3.17 and 3.18 that again, there are significant differences for the PTV\_5000. The hotspot is statistically lower from the RP optimised plan compared to the manually optimised. And between models there were some statistical differences.

The homogeneity index was statistically higher for the model 4 and 5, but still within acceptable margins.

But the D95% was statistically different for all the models, and even worse for the model 5. For the other model, it was lower but within acceptable margin.

Table 3.17: Mean and standard deviation for the model parameter of PTV\_5000\_hotspot and PTV\_5000\_eval

PTV_5000_hotspot	MO	RP1	RP2	RP3	RP4	RP5
D0.1cc [Gy]	55.39 $\pm$ 1.92	54.21 $\pm$ 0.61	54.09 $\pm$ 0.68	54.88 $\pm$ 0.68	54.80 $\pm$ 0.74	55.05 $\pm$ 0.77
HI	0.06 $\pm$ 0.01	0.06 $\pm$ 0.01	0.060 $\pm$ 0.009	0.069 $\pm$ 0.007	0.069 $\pm$ 0.009	0.08 $\pm$ 0.01
PTV_5000_eval						
D95% [Gy]	48.97 $\pm$ 0.39	48.83 $\pm$ 0.20	48.80 $\pm$ 0.18	48.78 $\pm$ 0.22	48.63 $\pm$ 0.19	48.25 $\pm$ 0.27

Table 3.18: P-value for comparison of PTV\_5000\_hotspot and PTV\_5000\_eval parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
PTV_5000_hotspot									
D0.1cc	< 0.01	< 0.01	0.88	0.17	< 0.01	0.24	0.03	< 0.01	0.29
HI	< 0.01	< 0.01	0.98	0.17	< 0.01	0.88	0.65	0.05	0.84
PTV_5000_eval									
D95%	< 0.01	< 0.01	< 0.01	0.04	0.05	0.24	0.10	< 0.01	0.01

### 3.1.2.3 Rectum

As we can see on table 3.19 and 3.20, when comparing the MO plans with the RP optimised plans, we can easily see that statistically speaking, all the 5 RP models were better than the manually optimised one for the Rectum.

Out of the 5 models, the best for the rectum was the model 5.

Table 3.19: Mean and standard deviation for the model parameter of Rectum

Rectum	MO	RP1	RP2	RP3	RP4	RP5
V62Gy [%]	8.97 $\pm$ 4.90	7.11 $\pm$ 3.80	6.94 $\pm$ 3.81	7.23 $\pm$ 3.95	7.33 $\pm$ 3.93	5.93 $\pm$ 3.36
V53Gy [%]	16.53 $\pm$ 6.88	13.00 $\pm$ 5.98	12.42 $\pm$ 5.85	12.85 $\pm$ 6.21	12.60 $\pm$ 5.98	11.07 $\pm$ 5.52
V44Gy [%]	35.24 $\pm$ 7.44	27.67 $\pm$ 8.46	26.19 $\pm$ 8.46	25.53 $\pm$ 8.37	24.58 $\pm$ 7.85	21.82 $\pm$ 8.29
V35Gy [%]	54.85 $\pm$ 7.76	48.45 $\pm$ 9.02	45.34 $\pm$ 90.92	41.27 $\pm$ 8.62	38.43 $\pm$ 8.40	34.82 $\pm$ 9.06
V27Gy [%]	73.35 $\pm$ 7.85	74.05 $\pm$ 8.62	70.04 $\pm$ 8.72	62.97 $\pm$ 8.79	58.28 $\pm$ 8.43	53.25 $\pm$ 7.86
D30% [Gy]	46.06 $\pm$ 3.42	42.97 $\pm$ 4.50	41.53 $\pm$ 4.17	40.99 $\pm$ 4.57	40.06 $\pm$ 4.74	38.10 $\pm$ 5.08
D25% [Gy]	48.40 $\pm$ 3.61	45.05 $\pm$ 3.86	44.12 $\pm$ 4.12	43.94 $\pm$ 4.64	43.20 $\pm$ 4.78	41.12 $\pm$ 5.12
D53% [Gy]	36.00 $\pm$ 4.06	33.69 $\pm$ 3.10	32.57 $\pm$ 3.49	30.53 $\pm$ 3.53	28.98 $\pm$ 3.40	27.45 $\pm$ 3.34
D0.1cc [Gy]	65.43 $\pm$ 1.00	65.18 $\pm$ 1.50	65.30 $\pm$ 1.58	64.75 $\pm$ 1.51	65.16 $\pm$ 1.69	64.91 $\pm$ 2.37

Table 3.20: P-value for comparison of rectum parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Rectum									
V62Gy	0.15	0.17	0.92	0.29	1.00	0.41	1.00	< 0.01	0.29
V53Gy	0.07	0.10	0.90	0.17	1.00	0.10	1.00	< 0.01	0.65
V44Gy	< 0.01	< 0.01	0.69	< 0.01	0.97	< 0.01	1.00	< 0.01	0.45
V35Gy	< 0.01	< 0.01	0.47	< 0.01	0.85	< 0.01	0.97	< 0.01	0.65
V27Gy	0.02	< 0.01	0.22	< 0.01	0.17	< 0.01	0.85	< 0.01	0.29
D30%	< 0.01	< 0.01	0.78	< 0.01	0.65	< 0.01	0.97	< 0.01	0.45
D25%	< 0.01	< 0.01	0.75	< 0.01	0.97	< 0.01	1.00	< 0.01	0.45
D53%	< 0.01	< 0.01	0.21	< 0.01	0.29	< 0.01	0.84	< 0.01	0.17
D0.1cc	0.37	0.65	0.23	0.05	0.03	0.65	0.03	< 0.01	0.03

### 3.1.2.4 Anal canal

As we can see on table 3.21 and 3.22, the only statistical difference is between the RP model 5 optimised and the MO plan. The other 4 models, even if the DMean were slightly lower, it was not enough to be a statistical difference.

Table 3.21: Mean and standard deviation for the model parameter of anal canal

Canal_Anal	MO	RP1	RP2	RP3	RP4	RP5
Dmean [Gy]	$16.97 \pm 7.44$	$14.33 \pm 6.38$	$13.52 \pm 5.93$	$12.78 \pm 5.71$	$12.24 \pm 5.65$	$10.72 \pm 4.63$

Table 3.22: P-value for comparison of anal canal parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Canal_Anal									
Dmean	0.38	0.45	1.00	0.29	1.00	0.17	0.97	0.02	0.84

### 3.1.2.5 Bladder

As we can see in table 3.23 and 3.24, we can clearly see that the hotspot for the RP models were statistically smaller and more consistent when compared to the MO plans and the D53% was statistically smaller for the models from 2 to 5.

Table 3.23: Mean and standard deviation for the model parameter of bladder

Bladder	MO	RP1	RP2	RP3	RP4	RP5
V49Gy [%]	$26.75 \pm 10.31$	$24.31 \pm 11.52$	$23.96 \pm 11.15$	$23.80 \pm 11.60$	$23.02 \pm 11.45$	$21.36 \pm 10.97$
V62Gy [%]	$9.39 \pm 5.67$	$8.24 \pm 5.14$	$8.23 \pm 5.08$	$8.50 \pm 5.41$	$8.66 \pm 5.54$	$7.97 \pm 5.04$
D53% [Gy]	$38.60 \pm 4.70$	$36.77 \pm 4.83$	$36.70 \pm 4.68$	$36.62 \pm 4.73$	$35.58 \pm 4.82$	$34.32 \pm 4.78$
D0.1cc [Gy]	$67.64 \pm 0.83$	$67.07 \pm 0.28$	$67.04 \pm 0.23$	$67.00 \pm 0.26$	$67.52 \pm 0.30$	$67.22 \pm 0.17$

Table 3.24: P-value for comparison of bladder parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Bladder									
V49Gy	0.78	0.65	0.95	0.65	0.97	< 0.01	1.00	0.17	0.84
V62Gy	0.72	0.65	0.99	0.84	1.00	0.17	1.00	0.29	0.84
D53%	0.76	0.45	0.87	0.45	0.97	0.84	1.00	0.10	0.97
D0.1cc	0.73	0.84	0.97	0.45	0.29	0.29	< 0.01	< 0.01	< 0.01

### 3.1.2.6 Sigmoid colon

As we can see on table 3.25 and 3.26, there were only statistical differences between MO plans and the model 4 and 5 for the doses below 44Gy.

Table 3.25: Mean and standard deviation for the model parameter of sigmoid colon

Colon_Sigmoid	mo	RP1	RP2	RP3	RP4	RP5
V62Gy [%]	0.00 $\pm$ 0.00	0.00 $\pm$ 0.00	0.00 $\pm$ 0.000	0.00 $\pm$ 0.00	0.00 $\pm$ 0.00	0.00 $\pm$ 0.00
V53Gy [%]	0.07 $\pm$ 0.23	0.02 $\pm$ 0.10	0.011 $\pm$ 0.04	0.01 $\pm$ 0.05	0.01 $\pm$ 0.05	0.01 $\pm$ 0.04
V44Gy [%]	17.36 $\pm$ 10.86	13.27 $\pm$ 9.81	12.76 $\pm$ 9.37	12.16 $\pm$ 9.08	11.33 $\pm$ 8.72	10.41 $\pm$ 7.98
V35Gy [%]	39.37 $\pm$ 13.96	31.30 $\pm$ 16.28	30.98 $\pm$ 17.19	29.40 $\pm$ 15.45	26.37 $\pm$ 13.28	24.05 $\pm$ 12.28
V27Gy [%]	61.20 $\pm$ 12.92	58.48 $\pm$ 20.50	56.60 $\pm$ 20.32	51.38 $\pm$ 19.46	48.55 $\pm$ 18.81	44.17 $\pm$ 17.32
D30% [Gy]	38.08 $\pm$ 5.23	34.56 $\pm$ 6.38	34.29 $\pm$ 6.55	33.38 $\pm$ 7.22	32.41 $\pm$ 7.18	31.48 $\pm$ 7.10
D25% [Gy]	39.76 $\pm$ 5.08	36.40 $\pm$ 6.45	36.06 $\pm$ 6.69	35.42 $\pm$ 7.03	34.48 $\pm$ 7.06	33.64 $\pm$ 7.06
D53% [Gy]	29.85 $\pm$ 5.53	28.51 $\pm$ 5.56	28.31 $\pm$ 5.75	26.63 $\pm$ 6.22	25.39 $\pm$ 6.05	24.07 $\pm$ 5.68
D0.1cc [Gy]	51.05 $\pm$ 2.27	50.85 $\pm$ 2.14	50.70 $\pm$ 1.71	51.02 $\pm$ 1.93	50.82 $\pm$ 1.86	50.67/ $mp$ 2.04

Table 3.26: P-value for comparison of sigmoid colon parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Sigmoid colon									
V62Gy [%]	1.00	0.97	1.00	1.00	1.00	1.00	1.00	0.33	1.00
V53Gy [%]	0.46	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.60
V44Gy [%]	0.88	0.35	0.76	0.52	0.85	0.57	0.98	0.35	0.93
V35Gy [%]	0.53	0.11	0.29	0.39	0.88	0.29	1.00	0.03	0.88
V27Gy [%]	0.94	0.42	0.46	0.40	0.96	0.40	0.97	0.10	0.59
D30% [Gy]	0.99	0.99	1.00	0.89	1.00	0.89	1.00	0.67	0.89
D25% [Gy]	0.99	0.90	0.99	0.89	1.00	0.89	1.00	0.45	0.89
D53% [Gy]	0.99	0.99	1.00	0.99	1.00	0.99	1.00	0.90	0.89
D0.1cc [Gy]	1.00	0.90	0.99	0.99	1.00	0.99	1.00	0.99	1.00

### 3.1.2.7 Bowel small

As we can see on table 3.27 and 3.28., there are not any statistical difference. The high standard deviation is due to one exception, in a planification where it was not optimised at all for the Bowel Small. But for the rest, there is not a statistical change, even if we can see a decrease in the constraints.

Table 3.27: Mean and standard deviation for the model parameter of small bowel

Bowel_Small	Treat	RP1	RP2	RP3	RP4	RP5
V45Gy [cc]	23.30 $\pm$ 42.26	17.12 $\pm$ 32.62	2.01 $\pm$ 2.35	3.01 $\pm$ 5.50	2.81 $\pm$ 4.93	1.75 $\pm$ 1.97
D2% [Gy]	41.26 $\pm$ 8.97	39.01 $\pm$ 9.77	38.22 $\pm$ 10.48	38.96 $\pm$ 9.92	38.48 $\pm$ 10.13	38.04 $\pm$ 10.10
D0.1cc [Gy]	48.29 $\pm$ 7.70	48.03 $\pm$ 8.24	47.78 $\pm$ 8.34	48.17 $\pm$ 8.51	47.94 $\pm$ 8.44	47.31 $\pm$ 8.69
#RED	1.17 $\pm$ 0.94	1.70 $\pm$ 0.88	1.45 $\pm$ 0.9625004	1.26 $\pm$ 1.01	1.43 $\pm$ 0.66	1.19 $\pm$ 0.60

Table 3.28: P-value for comparison of small bowel parameter, in green the p-value lower than 0.05

	MO vs RP1	MO vs RP2	RP1 vs RP2	MO vs RP3	RP2 vs RP3	MO vs RP4	RP3 vs RP4	MO vs RP5	RP4 vs RP5
Small bowel									
V45Gy [cc]	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
D2% [Gy]	1.00	1.00	0.99	0.99	0.99	1.00	1.00	1.00	0.98
D0.1cc [Gy]	0.95	1.00	0.95	0.99	1.00	0.95	0.99	0.97	1.00

## 3.2 comparison with other dose prescription

As already stated, I also tested the best of the 5 models for other dose prescription, RP4. One with higher dose levels and one with smaller dose levels. And I compared it with the manually optimised plans. (cf 2.2.1.2 and 2.2.1.3)

For the 70Gy prescription the set I compared was composed of 10 treatment plans : 7 with lymph nodes and 3 without lymph nodes.

For the 60Gy prescription the set I compared was composed of 20 treatment plans : 9 with lymph nodes and 11 without lymph nodes.

### 3.2.1 PTV\_High\_eval

As we can see on table 3.29 and 3.30 there was only a statistical difference for the D95% on the 70Gy prescription.

Table 3.29: Mean and standard deviation for other dose levels PTV\_High\_eval

	MO	RP		MO	RP
PTV_6000_eval			PTV_7000_eval		
D95% [Gy]	$58.61 \pm 0.41$	$58.56 \pm 0.12$	D95% [Gy]	$68.28 \pm 0.35$	$68.22 \pm 0.46$
D0.1cc [Gy]	$62.12 \pm 0.51$	$62.55 \pm 0.49$	D0.1cc [Gy]	$72.42 \pm 0.46$	$72.80 \pm 0.59$
HI	$0.055 \pm 0.014$	$0.055 \pm 0.007$	HI	$0.054 \pm 0.007$	$0.60 \pm 0.0022$
CIP100	$0.49 \pm 0.06$	$0.49 \pm 0.01$	CIP100	$0.51 \pm 0.05$	$0.51 \pm 0.02$
CIP95	$0.87 \pm 0.04$	$0.88 \pm 0.02$	CIP95	$0.85 \pm 0.04$	$0.86 \pm 0.02$

Table 3.30: P-Value for comparison of different dose level, in green the p-value lower than 0.05

	MO vs RP		MO vs RP
PTV_6000_eval		PTV_7000_eval	
D95%	0.99	D95%	< 0.01
D0.1cc	0.42	D0.1cc	0.08
HI	0.98	HI	0.56
CIP 100	0.98	CIP 100	0.08
CIP 95	0.76	CIP 95	0.08

### 3.2.2 PTV\_Low\_eval and PTV\_Low\_hotspot

As we can see on table 3.31 and 3.32, for the PTV\_Low\_eval and PTV\_Low\_hotspot, there were not any statistical differences on any of the constraints.

Table 3.31: Mean and standard deviation for other dose levels  $PTV_{Low\_eval}$  and  $PTV_{Low\_hotspot}$ 

	MO	RP		MO	RP
PTV_4400_hotspot	PTV_5775_hotspot				
D0.1cc [Gy]	$46.26 \pm 0.99$	$46.48 \pm 1.26$	D0.1cc [Gy]	$60.94 \pm 0.64$	$61.00 \pm 1.13$
HI	$0.059 \pm 0.013$	$0.061 \pm 0.014$	HI	$0.074 \pm 0.028$	$0.067 \pm 0.025$
PTV_5000_eval	PTV_5775_eval				
D95% [Gy]	$43.09 \pm 0.24$	$43.04 \pm 0.26$	D95% [Gy]	$56.25 \pm 0.59$	$56.28 \pm 0.59$

Table 3.32: P-Value for comparison of different dose level 5000 eval and 5000 hotspot, in green the p-value lower than 0.05

	MO vs RP		MO vs RP
PTV_4400_hotspot		PTV_5775_hotspot	
D0.1cc	0.56	D0.1cc	0.99
HI	0.56	HI	0.99
PTV_4400_eval		PTV_5775_eval	
D95%	0.82	D95%	0.99

### 3.2.3 Rectum

As we can see on table 3.33 and 3.34, there were again no statistical difference for any of the constraints. But even if the difference were not statistically significant, we can still see a decrease in all of the constraints.

Table 3.33: Mean and standard deviation for other dose levels Rectum

	MO	RP		MO	RP
Rectum_60			Rectum_70		
V60Gy [%]	$0.09 \pm 0.16$	$0.05 \pm 0.06$	V60Gy [%]	$21.65 \pm 8.65$	$20.01 \pm 9.44$
V50Gy [%]	$14.05 \pm 5.98$	$12.88 \pm 5.75$	V50Gy [%]	$34.02 \pm 8.10$	$32.29 \pm 9.97$
V40Gy [%]	$29.65 \pm 6.93$	$25.67 \pm 8.44$	V40Gy [%]	$46.96 \pm 8.83$	$43.11 \pm 10.83$
V30Gy [%]	$49.51 \pm 8.55$	$41.09 \pm 12.01$	D30% [Gy]	$53.30 \pm 7.20$	$50.66 \pm 8.78$
D0.1cc [Gy]	$59.76 \pm 0.32$	$59.62 \pm 0.32$	D25% [Gy]	$56.86 \pm 6.96$	$54.50 \pm 7.84$
			D53% [Gy]	$35.28 \pm 6.42$	$34.81 \pm 6.33$
			D0.1cc [Gy]	$69.43 \pm 0.61$	$69.57 \pm 0.57$

Table 3.34: P-Value for comparison of different dose level rectum, in green the p-value lower than 0.05

	MO vs RP		MO vs RP
Rectum (60Gy)		Rectum (70Gy)	
V60Gy	0.85	V60Gy	0.76
V50Gy	0.85	V50Gy	0.76
V40Gy	0.17	V40Gy	0.76
V30Gy	0.08	D30%	0.76
D0.1cc	0.17	D25%	0.76
		D53%	0.76
		D0.1cc	0.40

### 3.2.4 Anal canal

In table 3.35 and 3.36, we can see that there was a statistical difference for the V28Gy on the lower prescription, and even for the V32Gy, even if the p-value was not smaller than 0.05, it was still close and gave us a remarkable decrease of the dose received by the anal canal.

Table 3.35: Mean and standard deviation for other dose levels Canal Anal

	MO	RP		MO	RP
Canal Anal 60Gy			Canal_Anal 70Gy		
V28Gy [%]	24.32 ± 10.98	15.32 ± 9.32	D35% [Gy]	13.64 ± 13.66	9.20 ± 12.13
V32Gy [%]	20.36 ± 9.78	13.20 ± 8.39	D40% [Gy]	10.91 ± 12.16	7.33 ± 10.37

Table 3.36: P-Value for comparison of different dose level canal anal, in green the p-value lower than 0.05

	MO vs RP		MO vs RP
Canal_Anal		Canal_Anal	
V28Gy	< 0.01	D35%	0.70
V32Gy	0.07	D40%	1.00

### 3.2.5 Small bowel and sigmoid colon

In table 3.37 and 3.38 we can see that for this 2 OAR too there is not any statistical differences.

Table 3.37: Mean and standard deviation for other dose levels Bowel small and sigmoid colon

			MO	RP
Colon_Sigmoid 70				
V60Gy [%]			$0.19 \pm 0.47$	$0.13 \pm 0.34$
V50Gy [%]			$17.18 \pm 13.23$	$16.92 \pm 13.53$
V40Gy [%]			$29.52 \pm 20.65$	$24.16 \pm 22.10$
D30% [Gy]			$37.34 \pm 14.23$	$35.56 \pm 14.97$
D25% [Gy]			$39.65 \pm 14.66$	$37.48 \pm 15.35$
D53% [Gy]			$27.69 \pm 11.91$	$26.82 \pm 13.41$
D0.1cc [Gy]			$55.73 \pm 15.48$	$55.18 \pm 9.56$
Bowel_Small 60	MO	RP	Bowel_Small 70	
V42.86Gy [cc]	$21.05 \pm 33.18$	$16.80 \pm 27.78$	V45Gy [cc]	$3.76 \pm 7.09$ $3.08 \pm 4.55$
D2% [Gy]	$25.42 \pm 17.93$	$21.51 \pm 17.94$	D2% [Gy]	$34.38 \pm 13.37$ $35.65 \pm 14.14$
D0.1cc [Gy]	$37.06 \pm 13.85$	$35.80 \pm 15.49$	D0.1cc [Gy]	$43.32 \pm 15.48$ $47.11 \pm 16.55$

Table 3.38: P-value for model comparison for other dose levels for sigmoid colon and bowel small, in green the p-value lower than 0.05

			MO vs RP
Colon_Sigmoid 70			
V60Gy			0.78
V50Gy			1
V40Gy			0.63
D30%			0.98
D25%			0.98
D53%			0.98
D0.1cc			0.98
Bowel_Small 60	MO vs RP	Bowel_Small 70	
V42.86Gy	1.00	V45Gy	0.99
D2%	1.00	D2%	1
D0.1cc	0.79	D0.1cc	0.62

### 3.3 Comparison with other techniques

#### 3.3.1 comparison with IMRT vs VMAT using RapidPlan for the same models

While comparing IMRT and VMAT, I chose non to do a p-value test, because the two different techniques will show us different results, this has already been tested in the literature [52]. .

This analysis was mostly to see if RapidPlan could give us adequate planifications for IMRT while using a RapidPlan model that has only VMAT planifications in its model.

**3.3.1.1 PTV\_6600\_eval**

Table 3.39: Mean and standard deviation for other techniques on the PTV\_6600\_eval

	MO	IMRT 5 1	IMRT 5 2	IMRT 7 1	IMRT 7 2
PTV_6600_eval					
D95% [Gy]	$64.43 \pm 0.36$	$63.20 \pm 0.36$	$63.53 \pm 0.26$	$63.93 \pm 0.27$	$63.84 \pm 0.18$
D0.1cc [Gy]	$68.35 \pm 0.66$	$68.67 \pm 0.72$	$68.76 \pm 0.39$	$68.01 \pm 0.59$	$68.28 \pm 0.40$
HI	$0.054 \pm 0.009$	$0.085 \pm 0.012$	$0.079 \pm 0.008$	$0.061 \pm 0.017$	$0.067 \pm 0.005$
CIP 100	$0.50 \pm 0.07$	$0.48 \pm 0.01$	$0.49 \pm 0.01$	$0.49 \pm 0.07$	$0.48 \pm 0.01$
CIP 95	$0.88 \pm 0.01$	$0.89 \pm 0.02$	$0.89 \pm 0.02$	$0.88 \pm 0.02$	$0.89 \pm 0.02$

We can see on table 3.38 that the manually optimised plans are still better than the planifications done with IMRT and RapidPlan.

**3.3.1.2 PTV\_5000\_eval and PTV\_5000\_hotspot**

Again we can clearly see on table 3.39 that the D95% was lower on all the IMRT planification while all the hotspot were higher.

Table 3.40: Mean and standard deviation for other techniques on the PTV\_5000\_hotspot and PTV\_5000\_eval

	MO	IMRT 5 1	IMRT 5 2	IMRT 7 1	IMRT 7 2
PTV_5000_hotspot					
D0.1cc [Gy]	$53.18 \pm 2.62$	$54.30 \pm 2.69$	$54.57 \pm 2.04$	$53.44 \pm 2.20$	$53.43 \pm 1.55$
HI	$0.061 \pm 0.032$	$0.125 \pm 0.039$	$0.128 \pm 0.023$	$0.090 \pm 0.034$	$0.094 \pm 0.013$
PTV_5000_eval					
D95% [Gy]	$48.88 \pm 0.88$	$46.92 \pm 0.96$	$47.11 \pm 0.57$	$47.99 \pm 0.57$	$47.83 \pm 0.35$

**3.3.1.3 Rectum**

We can see on table 3.40 that all the objectives were similar while comparing IMRT and MO planifications, while the hotspot were a bit lower.

Table 3.41: Mean and standard deviation for other techniques on the Rectum

	MO	IMRT 5 1	IMRT 5 2	IMRT 7 1	IMRT 7 2
Rectum					
V62Gy [%]	$8.60 \pm 2.60$	$7.68 \pm 2.47$	$7.88 \pm 2.55$	$7.78 \pm 2.56$	$7.85 \pm 2.67$
V53Gy [%]	$14.34 \pm 4.89$	$16.49 \pm 4.03$	$15.47 \pm 3.81$	$14.05 \pm 4.01$	$15.01 \pm 3.96$
V44Gy [%]	$26.45 \pm 6.48$	$29.96 \pm 6.16$	$28.89 \pm 6.12$	$26.24 \pm 5.99$	$27.84 \pm 6.77$
V35Gy [%]	$38.98 \pm 7.84$	$50.30 \pm 9.06$	$50.82 \pm 9.69$	$43.86 \pm 8.14$	$43.21 \pm 8.64$
V27Gy [%]	$54.72 \pm 12.65$	$70.17 \pm 12.32$	$69.19 \pm 13.26$	$62.69 \pm 10.35$	$62.07 \pm 10.13$
D30% [Gy]	$40.44 \pm 3.56$	$43.74 \pm 3.35$	$43.18 \pm 4.20$	$41.15 \pm 3.83$	$42.03 \pm 4.96$
D25% [Gy]	$43.94 \pm 3.49$	$46.49 \pm 3.16$	$45.89 \pm 3.70$	$44.01 \pm 3.32$	$45.00 \pm 4.03$
D53% [Gy]	$27.45 \pm 4.18$	$33.06 \pm 4.75$	$33.12 \pm 4.71$	$30.42 \pm 4.18$	$30.35 \pm 5.15$
D0.1cc [Gy]	$65.69 \pm 0.31$	$65.37 \pm 0.23$	$65.42 \pm 0.27$	$65.23 \pm 0.49$	$65.34 \pm 0.29$

### 3.3.1.4 Anal Canal

We can see on table 3.41 that the mean doses were similar across the planifications.

Table 3.42: Mean and standard deviation for other techniques on the anal canal

	MO	IMRT 5 1	IMRT 5 2	IMRT 7 1	IMRT 7 2
Canal_Anal					
Dmean [Gy]	$13.91 \pm 9.30$	$14.47 \pm 6.75$	$14.12 \pm 6.49$	$13.56 \pm 6.54$	$13.70 \pm 6.49$

### 3.3.1.5 Bladder

We can see on table 3.42 that again the objectives were similar across the 5 planifications.

Table 3.43: Mean and standard deviation for other techniques on the bladder

	MO	IMRT 5 1	IMRT 5 2	IMRT 7 1	IMRT 7 2
Bladder					
V49Gy [%]	$18.22 \pm 9.30$	$17.08 \pm 8.99$	$16.49 \pm 9.12$	$17.68 \pm 8.75$	$16.54 \pm 9.44$
V62Gy [%]	$7.83 \pm 4.18$	$7.19 \pm 4.04$	$7.23 \pm 4.03$	$7.46 \pm 4.12$	$7.39 \pm 4.35$
D53% [Gy]	$23.15 \pm 15.20$	$24.87 \pm 14.17$	$23.37 \pm 14.70$	$23.35 \pm 4.01$	$22.59 \pm 12.98$
D0.1cc [Gy]	$67.78 \pm 0.58$	$67.49 \pm 0.54$	$67.44 \pm 0.45$	$67.02 \pm 0.49$	$67.10 \pm 0.41$

### 3.3.1.6 Sigmoid Colon

We can see on table 3.43 that the objectives were a bit higher on the IMRT planifications, not by a lot, but we can still see the difference.

Table 3.44: Mean and standard deviation for other techniques on the sigmoid colon

	MO	IMRT 5 1	IMRT 5 2	IMRT 7 1	IMRT 7 2
Colon_Sigmoid					
V53Gy [%]	$0.01 \pm 0.33$	$0.11 \pm 0.31$	$0.09 \pm 0.15$	$0.04 \pm 0.07$	$0.02 \pm 0.05$
V44Gy [%]	$6.61 \pm 9.50$	$6.85 \pm 10.10$	$7.45 \pm 8.87$	$6.93 \pm 8.78$	$6.47 \pm 9.26$
V35Gy [%]	$14.90 \pm 21.08$	$20.25 \pm 19.05$	$17.94 \pm 18.35$	$17.98 \pm 16.44$	$15.46 \pm 15.19$
V27Gy [%]	$28.65 \pm 28.80$	$33.10 \pm 29.26$	$35.30 \pm 27.01$	$30.60 \pm 23.87$	$27.07 \pm 23.41$
D30% [Gy]	$20.83 \pm 17.37$	$22.17 \pm 16.36$	$21.46 \pm 16.41$	$21.36 \pm 15.82$	$20.59 \pm 15.33$
D25% [Gy]	$21.86 \pm 17.83$	$23.40 \pm 16.78$	$22.65 \pm 17.01$	$22.79 \pm 16.46$	$22.00 \pm 16.02$
D53% [Gy]	$15.34 \pm 13.88$	$16.36 \pm 14.26$	$17.56 \pm 12.87$	$15.68 \pm 12.34$	$15.35 \pm 11.49$
D0.1cc [Gy]	$42.73 \pm 21.29$	$42.14 \pm 20.88$	$42.56 \pm 20.97$	$42.29 \pm 20.63$	$41.90 \pm 19.69$

### 3.3.1.7 Bowel Small

We can see on table 3.44 that the objectives were similar for the 5 planifications.

Table 3.45: Mean and standard deviation for other techniques on the bowel small

	MO	IMRT 5 1	IMRT 5 2	IMRT 7 1	IMRT 7 2
Bowel_Small					
V45Gy [cc]	$1.60 \pm 1.98$	$1.52 \pm 1.98$	$1.56 \pm 2.07$	$1.66 \pm 2.05$	$1.64 \pm 2.02$
D2% [Gy]	$25.48 \pm 20.63$	$25.48 \pm 20.19$	$25.55 \pm 20.50$	$25.84 \pm 20.41$	$25.85 \pm 20.57$
D0.1cc [Gy]	$30.22 \pm 23.03$	$30.08 \pm 22.39$	$30.46 \pm 22.60$	$30.21 \pm 22.43$	$30.35 \pm 22.54$

## 3.4 comparison with new models

### 3.4.1 Comparison for 2 new models

I will now test the 2 models : RP\_WO and RP\_SP that I mentioned (Cf 2.1.5.1.6 and 2.1.5.1.7). I analysed the results to see the effects of the closed loop strategy (RP\_SP) and the effect of the structures "\_in" and "\_out" (RP\_WO).

#### 3.4.1.1 PTV\_6600\_eval

As we can see on table 3.45 and 3.46, the only two models there were not statistically different for the PTV\_6600\_eval were the RP4 and RP\_WO.

As before, the CIP100 was consistent across all the models.

And when using a RapidPlan model, the standard deviation was lowered, which means the planification were more consistent.

Table 3.46: Mean and standard deviation for comparison of new models for the PTV\_6600\_eval

	MO	RP	RP_WO	RP_SP
PTV_6600_eval				
D95% [Gy]	$64.58 \pm 0.43$	$64.41 \pm 0.14$	$64.41 \pm 0.19$	$64.50 \pm 0.10$
D0.1cc [Gy]	$68.24 \pm 0.64$	$68.52 \pm 0.51$	$68.69 \pm 0.48$	$68.30 \pm 0.38$
HI	$0.050 \pm 0.014$	$0.062 \pm 0.007$	$0.065 \pm 0.008$	$0.058 \pm 0.005$
CIP 100	$0.49 \pm 0.09$	$0.49 \pm 0.01$	$0.49 \pm 0.01$	$0.49 \pm 0.01$
CIP 95	$0.85 \pm 0.06$	$0.88 \pm 0.02$	$0.89 \pm 0.02$	$0.88 \pm 0.02$

Table 3.47: P-Value for for comparison of new models for the PTV\_6600\_eval

	MO vs RP4	MO vs WO	RP4 vs WO	MO vs SP	RP4 vs SP
PTV_6600_eval					
D95% [Gy]	< 0.01	< 0.01	0.33	< 0.01	< 0.01
D0.1cc [Gy]	0.02	< 0.01	0.15	0.10	0.15
HI	< 0.01	< 0.01	0.15	< 0.01	0.04
CIP 100	0.10	0.08	1.00	0.10	1.00
CIP 95	< 0.01	< 0.01	0.90	< 0.01	0.10

#### 3.4.1.2 PTV\_5000\_eval and PTV\_5000\_hotspot

As we can see on table 3.47 and 3.48, the only statistical differences were when comparing the RP\_WO and MO planifications and RP4 and RP\_SP.

Table 3.48: Mean and standard deviation for comparison of new models for the PTV\_5000\_eval and PTV\_5000\_hotspot

	MO	RP	RP_WO	RP_SP
PTV_5000_hotspot				
D0.1cc [Gy]	$53.58 \pm 2.15$	$53.06 \pm 1.57$	$53.15 \pm 1.62$	$53.02 \pm 1.74$
HI	$0.063 \pm 0.017$	$0.063 \pm 0.012$	$0.068 \pm 0.013$	$0.061 \pm 0.016$
PTV_5000_eval				
D95% [Gy]	$49.00 \pm 0.38$	$48.89 \pm 0.27$	$48.79 \pm 0.32$	$48.92 \pm 0.39$

Table 3.49: P-Value for comparison of new models for the PTV\_5000\_eval and PTV\_5000\_hotspot

	MO vs RP4	MO vs WO	RP4 vs WO	MO vs SP	RP4 vs SP
PTV_5000_hotspot					
D0.1cc [Gy]	0.23	0.33	0.90	0.06	0.62
HI	0.77	0.10	0.33	0.46	0.23
PTV_5000_eval					
D95% [Gy]	0.06	< 0.01	0.23	0.77	< 0.01

### 3.4.1.3 Rectum

As we can see on table 3.49 and 3.50, the RP\_WO was comparatively similar to the RP4 across all range of doses while having a statistically higher hotspot.

While the RP\_SP was statistically worse than the RP4 at lower doses.

But when comparing RP\_SP with the MO planifications, all of the objectives were still statistically better across all ranges of doses.

Table 3.50: Mean and standard for comparison of new models for the rectum

	MO	RP	RP_WO	RP_SP
Rectum				
V62Gy [%]	$10.58 \pm 4.13$	$8.95 \pm 3.58$	$8.65 \pm 3.49$	$9.69 \pm 3.92$
V53Gy [%]	$19.21 \pm 6.32$	$15.30 \pm 5.53$	$14.98 \pm 5.64$	$16.52 \pm 5.89$
V44Gy [%]	$35.24 \pm 7.15$	$26.07 \pm 7.12$	$25.88 \pm 8.33$	$28.45 \pm 7.30$
V35Gy [%]	$52.04 \pm 8.87$	$37.75 \pm 8.27$	$39.21 \pm 10.83$	$42.71 \pm 8.23$
V27Gy [%]	$67.54 \pm 11.42$	$52.96 \pm 9.96$	$55.86 \pm 12.36$	$60.18 \pm 9.78$
D30% [Gy]	$46.44 \pm 4.70$	$40.26 \pm 5.44$	$40.21 \pm 5.73$	$42.55 \pm 4.67$
D25% [Gy]	$49.21 \pm 4.52$	$44.13 \pm 5.19$	$43.77 \pm 5.50$	$46.08 \pm 4.64$
D53% [Gy]	$33.67 \pm 6.54$	$26.73 \pm 4.86$	$27.98 \pm 5.62$	$29.67 \pm 4.90$
D0.1cc [Gy]	$65.50 \pm 0.70$	$65.43 \pm 1.12$	$66.23 \pm 1.64$	$65.35 \pm 0.87$

Table 3.51: P-Value for comparison of new models for the rectum

	MO vs RP4	MO vs WO	RP4 vs WO	MO vs SP	RP4 vs SP
Rectum					
V62Gy [%]	0.15	0.06	0.90	0.46	0.90
V53Gy [%]	0.04	< 0.01	0.98	0.15	0.90
V44Gy [%]	< 0.01	< 0.01	0.98	< 0.01	0.33
V35Gy [%]	< 0.01	< 0.01	0.62	< 0.01	< 0.01
V27Gy [%]	< 0.01	< 0.01	0.33	< 0.01	< 0.01
D30% [Gy]	< 0.01	< 0.01	1.00	< 0.01	0.06
D25% [Gy]	< 0.01	< 0.01	1.00	< 0.01	0.33
D53% [Gy]	< 0.01	< 0.01	0.33	< 0.01	< 0.01
D0.1cc [Gy]	0.23	< 0.01	< 0.01	< 0.01	0.15

### 3.4.1.4 Anal canal

As we can see on table 3.51 and 3.52, RP4 and RP\_WO were statistically better than the manually optimised plans, but between the RapidPlan models there are no statistical differences.

Table 3.52: Mean and standard deviation for comparison of new models for the anal canal

	MO	RP	RP_WO	RP_SP
Anal Canal				
Dmean [Gy]	$16.72 \pm 7.49$	$12.79 \pm 6.66$	$12.60 \pm 6.54$	$14.21 \pm 7.03$

Table 3.53: P-Value for comparison of new models for the anal canal

	MO vs RP4	MO vs WO	RP4 vs WO	MO vs SP	RP4 vs SP
Canal_Anal					
Dmean [Gy]	< 0.01	< 0.01	1.00	0.23	0.46

#### 3.4.1.5 Bladder

As we see on table 3.53 and 3.54, the performance of the models are the same on what we saw with the anal canal.

Table 3.54: Mean and standard for comparison of new models for the bladder

	MO	RP	RP_WO	RP_SP
Bladder				
V49Gy [%]	$22.42 \pm 10.61$	$19.21 \pm 10.47$	$18.39 \pm 10.01$	$19.94 \pm 11.10$
V62Gy [%]	$9.99 \pm 5.83$	$9.10 \pm 5.64$	$8.74 \pm 5.26$	$9.40 \pm 5.98$
D53% [Gy]	$26.40 \pm 14.47$	$22.56 \pm 13.49$	$22.72 \pm 13.34$	$23.77 \pm 14.04$
D0.1cc [Gy]	$67.62 \pm 0.65$	$68.00 \pm 0.64$	$68.10 \pm 0.67$	$67.79 \pm 0.50$

Table 3.55: P-Value for comparison of new models for the bladder

	MO vs RP4	MO vs WO	RP4 vs WO	MO vs SP	RP4 vs SP
Bladder					
V49Gy [%]	0.04	0.04	0.77	0.46	0.77
V62Gy [%]	0.50	0.33	0.98	0.77	0.98
D53% [Gy]	< 0.01	0.02	1.00	0.06	0.90
D0.1cc [Gy]	< 0.01	< 0.01	0.62	0.10	0.23

#### 3.4.1.6 Sigmoid colon and small bowel

As we can see on table 3.55 and 3.56, there were no statistical differences at all even if the manually optimised plans seems having a higher mean across the objectives. This phenomena is due to their high standard deviation, which will not allow the test to confirm the statistical differences.

Table 3.56: Mean and standard deviation for comparison of new models for the Sigmoid colon

	MO	RP	RP_WO	RP_SP
sigmoid colon				
V62Gy [%]	$0.02 \pm 0.08$	$0.01 \pm 0.06$	$0.01 \pm 0.06$	$0.02 \pm 0.08$
V53Gy [%]	$0.10 \pm 0.32$	$0.06 \pm 0.22$	$0.05 \pm 0.21$	$0.06 \pm 0.25$
V44Gy [%]	$9.05 \pm 10.76$	$5.86 \pm 7.71$	$5.52 \pm 7.37$	$6.16 \pm 8.07$
V35Gy [%]	$20.43 \pm 20.62$	$13.46 \pm 14.94$	$13.84 \pm 16.18$	$14.08 \pm 15.41$
V27Gy [%]	$31.79 \pm 29.87$	$24.64 \pm 25.68$	$24.97 \pm 26.74$	$26.78 \pm 26.95$
D30% [Gy]	$21.49 \pm 17.24$	$18.09 \pm 14.95$	$17.99 \pm 15.04$	$18.75 \pm 15.35$
D25% [Gy]	$22.88 \pm 17.80$	$19.46 \pm 15.73$	$19.28 \pm 15.76$	$20.09 \pm 16.07$
D53% [Gy]	$16.18 \pm 13.97$	$13.81 \pm 11.97$	$14.13 \pm 12.42$	$14.74 \pm 12.76$
D0.1cc [Gy]	$42.00 \pm 22.09$	$40.80 \pm 22.40$	$40.53 \pm 22.45$	$40.08 \pm 22.61$
Bowel_Small				
V45Gy [cc]	$13.57 \pm 29.12$	$1.49 \pm 3.33$	$0.89 \pm 1.38$	$0.96 \pm 1.41$
D2% [Gy]	$25.02 \pm 20.14$	$22.74 \pm 18.95$	$22.07 \pm 18.81$	$23.29 \pm 19.08$
D0.1cc [Gy]	$29.42 \pm 23.00$	$28.96 \pm 23.02$	$28.23 \pm 23.03$	$29.36 \pm 23.10$

Table 3.57: P-Value for comparison of new models for the sigmoid colon

	MO vs RP4	MO vs WO	RP4 vs WO	MO vs SP	RP4 vs SP
Colon_Sigmoid					
V62Gy [%]	1.00	1.00	1.00	1.00	1.00
V53Gy [%]	0.98	0.98	1.00	0.91	0.82
V44Gy [%]	0.34	0.21	1.00	0.70	0.88
V35Gy [%]	0.05	0.18	1.00	0.15	0.88
V27Gy [%]	0.27	0.43	0.93	0.60	0.98
D30% [Gy]	0.35	0.35	1.00	0.35	1.00
D25% [Gy]	0.24	0.24	1.00	0.35	1.00
D53% [Gy]	0.35	0.50	1.00	0.67	0.95
D0.1cc [Gy]	0.84	1.00	0.95	0.84	1.00
Bowel_Small					
V45Gy [cc]	0.16	0.09	0.92	0.10	0.72
D2% [Gy]	0.68	0.56	1.00	0.67	1.00
D0.1cc [Gy]	0.99	0.36	0.88	0.99	0.96

## Chapter 4

# Discussion

As in chapter 3, I highly advise to look at the third appendix when reading this chapter, it may lead to a faster understanding.

### 4.1 Implementation of RapidPlan

The version of RapidPlan I used was the first one that uses gEUD, thus is a new technique and still suffer from immaturity.

During the implementation of RapidPlan, I tried different strategies as already stated with the goal to create the best model possible.

The simplest was to put the objectives on the PTV\_6600\_eval, PTV\_5000\_hotspot and PTV\_5000\_eval. I used the most used constraints utilised in the service and the most important feature for this work were the different constraints to the OAR's.

#### 4.1.1 Double gEUD combined

A double gEUD is when I used two different gEUD for the same OAR.

I started by using a double gEUD (RP1, RP2) on all the "OAR\_out" but that lead to a worse sparring of the OAR and a worse coverage of the PTV\_6600 and the PTV\_5000 when compared to models done with a single gEUD (RP3, RP4 and RP5). This is due to the fact that RapidPlan was intended to work with simpler constraints that work on a single point of the DVH in contrast of the gEUD that work on all the DVH curve (cfrt 1.4). Hence the double gEUD led to a overlapping and maybe contradictory constraint, comparatively to the upper and lower where the overlapping is more difficult to achieve. But with the nature of the gEUD they will overlap over a dose range, and they will give us a worse results. Double gEUD can lead us to better results when manually optimised by a trained physicist, but for now it does not fit well with RapidPlan. RapidPlan still needs refinements about how it calculates the gEUD

constraints when using double gEUD. In fact the lowest gEUD possible in this case may not be the best, it would be better to have a compromise between the two.

### 4.1.2 Single gEUD

When using a single gEUD and one or more upper on the OAR (RP3, RP4 and RP5), RapidPlan started to give better results compared to the models created before (RP1, RP2) by having a better coverage of the 2 PTV' and a better OAR sparing across the whole DVH. This was due to the change of the double gEUD up to a single one, this manoeuvre led to better constraints set by RapidPlan.

After introducing the single gEUD model, the greatest difficulty was to optimise the priorities of the objectives and to add some upper objectives in order to help RapidPlan to do a better planification.

### 4.1.3 Auto-generated priorities

RP5 had the same constraints as RP4. The only differences were the priorities who were auto-generated by RapidPlan like so they were not fixed by the creator of the model.

As said in the literature, having fixed priorities for pelvic treatment would give us better planifications when using RapidPlan, but I wanted to explore to see the feedback that I would receive using gEUD in a RapidPlan model. That is the main reason why I used the first method. The results were clear, across all the OAR there was a sharp improvement. But in the meantime the loss in the PTVs coverage was too great to be considered as acceptable.

This is due to the fact that gEUD are powerful constraints that work on all the DVH and not only on specific points of it. This means that RapidPlan is still not mature enough to use auto-generated priorities with gEUD because it sets too high priorities for the geometry of the patient.

### 4.1.4 PTV behaviour

As expected from RapidPlan, the standard deviation of the PTVs' constraints were lower than the ones compared to the manual optimisation (cf 1.4.2). Thus having a better interplanification consistency.

Another important aspect was that the D95% for RP models were always lower than the MO planifications, but the CIP95 were always higher. This means that the coverage and conformity were always better for the RP models while the minimum dose received by the 95% of the volume was lower. This was not a problem because the D95% were still higher than the constraints of the clinical protocol set by the radiotherapist.

The HI was higher when using the RP models.

### 4.1.5 OAR behaviour

Across the 5 models, the OARs had mainly the same behaviour, the biggest difference was the amplitude of those differences. This means that the difference on the doses when comparing OARs were similar. The consequence of this behaviour was that the standard deviation of the OARs constraints were very close in every model.

This behaviour was to be expected. In fact, prostate treatments are similar to the treatment of a sphere, when without lymph nodes and of a cylinder when with lymph nodes. That is the reason why, when optimising, we lower the dose all around in about the same way. This may not be true due to the priorities of the OAR, but in this work the ratio of the priorities did not change a lot.

### 4.1.6 Hotspots

The average hotspots when comparing RP planifications with the MO have a big dependency on the considered structure.

For the PTV\_6600\_eval the hotspot were slightly higher for RP planifications on average but with a smaller standard deviation. This is also one of the factor that led to the higher HI for the RP planifications.

For the PTV\_5000\_hotspot they were always lower with a smaller standard deviation for RP planifications.

The rectum had a lower hotspot with the same standard deviation. In other papers they found that RP almost always led to a higher hotspot, but this was not the case, in this work. The reason is probably due to the fact that I used the OAR structure "\_in" and "\_out".

### 4.1.7 Differences for treatment with lymph nodes and without lymph nodes

The biggest difference when comparing the RP planifications and MO planifications with or without lymph nodes was that with lymph nodes there was a biggest increment in OAR sparing. The coverage of the PTVs was slightly worse, but this was not a big problem because the decrease was still within acceptable margin, and the gain in OAR was better than the lost coverage of the PTVs. Physicist may need to optimise manually more after using RapidPlan for prostate treatment with lymph nodes.

This was due to the fact that RapidPlan generally prioritise the OAR sparing.

Thus a model for two different geometries can be done if there are at least 20 plans for each geometry in the model set.

#### 4.1.8 Best RP Models

I previously said, the best of the 5 models I created during the implementation was RP4. The reason is that it gives a similar coverage of the two PTVs while still having a better OAR sparring than the MO planifications.

The rectum was the OAR where we saw the biggest improvements, this concerns the case of planifications with or without lymph nodes.

Regarding the other OARs there were big improvements. Nevertheless they were not big enough to be statistically significant because of the high standard deviation.

## 4.2 Usage of RapidPlan models trained with a specific dose prescription for other dose prescriptions

The RapidPlan optimised planifications were done with the RP4, which is the best amongst the 5 models that I created.

I averaged the results of 10 cases for the 70Gy prescription (8 with lymph nodes and 2 without lymph nodes) and 20 cases for the 60Gy prescription (10 with lymph nodes and 10 without lymph nodes).

This indicates that the statistical importance was less compared to other tests. Nonetheless they were the only cases made with those prescription in the 2 years span.

### 4.2.1 Coverage of the PTVs

While using a RapidPlan model created with another dose prescription than the one of the planification we can see that there are no big statistical differences for the coverage of the PTVs. And that is a good news, because on the tests done in the precedent section we saw that the D95% was lower but the CIP95 was higher. In this particular case there were no differences, which is a positive way to show that it has not gone worse.

The standard deviations were the same, they did not decrease as when comparing RP4 for the 66Gy prescription with MO, but they maintained approximately the same. The only exception was the hotspot of the PTV\_5000\_hotspot. This exception was probably due to difference in the dose ratio of the two PTVs. As a consequence of the added margin of 8mm to create the PTV\_low\_hotspot is probably not adequate for these two cases prescriptions, but it could be modified by the physicist beforehand.

### 4.2.2 OAR sparring

There were no statistical differences in the OAR constraints, nonetheless they were slightly lower while using RapidPlan. The standard deviation were always higher or the same(excluded

some rare exceptions), oppositely in what I have explained in the last section. Once again, this may be due to the constraints not being enough powerful in some planifications and too powerful in others. It all depends on the geometry of the patient.

The model was created on purpose for the 66Gy prescription, this is why this model may not be the best for those other prescriptions.

### 4.2.3 Differences between the two dose prescriptions

I expected the results not to be different depending on the dose prescription when comparing the RapidPlan with the MO planifications and my expectation were met. This is was due to the ratio of the two dose levels.

This can be explained with the fact that the most important parameter for RapidPlan is the ratio between the different DVH of the PTVs and OARs rater than the absolute dose of them.

Consequently this RapidPlan model can be used as a starting point for planifications with other dose prescriptions and it should be similar to a manually optimised planification.

## 4.3 Usage of RapidPlan model trained with a VMAT treatment used for a IMRT treatment

In order to compare the use of RapidPlan for a different treatment technique, I averaged the value of 20 planifications (11 without lymph nodes and 9 with lymph nodes). My main goal was to have faster results. I only compared 20 planifications because I would not have done the KS test. In fact, as I already said, I did not want to assert the differences between IMRT and VMAT, but to see if it could give us an achievable planification. I already knew there would be differences in comparing IMRT and VMAT.

With those comparisons I wanted to see if RapidPlan would give coherent results for another technique.

This has already been tested in the literature, however I wanted to see if a RapidPlan model with gEUD would still give acceptable results[34].

### 4.3.1 Number of beam

The quality of the planification treatment will get better as the number of beams increase. This has already been proved multiple times [53].

I tried with 5 and 7 beams with two different geometry to attempt and test if the results would be acceptable or not. In the end, acceptable planifications were achieved only for treatments without lymph nodes, but it was because of not having enough beams.

The constraints generated by RapidPlan were coherent.

In the hypothesis I would have continued to add beams, we would have had acceptable results even for the treatment with lymph nodes.

### 4.3.2 RapidPlan usage

Unfortunately, I could not compare MO planifications of IMRT with a IMRT RP planification, because this kind of planification was not done in the last two years at the CHU Namur. Yet the constraints generated by RapidPlan for this technique were acceptable for this kind of approach. In fact those were the expected results for IMRT planifications, consequently I can conclude that RP4 can be used for IMRT planification. However it is still advisable to manually fine tune to get an even better planifications.

These conclusions are the same as the ones that I found in the literature, hence the use of gEUD will not change their results [34].

I still advise to add some IMRT planification into the RapidPlan model if the model would be used daily also for IMRT planifications. Or creating a model for it.

## 4.4 RapidPlan models with manual planifications in the model and without personalised structures

During my work at CHU Namur I created two extra models. The first was created with the same constraints as RP4 but with all the planifications in the model set were MO planifications, thus not taking advantage of the closed loop strategy. This model was created to quantify the amelioration due to the closed loop strategy. The second was created without "\_in" and "\_out" structures. This model was created in order to quantify the amelioration we have achieved with the use to those two structures.

### 4.4.1 RapidPlan model with standard planifications

With this model, the changes are in the same direction as the improvements of RP4, but to a smaller degree.

The planifications done with this model are in the middle of the MO planifications and the RP4 planifications. This was an expected results. Because the closed loop strategy helped us in widening the differences for the model.

The D95% of the PTV\_6600\_eval and the PTV\_5000\_eval was better in this model than the RP4, same for the homogeneity index. But this model lost some of the gains in the OAR sparing of the low to middle doses.

In addition almost all of the standard deviation were bigger than the standard deviation of the model RP4.

The lost of OAR sparing was greater than the gain of the D95% on the 2 PTVs, hence I considered that the RP4 was the best of the two as expected. Furthermore, the closed loop strategy is a good strategy when implementing RapidPlan.

#### 4.4.2 RapidPlan model without "\_in" and "\_out" structures

When comparing this model to the RP4, all the results were almost the same. The biggest differences were the hotspot for the OAR the PTVs. They were always higher than the RP4 planifications. The biggest drawback were the hotspots of the rectum, indeed the average hotspot was higher than the limit set by the clinical protocol. Even the hotspots of the other OARs, even if they were not statistically different, they were always higher and their clinical objectives were met with more difficulties than when using the RP4 model.

The biggest benefit of this model, is that it is a faster model to use due to not having to create all the OAR "\_in" and "\_out", as a consequence its use becomes more efficient.

The results of this model were closer to what we have seen on the literature, with higher hotspot seen when utilising RP model compared to MO planifications. The use of "\_in" and "\_out" structures helped to not have hotspot on the structures. Although it may not have been the only reason, it is possible that the priorities set on the upper constraints for the hotspot on the OAR were not high enough, but if I changed them to be higher, they may have worsen the coverage of the isodose 95% of the PTVs.

When choosing which model was the best by considering efficiency and quality, I think the RP4 model was fitting better that position thanks to its results. If we think of the usage of the RP\_WO model as a starting point for the planification, it can be seen as a better model, because afterwards the physicist could lessen the hotspot with some manual modifications. After all it is a matter of preference when choosing which one of the two model is better (RP4 or RP\_WO).

## Chapter 5

# Conclusion

RapidPlan is a powerful tool that can help physicist to achieve good planification faster, easier and in a more reliable way without taking into account the experience. It can helps greatly the efficiency of a radiotherapy department.

Yet there are still great drawbacks. When creating a RapidPlan model for a department, the quality of the model is dependant on the experience of the physicist who creates it. An experienced physicist could create a good model in a matter of hours, but for a newly physicist it could take some days. The implementation time will be higher if the physicist wants to do a quantified comparison of the models to try and achieve an even preciser model, but in my experience, the quantifying of the changes is not a required step.

### 5.1 Usage for a different prescription or treatment technique

RapidPlan is also a good tool to use when optimising a planification of the target organ that has a different dose prescription or a different treatment technique than the one that are in the model. It would be better if the model would be adapted to them, but because of the implementation of RapidPlan, this process is a time consuming work. It would not be time efficient to create a model for each dose prescription or technique for a specified organ.

### 5.2 Usage of gEUD

The usage of gEUD in a RapidPlan model was never done before. Indeed, RapidPlan implemented the gEUD only in late September 2021. Thanks to the work made in this thesis, I could tell that the gEUD is a really powerful tool if used in a good manner, and the use of it could simplify the objectives for the planification treatment. But RapidPlan sometimes push too much the gEUD objective having as a consequence a better OAR sparing but a worsened

PTVs coverage.

The use of a double gEUD constraint could be a great idea, but more studies should be done and it should be used with more caution. I think that the way RapidPlan set the constraints of the objective is not adequate to a double gEUD and should be refined more. For a single gEUD there are no problems for RapidPlan to set a good constraint.

### 5.3 Closed loop strategy

The usage of the closed loop strategy is the foundation for a RapidPlan implementation. Without it, the implementation would not be as refined as it should be. The biggest help this strategy can give, is to improve planifications that were not as optimised as they could have been.

This strategy could not be used, if the planifications in the model are known to be the best for their respective geometry. But because there is not a way of knowing that, using the closed loop strategy would always gives us better results or in the worst case scenario, the same result.

### 5.4 Personalised structure : "\_in" and "\_out"

The usage of the structure "\_in" and "\_out" were really useful to cushion the hotspot due to RapidPlan. However the creation of those structure can take some time and it can reduce the efficiency of RapidPlan. Nevertheless the creation of them could be made faster with a personalised script to implement in the TPS Eclipse. This would render the process of using RapidPlan more efficient and it would also add some time to the implementation of it.

The choice to use RP4 instead of RP\_WO is a personal one. Some physicist may prefer RP\_WO because it would be faster in addition the physicist could use it as a starting point for a subsequent optimisation. Some would prefer RP4 because even if it takes a longer time to use it, it would be more probable to give a satisfactory optimisation without the need to optimise it even further.

My personal choice would be to use RP4, because it would give me a better starting point if I want to optimise it further, also I think it is easier to optimise a planification when using those structures because it would be easier to optimise when the structure are more segmented by working on smaller and more important parts of the structures. I chose the quality of the model rather than the efficiency.

Between RP4 and RP\_WO there is no worse or better model, what really matter is the personal choice made by the physicist.

# Bibliography

- [1] Ionizing radiation, health effects and protective measures [WWW Document], n.d. URL <https://www.who.int/news-room/fact-sheets/detail/ionizing-radiation-health-effects-and-protective-measures>
- [2] Pusey, Wm. Allen (1900). "Roentgen rays in the treatment of skin diseases and for the removal of hair". *Journal of Cutaneous Diseases Including Syphilis*. 18: 302–318.
- [3] Lederman M. The early history of radiotherapy: 1895-1939. *Int J Radiat Oncol Biol Phys*. 1981;7:639-648.
- [4] Thames HD Jr. Early fractionation methods and the origins of the NSD concept. *Acta Oncol*. 1988;27:89-103.
- [5] Quimby EH. The history of dosimetry in roentgen therapy. *Am J Roentgenol Radium Ther*. 1945;54:688-703.
- [6] Palta JR, Mackie R, Chen Z. Intensity-modulated radiation therapy- the state of the art. Madison: Medical Physics Publishing; 2003:1-23.
- [7] Sternick ES. The theory and practice of intensity modulated radiation therapy. Madison: Advanced Medical Publishing; 1997.
- [8] Zeman, E.M., Schreiber, E.C., Tepper, J.E., 2020. Basics of Radiation Therapy, in: Abeloff's Clinical Oncology. Elsevier, pp. 431-460.e3. <https://doi.org/10.1016/B978-0-323-47674-4.00027-X>
- [9] Funk, R.K., Stockham, A.L., Laack, N.N.I., 2016. Basics of Radiation Therapy, in: Clinical Cardio-Oncology. Elsevier, pp. 39–60. <https://doi.org/10.1016/B978-0-323-44227-5.00003-X>
- [10] Ionizing Radiation Interactions ||*OncologyMedicalPhysics*, n.d URL <https://oncologymedicalphysics.com/radiation-interactions/>
- [11] Treatment volume , n.d. URL [https://www.radiation-therapy-review.com/Treatment\\_Volume.html](https://www.radiation-therapy-review.com/Treatment_Volume.html)
- [12] van Herk, M., Remeijer, P., Rasch, C., Lebesque, J.V., 2000. The probability of cor-

rect target dosage: dose-population histograms for deriving treatment margins in radiotherapy. *International Journal of Radiation Oncology\*Biology\*Physics* 47, 1121–1135. [https://doi.org/10.1016/S0360-3016\(00\)00518-6](https://doi.org/10.1016/S0360-3016(00)00518-6)

[13] Nenot, J.-C., 2009. *Recommandations 2007 de la Commission internationale de protection radiologique*, Publication de la CIPR. Éd. Tec & doc, Paris.

[14] Drzymala, R.E., Mohan, R., Brewster, L., Chu, J., Goitein, M., Harms, W., Urie, M., 1991. Dose-volume histograms. *International Journal of Radiation Oncology\*Biology\*Physics* 21, 71–78. [https://doi.org/10.1016/0360-3016\(91\)90168-4](https://doi.org/10.1016/0360-3016(91)90168-4)

[15] Cheng, C.-W., Das, I.J., 1999. Treatment plan evaluation using dose-volume histogram (DVH) and spatial dose-volume histogram (zDVH). *International Journal of Radiation Oncology\*Biology\*Physics* 43, 1143–1150. [https://doi.org/10.1016/S0360-3016\(98\)00492-1](https://doi.org/10.1016/S0360-3016(98)00492-1)

[16] Fluence Rate [WWW Document], n.d. . Ionactive. URL <https://ionactive.co.uk/resource-hub/glossary/fluence-rate>

[17] *Radiation Therapy Physics*, Hendee W., Ibbott G. and Hendee E. (2005) Wiley-Liss Publ., ISBN 0-471-39493-9

[18] 8.3.2 - Descriptors Of Dose Distribution (Photons) - OzRadOnc [WWW Document], n.d. URL <http://ozradonc.wikidot.com/descriptors-of-dose-distribution-photons>

[19] Taylor, A., Powell, M.E.B., 2004. Intensity-modulated radiotherapy—what is it? *Cancer Imaging* 4, 68–73. <https://doi.org/10.1102/1470-7330.2004.0003>

[20] Fogliata, A., Thompson, S., Stravato, A., Tomatis, S., Scorsetti, M., Cozzi, L., 2017. On the gEUD biological optimization objective for organs at risk in Photon Optimizer of Eclipse treatment planning system. *J Appl Clin Med Phys* 19, 106–114. <https://doi.org/10.1002/acm2.12224>

[21] Bell, J.P., Patel, P., Higgins, K., McDonald, M.W., Roper, J., 2018. Fine-tuning the normal tissue objective in eclipse for lung stereotactic body radiation therapy. *Medical Dosimetry* 43, 344–350. <https://doi.org/10.1016/j.meddos.2017.11.004>

[22] Rawla, P., 2019. Epidemiology of Prostate Cancer. *World J Oncol* 10, 63–89. <https://doi.org/10.14740/wjon1191>

[23] What Is Prostate Cancer? [WWW Document], n.d. URL <https://www.cancer.org/cancer/prostate-cancer/about/what-is-prostate-cancer.html>

[24] Woodrum, D.A., Kawashima, A., Gorny, K.R., Mynderse, L.A., 2016. Targeted prostate biopsy and MR-guided therapy for prostate cancer. *Abdom Radiol* 41, 877–888. <https://doi.org/10.1007/s00261-016-0681-3>

[25] Fogliata, A., Cozzi, L., Reggiori, G., Stravato, A., Lobefalo, F., Franzese, C., Franceschini, D., Tomatis, S., Scorsetti, M., 2019. RapidPlan knowledge based planning: iterative

learning process and model ability to steer planning strategies. *Radiat Oncol* 14, 187.  
<https://doi.org/10.1186/s13014-019-1403-0>

[26] Scaggion, A., Fusella, M., Roggio, A., Bacco, S., Pivato, N., Rossato, M.A., Peña, L.M.A., Paiusco, M., 2018. Reducing inter- and intra-planner variability in radiotherapy plan output with a commercial knowledge-based planning solution. *Physica Medica* 53, 86–93.  
<https://doi.org/10.1016/j.ejmp.2018.08.016>

[27] Hussein, M., Heijmen, B.J.M., Verellen, D., Nisbet, A., 2018. Automation in intensity modulated radiotherapy treatment planning—a review of recent innovations. *BJR* 91, 20180270.  
<https://doi.org/10.1259/bjr.20180270>

[28] RapidPlan 15.5 Implementation, Varian, Skills Circle, 2018.

[29] Fusella, M., Scaggion, A., Pivato, N., Rossato, M.A., Zorz, A., Paiusco, M., 2018. Efficiently train and validate a RapidPlan model through APQM scoring. *Med. Phys.* 45, 2611–2619. <https://doi.org/10.1002/mp.12896>

[30] Eclipse Photon and Electron Reference Guide. Doc. ID. P1012333-001-A. Varian Medical System; 2015

[31] Fogliata, A., Cozzi, L., Reggiori, G., Stravato, A., Lobefalo, F., Franzese, C., Franceschini, D., Tomatis, S., Scorsetti, M., 2019. RapidPlan knowledge based planning: iterative learning process and model ability to steer planning strategies. *Radiat Oncol* 14, 187.  
<https://doi.org/10.1186/s13014-019-1403-0>

[32] Gysen, K., O’Toole, J., Le, A., Wu, K., Schuler, T., Porter, B., Kipritidis, J., Atyeo, J., Brown, C., Eade, T., 2020. Rolling out RapidPlan: What we’ve learnt. *J Med Radiat Sci* 67, 310–317. <https://doi.org/10.1002/jmrs.420>

[33] Nakamura, K., Okuhata, K., Tamura, M., Otsuka, M., Kubo, K., Ueda, Y., Nakamura, Y., Nakamatsu, K., Tanooka, M., Monzen, H., Nishimura, Y., 2021. An updating approach for knowledge-based planning models to improve plan quality and variability in volumetric-modulated arc therapy for prostate cancer. *J Appl Clin Med Phys* 22, 113–122.  
<https://doi.org/10.1002/acm2.13353>

[34] Wu, H., Jiang, F., Yue, H., Zhang, H., Wang, K., Zhang, Y., 2016. Applying a RapidPlan model trained on a technique and orientation to another: a feasibility and dosimetric evaluation. *Radiat Oncol* 11, 108. <https://doi.org/10.1186/s13014-016-0684-9>

[35] Fogliata, A., Belosi, F., Clivio, A., Navarria, P., Nicolini, G., Scorsetti, M., Vanetti, E., Cozzi, L., 2014. On the pre-clinical validation of a commercial model-based optimisation engine: Application to volumetric modulated arc therapy for patients with lung or prostate cancer. *Radiotherapy and Oncology* 113, 385–391. <https://doi.org/10.1016/j.radonc.2014.11.009>

[36] Schubert, C., Waletzko, O., Weiss, C., Voelzke, D., Toperim, S., Roeser, A., Puccini, S., Piroth, M., Mehrens, C., Kueter, J.-D., Hierholz, K., Gerull, K., Fogliata, A., Block, A., Cozzi, L., 2017. Intercenter validation of a knowledge based model for automated planning of

volumetric modulated arc therapy for prostate cancer. The experience of the German RapidPlan Consortium. *PLoS One* 12, e0178034. <https://doi.org/10.1371/journal.pone.0178034>

[37] Wang, J., Hu, W., Yang, Z., Chen, X., Wu, Z., Yu, X., Guo, X., Lu, S., Li, K., Yu, G., 2017. Is it possible for knowledge-based planning to improve intensity modulated radiation therapy plan quality for planners with different planning experiences in left-sided breast cancer patients? *Radiat Oncol* 12, 85. <https://doi.org/10.1186/s13014-017-0822-z>

[38] Li, N., Carmona, R., Sirak, I., Kasaova, L., Followill, D., Michalski, J., Bosch, W., Straube, W., Mell, L.K., Moore, K.L., 2017. Highly Efficient Training, Refinement, and Validation of a Knowledge-based Planning Quality-Control System for Radiation Therapy Clinical Trials. *Int J Radiat Oncol Biol Phys* 97, 164–172. <https://doi.org/10.1016/j.ijrobp.2016.10.005>

[39] Ueda, Y., Monzen, H., Fukunaga, J., Ohira, S., Tamura, M., Suzuki, O., Inui, S., Isono, M., Miyazaki, M., Sumida, I., Ogawa, K., Teshima, T., 2020. Characterization of knowledge-based volumetric modulated arc therapy plans created by three different institutions' models for prostate cancer. *Reports of Practical Oncology Radiotherapy* 25, 1023–1028. <https://doi.org/10.1016/j.rpor.2020.08.011>

[40] Spratt DE, Pei X, Yamada J, et al. Long-term survival and toxicity in patients treated with high-dose intensity modulated radiation therapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys*. 2013;85(3):686–692.

[41] Dearnaley DP, Jovic G, Syndikus I, et al. Escalated-dose versus control-dose conformal radiotherapy for prostate cancer: long- term results from the MRC RT01 randomised controlled trial. *Lancet Oncol*. 2014;15(4):464–473

[42] Kubo, K., Monzen, H., Ishii, K., Tamura, M., Nakasaka, Y., Kusawake, M., Kishimoto, S., Nakahara, R., Matsuda, S., Nakajima, T., Kawamorita, R., 2019. Inter-planner variation in treatment-plan quality of plans created with a knowledge-based treatment planning system. *Physica Medica* 67, 132–140. <https://doi.org/10.1016/j.ejmp.2019.10.032>

[43] Chang, A.T.Y., Hung, A.W.M., Cheung, F.W.K., Lee, M.C.H., Chan, O.S.H., Philips, H., Cheng, Y.-T., Ng, W.-T., 2016. Comparison of Planning Quality and Efficiency Between Conventional and Knowledge-based Algorithms in Nasopharyngeal Cancer Patients Using Intensity Modulated Radiation Therapy. *International Journal of Radiation Oncology\*Biology\*Physics* 95, 981–990. <https://doi.org/10.1016/j.ijrobp.2016.02.017>

[44] Fogliata, A., Belosi, F., Clivio, A., Navarria, P., Nicolini, G., Scorsetti, M., Vanetti, E., Cozzi, L., 2014. On the pre-clinical validation of a commercial model-based optimisation engine: Application to volumetric modulated arc therapy for patients with lung or prostate cancer. *Radiotherapy and Oncology* 113, 385–391. <https://doi.org/10.1016/j.radonc.2014.11.009>

[45] Kamima, T., Yoshioka, M., Takahashi, R., Sato, T., 2019. Impact of DVH Outliers Registered in Knowledge-based Planning on Volumetric Modulated Arc Therapy Treatment Planning for Prostate Cancer. *Nippon Hoshasen Gijutsu Gakkai Zasshi* 75, 151–159. [https://doi.org/10.6009/jjrt.2019\\_JSRT\\_75.2.151](https://doi.org/10.6009/jjrt.2019_JSRT_75.2.151)

[46] Kuekkong, K., Pleanarom, S., Dankulchai, P., Tangboonduangjit, P., Tuntipumiamorn, L., 2019. Application of the RapidPlan knowledge-based treatment planning system for radiation therapy of prostate cancer patients. *Journal of Thai Association of Radiation Oncology* 25, 29–42.

[47] Paddick, I., 2000. A simple scoring ratio to index the conformity of radiosurgical treatment plans: Technical note. *Journal of Neurosurgery* 93, 219–222. [https://doi.org/10.3171/jns.2000.93.supplement\\_3.0219](https://doi.org/10.3171/jns.2000.93.supplement_3.0219)

[48] Kataria, T., Sharma, K., Subramani, V., Karrthick, K.P., Bisht, S.S., 2012. Homogeneity Index: An objective tool for assessment of conformal radiation treatments. *J Med Phys* 37, 207–213. <https://doi.org/10.4103/0971-6203.103606>

[49] Chang, S.D., Gibbs, I.C., Sakamoto, G.T., Lee, E., Oyelese, A., Adler, J.R., 2005. Staged stereotactic irradiation for acoustic neuroma. *Neurosurgery* 56, 1254–1261; discussion 1261–1263. <https://doi.org/10.1227/01.neu.0000159650.79833.2b>

[50] AAT Bioquest, Inc. (2022, July 1). Quest Graph™ Kolmogorov-Smirnov (K-S) Test Calculator. AAT Bioquest. <https://www.aatbio.com/tools/kolmogorov-smirnov-k-s-test-calculator>.

[51] "Definition of ALGORITHM". Merriam-Webster Online Dictionary. Archived from the original on February 14, 2020. Retrieved November 14, 2019.

[52] Lomas, S., Bachand, F., Lim, P., Fong, M., Stewart, E., Aquino-Parsons, C., n.d. A Comparison of 3DCRT, IMRT, and VMAT Pelvic Radiation for Qualitative and Quantitative Toxicity. *Cureus Journal of Medical Science*.

[53] Fischer-Valuck, B.W., Rao, Y.J., Michalski, J.M., 2018. Intensity-modulated radiotherapy for prostate cancer. *Transl Androl Urol* 7, 297–307. <https://doi.org/10.21037/tau.2017.12.16>