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MSc Thesis
Industrial Engineering and Management

ProaRT:
Preventing delays via proactive linac-capacity planning.

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Management Summary

In this thesis we study how to optimize the logistical planning of the linear accelerators (linacs) in a radiotherapy process. In this complex healthcare process, cancer patients undergo from one up to 35 daily sessions of radiation under a linac, according to its type, in order to shrink or kill the tumor. Due to the medical and technological constraints of the treatments, some patients can only be treated in some of the linacs. Moreover, for some patients, delays in the start of treatment can compromise the quality of the care process. Thus, the challenge of the logistical planning of the linacs resides in assuring that feasible linac capacity is swiftly available for treating new and uncertain coming patients. We define this challenge as the linac capacity planning problem. This problem consists in the allocation of linac capacity (or linac time), in advance and for a mid-term horizon, to different types or categories such that categorized access times (time a patient waits to begin treatment) are minimized.

In order to tackle the linac capacity planning problem, we develop a mathematical method called ProaRT. This method allocates linac capacity to the different categories (patient-types) in advance by setting a threshold on the time a linac can be used to treat a category. In this thesis, we consider linac capacity to be measured in timeslots, where each timeslot corresponds to one session of radiation. For this reason, the allocation ProaRT does can be seen as the maximum number of patients from a category that can be treated on a linac, any given day. The maximum number of patients yielded by ProaRT is calculated via a simulation-and-heuristic approach. The heuristic approach handles the problems characteristics (e.g. linac constraints, daily sessions of radiation, etc.). The simulation part of the approach handles the uncertainty in the arrivals and the mid-term horizon (for in advance planning).

We carry out a series of theoretical and practical experiments with ProaRT to test how well it tackles the problem. The data used for the experiments is based on the current situation of the NKI-AVL. In experiments we compare planning through ProaRT and planning through open access scheduling (planning a patient as early as possible), which is the current way of working of the NKI-AVL. In ProaRT day-to-day scheduling of patients is done as follows: all sessions of radiation of a patient are planned on the earliest available linac that (1) has less than the number of maximum patients (given by the ProaRT table) planned and that (2) has the least number of total planned patients. The theoretical experiments show that ProaRT can achieve up to 90% lower access times compared to an open access scheduling approach. Nevertheless, the more linac constraints and uncertainty in the arrival of patients there are, the less the impact of ProaRT. In our most constrained and uncertain experiment, ProaRT could only achieve 8% improvements. In the practical experiments exclusive for the NKI-AVL, we observe that access times in the current situation, and due to linac capacity, are not high, i.e. 0.24 days on average for all patients. ProaRT can reduce this time to an even smaller value of 0.05 days. Similar reductions are found in all practical cases analyzed. Furthermore, in some cases, ProaRT had the additional benefit of leveling categorized access times, i.e. less variation among the longest and shortest access time. With these experiments we demonstrate that in advance linac capacity allocation, through ProaRT can significantly improve the logistic planning of the linacs in a radiotherapy process.

Acknowledgement

At the beginning of my master assignment, having a mathematician, two physicists and a medical doctor as my supervisors seemed an impossible challenge. However, the challenge turned out to be a great learning experience in which I broaden my knowledge thanks to the brightness and experience of all of them. I am thankful for their positive feedback and constructive criticism, but most important for their inspiration to and motivation towards doing this and further research.

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Arturo E. Pérez Rivera
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Contents

Chapter 1
Introduction

In this chapter we introduce the project structure and the research design of this thesis. In Section 1.1 we give a short opening on why the healthcare industry is in need of analyzing and optimizing their processes and how this industry can fulfill its need. In Section 1.2 we present the NKI-AVL, the institution in which this project is executed, and briefly describe the care process that is studied. Furthermore, in Section 1.3 we describe the relevance of this study for the NKI-AVL's mission. In Section 1.4 we establish the goal of this research and formalize the problem statement that we work upon. Finally, in Section 1.5 we pose the research questions we strive to answer in this thesis and how we plan to do so. These questions are the drivers used to attain the research's goal and to solve the problem statement.

1.1 Healthcare and Operations Research

Nowadays, the healthcare business has become a strong topic of discussion for different groups of people, ranging from patients receiving care and specialists giving treatment up to insurance companies competing in the industry and governments controlling it. These groups of stakeholders bring separate and conflicting goals to the discussion table, which makes it difficult for managers to fulfill, in an effective way, the objectives of all parties (Carter, 2002). The industry is continuously pressured to deliver higher quality treatments, to have more available services and to lower its costs. Over the last decade, this pressure has been a motivation to achieve better diagnosis methods and more effective treatments. The human genome depiction, minimal invasive robotic surgery and targeted therapies for cancer are a few examples of the improvements that have been materialized in the quality of healthcare (Cox and Peck, 2009). However, all around the world, the availability and costs of the healthcare services have not experienced improvements of the same magnitude.

Financial sustainability is expected to be one of the major issues in organizing hospital care in the coming years. In the Netherlands, the Worldwide Health Organization (2011) reports that the government expenditure on healthcare per capita (in Euros at exchange rate) increased from €1925 in the year 2000 to €5593 in 2010. Although costs have significantly increased in the Netherlands over the last decade (191%), healthcare resources have not. For example, the number of hospital beds per thousand inhabitants went from 55.4 in the year 2000 to 55.0 in the year 2009 even though hospital admissions increased from 1485 to 1899 over the same period of time (Centraal Bureau voor de Statistiek, 2011). This is not only an indicator of capacity, but also an indicator of availability of inpatient services (World Health Organization, 2011). Just as everywhere else in the world, *everyone* in the Netherlands is in need of more cost-and-resource efficient healthcare institutions to guarantee access to the entire population.

On an institutional level, increasing costs pressures lead to a need of continuously balance various aspects of care quality with care-resources efficiency. For this reason, healthcare institutions are giving more and more attention to managing their processes in the best way. Most important of all, they are investing on optimizing their *healthcare logistics*. Finding a perfect balance in healthcare logistics is a challenging task since the objectives and interests from the parties involved are conflicting most of the time. Fortunately, similar problems faced by other industries have been engaged by *operations research*. This field of research, which is the scientific study of quantitative decision making, offers important ways to analyze and optimize logistical processes. The trade-offs between costs, resources and demand of healthcare services are increasingly being studied by both healthcare organizations and the operations research community, and techniques have been proven to be of great help for engaging the financial sustainability vs. quality of care problem.

This thesis is carried out in this field of operations management and operations research applied into healthcare. An oncological care process is studied in the Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital (NKI-AVL). We aim to explore scenarios for logistical improvement and deduct guidelines for the tactical and operational planning of this process. The institution and the oncological care process are presented in the following sections.

1.2 The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital

The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital is a comprehensive cancer institution in Europe doing state of the art research and treatment in the cancer field. Since its foundation in 1913, the NKI-AVL has been a place “where patients suffering from malignant growths could be treated adequately and where cancer and related diseases could be studied” (The Netherlands Cancer Institute, 2006b). The NKI-AVL merges scientific research and clinical application into one single independent organization and a highly collaborative atmosphere in Amsterdam, the Netherlands (Figure 1). This interaction helps developing and improving knowledge about cancer, and most important of all, helps in the clinical application of the best diagnosis, treatment and nursing care for patients who suffer from this terrible disease. The NKI-AVL cooperates and shares knowledge with multiple research institutes, universities and academic hospitals both nationally and internationally. In addition to this, it continuously transfers theoretical knowledge to practice by training and education of medical and scientific professionals in the field of oncology.

Figure 1 - The NKI-AVL in Amsterdam, the Netherlands

As a research institute, the NKI-AVL focuses on three major areas of research: fundamental, clinical and translational cancer research. In its facilities, fundamental studies about the biological processes of normal and cancer cells are performed. To do these studies, the NKI-AVL possesses cutting-edge technologies and laboratories, which are used by the more than 500 scientists and scientific support personnel. These technologies cover important subjects of cancer research, and have a special emphasis on cell-based screens, mouse tumor models, cell biology, structural biology and epidemiology (The Netherlands Cancer Institute, 2012). Nevertheless, the research goals of the NKI go beyond a better theoretical understanding of cancer. The institute also organizes diverse clinical trials of new forms of diagnosing and treating cancer. As part of the translation research program, the results of these clinical trials are converted to clinical applications and improved therapies that aim to better identification of cancers and improved patient's health and life expectancy.

The Antoni van Leeuwenhoek Hospital, which is the NKI-AVL's clinic, houses around 140 different medical specialists, 180 beds, five operating rooms and nine irradiation units. It is the only dedicated cancer centre in the Netherlands and receives around 24000 new patients each year. In order to have a better understanding of each patient's cancer, the NKI-AVL specialists have access to many different diagnostic facilities from the areas of pathology, radiology, nuclear medicine and clinical laboratory. With these tools, oncologists can design the best tailored treatment for patients. These treatments often consist of a combination of conventional surgery, chemotherapy and/or radiotherapy. Specialized treatments such as robotic assisted surgery, photodynamic therapy and image guided radiotherapy are also used to fight cancer. In addition to the excellent cancer facilities, patients have a dedicated unit comprising psychologists, social workers, information officers and others who offer them, and their relatives, support in dealing with cancer (The Netherlands Cancer Institute, 2006a).

In accordance with the NKI-AVL's mission of guarantying cancer patients the best care possible, support studies on resource and logistics management have been executed. These studies aim to balance the quality of care with the efficient use of the resources. Operations management and operation research investigations, like the ones from Vanberkel *et al.* (2010) and van Lent *et al.* (2010), demonstrate the interest of the NKI-AVL on assuring patients a promptly access to all the means of treatment. In line with this support research, this project looks into one specific treatment form: the radiotherapy treatment process. A study of the best way to plan and control this process, from a logistical and operational perspective, is carried out in this thesis.

1.1.1 Radiation Treatment or Radiotherapy

Radiotherapy is a way of treating cancer through the use of high energy radiation (U.S. Department of Health, 2010). This radiation can be delivered to a patient's tumor by an external beam from an irradiation machine or by some radioactive material placed near it. As radiation goes through normal and cancer cells in the body, genetic damage occurs which either stops cells from multiplying or kills them (The Netherlands Cancer Institute, 2006b). In this study, we focus on the external-beam radiotherapy which is the process of treating different cancer patients with radiation from specialized machines such as the one seen in Figure 2.

Radiotherapy is a complex way of treatment, which involves many medical, technical and logistical considerations. An extended explanation of this process and a depiction of the current situation in the NKI-AVL are presented in Chapter 2 of this thesis.

Figure 2 - Radiotherapy at the NKI-AVL

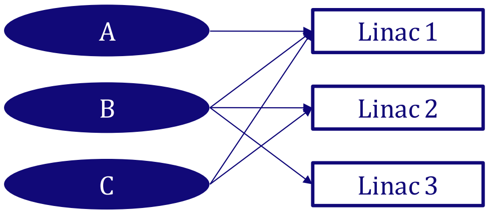
Currently, the NKI-AVL radiotherapy department treats approximately 4500 new patients every year. Each patient is categorized into one out of approximately 70 care plans. The demand for this type of care, which is currently around 95 new patients per week, is expected to steadily grow. In order to give this type of treatment, the NKI-AVL has nine state-of-the-art linear accelerators (linacs). However, since the incoming patients have care plans and the linacs have different technical characteristics (e.g. radiation type, energy level, etc.), not all machines are suitable for treating all patients. In addition, depending on the location of the cancer, the size of tumor and other medical aspects, patients need a different amount of radiation, which is usually given in different sessions (fractions) under a linac. The number of times a patient has to receive radiation can vary from one single fraction up to 35 fractions. These fractions need to be in consecutive days, or sometimes twice a day, in order to achieve the best results possible. To assure that radiation is under control and precisely targeted, periodic maintenance inspections are mandatory for all machines.

1.3 Research Motivation

In the spirit and ambition of the NKI-AVL to make important contributions to the cancer field, but most important, to the care of patients who suffer from this disease our research looks into the radiotherapy capacity planning. With a supply of different linacs, demand for different treatments must be satisfied as soon as possible and using the resources as much as possible. The problem becomes challenging when we consider that not all linacs are able to treat all care plans (e.g. cancer types), and that the different care plans require a different number of fractions under a linac. Moreover, patient arrivals vary from week to week. With the treatment constraints and uncertainty in arrivals, a good plan of the linac capacity must be designed *in advance* in order to achieve the time and resource related goals.

As an illustration of the logistical challenge mentioned above, let's consider the simple and deterministic example presented in Figure 3. On a given week, we have a certain number of patients, from three care plans: A, B and C, which have already been diagnosed and are ready to start radiotherapy. In order to treat these incoming patients, we have three treatment linacs: 1, 2 and 3. All linacs have the same fixed capacity and can execute the same amount of treatments, however due to medical and technical reasons, not all patients can go to all linacs. We consider that patients from care plan A can only go to linac 1; patients from care plan B can go to any linac and patients from care plan C can only go to linacs 1 and 2. From the numerical instance in Figure 3, we observe that the total capacity (450) is enough to start treatment for the number of incoming patients (400).

Care Plan	New Patients
A	50
B	200
C	150



Linac	Capacity
1	150
2	150
3	150

Figure 3 - Planning example of linac capacity

If all patients in this example show up at the same time, it is easy to determine an allocation where all patients can start during the given week. For example, all patients from A can go to linac 1 and all patients from C can go to linac 2 as seen in Table 1 (i). However, if patients come in a different order, then there are several ways that they may be assigned. Suppose, for illustration purposes, that all patients from type B arrive first, all patients type A arrive second and all patients type C arrive last. If the patients are assigned according to the order of their arrival to the first available machine, without any other logistical consideration, a completely different plan can result, as seen in Table 1 (ii). Although there is enough capacity to treat every incoming patient, the poor planning in this example results in 25% less patients treated during that week and a reduction from 89% to 67% utilization. In addition, 100 patients could not start the treatment in this first come first served manner.

Table 1 - Possible allocations for the planning example of linac capacity:

Care Plan:	A	B	C	Total	Unused Cap.
Linac 1	50	100	-	**150**	**0**
Linac 2	-	-	150	**150**	**0**
Linac 3	-	100	-	**100**	***-50***
Started	**50**	**200**	**150**	**400**	**N.A.**
Delayed	**0**	**0**	**0**	**0**	**N.A.**

(i)

Care Plan:	A	B	C	Total	Unused Cap.
Linac 1	-	150	-	**150**	**0**
Linac 2	-	50	100	**150**	**0**
Linac 3	-	-	-	**0**	***-150***
Started	**0**	**200**	**100**	**300**	**N.A.**
Delayed	***-50***	**0**	***-50***	***-100***	**N.A.**

(ii)

The radiotherapy process at the NKI-AVL is much more complex and has many other inputs that the ones shown in this simplistic example. For instance, an exhaustive series of inspections is carried out by maintenance engineers that ensure the linacs are in the best state possible to deliver treatment. While these inspections are being executed, no patients can be treated on the linac. As a solution to this situation, one of the nine linacs is used as a “backup” device, i.e while maintenance is given to a linac, the backup linac treats the patients planned in the maintained linac. However, if both maintenance inspections and treatments could be planned simultaneously, the backup linac could be used for treating patients the entire time. From a patients’ perspective, it is necessary to promptly and uninterruptedly receive treatment. From a business’ perspective, it is important that the linac capacity is utilized at its maximum, and that linacs are not being idle when there are patients waiting for treatment.

Healthcare processes involve many uncertain medical conditions which are known only when the patients arrive. The radiotherapy process is no exception to this fact. Besides the uncertainty of how many patients will arrive in the future, there is also uncertainty in the duration and the type of treatment they will require (e.g. number of fractions, radiation type). If the planning and control is not robust to these uncertainties undesired consequences can occur, such as delayed patients and capacity not being used. To avoid these unfavorable situations and to pursue patient’s and institution’s objectives while taking into account the constraints imposed by the radiotherapy process itself, an operations research studies is of utmost importance.

1.4 Research Goal and Problem Statement

In the previous sections, a general impression of the purpose of this study was presented. In this section, we point out the specific intent with which this thesis is done at the department of radiotherapy in the NKI-AVL. The variables that are analyzed in this research are the planning decisions for patients’ treatments on the linacs of the radiotherapy process. We study the relation between these planning decisions and the patient’s objective of swiftly starting treatment and the business’s objective of having the largest number of patients being treated (capacity utilized at its maximum). This is done through two performance indicators: (i) ‘access time’ which is the time between patients are ready to receive treatment (diagnosed and prepared) and the first fraction of radiotherapy and (ii) ‘linac utilization’ which is the ratio of time the linacs are being used over total available time. The scope of the variables is for care plans (as opposed to individual patients) and the time for the relations (indicators) is a mid-term horizon. The Research Goal and the Problem Statement of this thesis are:

Research Goal:
To develop a tactical planning and control methodology for the allocation of linac capacity of a radiotherapy process, to categorized patients, that minimizes the access time of the different categories and maximizes the number of patients treated while taking all process constraints and characteristics.
Problem Statement:
How can the time available of the linacs be allocated, in advance, to treatment of patient groups to ensure the shortest access times for categorized cancer patients and the largest number of patients treated can be achieved in the radiotherapy process in the NKI-AVL?

Although from queuing theory it is known that lower waiting (access) time and higher utilization (larger number of patients treated) are two opposite objectives (Winston and Goldberg, 2004), the underlying assumption is that the process is being planned at its best (and sometimes only) planning method. Minimizing waiting time and maximizing utilization is not possible if a service process is in this situation, and hence in the 'efficient frontier' of its logistical performance. However, if the process is not on its efficient frontier (as seen with the red dot in Figure 4) because of a given reason, e.g. the planning methodology used as the illustration example from Section 1.3, then there are three possible improvements: (i) access time can be decreased while maintaining the same utilization level, (ii) utilization can be increased while keeping a constant access time or (iii) both access time and utilization might be improved as see in Figure 3. We believe this situation is possible in the linac capacity from the radiotherapy department of the NKI-AVL, and therefore, we strive in our research goal to optimize these two performance indicators which are relevant for both patients and institution perspectives.

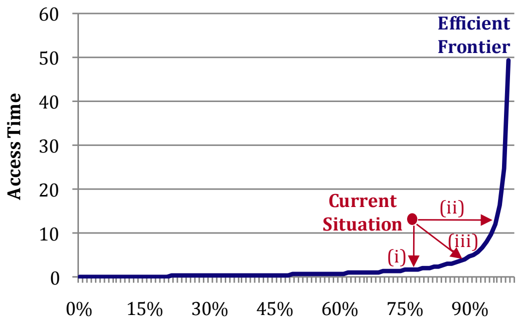


Figure 4 - Utilization in queuing theory

1.5 Research Questions and Methodology

To achieve the research goal of this project, and to find a solution to the problem statement, we pose a series of research questions to guide the work by the scientific method. In this section we present these research questions and briefly explain how each of them is approached. Furthermore, in this section we give indications on the structure of the remainder of the thesis.

The radiotherapy process is a complex one, especially when it is done at comprehensive cancer center such as the NKI-AVL. In a comprehensive cancer center, new research developments are constantly translated into clinical applications, reason why treatments are highly constrained and continuously changing. Our focus of the entire process is the actual treatment (patient going under a linac). To optimize it from a logistical planning perspective, we first should analyze how the planning and the control for this process are currently done, observe their advantages and delineate potential improvements for their drawbacks. We should also know what the current logistical performance of this planning and control is for the different categories of patients. Although performance can have different meanings and different purposes, we consider performance to be the impact that the current way of working has on the access time of patients and the utilization of the machines. All of these aspects bring us to our first research question:

1. What is the current situation of the radiotherapy linac capacity and its demand at the NKI-AVL?

To answer this question, we use a series of interviews and meetings with the people involved in the process, the experts. Visits to the actual process steps (when they are being executed) are realized, such that observations from an outsider's eye can be the base for discussions during the interviews and meetings. Documentation about the radiotherapy process and the regulations that govern each of the steps is reviewed to have a complete depiction of the boundaries of each step in the process. The NKI-AVL as research centre collects and stores a vast amount of information. Since 2008, an electronic database of patients, treatments, appointments and other information is kept. A team of people is in charge of managing and controlling the records of this electronic database. Reports from this database are examined in order to determine which data are available. Afterwards, discussions with the department experts are done do determine which data are relevant. Finally, statistical analyses are used to get indications on the current performance and potential opportunities for improvement. In these ways, we deal with Research Question 1. The findings with respect to this question can be found in Chapter 2 of this thesis.

In a very abstract level, the radiotherapy linac capacity planning can be seen as the question of how to satisfy a demand of cancer treatment with a supply of linac-time. However, the answer should be specific for the characteristics of radiotherapy treatment process (e.g. constrained supply, recurring demand, etc.) and for the desired objectives (e.g. meet demand, minimize waiting times, etc.). Quantitative methods that handle these characteristics are crucial for correctly building an answer. It is important to know what methods have been, and can be, used to plan the linacs including all pertinent process characteristics. Furthermore, within the aforementioned abstract level of a supply-demand process, comparisons can be made to other healthcare and manufacturing processes that have some of the linac capacity planning characteristics and where the operations research field has developed diverse planning methods. These knowledge aspects bring us to our second research question:

2. What factors and quantitative methods are relevant for planning the radiotherapy linac capacity?

To come up with a good answer to this question, a review and analysis of relevant scientific literature is done. In addition to quantitative methods used specifically for the linac capacity, we also study methods for similar healthcare and manufacturing processes. Naturally, each method comes with its own set of requirements and formulations for their process. A comparison of similarities and differences between their intended process characteristics and the radiotherapy process is done. Furthermore, we evaluate the advantages and disadvantages of each of the method with respect to the complete description of the process from Chapter 2. This allows us to define the relevant aspects of the radiotherapy linac capacity planning in an institution such as the NKI-AVL. The findings with respect to this question can be found in Chapter 3 of this thesis.

From a mathematical point of view, modeling the radiotherapy linac capacity planning, with NKI-AVL's characteristics, is a challenging combinatorial optimization problem. The challenge is in mathematically formulating all aspects of the process into a model and solving the resulting model for relevant process characteristics, such that it achieves its goal theoretically and practically. For this reason, we pose our third research question:

3. What is a useful planning method for radiotherapy linac capacity with NKI-AVL's characteristics?

Based on the guidelines from Research Question 1 (i.e. operations research literature) this question is embarked upon. We develop a mathematical model of the radiotherapy linac capacity by reviewing and verifying characteristics, representation levels and assumptions with experts in the process from the NKI-AVL. What is more important, we design a solution methodology that is able to solve the resulting model in a convenient, time-efficient and goal-effective way. To test the usefulness of the proposed planning method, we make a series of numerical (i.e. theoretical) experiments for the different levels of key process factors and present their results with respect to the planning objectives. The model, method, experiments and all relevant considerations can be found in Chapter 4 of this thesis.

Even though in Research Question 3 we build a model and a method that comply with NKI-AVL characteristics, we test them only against theoretical instances and strict performance indicators. It is of our interest also to study practical instances and to look into more detail all the differences between the proposed method and the current way of working. This brings us to our fourth and last research question:

4. What would be the benefits of implementing the proposed planning method for the NKI-AVL?

In order to answer this question, we conduct a case study that compares the proposed planning methodology (resulting from Research Question 2) and the current way of working (derived from Research Question 1). A series of representative cases (e.g. increment in arrival of patients, change in working time, change in types of linacs, etc.) are chosen and analyzed through a computer simulation. Besides the strict performance indicators, other aspects of the output from the proposed method (e.g. equity for different patients, differences between linacs, access time behavior, etc.) are analyzed to evaluate the effects of using the proposed planning method in the NKI-AVL. The findings with respect to this question can be found in Chapter 5 of this thesis.

Chapter 2
Radiotherapy in the NKI-AVL

In this chapter we describe the process of treating cancer with radiation and the current situation of this process in the NKI-AVL. In Section 2.1 we briefly explain what radiotherapy is and how radiation is used for fighting cancer. In Section 2.2 we present an overview of the steps in the radiotherapy process. In Section 2.3 we describe the demand and supply for this type of cancer treatment in the NKI-AVL. In Section 2.4 we show how the current planning and control of the treatment capacity is done, and what the opportunities for improvement are. Moreover, we present the current performance of the radiotherapy process in the NKI-AVL in terms of access time and utilization. Finally, in Section 2.5 we summarize the key points of the radiotherapy process in the NKI-AVL.

2.1 Radiotherapy (RT) and Cancer

'Cancer' is a general term used for a group of diseases in which abnormal cells in some site of the body reproduce out of control and are able to spread to (or invade) other parts of it. The more than hundred cancer diseases differ from the place they originated, e.g. lung cancer and prostate cancer, and several other characteristics such as growing rate and response to treatment. Furthermore, when cancer cells spread to other organs in a process called metastasis, they keep some characteristics from the original site and hence are named accordingly, e.g. metastatic breast cancer in the lung rather than lung cancer. Even though cancer is a lifethreatening disease that accounts for millions of deaths worldwide, the improvements in knowledge about its nature and its treatments have increased the chance of survival. In the Netherlands, the Dutch Cancer Society –*KWF Kankerbestrijding*– (2011) reports that almost 60% of all patients diagnosed are still alive after five years. Considering that in the Netherlands one in three people get cancer, and it is the principal cause of death of the country, faster and better diagnosis and treatments if of high importance for Dutch society.

Radiotherapy (RT) is, along with surgery and chemotherapy, one of the most common ways of treating cancer. Cancer institutions worldwide and evidence-based medical research show that approximately 50% of all cancer patients receive radiotherapy as part of their overall treatment (Delaney *et al.*, 2005). The RT treatment consists of the use of controlled high energy radiation to kill cancer cells. When radiation goes through the body, it damages cells' DNA in such a way, that cells either stop growing, i.e. reproducing, or they simply die. Radiation is able to shrink cancer tumors and/or completely eliminate them with the help of natural processes in the body. Radiation can be delivered in two ways: either by internal implants placed near the cancer tumor or by linear accelerators (linacs) such as the one seen in Figure 5. When radiation is aimed and delivered by this kind of specialized machines it is known as external-beam radiotherapy. In this thesis we are interested only in external-beam radiotherapy, i.e. radiation treatment that is delivered by linear accelerators, which is the most common type.

Figure 5 - Linac at the NKI-AVL

Patients that receive external-beam radiotherapy can have it as a stand-alone treatment, or as part of a combination of different oncological treatments. For example, radiotherapy can be used before surgery to reduce a tumor's size. It may also be used after chemotherapy to kill remaining cancer cells. In the NKI-AVL, patients are labeled as "trajectory" patients if there is a coordination needed with surgery or chemotherapy. RT can be given with a radical (or curative) intent or with palliative (symptoms relieving) purposes such as pain relieving and bleeding control. Palliative RT is always urgent since the cancer tumors might be interfering with basic body functions. Examples of cancer locations that require immediate palliative RT are bone and esophagus tumors, which besides causing pain also reduce the ability of a patient to move (possibly permanent paralysis) or to eat and breathe. Likewise, a swift start of radical RT has proven to be essential in tumor control for some fast-growing cancers (Seel and Foroudi, 2002). Therefore, correct *timing* of radiotherapy and its coordination with other forms of treatment is important to achieve the objective with which RT is given to a patient.

Many factors have to be appraised in order to assure the person's wellbeing and maximize his or her life expectancy in the RT treatment. An effective radiation treatment plan depends on medical aspects such as the location, stage and type of cancer as well as the specific condition of the patient (Pérez, 2004). It also depends on technical parameters such as radiation type (photos or electrons), radiation energy, shape and angle of the beams of radiation, etc. An example of the influence of shape of radiation, in an RT method called intensity modulated radiotherapy (IMRT) small devices called multi leaf collimators are used to shape and localize the beam of radiation coming out of a linac (as seen in Figure 6) such that healthy tissue has the minimum damage from the radiation. Oncologists, physicists and specialized RT therapists work together, as a multidisciplinary team, to define the best way of giving the RT treatment. After all factors are analyzed and the treatment plan is defined, the patient is ready to start receiving radiation from a linac that can be configured according to the chosen technical parameters.

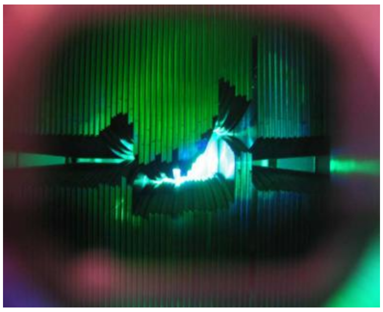


Figure 6 – Multi leaf collimator (MLC) in a linac

An important characteristic of the treatment is its distribution over time. The total dose of radiation prescribed is divided into "fractions" in order to minimize the damage to non-cancerous tissue (Barendsen, 1982). Fractions (sessions of radiation) are usually given on a daily basis. However, in the last years, research has been going on about other rates of irradiation such as *hypofractionation* where larger doses are given less than once per day. Depending on the treatment plan, a patient can receive a single fraction up to 35 fractions. In case of a patient receiving more than one fraction, he or she has often to "return" to the hospital for several days. Medical studies have shown that, for some types of cancer, interruptions on consecutive sessions of radiotherapy can significantly affect treatment outcome (The Royal College of Radiologists, 2008). Also, evidence exists that for some sites, cancer control is adversely affected if there are prolonged waiting times to receive the first fraction (Seel and Foroudi, 2002). As mentioned by Petrovic *et al.* (2006) an appropriate scheduling method that effectively manages the treatment over time is necessary for a successful outcome.

2.2 Overview of the Logistics in the RT Process

The radiotherapy process is a complex collection of interrelated and interdependent actions. From a logistical perspective, we can divide the process into a pre-treatment and a treatment phase, similar to the division presented by Kapamara *et al.* (2006) and Petrovic *et al.* (2011). Every action in both phases usually has precedence relationships, meaning they cannot start until the previous actions have been finished. Furthermore, for each action there are different resources and personnel involved. The assignation of resources to a patient depends on his or her cancer type and the requirements of the radiation oncologist, who leads the specialized team that executes the process. In this section we have aggregated the actions of both phases of the radiotherapy process at the NKI-AVL in four steps as shown in Figure 7. We now generally describe these steps, their actions, resources and personnel. Afterwards we delimit and define the part of the radiotherapy process which we study in the remaining chapters of this thesis.

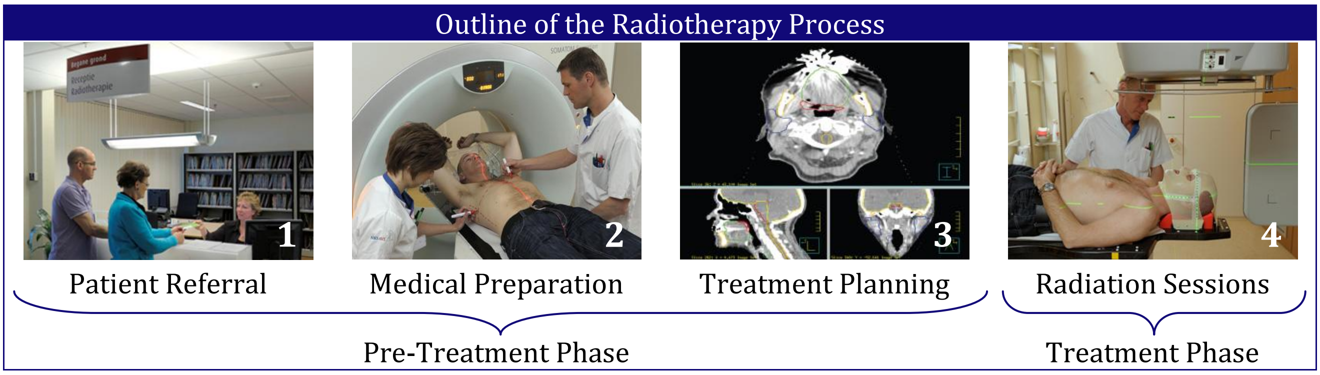


Figure 7 - Outline of the Radiotherapy Process

1. Patient Referral: Patients are referred to the radiotherapy department of the NKI-AVL by other hospitals (referring specialists) as well as internal policlinics. Information is transferred to the department and to a radiation oncologist. The radiation oncologist decides then which additional studies are required to determine a patient's condition. In a personal interview between the radiation oncologist and the patient, the goal of the treatment is explained, as well as the possible side effects. If the patient and the doctor decide to proceed with a treatment, appointments for the second step, the "Medical Preparation", are scheduled. In addition, patients at the NKI-AVL go through an information interview, in which a detailed explanation of radiotherapy and practical issues of this type of treatment are given.

2. Medical Preparation: It is important that the localization of the tumor is well known in order to determine the precise area that will be irradiated. For this purpose, a computed tomography

(CT) scan of the patient is taken. Depending on the patient's characteristics and cancer type, other medical examinations (e.g. MRI, PET, blood tests) might be done during this step in order to gather all information necessary for the actual treatment. During the CT scan, body marks are made with a special ink. These marks (dots and lines) serve as a guiding reference to ensure the patient is irradiated in the desired location every time (since radiotherapy treatments usually last for several weeks). Also in this step, special immobilization devices such as casts and masks might be molded from a patient, depending on the location of the cancer.

3. Treatment Planning: Once the location information is digitalized and all the medical preparations done, dosimetrists are able to define the technical settings of the treatment plan. This treatment plan is based on the radiation oncologist requirements (e.g. radiation dose to the tumor, maximum dose for surrounding non-cancerous tissue, safest angles, etc.). With the help of a computer, a contour of the treated area is made. The sophisticated software installed in these computers is able to do a multi-objective optimization of the dose, beam shape, angles and other criteria such that the best technical settings are achieved. After the optimization is done, the resulting plan is presented to the radiation oncologist. If approved by the radiation oncologist, the treatment settings (e.g. angles of radiation, dose, etc.) are automatically loaded into a linac and the patient is able to begin his or her radiation fractions.

4. Radiation Sessions (Fractions): The first three steps make up the pre-treatment phase of the radiotherapy process. The last step consists of the actual treatment with radiation. Radiation has to be delivered by a linac that is able to be configured according to the plan defined in previous steps. For every radiation session, or fraction, radiation therapists will check that all settings are correct and that the patient is positioned and aligned with the marks done during the CT-scan. Once everything is in order, the linac will start delivering the fraction of radiation that was planned. Depending on the treatment plan, a patient will receive one up to 50 daily fractions (sometimes twice per day or other rates) which almost always have the same radiation settings. In the NKI-AVL, most fractions are given in a timeslot of 15 minutes, independent of the cancer or treatment type. For certain highly complex irradiations, two timeslots might be required. After all fractions are finished, patients receive follow-up care specialized to his or her condition.

Figure 8 - Large maintenance inspection on a linac

Maintenance Inspections: The control over the positioning and the amount of radiation delivered is paramount for radiotherapy. To guarantee this control, periodical maintenance inspections are done on all linacs. National and international conventions regulate the frequency with which these inspections are done. They also determine the protocols and standards to be followed in every inspection. If necessary, corrective maintenance actions (e.g. parts replacement) are executed on a linac during these inspections. Furthermore, during the time the inspections are carried on, no patients can be treated on the linacs. There are several types of inspections in which different quality checks are performed. The duration of these different inspections varies from a couple of hours to a couple of days. In the NKI-AVL, there is a dedicated technical team to carry out the small weekly inspections as well as some of the long daily ones (as seen in Figure 8). There are also contracted inspections with the manufacturer of the linacs, in which additional small updates are sometimes installed on the linacs.

Quality Assurance: In the NKI-AVL, a multidisciplinary team, within the Clinical Physics and Instrumentation section of the RT department, carries out activities and projects to make sure that linacs work as planned, that the software systems and applications are up and that instruments for the mechanical maintenance are ready. A team of clinical physicists permanently works on projects of dosimetry (dose calculation methods), radiation protection, medical recording and analyzing of data, etc. The projects are both at internal and external levels, always with the aim of assuring that all critical processes to the RT treatment continue unaffected.

The RT Treatment Process in the NKI-AVL

In the NKI-AVL, all the actions of the radiotherapy process explained above are done within one department (e.g. CT-scans, maintenance inspections, etc.). The department of Radiation Oncology employs approximately 250 staff members, who work on the entire process and also on various research projects. In this research thesis, we are interested in the last step of the overall radiotherapy process, the radiation sessions, as seen in Figure 9. From a logistic perspective, planning this step is a complex task since (1) there are constraints to which linac a patient can go depending on his or her type of treatment (see Section 2.3.2), (2) the number of (daily) sessions varies among the patients (see Appendix 1) and (3) there is uncertainty in the number of patients who will come in the future (see Appendix 5). In this thesis we research how to cope with these characteristics in order to achieve minimum delays in this step, and hence lower waiting times in the overall process.

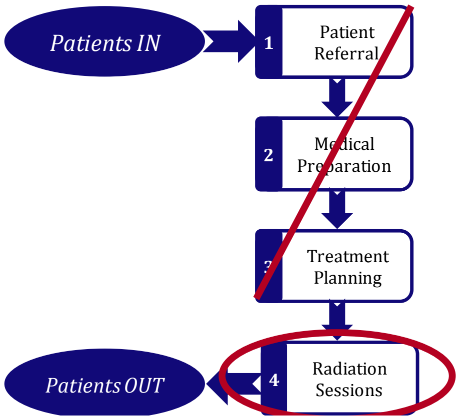


Figure 9 - Radiotherapy process considered in this thesis

2.3 Demand and Supply for Radiation Sessions

There are different types of “demands” and “supplies” for the last step of the radiotherapy process in the NKI-AVL. Patients have a personalized treatment (e.g. individual contour of irradiation area, individual dose fractionation, etc.), which can be categorized into a specific care plan (CP). Patients with the same care plan usually have the same fractionation scheme (i.e. number of radiation sessions over time). Furthermore, the linac configuration (e.g. Cone Beam CT, use of electrons, etc.) required among patients of the same care plan is identical. The radiation is delivered by a set of different linacs. Each linac has its own technical characteristics which allow it, or not, to deliver radiation sessions to a patient from a given care plan. In this section we present general information about the care plans and the linacs, which are important from a logistical point of view.

2.3.1 Care Plans (CPs)

In the NKI-AVL Radiation Oncology department there are approximately 4500 new patients treated each year. Every week, around 95 new patients arrive for treatment. What we refer as a “new” patient might be a returning patient for a new treatment. There is variability in the arrival of new patients as seen in Figure 10. These patients are categorized into different care plans (CPs). Each care plan defines how many fractions a patient needs and which linacs can deliver these fractions of radiation. Currently there are approximately 60 CPs in the NKI-AVL. However, some of these CPs are identical with

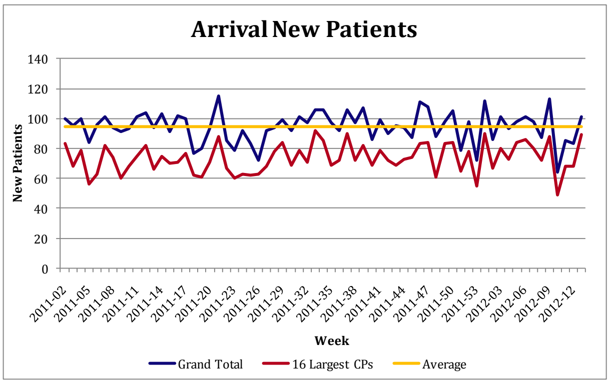
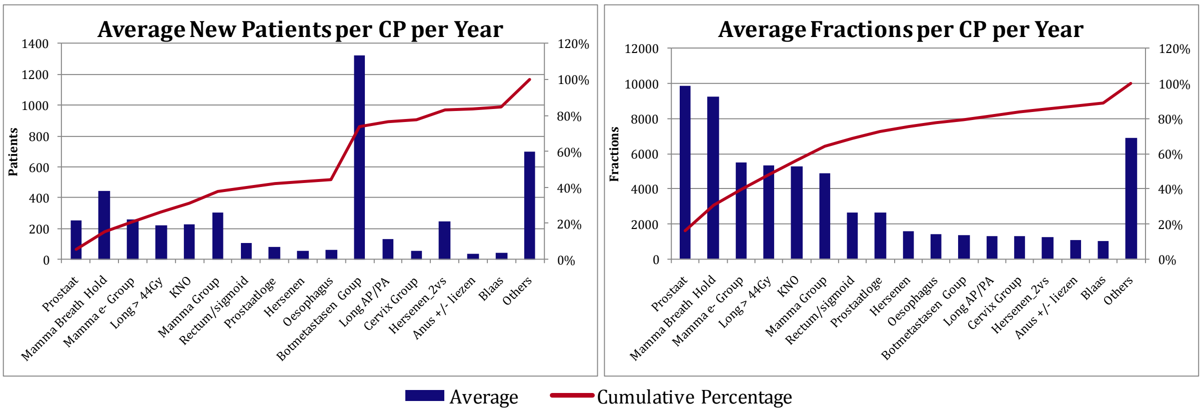


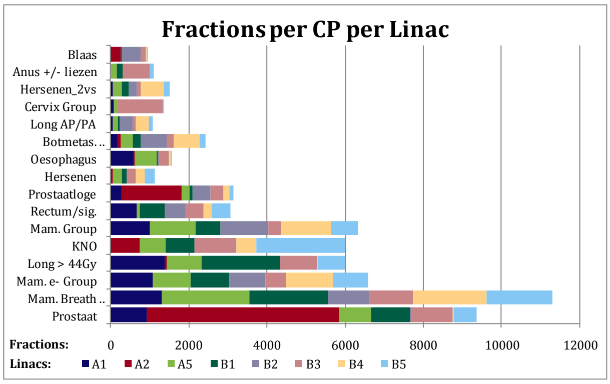
Figure 10 - New patients per week from January 2011 until March 2012

respect to the relevant logistic characteristics (i.e. number of fractions and feasible linacs). By merging these identical CPs, we can reduce the list up to approximately 45 CPs. The number of new patients in a year varies from 1 up to approximately 1300 per CP. Also, the number of fractions from these CPs varies from 1 up to 39 on average. The demand of a CP for linac time in a year is the multiplication of the average number patients and the number of fractions. In Appendix 1 we show the ordered (from highest to lowest demand) list of CPs in the NKI-AVL. The first 16 CPs (35% of the total number of CPs) account for approximately 80% of the average new patients and 90% of the average fractions given per year, as seen in Figure 11 (CP names in Dutch). We refer to these CPs as the 16 largest. These numbers are valid for the most recent data (from 2011 until the first quarter of 2012). CPs are dynamic over time, meaning that the number of fractions or the set of feasible linacs changes whenever new ways of treatment are developed.



Explanation about data used to build these graphs can be found in Appendix 1.

Figure 11 – Sixteen largest CPs demand information



Data used for this graph can be found in Appendix 4.

Figure 12 - Fractions per CP per linac, delivered from January 2011 until March 2012

Every year, the NKI-AVL radiotherapy personnel schedule approximately 63000 fractions of radiation. These fractions can be delivered by 9 linacs, from which one is used only as a backup machine. Due to the technical specifications of the radiation in a CP's treatment plan, not all linacs are capable of delivering a CP's fraction. On average, a CP can make use of 7 linacs (75% of 9 available machines). However, some CPs can only use 3 linacs (the CPs that require electron radiation). Detailed information about the relationship between CPs and linacs and some current usages can be found in Appendix 2 and Appendix 3 respectively. In Figure 12 we can see the distribution of the fractions of the 16 largest CPs over the different linacs. We observe that some CPs have most of their fractions (e.g. CP1 in linac A2), suggesting that some implicit, logistical preference, is also taken into account in the scheduling besides the technical capabilities.

A patient's CP is related to the site where the cancer is. As explained in Section 2.1, different cancer sites have different growing rates and hence different "urgencies" for beginning treatment. Seel and Foroudi (2002) carried out a literature study to determine the effects of long waiting times in radical RT for different sites. They concluded tumor control might be negatively affected for some sites such as head-and-neck cancers. Furthermore, they report evidence for prostate cancer to not be affected by delays in starting RT treatments if hormones are used. For palliative RT treatments, prolongation of symptoms might result in unnecessary suffering and the need for other interventions that have adverse effects (D'Souza *et al.*, 2001). For some specific palliative treatments, such as pain relieving for bone metastases, prompt treatment can help reduce the morbidity of this cancer type (Lutz *et al.*, 2011). In the NKI-AVL, patients gets a waiting time target set by the radiation oncologists, time which is used by the planner to schedule the fractions of the different patients. Waiting time targets, and hence "urgencies" for beginning treatment, are different among the CPs. This is quantified in Chapter 5.

2.3.2 Linear Accelerators (linacs)

The fractions of radiation are delivered by specialized machines that accelerate electrons. In the NKI-AVL there are currently 9 of these machines, or linear accelerators (linacs). These linacs are placed in special rooms (shelters) which isolate them for safety purposes. There are 10 of these bunkers, from which one is continuously used for installing and testing a new machine. The oldest linac in use dates from 2003 and the newest one was installed by 2010. Out of the 9 linacs in use, one serves as a substitute linac for when the periodic maintenance inspections are carried on. Each linac has a team of 5 radiation technologists or therapists that control the machine when the fractions are given. For the purpose of this research we consider that the machine and its staff is a single unit to which we refer as linac.

The linacs in the NKI-AVL have special characteristics that allow them to give different types of treatment. These characteristics act as technological constraints on which CPs can be treated on the linacs. For example, there are 3 linacs (33%) which can deliver radiation from both photons and electrons. All linacs have an EPID (electronic portal imaging device) which can verify, in vivo, the dose of radiation that is being delivered in each fraction. This device allows high precision irradiation techniques to be executed in all linacs. Furthermore, 6 linacs (67%) have special equipment that allows Cone-Beam CT. A further explanation of these technologies and medical terms can be found in the Glossary.

Table 2 - Summary of Linacs' Capabilities:

Linac 'x' =	A1	A2	A4*	A5	B1	B2	B3	B4	B5
CPs with Linac 'x' as an Ideal Linac	30	12	0	28	25	15	29	18	20
CPs with Linac 'x' as a Tech. Feas. Linac	15	0	37	14	18	6	14	8	23
Treatable CPs in Linac 'x'	45	12	37	42	43	21	43	26	43
Percent of CPs	98%	26%	80%	91%	93%	46%	93%	57%	93%

**A4 is the substitute or 'backup' linac. Explanation about data used to build this table can be found in Appendix 2.*

In Table 2 we observe that the majority of linacs can treat the majority of care plans (treatable CPs percentage is out of the 46 CPs mentioned earlier and found in the Appendices). However, the number of treatable CPs in a linac consists of 'ideal' and 'technically feasible' relationships. This distinction in the relationships linac-CP is based on medical staff reasons. If a linac and a CP have the 'technically feasible' relation it means that all radiation settings can be configured in the machine. However, the radiation therapists operating the linac might not have enough experience with treating such kind of patient (from a CP) before and hence the linac is not 'ideal'. This situation usually occurs with new CPs (new RT treatments) and CPs that seldom occur. On the other hand, linacs that have an 'ideal' relationship with a CP have medical 'preference' for delivering the fractions. This distinction is specific to the NKI-AVL, and can be reviewed in detail in Appendix 2.

The actual resource capacity or supply for the RT treatments we consider in this thesis is linac time. Linacs work for 5 days per week. Every day is divided into timeslots of 15 minutes. There are 35 of these timeslots each day, for a total capacity of around 9000 timeslots per linac per year. These timeslots have been chosen to last 15 minutes because that is approximately the duration of any fraction (of any CP), with a very few exceptions. Although fractions require to be given daily, when the treatment plan is designed, the weekend breaks are taken into account. The total current resource capacity per year is of approximately 73000 timeslots (for 8 linacs). The current demand-to-capacity ratio is of approximately 87%. However, this does not mean that all linacs are delivering fractions in 87% of their timeslots. Furthermore, the capacity used depends not only on the 'feasibility' or 'preference' of a linac, but also in the planning method. A deeper overview of fractions delivered (timeslots used) per linac is given in Section 2.4.

In practice, each linac has less than 9000 timeslots per year. Approximately 660 timeslots are used for mandatory maintenance inspections every year in every linac. Maintenance inspections account for 7% of a linac's capacity per year. For this reason, a 'backup' linac is used for the total 5280 timeslots the other linacs are being inspected. The three main types of inspections are presented in Table 3. In all of these inspections quality checks are done. With the help of dosimetry equipment, data is collected and compared to radiation dose and position standards. If corrective actions are required, a team of maintenance engineers and physicists will do them immediately. Thanks to this kind of preventive maintenance are hardly ever down due to technical failures. At the moment, only one linac is inspected at a time although there is enough dosimetry equipment and personnel to inspect two simultaneously. The main reason for doing this is to maximize the consecutive capacity. Since there is one 'backup' linac, daily treatments can continue at the same time, without interruptions (skipped days) or overtime work.

Table 3 - Periodic Maintenance Inspections:

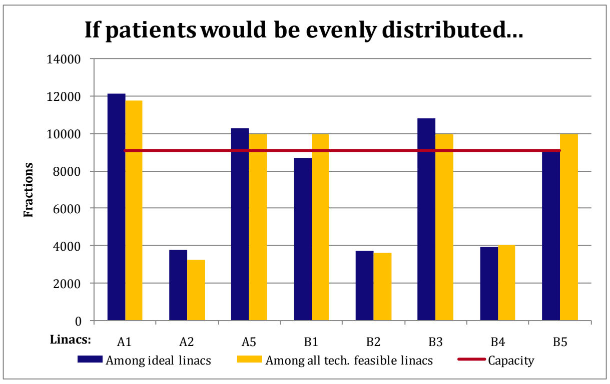
Maintenance Type	Duration	Frequency
Short In-House	2.5 hours	Weekly
Large In-House	2 days	Yearly
Vendor Contracted	1 day	Twice per year

2.4 Current RT Scheduling and Performance

An 'Appointment Office' (AO) is in charge of scheduling the different parts of the RT process. This office is in charge of planning when and where patients will be scheduled for their different steps and actions in the RT process within the department. The AO schedules the process individually for every patient immediately after referral. As mentioned before, the referral is done by another hospital (specialist) or by a policlinic from the NKI-AVL. In this referral the patient's diagnostic, care plan and special requirements dictated by the radiation oncologist are provided to the AO. Furthermore, in addition to the referral information, the AO has pre-defined procedures for planning the appointments. In this section we briefly explain how the AO schedules the treatment phase of the process, i.e. the fractions in the linacs. Furthermore, we give an indication of what is the current logistical performance of the linacs and the times to begin treatment.

The AO schedules the fractions of every patient to start as soon as possible, in a linac that is able to deliver the entire treatment without interruptions (i.e. all fractions are scheduled in the same linac). In logistics, this way of scheduling is known as First Come First Served (FCFS) or in some healthcare settings as open-access scheduling. In spite of the name, 'first' patients are not necessarily 'first' treated! In a patient's referral, there might be a mandatory waiting period. This mandatory waiting time can occur, for example, if a patient had surgery and needs the wound to heal. In addition to this and other medical considerations, patients are scheduled to receive their fractions according to a document (procedure) called 'Logistic Overview'. This procedure dictates which linacs can treat which care plans and all time related considerations of the fractions (e.g. daily or twice per day, one or two timeslots, etc.). With all these information, the AO plans the entire number of fractions of a patient. Even though patients have, for some care plans, several weeks of fractions that are planned since the beginning, appointments are handed out on a weekly basis. Every Thursday, a patient receives his or her set of appointments for next week, i.e. time and linac that will deliver the fractions. This gives some freedom to the AO of re-scheduling some fractions, for example, when there is an unscheduled or unforeseen maintenance in one of the linacs.

The main goal of the AO is to schedule patients according to the requirements from the radiation oncologists. Nevertheless, they also try to fulfill other patient and staff desires as much as possible. For example, some patients like to have their fractions in the afternoon and some staff would prefer to treat patients from different CPs. To illustrate that these desires can have an influence on the schedule performance, we consider the following example. Suppose the 252 patients that come on average from CP1 are distributed evenly into the 6 ideal linacs for this CP, i.e. 42 patients per linac per year. If we would do this for all CPs, such that the staff at each linac has the largest variety of CPs per year, we would end with some linacs that use only half of their capacity and others that use 30% more (see Figure 13). This example, although very unlikely to happen, shows that improper management of the combination patient-fractions, can lead to inefficient use of capacity.



Data used for this graph can be found in Appendix 1 and Appendix 2.

Figure 13 - Example of maximizing staff desires

In 2011 and the first quarter of 2012, each of the nominal eight linacs (A1, A2, A3, A5…B5) delivered on average 9800 fractions (7800 per year). The backup linac (A4) delivered 5000 fractions during this period (4000 per year). We can see from Figure 14 that currently, most of the linacs are being used at is maximum capacity, i.e. nominal working time excluding the time for the maintenance inspections. It is interesting to point out that even when not all linacs can treat all CPs, they all are approximately delivering the same amount of fractions. Taking a look back at Figure 12, we notice that CP1 is treated more in linac A2 than in any other linac (53% of the patients). Half of the patients from CP1 do not come just in time when for A2 to be the first linac available, supporting the existence of some implicit logistic preferences..

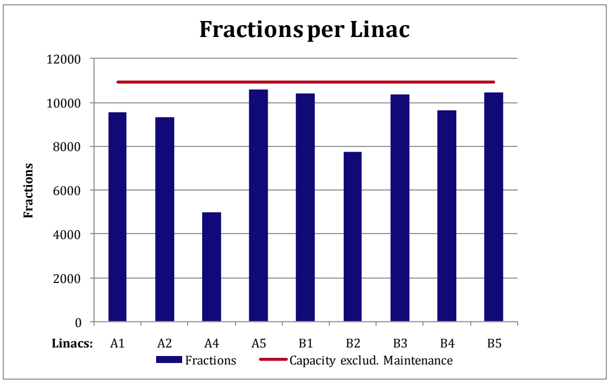


Figure 14 - Fractions per linac delivered from January 2011 until March of 2012*

In this thesis, we define utilization as the number of fractions delivered over the total linac capacity. Over the last year, the NKI-AVL utilization has been approximately 90%, as seen in Figure 15. The current way of defining the linac capacity (Method A) is by assuming linacs can work all nominal time, including the maintenance inspection timeslots (due to backup linac use). We present another definition (Method B), which excludes maintenance inspections but includes backup linac capacity. Both methods yield approximately the same utilization.

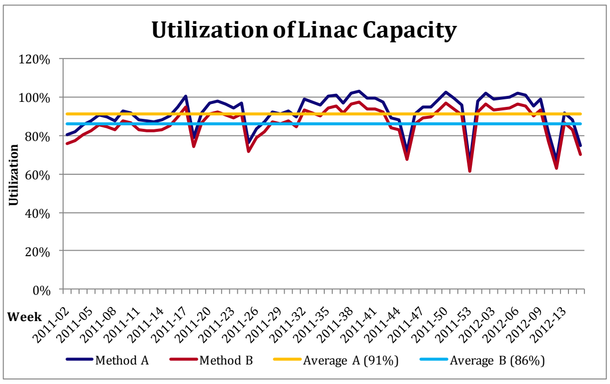


Figure 15 – Weekly utilization of linac capacity from January 2011 until March of 2012*

**Data from the MOSAIQ report 'Overzicht Capaciteit' was used to build these figures. Fractions given during weekends were filtered out.*

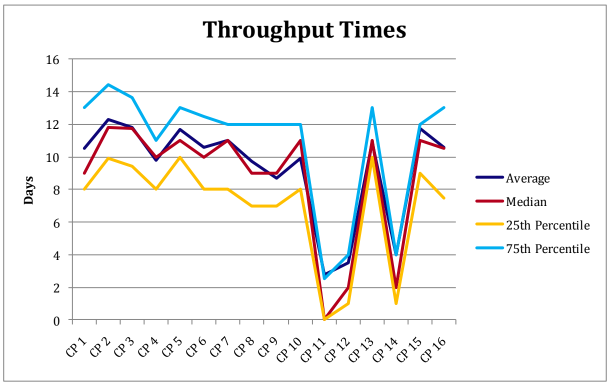
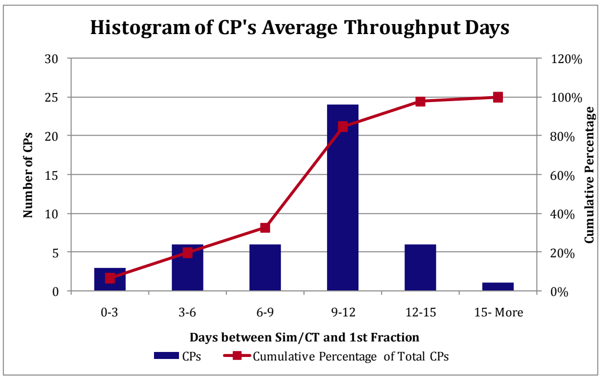
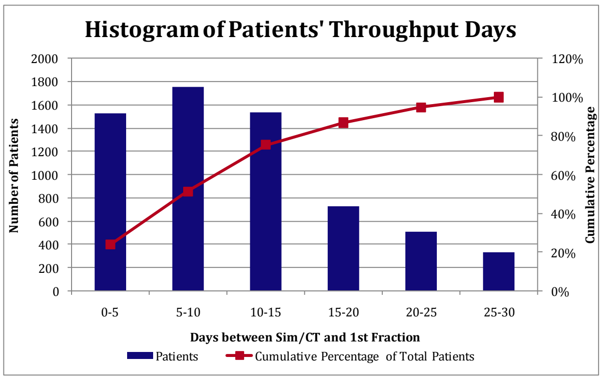


Figure 16 - Throughput time between Sim/CT and 1st Fraction for the largest 16 CPs

Information about waiting times is not directly available. A record is kept about the two throughput times of patients. The first one is the throughput from steps 1 and 2, i.e. from the diagnostic or referral up to the simulation/scans. The second one is from the end of step 2 to the beginning of the last step, i.e. from the end of the simulation/scans up to the first fraction. Statistics of this second throughput time, from January 2011 until March of 2012, and for the largest 16 CPs. This throughput time includes the duration of step 3 (treatment planning) and other times (including waiting times for RT treatment due to the linac being occupied). An important remark is that the treatment planning lasts approximately 4 days for the CPs that require it. We can assume that part of the remaining throughput time is in part due to the linacs being occupied with other patient-fractions. However, this can only be very rough indication since the appointments for the fractions are scheduled since the beginning.





**A4 is the substitute or 'backup' linac. Explanation about data used to build this table can be found in Appendix 2.*

Figure 17 - Histograms for throughput days from the Sim/CT to the first fraction

2.5 Summary

In this chapter the current situation of the NKI-AVL's radiotherapy process is described. Moreover, data about the treatment demand (patient-type and fractionation-scheme) as well as linac capabilities and capacity use is analyzed. The key points to keep in mind are:

- Radiation therapy in the NKI-AVL is given using the latest forms of treatments and different, state-of-the-art linacs. This is valuable for the quality of care, but introduces a challenging in managing the capacity for all patients, current and future ones.
- The demand for treatment differs among the CPs. The number of fractions, the set of 'ideal' linacs, the different 'urgencies' increase the complexity of planning the capacity.
- The number of new patients per week varies from CP to CP and from week to week. On average, the combination of new patients and the number of fractions they need requires 87% of the installed capacity.

The tradeoff between waiting times and utilization is a complex one due to the demand coming from the combination of patient-type and fractionation-scheme. In the NKI-AVL, one of the largest group in number of patients, bone metastases, is the one that receives the least number of fractions and the one that has the highest urgency to start treatment. On the other hand, the Prostate group, which one of the largest in terms of patient-fraction combination has less urgency to start treatment the bone metastases but uses more capacity.

“What I began by reading,
I must finish by acting.”
Henry D. Thoreau (1817-1962)

Chapter 3
Literature Review

In this chapter we present a brief overview of the scientific literature related to the *logistic planning* of the radiotherapy (RT) process. In the healthcare industry, logistic planning is concerned, among others questions, with how to allocate valuable resources (Rais and Viana, 2011). Specifically, the resources of the RT process which we plan in this thesis are the linear accelerators, or linacs. We begin by introducing the characteristics of the logistic planning of linacs and define the Linac Capacity Planning Problem (LCPP) in Section 3.1. According to this characterization, we decide upon which literature to review. Then, in Section 3.2, we look at different approaches that have been used for linac capacity planning and we evaluate their strengths and weaknesses with respect to our definition of the LCPP. In Section 3.3 we study a few examples of planning approaches of similar healthcare resources. From these examples we get insights on how the different healthcare objectives and uncertainties can be incorporated into a single planning approach. In a comparable way, in Section 3.4 we broaden the scope and briefly take a look at examples of logistic planning in ‘related’ manufacturing businesses. From these examples we extract ideas for potential planning decisions, and the implications they have in the ‘production’ processes. Finally, in Section 3.5, we recap the main points obtained from the literature reviewed and state the contribution of our work to the linac logistic planning knowledge.

3.1 Introduction to Linac Planning

Radiotherapy (RT) is a complex healthcare process in which many resources are used for providing the necessary care to a patient. The decisions on which resource to use (i.e. allocate) for a patient or a group of patients depend on all sort of criteria, including medical, technical and patient preference factors. In the *medical planning* of the RT process a radiation oncology team decides upon the treatment plan for a patient (e.g. dose of radiation, number of fractions, shape and angles of beams, etc.) thus providing resource requirements for the treatment. In the *logistic planning* of the RT process, a support-staff team checks which resources fulfill the medical requirements, and from these, decides upon which resources to use. The main objective of both types of planning is to achieve the highest quality in the treatment of patients. In logistical aspects, this objective is translated into patients having prompt access to the resources they need. In RT treatment, long waiting times can impair tumor control for some cancers (Dodwell and Crellin, 2006) and add psychological stress to patients (Mackillop, 2007). The management of the resources (e.g. linear accelerators, CT scanners, radiotherapists) through adequate logistic planning can help providing the necessary *and best* care for a patient.

From all the resources needed for the external-beam RT treatment of a patient, we focus on the one used by all patients (and from which the treatment derives its name): the radiation machines or linear accelerators (linacs). We define the Linac Capacity Planning Problem (LCPP) as the part of the logistic planning of the RT process in which decisions on how to allocate the *linac capacity*, or the available time of the linacs for treating patients, are done with the objective of minimizing access times. In our context, *access time* is the time a patient has to obligatory wait before beginning treatment. Since the linacs are used until the last phase of the process (the actual treatment), we define access time to be the time between the end of the 'pre-treatment' phase (treatment medical planning phase) and the first fraction of radiation (start of treatment).

Figure 18 – Example of medical and logistic planning interaction

The objective of LCPP is straightforward, but the decisions to achieve the objective are more complex. First of all, the allocation decisions in this problem are interrelated to, and dependent of, the medical planning of the RT process, as seen in Figure 18. This relationship makes the linac capacity a *constrained resource*. Even though RT treatments are individual for each patient, the medical constraints on the linacs usually apply for grouped patients, e.g. cancer types. For this reason, we consider decisions in the LCPP to be done for *categories* of patients, rather than individuals. These categories are different and have all medical characteristics (e.g. which linacs are feasible to deliver the treatment) known. Furthermore, the decisions for the categorized patients can be reactive, i.e. when a patient arrives, or proactive, i.e. before the patient arrives. Reactive decisions have the benefit that individual patient information is known and therefore there is much lower *uncertainty* than in the proactive decisions. Nevertheless, Petrovic and Leite-Rocha (2008) state that research should be done on how to improve reactive, day-to-day decisions with 'look-ahead' techniques that provide a robust solution for current and future patients. In favor of this, and the aforementioned characteristics, we define the decisions in the LCPP decisions to be how to allocate constrained linac capacity to categorized patients in advance, i.e. before the patients arrive.

When planning in advance, logistic decisions in healthcare can differ greatly as explained in the framework for healthcare operations management by Hans *et al.* (2012) (see Appendix 6). Using this framework, the level of LCPP decisions can range from *strategic* (e.g. which kind of linacs to buy) down to the *operational offline* (e.g. what to do when a linac breaks down). As the level of in-advance decisions decreases, two important characteristics of these decisions also decrease: (1) the *uncertainty* in the information used and (2) the *planning horizon* or the time extent when decisions should be effective. With respect to the uncertainty, LCPP decisions must take into account information about the variability in the arrival of patients such that the decisions can benefit future patients. This variability in the arrival of patients is the only form of uncertainty we consider in the LCPP, i.e. linac capacity and categories' medical information in the LCPP are assumed to be certain. Linac capacity (e.g. number, type and working time of linacs) is usually fixed for a long period of time (e.g. several years). However, medical information, such as fractionation scheme and feasibility of linacs, is constantly changing as improvements and new treatments are discovered. For this reason, we consider the planning horizon for the LCPP decisions to be of a medium extension, i.e. six months to one year.

When decisions include uncertain and certain information, and they are effective for a medium-term horizon, they are placed in the *tactical* level of the framework for healthcare operations management by Hans *et al.* (2012). As explained by the authors of the framework, tactical decisions are restricted to decisions from the upper strategic level (e.g. fixed number and type of linacs). In turn, tactical decisions bound the decisions that can be made in the operational level (e.g. in which linac a patient can be treated according to the LCPP allocation). For this reason, the operational characteristics of the treatment phase of the RT process (such as patients returning to receive several daily fractions) must be also included in the tactical level decisions, thus increasing the complexity of making them. In order to find how to cope with these characteristics of the LCPP (which are summarized in Table 4) and find a way to develop a tactical level solution, we make a review the relevant scientific literature.

Table 4 - Summary of LCPP Characteristics:

Resources (supply)	Treatments (demand)	Decisions
• Fixed number of linacs • Fixed working time • Constrained linacs (i.e. not all of them can treat all patients)	• Categorized patients • Recurrent use of resources (daily fractions) • Different urgencies to start treatment • Uncertain arrival of patients	• Allocation of linac capacity to categorized patients • Tactical level • Medium-term horizon

3.1.1 Design of the Review

As pointed by Royston (2009), day-to-day activities and resource-constrained operations in healthcare are increasingly being analyzed with operations research (OR) techniques. Through mathematical analyses, OR techniques provide quantitative support for complex but specific decision making, such as the one required by our LCPP. In our review, we search for literature that deals with such kind of approaches and which is directly or indirectly applicable to the LCPP. We divide the search into three topics: (1) linac planning and scheduling, (2) healthcare resource planning and (3) industrial resource planning. For the first topic, we search literature about quantitative linac capacity decisions. We confine the search to linacs only, filtering out literature about other parts or resources of the RT process. Since tactical decisions are limited by strategic ones, at the same time while they limit the operational ones, we review literature on all three levels of planning for this first topic. In this first topic the aim is to briefly study what has been done. For the second topic, which is indirectly applicable, but in the same domain of the LCPP (i.e. healthcare), we specifically select literature in which constrained resources are planned, at a tactical level, for categorized patients whose arrival is uncertain. In this second topic the aim is to study how these characteristics have been mathematically approached and the effectiveness of such approaches. Finally, for the last topic, the application domain of OR is extended to manufacturing business that share all characteristics of the LCPP, with the (only) difference that demand is not in the form of patient treatments. We now shortly discuss the relevant literature to the criteria just described and note down the important remarks from the scientific theory to the solution of the LCPP.

3.2 Linac Capacity Planning and Scheduling

From the early days of radiotherapy up to the present day, a variety of studies on how to quantify an adequate supply of linacs to meet treatment demand have been done. Since the 1990's, researchers have gone beyond examining ways of calculating necessary linacs to meet demand and have studied mathematical ways of guaranteeing this demand is satisfied as soon as possible. The questions asked in this kind of studies range from the strategic (planning) ones, e.g. how many linacs are needed for the next years, down to the operational (scheduling) ones, e.g. how to book the fractions of a new patient. Although there is a large choice of which questions to answer if low waiting times for RT treatments are desired, Conforti *et al.* (2010) and Petrovic and Leite-Rocha (2008) report that the scientific literature has scarcely considered all possible questions. In this section we give an overview of which questions about managing RT capacity have been reported in the scientific literature, and how well these questions tackle the problem considered in this thesis, the LCPP. Rather than exhaustively analyzing how each and all of the studies are done, we describe key aspects of the questions asked and the answers provided. For a larger and more comprehensive review of planning literature for the RT capacity we refer to Leite-Rocha (2011). To present how linac capacity planning is done, we use the healthcare operations framework of Hans *et al.* (2012).

3.2.1 Strategic linac capacity "planning"

We label strategic linac capacity questions as "planning" questions because they include uncertainty of what might happen in the future. In the strategic level this uncertainty tends to be large since the decisions are for the long-term. The main type of questions studied at this level deal with "how many" and "which type" of linacs are required to satisfy future RT demand. We find that most of the studies concerning these questions are approached on a regional (as opposed to institutional) scale. For example, Erridge *et al.* (2007) use medical factors (such as cancer incidence, radiotherapy usage for the different cancers, etc.) in combination with statistic and probability formulae for forecasting the demand and predicting the machine capacity required for the *entire* Scotland population for 2015. Nevertheless, Postma and Terpstra (2002) show that even with simple formulae and statistical indicators of RT data from the Netherlands, a balance between regional (in their case national) and institutional decisions is necessary for 'expertise-requiring' planning, such as linac capacity planning. An example of regional-institutional interaction is the QUARTS (QUAntification of Radiation Therapy Infrastructure and Staffing Needs) model of Bentzen *et al.* (2005). Their model determines, through the use of epidemiological data, European guidelines (i.e. benchmarks of linac throughput) and forecasting methods, the required number of linacs required per population per year. In these studies we observe the importance of representative medical information and statistics to cope with the characteristics of strategic linac capacity planning questions.

An important remark in the aforementioned studies is that their approach assumes that the required capacity must be equal to the expected demand. However, from the logistic planning knowledge, in this case queuing theory, we know that waiting times grow exponentially when demand approaches capacity. There is, however, some strategic research that has taken this into account. For example, Thomas *et al.* (2001) propose a queuing theory method to calculate the overcapacity needed to meet waiting time targets. With their approach, they devise a formula that determines the level of excess capacity needed in order to see patients without a waiting list. A variation of this model is then presented in Thomas (2003), in which Monte Carlo simulation is used rather than queuing theory. Although this study does consider categorized patients with different urgencies to start treatment, it assumes (as every other strategic study reviewed) that linacs are able to treat all patients, and hence not comply with the constrained resources of the LCPP. Nonetheless, in these studies we observe that strategic linac capacity planning questions *must go beyond* the "how many" and "which type" of linacs are required for meeting future demand. Strategic decisions must consider their effect in lower levels in order to guarantee a good performance when executed.

3.2.2 Operational linac capacity "scheduling"

On the opposite level of strategic linac capacity questions we have the operational ones. We label these questions as "scheduling" questions because they include fewer uncertainties than "planning" ones, although they are done for the future as well. The main type of questions studied at this level deal with "when" and "in which linac" should a patient be treated. These questions imply decisions for a shorter time horizon, e.g. daily or weekly horizon, since they refer to individual patients rather than the entire population. Nevertheless, answering the questions from this level is still complex due to the large number of constraints and interactions in the RT process, thus attracting researchers' attention. The earliest study about how to schedule RT treatments in the best way was carried out by Larsson (1993). He develops a model based in arithmetic formulae in order to estimate the starting day of a patient, given a current waiting list. The model was completely automated in a spreadsheet, allowing the user, i.e. the planner, to check the different scheduling options for a patient and to choose the best one. A more recent, but similar, booking tool is presented in Thomsen and Nørrevang (2009). Their model allows the planner to derive future waiting times curves for the different options for scheduling a patient today. Again, these future indicators are derived from arithmetic formulae and medical information and are used as support for the planner. In both studies only support information is given to the planner, but there is no explicit optimization of waiting times for the decisions.

More than indicating-tool studies, there are studies that explicitly aim to improve the performance of scheduling. There have been researchers that, with OR methods have developed rules of "when" and in "which linac" a patient should be scheduled. For example, Petrovic and Leite-Rocha (2008) use a *parameterized* construction-and-improvement heuristic to schedule patients at the end of a day. Some of the parameters in the construction part of their heuristic include how close to the 'due date' (e.g. waiting time target) will the planner try to schedule a patient and how long can the planner wait to do a schedule for a group of categorized (e.g. urgent, non-urgent) patients. Their improvement approach is GRASP. Through a simulation with 4 different linacs, the authors conclude that their proposed approach performs better (than the current way of working of the study hospital in the UK) as long as linac capacity is enough to satisfy the incoming patients. On their sensitivity analysis, they observe that when they double and triple the number of linacs, their heuristic significantly takes longer computational time to run. Kapamara (2009) and Petrovic *et al.* (2011) use a similar approach of a construction-and-improvement heuristic for the entire RT process. Opposite of the previous example, in both studies *greedy* construction heuristics are used (e.g. plan urgent patient as soon as possible). After the schedule has been constructed, the authors use as their improvement approach 'steepest' hill climbing and a multi-objective genetic algorithm. The main conclusion of these three studies is that heuristics or *simple rules* for making the decisions (e.g. plan a number of days from now, plan this patient first, etc.) can improve the waiting time performance. Furthermore, with advanced OR methods such as the improvement heuristics the resulting schedule can be 'improved' under the assumption that this can be done for patients grouped over a planning horizon (e.g. a schedule can be finalized after a day).

Heuristics are usually are 'easy to understand' rules that improve performance. However, if the assumption the scheduling for patients that are grouped over a planning horizon is true, then the OR method that guarantees the best scheduling performance is mathematical programming. Conforti *et al.* (2008) propose such an approach. By modeling the scheduling problem as mixed integer linear programming (MILP) model they develop an optimal weekly schedule for the patients that have been grouped for a week. They benchmark their approach against real-world data of a hospital in Italy that has 1 linac and show that, not only waiting times could have been shorter, but also more patients could have been treated if their MILP would have been used. We find a similar, but more complex MILP model in Conforti *et al.* (2010). The authors include a set of machines, rather than a single one, different working times per machine per day, a priority value for each patient, set up times, amongst other considerations. To test their approach, they develop six scenarios based on real data, with 2 linacs. They report that computational time does become large in one of the six scenarios, but short enough to be used in real practice. From these two studies we observe that modeling the complex RT treatment scheduling process with mathematical programming is possible, therefore the possibility to always obtain the optimal schedule. However, due the different components of the process itself, the model is not always practical (and sometimes impossible) to solve computationally for large problems (e.g. 'large' number of linacs or patients).

3.2.3 Tactical linac capacity planning

From the strategic planning perspective, Erridge *et al.* (2007) suggest that further research on how to meet the projected demand also considering the waiting times is needed. Thomas (2003), who already considers waiting time in his strategic study, indicates that further research is needed to manage access rates and fractions per course if linac capacity is already planned considering waiting times. From the operational perspective, Conforti *et al.* (2010) point out it is important to handle the uncertainty that affects the scheduling model in an appropriate way. Petrovic and Leite-Rocha (2008) suggest the use of 'look-ahead techniques' as an extension of operational scheduling. Strategic studies of RT linac capacity suggest there is a need to consider lower-level planning aspects, i.e. waiting times. Operational studies of RT linac capacity suggest there research should be done on how to incorporate upper-level planning aspects, i.e. uncertainty. Nevertheless, a very few studies that have looked at this "middle" planning level (or tactical planning level in the framework of healthcare operations of Hans *et al.* (2012) of the RT linac capacity.

Although there main objective is to develop an operational method, Petrovic and Leite-Rocha (2008) include an implicit "tactical decision" on their operational model. They include a parameter (whose value is decided by the planner) that tells how much capacity to reserve for urgent patients. All other patients are scheduled up to a certain limit imposed by this capacity reserved for urgent patients. They use a value of 10% for this parameter, but with no methodology to optimize it over all the uncertainties of the RT linac capacity planning problem. A similar study that includes an implicit "tactical aspect" is the one by Munro and Potter (1994). In their study, they use a Monte-Carlo simulation to analyze the effect of allocating "machine-hours" to three different categories. Their model, which is built in a spreadsheet, allows the user to see the expected tradeoff between allocated machine hours (to the three categories). The user (i.e. the planner) has then to decide how much machine hours to allocate, in a "numerical enumeration" of waiting times. From these two studies we observe that there have been ideas on how to link the strategic and the operational decisions through tactical aspects, but no real optimization of the scheduling or planning decisions have been done (i.e. they are left to the user to decide).

3.3 Healthcare Resource Planning

In healthcare organizations that provide specialized treatments or care, resources (e.g. infrastructure, specialized drugs, personnel, etc.) are generally expensive and unique. In addition, these organizations face uncertain demand for these treatments, and therefore the use of their specialized resources. Not only the number of patients that will arrive in the near future is unknown, but also the type and priority of the specialized care they will need is variable. Due to the nature of the medical treatments, and the resources used to provide it, these organizations have challenges when defining an effective logistical plan. According to Leite-Rocha, (2011) the challenge of planning in specialized clinics is to reserve enough capacity for prioritized patients while maintaining a high utilization of resources. In this section, we present a few examples on how this challenge is tackled, i.e. how healthcare resources have been planned to meet uncertain and categorized demand in constrained healthcare processes. Furthermore, we review the different forms that healthcare objectives can take.

An outpatient resource that is similar to a linac in the RT process, from a logistical perspective, is a CT-scanner in a diagnostic facility. Vermeulen *et al.* (2009) present an adaptive heuristic approach for resource allocation of CT scanners. In their study, they consider patients to be grouped according to different medical attributes. They consider a set of scanners to have different 'timeslot-type specification' (TTS) per day. These TTS restrict which patients (from the different groups) can be scheduled on them. They develop a model to optimize these TTS variables for the mid- and short-term, considering an uncertain arrival of patients in the future. The model schedules each patient on the first TTS available. After scheduling a patient, their model re-adjusts the TTS (according to the attributes or category of the scheduled patient) with the goal of maximizing the expected number of patients scanned on-time (i.e. within a medical time window). The re-adjustment of TTS is done through a patient-arrival simulator and a heuristic algorithm. Furthermore, their model is equipped to adjust capacity in-advance if necessary, i.e. increasing or decreasing the opening times of the CT scanners. The authors test their approach using real-life data and a simulation from a hospital in the Netherlands and show that benefits can be gained in efficiency of resource usage and 'on-time' performance for all groups. Their main contribution, to the planning literature of CT scanners, is the reduction of the gap between the strategic-only and the operational-only planning literature by a tactical method that links to the two.

A different approach for a diagnostic resource is developed by Patrick *et al.* (2008). They consider similar demand characteristics (i.e. grouped patients, different priorities for diagnostic, uncertainty in the arrivals) and capacity characteristics (i.e. deterministic service time) as the previous example. However, their approach is based on a Markov Decision Process (MDP) model rather than a heuristic approach. Their model's goal is to minimize a cost function of waiting times and lateness (with respect to a time window) of patients, in addition to overtime use of capacity. A MDP approach outputs a 'policy' for scheduling, which in this case gives rules of when to book a patient in nominal or overtime, according to a given 'state' of the system. However, there are so many 'states' of the system that the problem becomes impossible to solve directly. The authors overcome this issue with a complex approximate dynamic programming technique. They test their approach using real-life data and a simulation from a hospital in Canada, for small and large instance settings. Their approach outperforms the current way of working of the hospital and proves to be robust to small changes in the parameters (e.g. same policy for an increment in demand). Their main contribution is the design of a method that schedules patients through policies (or rules defined in advance) that are robust to the uncertainties inherent to healthcare processes. As a concluding remark, the authors also state that their approach is applicable in surgical scheduling and scheduling of radiation treatment. However, they point out that for the latter one, a complication of the modeling approach is that it involves a series of appointments rather than a single one.

A last example of a healthcare-resource planning that has been approached through tactical methods is the operating room. Although different from the linacs, operating rooms also face uncertainties in the operational scheduling and many constraints for the strategic planning. Van Oostrum *et al.* (2008) develop a master surgical scheduling approach for the tactical planning of this resource. They consider different types of surgical procedures, each with a stochastic duration. They define, for each operating room, a cyclic 'master surgical schedule' (MSS) that specifies a list of surgery types that can be performed every day. A MSS restricts which patients (from the different types of surgical procedures) can be scheduled for an operating room on a given day. They construct a mathematical programming model with probabilistic constraints and use a column generation technique to construct MSSs that minimize the required capacity and level hospital bed requirements. The authors test their complex approach using real-life data from a large hospital in the Netherlands. In the test they build weekly, two-weeks and monthly MSSs for a capacity of 5 up to 20 operating rooms and conclude that, within reasonable computational times, it is possible to obtain schedules. Their main contribution is the development of a cyclic (i.e. repeating) tactical plan that reduces planning efforts while attaining strategic and operational goals.

From these few examples of planning healthcare resources for categorized patients, we can derive several indications on how to tackle the challenges of the LCPP. There are different mathematical approaches (e.g. heuristics, MDP, MILP with stochastic constraints, etc.) to handle the uncertainty in the arrival of patients and the patient-related objectives (e.g. minimizing waiting times, maximizing patients served within a timeframe, etc.). Independent of the approach, some form of allocation of capacity to the different categories is obtained with the approaches. These allocation plans provide guidelines on when and where a patient can be scheduled (i.e. use the resource) that prove, for real-life data, to be better than not having them. Depending on the objective or objectives considered, and the size of the problem characteristics (i.e. number of resources, categories, etc.), some approaches that handle the uncertainty are not directly applicable. For instance, the MDP and the MILP-with-stochastic-constraints require additional (usually approximation or heuristic) techniques to provide an answer (a plan). From this section, the two main observations about healthcare resource planning are that (1) plans in the form of in-advance capacity allocation can improve current way of working with respect to patient-related objectives and that (2) combined mathematical techniques are required to handle all characteristics of healthcare processes.

3.4 Manufacturing Resource Planning

In this section we broaden the scope of the study to manufacturing businesses that use a constrained supply of machines to produce and satisfy a demand of different types of products. Pinedo (2005) provides a framework to classify the scheduling in this manufacturing environments according to their machine, job (product) and objective characteristics. Using this framework, we can describe the LCPP as the scheduling problem of having parallel machines (with machine eligibility restrictions and recirculation) in which there are weighted jobs (with release dates) that must be scheduled in such a way that the total weighted completion time is minimized. Although his focus is on operational scheduling rather than tactical planning, Pinedo provides indications on 'look-ahead' solution approaches (e.g. 'composite dispatching' heuristics). Based on these 'look-ahead' indications by Pinedo, as well as the characteristics of the LCPP in his framework, we present a few examples of businesses problems. Our objective in this section is to obtain ideas for tactical decisions and understand the interaction between these tactical decisions and the manufacturing characteristics. It is not our goal to completely depict the LCPP to a specific manufacturing problem or to survey all possible examples that are applicable. For the purpose of conceptualizing the entire RT process, and a exhaustive review of RT examples, as a manufacturing process we refer to Kapamara (2006) and Leite-Rocha (2011) respectively.

We begin by presenting a study done by Aghezzaf *et al.* (2010). In this study, the authors consider a production system with uncertain demands of finished products, inspired in a medical and graphical film manufacturer. They test stochastic and deterministic MILP approaches for reserving production capacity for product families and at each stage of the production system. All of these approaches have the objective of minimizing costs and are tested under several levels of demand variability and capacity tightness. Their numerical experiments report that average costs are 6% lower in the stochastic model for high variability and capacity tightness, but they show significantly more variation than the deterministic model. Furthermore, they report that the stochastic model becomes computationally more expensive (running time of hours) than the deterministic one (running time of minutes) as instances become large (i.e. 5 product families, 6 week planning horizon, 2 stages). Thus, they recommend the deterministic MILP model for defining the tactical variables of reserved time for product families. An important remark is that, although the model is labeled as deterministic, the reserved capacity (called the 'cushion level') is built in the model similar to a 'safety stock' of production capacity. For this 'cushion level', the demand is assumed to be stochastic, but with known average and standard deviation. It is also assumed that a 'service level' (i.e. probability of not meeting demand) is known for the model to work. The main contribution of this study is the deterministic 'cushion level' MILP that performs (in terms of costs) as good as the stochastic one under some circumstances (e.g. capacity tightness), for a far less computational time. Furthermore, for those circumstances where the stochastic model performs better, the deterministic model shows less variation in the costs (in a series of numerical experiments) leading to a more robust planning method.

In contrast to the MILP based approach of the previous study, Almada-Lobo *et al.* (2008) present a research about composite dispatching rules with a variable neighborhood search (i.e. a metaheuristic approach) for the tactical planning of a glass container manufacturer. The technologies of the machines used for molding the glass restrict which containers can be produced on them. In addition, the furnaces have sequence dependent setup times according to the color of the glass paste to be processed. Both furnaces and machines are completely automated and work 24 hours per day, 7 days per week. In this highly constrained and massive production environment, their goal is to build a yearly plan that assigns colors to furnaces and products to machines monthly, and that minimizes a multi-objective weighted function. To achieve this, first they build a plan through a composite dispatching rule. This rule assigns a 'priority index' to product-machine pairs and schedules, as soon as possible, the highest pair. Forecasts for the monthly demand of finished products are assumed to be known. The resulting plan is then improved by a variable neighborhood search, with a special 'neighborhood changing' scheme. The main contribution of this paper lies in this neighborhood changing scheme, which achieves better solutions (than the dispatching rule itself) at almost no computational cost, for a highly constrained and complex process. However, no indication is given about the performance when the forecasts are not as expected or any stochasticity in the demand of glass containers.

Last two examples of manufacturing businesses have been of small products (film and glass containers). Finally, we analyze a larger manufacturing environment, a build-to-order automobile production. More specifically, we analyze an engine manufacturer study done by Garcia-Sabater *et al.* (2012). They relate the mid- and short-term planning via two sequential (iterative) MILP models. Similar to the previous example, they consider forecasts for the different engine types (more than 40 variants) to be available for a 6 month horizon. They describe demand to be stable, and thus forecasts to be accurate. The tactical MILP, which they call master planning process, is used to decide production rates and down days for the different engine types on the assembly lines such that a multi-objective weighted function is minimized. The output is then used in a complex weekly MILP (with all industry specific constraints) that minimizes costs. They report the implementation in a real-life business, in which an additional algorithm relaxes some constraints in order to deliver a feasible plan when necessary.

Furthermore, their implementation included an algorithm to stop at the last feasible plan (with the lowest integrality gap) whenever the MILP became computationally too expensive. The two main contributions of this paper are (1) a model that links (and coordinates) mid- and short-term planning and (2) the results of a real-life implementation where additional benefits such as reducing planning complexity and stable planning of workers.

With this few, but representative examples (of the characteristics of the LCPP in Pinedo's framework) we observe that allocation (in advance) of machine time capacity can model in several forms and solved with different approaches. The allocation can be in the form of reserved capacity (such as the cushion levels), production rates, no work days, etc. We observe also that authors contribute with methods for making the different approaches more computationally efficient for real-life instances, which in part is due to the maturity of the knowledge for logistical planning in the manufacturing industry. We also see that, as processes get larger and more complex, the link between the tactical and the operational planning becomes more of an issue. For this reason, 'look-ahead' techniques that allocate capacity to different product families (rather than individual products) should be able to include the operational constraints to give an applicable solution to job-machine planning problems. As in healthcare applications, combined mathematical techniques are required to completely handle all characteristics of manufacturing tactical planning.

3.5 Summary and Contribution

In this chapter we briefly discussed the relevant scientific literature about linac capacity planning for the three hierarchical levels. Furthermore, we reviewed examples on how similar problems to the LCPP, in the healthcare and manufacturing industries, have been approached. The two key points of this chapter are:

- The majority of studies for planning the linac capacity have been done in the strategic and operational level. Strategic studies are usually medically oriented and do not include any logistical consideration (e.g. waiting times). On the other hand, operational studies usually do not include information about the process uncertainties (e.g. future patients) which can diminish their performance when applied in real-life. The tactical level studies, which relate the other two levels, have only been done for indication (support) purposes rather than optimizing ones.
- Similar processes to the RT linac capacity process can be found in the healthcare and manufacturing industries. Examples of tactical planning in these processes show that allocation of capacity, done in advance and for the different types of demand, can help achieve operational and strategic goals. There are different forms of allocating capacities, and different methods to do so. For similar processes to the RT linac capacity, a combination of mathematical techniques is required to capture, and cope with, problem characteristics.

Our contribution to the scientific literature is the design of a tactical planning methodology for radiotherapy linac capacity that handles uncertainty in the arrival of categorized cancer patients and minimizes the expected waiting times. The two main characteristics of this methodology are its (1) applicability in highly-constrained and large RT departments and that (2) relates the two levels of planning (tactical and operational) into a single solution. The output of this methodology is an allocation of capacity in the form of maximum linac-time that can be assigned to category. As described by van Oostrum *et al.*(2008), an implicit contribution of tactical approaches in practice is the simplification of scheduling while attaining the planning objectives of higher levels.

"Our problems are man-made,
therefore they may be solved by man..."
John F. Kennedy (1917-1963)

Chapter 4
ProaRT: A Solution to the LCPP

The Linac Capacity Planning Problem (LCPP) arises when a healthcare institution wants to minimize the access time of categorized patients by planning its linac capacity in advance. In this chapter we present "ProaRT", a solution (planning method) for the LCPP. We begin by presenting, in a nutshell, what is the linac capacity problem and what is our solution approach, in Section 4.1. In Section 4.2 we mathematically formulate the sets, inputs parameters, variables, objective and constraints that characterize the LCPP. In Section 4.3 we explain how ProaRT works and how its different parts tackle the problem characteristics. Furthermore, we indicate the assumptions we make in each part. In Section 4.4 we present a series of numerical experiments that provide insight in how the access time is influenced by 'in-advance' planning for different problem settings. In Section 4.5 we present a discussion about the approach and the results. Finally, in Section 4.6 we summarize the key points of modeling and solving the LCPP through ProaRT.

4.1 Problem and Solution in a Nutshell

In order to describe the linac capacity planning problem (LCPP), we begin by describing the relevant characteristics of the part of the radiotherapy process considered. A linear accelerator (linac) is a machine that delivers sessions of radiation to a cancer patient. We define linac capacity as the time from a group of linacs which can be used to treat different patients. We consider patients that need this kind of treatment to be categorized according to medical aspects. Each category (of patients) undergoes a different number of daily sessions of radiation, which are called fractions, and has a different urgency to start treatment (e.g. some categories can wait some days while others need immediate irradiation). Due to technical restrictions, the different categories can be treated only in some of the linacs. We call these restrictions linac feasibility constraints. We consider all aforementioned characteristics to be known and deterministic (e.g. number of fractions, linac feasibility constraints). However, we consider the arrival of patients (e.g. how many patients of each category will arrive next week) to be uncertain but statistically describable. With these considerations, we define the LCPP as follows:

> The LCPP in a nutshell:
> *We define the LCPP as the problem of allocating linac capacity in advance and to categories of patients such that the expected access times (i.e. times to start treatment) are minimized over a mid-term horizon while considering all process attributes (such as number of fractions, linac feasibility constraints, etc).*

In order to allocate linac capacity in advance, such that access times are minimized for the different categories of patients, we build a mathematical method we call "Proactive Radiotherapy" or shortly "ProaRT". In ProaRT we assume the linac capacity is measured in timeslots, and that one fraction lasts one timeslot, thus only one patient can be treated per timeslot. The allocation output of our method is a table that gives the maximum number of timeslots that can be used in a linac for a category. Due to our timeslot per patient assumption, this table gives a threshold on the number of patients from all categories that can be treated on a linac, any given day. An example of this kind of output is given in Table 5, where for instance, no more than 7 patients from category 1 can be treated daily on linac 3. ProaRT builds this table considering all process attributes for a mid-term horizon (e.g. 6 months). Furthermore, ProaRT's table is used in the day-to-day scheduling of patients as follows: all patient's daily fractions are planned on the earliest available linac that (1) has less than the number of maximum patients (given by the ProaRT table) planned and that (2) has the least number of total planned patients.

Table 5 - ProaRT's output table:

	Linac 1	Linac 2	Linac 3	...
Category 1	5	23	7	...
Category 2	11	2	0	...
Category 3	9	0	14	...
⋮	⋮	⋮	⋮	⋱

To obtain good values for the output table (i.e. thresholds that minimize the expected access times for the mid-term horizon), ProaRT uses a simulation and heuristic algorithm. Based on the arrival information and the length of the mid-term horizon, ProaRT builds samples of incoming patients. For each sample, or group of simulated patients, a local search algorithm finds thresholds (i.e. values for the table) that minimize the access time of the patients from that specific group. This means, that for each sample, the local search algorithm finds a different table. At the end, all tables are merged into a single one through applied statistics. This last table, which results from the statistical analysis of all sampled ones, is the output of the ProaRT method. In the following two sections we present a formal, and detailed, description of the problem and the solution method, respectively.

4.2 Formal Problem Description

The Radiotherapy Capacity Planning Problem (LCPP) consists in the design of an effective plan, for a mid-term horizon, that allocates in advance the linac capacity to categorized patients. This allocation must be done taking into account all process and treatment restrictions and, at the same time, considering the uncertainty in the arrival of patients. We say a plan for the LCPP is effective when it minimizes the access times in accordance to the healthcare organization's preferences and standards. To properly describe the LCPP, we first introduce the three main sets and their mathematical notation (all notation can be seen in Appendix 7). We consider different types of demand for RT treatment that comes from a set of categories $\mathcal{G}$, which is indexed with g and g'. We consider a set of linacs $\mathcal{M}$ (resource supply) to deliver the RT treatment, which is indexed with m and m'. We consider a plan must be constructed for a mid-term planning horizon $\mathcal{D}$, which is discretized in working days which are indexed with d and d'.

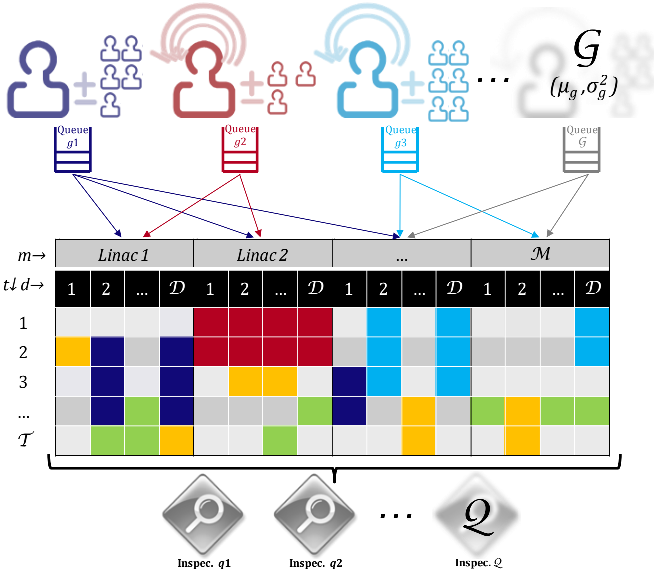
Expectations for the demand for treatment for the horizon $\mathcal{D}$ are known. We consider that for each category $g \in \mathcal{G}$ the number of patients that will "arrive" during a period of time is a stochastic variable with mean μ_g and variance σ_g^2. As explained in Section 2.2, when patients first arrive to the radiotherapy process, a pre-treatment phase is executed (e.g. CT scans, contouring, etc.). However, we consider the "arrival" of a patient in the LCPP to be the day at which the patient has completed his or her pre-treatment phase and is ready to receive radiation. Each category or care plan g has a constant number of fractions s_g (radiation sessions). We consider that all fractions of a patient must be given in the same linac $m \in \mathcal{M}$, or in a backup one while m is in maintenance. From a medical perspective, there are different effects of waiting time for different cancer sites, and hence different "importance factors" α_g for the different categories $g \in \mathcal{G}$. The higher the value of α_g the higher the importance of having lower waiting times for category g.These values work as 'penalties' in the objective function.

With respect to the resources, we consider all linacs in $\mathcal{M}$ to have the same working time (i.e. time for treating patients) during a day. The working time (capacity) of a linac is expressed in discrete timeslots $t \in \mathcal{T}$. We assume that any fraction of any category in any linac lasts one timeslot. Although all linacs share the same nominal time, each linac $m \in \mathcal{M}$ has its own technical characteristics, which might differ from the other linacs. To denote the technical (and medical) capability of linac m for treating category g, we use the binary parameter $f_{g,m}$. This parameter gets a value of one if linac m is able to treat a patient from category g, and zero otherwise. Another characteristic of the specialized resources in the LCPP is the series of different inspections $\mathcal{Q}$ that must be carried out in each $m \in \mathcal{M}$. Each inspection type $q \in \mathcal{Q}$ must be done periodically, at a fixed interval of r_q days between inspections. All inspections require the use of the same measuring devices. We define c as the number of measuring equipment the institution has, and hence as a limit on the number of simultaneous inspections that can be carried out. Moreover, an inspection q has a duration k_q timeslots in which no patient can be treated. Patients that cannot be treated in linac m due to maintenance are assumed to be treated in a backup linac. The maintenance schedule is assumed to be known in advance. We present a list of assumptions with respect to the resources and the demand for treatment in Table 6.

Table 6 - Assumptions of the LCPP:

Assumptions of the LCPP	
With respect to the linacs:	*With respect to the treatments:*
1. Linac capacity is fixed. 2. There is no overtime. 3. All fractions last one timeslot. 4. The categories that can be treated in a linac are constrained by medical factors. 5. Preventive maintenance is done in all linacs with a fixed frequency and known schedule. 6. There is one backup linac.	1. Demand arrives when pre-treatment phase of the radiotherapy is completed. 2. Treatment characteristics are the same for all patients from the same category. 3. Fractions are given on a daily basis for all categories. 4. All fractions of a patient are given in the same linac.

The main question in the LCPP is how much capacity (timeslots) should be allocated on the different linacs (in advance for the mid-term horizon $\mathcal{D}$) for the different categories in order to achieve a minimum weighted-function of the access times. We denote the capacity from linac $m \in \mathcal{M}$ allocated to category $g \in \mathcal{G}$ with the integer variable $V_{g,m}$. As explained in Section 4.1, $V_{g,m}$ represents the maximum number of timeslots that can be used for treating patients from category g on linac m. We define $\mathcal{F}_g(x)$ to be the total access time function (sum of all patients) of category g for a given tactical plan x. A tactical plan x is the vector (output table) consisting of all $V_{g,m}$ variables (thresholds) as seen in Constraint (2) . We define $\mathcal{X}$ as the feasible and finite decision space for x, which takes into account all assumptions and constraints in the LCPP (Constraint (3)) such as all fractions scheduled in one machine, linac-feasibility constraints, etc.. Finally, we denote the expectation of this function for the medium-term horizon by $\mathbb{E}^{\mathcal{D}}\left[\mathcal{F}_g(x)\right]$ and define the objective Z in Function (1). The objective function is then to minimize a penalized, total access time function (expected sum of all patients from all categories). The formal problem description and its mathematical formulation can be visualized in Figure 19 .



$$\min Z = \sum_{g \in \mathcal{G}} \alpha_g \cdot \mathbb{E}^{\mathcal{D}}\left[\mathcal{F}_g(x)\right] \qquad (1)$$

s.t.

$$x = \begin{bmatrix} V_{1,1} & V_{1,2} & \cdots & V_{1,m} \\ V_{2,1} & V_{2,2} & \cdots & V_{2,m} \\ \vdots & \vdots & \ddots & \vdots \\ V_{g,1} & V_{g,2} & \cdots & V_{g,m} \end{bmatrix} \qquad (2)$$

$$x \in \mathcal{X} \qquad (3)$$

Figure 19 - Graphical illustration and mathematical formulation of the LCPP

As seen in Figure 19, the access time function $\mathcal{F}_g(x)$ is “unclosed”, i.e. not explicitly defined in our formulation. This is to indicate its dependency in other decisions of planning and scheduling. The access time of a patient is defined as the number of days between his or her arrival and the start of treatment. The tactical plan x does not specifically say when a patient will start treatment, although it prohibits him or her to start treatment on a linac m if there are $V_{g,m}$ patients already planned from his or her category g on a given day. It is the operational scheduling which indicates the specific beginning of treatment, following the tactical plan x and all process considerations. The operational scheduling can be done in several ways, some of which can be found later in this chapter. Nonetheless, at a tactical level our objective is to minimize the expectation of this function for the mid-term horizon, thus the term $\mathbb{E}^{\mathcal{D}}\left[\mathcal{F}_g(x)\right]$ in the objective. From the aforementioned characteristics, we observe that sound solution (optimization method) for the LCPP must incorporate operational decisions and handle the stochastic nature of patients’ arrivals for the mid-term. As mentioned by Petrovic and Leite-Rocha (2008) in RT treatment scheduling ‘look-ahead techniques’ (tactical planning methods) must be an extension of day-to-day (operational) scheduling.

4.3 Formal Solution Description

We propose the use of a simulation-based meta-heuristic, which we call "ProaRT", to solve the LCPP. ProaRT first generates a collection $\mathcal{I}$ of patient-sets $\mathcal{P}_i$ for the time horizon $\mathcal{D}$. Then it minimizes a penalized access-time function $\mathcal{O}(\mathcal{P}_i)$ for each generated patient set $\mathcal{P}_i$ by designing a tactical plan x_i. Finally it constructs the overall best tactical plan x', through a statistical weighted-function $\mathcal{A}(\{x_1, x_2, \dots, x_{|\mathcal{I}|}\})$ of all designed tactical plans x_i's, that will achieve the goal from Equation (1). For this reason, we split the ProaRT method into three parts: (1) a patient-set generator, (2) a patient-set optimizer and (3) a statistical analyzer. The method has three sets of input parameters $\mathcal{H}^1, \mathcal{H}^2, \mathcal{H}^3$ for each part, respectively. These input parameters are user-defined and have a direct influence on the performance of the entire method. Moreover, the output of each part of the method is used in the following part, as can be seen in Figure 20, the graphical representation of ProaRT. In the following subsections we describe each part into more detail. An overview of the entire mathematical notation used in this chapter can be found in Appendix 7 and a short definition of technical terms in the Glossary.

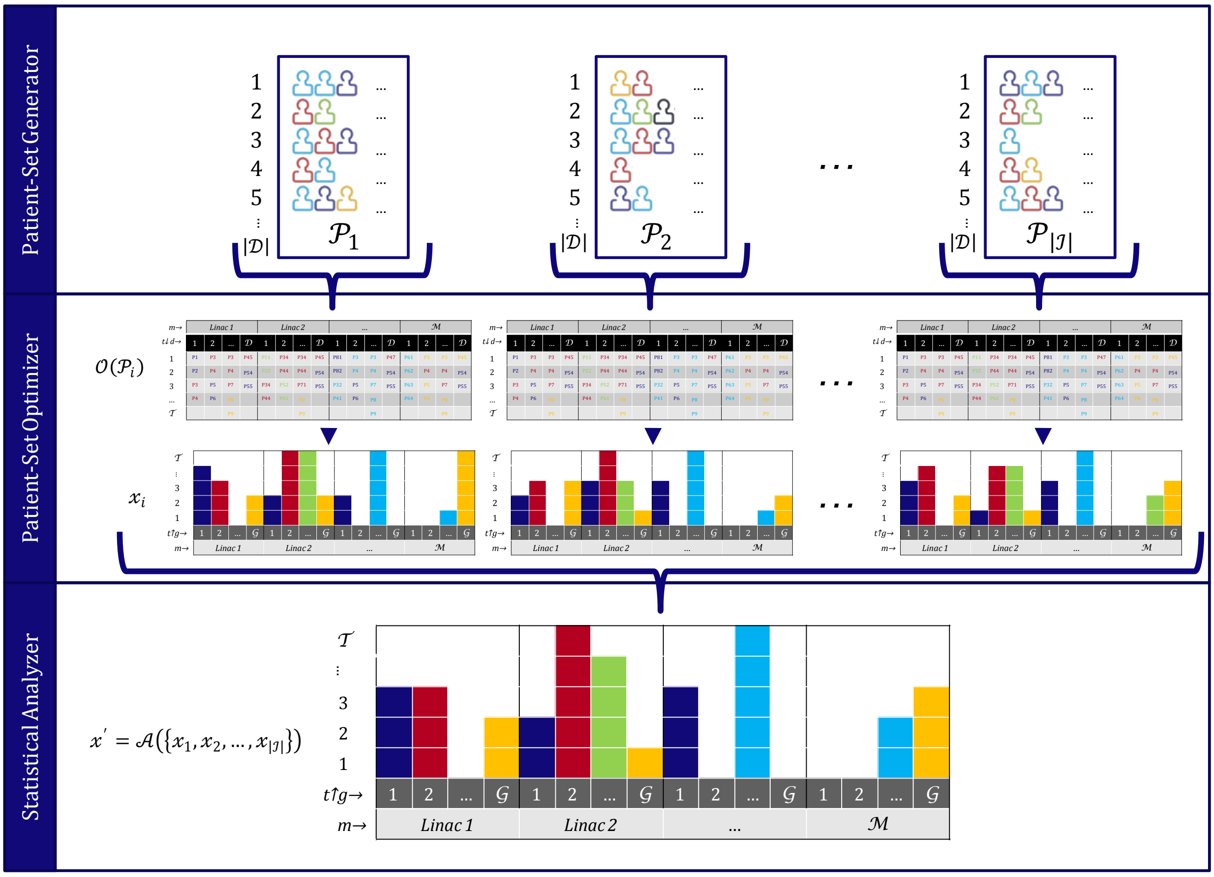


Figure 20 - Graphical representation of the ProaRT solution method

4.3.1 Patient-Set Generator

The first step in our solution method is the 'simulation-base' of ProaRT. We simulate the arrival of patients from all categories $g \in \mathcal{G}$ for the planning horizon $\mathcal{D}$, a total of $|\mathcal{I}|$ times. For each simulation $i \in \mathcal{I}$ we construct a set of patients $\mathcal{P}_i$, where each patient $p \in \mathcal{P}_i$ belongs to a category g and has a known arrival day a_p. The arrival of patients is built upon random variates from a Poisson distribution with rate λ_g, i.e. $\mu_g = \sigma_g^2 = \lambda_g$. This probability distribution is used because of its discrete and memory-less properties, and because evidence of a real-life radiotherapy department supports it as a mathematical representation of the arrivals (see Appendix 5). If the arrival rate λ_g is expressed in a longer time-unit than the days $d \in \mathcal{D}$ of the planning horizon (e.g. patients per week) then we use a factor φ to determine an arrival day a_p for every patient $p \in \mathcal{P}_i$ from a uniform distribution of days, i.e. $a_p \sim Uniform(1, \varphi)$, within the time-unit of λ_g. All the input parameters in $\mathcal{H}^1$ can be seen in Equation (4).

$$\mathcal{H}^1 = \{|\mathcal{I}|, \mathcal{G}, \mathcal{D}, \lambda_g \forall g \in \mathcal{G}, \varphi\} \tag{4}$$

From the parameters in $\mathcal{H}^1$, the number of simulations $|\mathcal{I}|$ is the only one that is not problem specific (as are the categories $\mathcal{G}$ and their arrival rates λ_g, for example). The value of $|\mathcal{I}|$ controls how much of the 'stochastic picture' the ProaRT method can capture. In every simulation $i \in \mathcal{I}$, random numbers are used to determine the number of patients in $\mathcal{P}_i$ and their arrival day. The larger the value of $|\mathcal{I}|$ the better the picture is, however, the method becomes computationally more expensive.

4.3.2 Patient-Set Optimizer

The second step in the ProaRT method minimizes a penalized access-time function $\mathcal{O}(\mathcal{P}_i)$ for each generated patient set $\mathcal{P}_i$ by designing a tactical plan x_i. We remind the reader that a tactical plan x_i is the vector consisting of all $V_{g,m}$ variables, which is the capacity from linac $m \in \mathcal{M}$ allocated to category $g \in \mathcal{G}$, for a simulation $i \in \mathcal{I}$. These $V_{g,m}$ variables define the maximum number of patients from category g that can be scheduled on linac m during any day d. In the RT planning literature, similar scheduling constraints can be found in Thomsen and Nørrevang (2009) and Petrovic and Leite-Rocha (2008). To design each tactical plan x_i, our method uses a Simulated Annealing (SA) algorithm. This 'meta-heuristic' varies the values of the $V_{g,m}$'s in a tactical plan x_i, evaluates $\mathcal{O}(\mathcal{P}_i)$ and adjust them in such a way that the best tactical plan is obtained. To explain in more detail how this is done, we have sub-divided this second step of the ProaRT method in two. First we will describe the SA algorithm (i.e. how $V_{g,m}$ is varied and how is the tactical plan x_i adjusted) and second how the penalized access-time function $\mathcal{O}(\mathcal{P}_i)$ is evaluated.

4.2.2.1 Simulated Annealing (SA)

Simulated Annealing is an useful optimization method for combinatorial problems whose objective function depends on many parameters (Kirkpatrick *et al.*, 1983). It has been widely and successfully applied in different planning problems as reported by Hans *et al.* (2008). Non-simulated annealing is a heat treatment process for a solid material in order to obtain certain physical properties. The material is heated to an initial temperature and then cooled down slowly until it reaches a desired temperature (so called thermal equilibrium). By small decreases in the temperature, different properties can be obtained in the material. In combinatorial optimization problems, the simulated version of this process does small changes in the decision variables (i.e. a local/random search method) for a "temperature" range with the objective of having a lower objective function value. For a complete description on how the SA algorithm works we refer the reader to Aarts and Korst (1989).

In the ProaRT method, our SA algorithm goes from the initial temperature $\tau^{initial}$ down to the final temperature τ^{final} through a proportional cooling system. Temperature is changed as follows: $\tau^{following} = \delta \cdot \tau^{current} | 0 < \delta < 1$, consequently the next temperature is $(1-\delta)\%$ less than the current one. While the algorithm is at a certain 'temperature', a number κ of single random changes (Markov chain length) in the decision variables $V_{g,m}$'s are made. For a single random change (neighborhood structure), first a category g' is randomly chosen, then a random feasible machine $m' | f_{g',m'} = 1$ chosen and finally a random value between zero and $|\mathcal{T}|$ is assigned to $V_{g',m'}$. This means that a "change" is just a new value between zero and the number of timeslots in one of the cells of a tactical plan x_i, i.e. $V_{g',m'}|f_{g',m'} = 1$. Every change that decreases the objective function $\mathcal{O}(\mathcal{P}_i)$ is accepted. On the other hand, every change that increases $\mathcal{O}(\mathcal{P}_i)$ is accepted with a temperature-dependent, monotonically and exponentially decreasing probability function $e^{-\eta/\tau}$ where η, just as τ, is updated for every change of temperature as follows: $\eta^{following} = (0.9 + \delta) \cdot \eta^{current}$. All the input parameters in $\mathcal{H}^2$ can be seen in Equation (5). A pseudo-code of the SA in the ProaRT can be seen in Table 7.

$$\mathcal{H}^2 = \{\tau^{initial}, \tau^{final}, \delta, \kappa, \eta^{initial}, \mathcal{O}(\mathcal{P}_i)\} \tag{5}$$

Table 7 - Pseudo-code of the SA in the ProaRT:

Pseudo-code of the SA in the ProaRT
1. Initialize all parameters in $\mathcal{H}^2$.
2. Empty all variables $V_{g,m}$.
3. While $\tau \geq \tau^{final}$ do
4. For $k = 1$ to κ do
5. CurrentSolution = $\mathcal{O}(\mathcal{P}_i)$.
6. Do random change in one $V_{g,m}$.
7. NewSolution = $\mathcal{O}(\mathcal{P}_i)$.
8. If (NewSolution≤CurrentSolution) or ($e^{-\eta/\tau}$ ≥Random(0,1)) then
9. Accept random change.
10. If (NewSolution≤BestSolution) then
11. Define BestSolution=NewSolution.
12. End If.
13. Else
14. Reject random change.
15. End If.
16. End For k.
17. Update $\tau = \delta \cdot \tau$.
18. Update $\eta = (0.9 + \delta) \cdot \eta$.
19. End While.
20. Define $x_i = [V_{g,m} \forall g, m]$.

To maximize the effectiveness of the method, all the SA parameters (Greek lettered ones from the set $\mathcal{H}^2$) must be chosen such that (1) all solutions are reachable and (2) a worse solution is almost always accepted close to the initial temperature but very rarely accepted when approaching the final temperature. In addition, we have included the parameter $\mathcal{O}(\mathcal{P}_i)$ in $\mathcal{H}^2$ to indicate that the way of evaluating a solution depends on the scheduling method used. This makes ProaRT a robust method since the approach is independent of the way of scheduling, which may vary from hospital to hospital. In the following subsection we elaborate more on how to evaluate $\mathcal{O}(\mathcal{P}_i)$.

4.2.2.2 Scheduling Methods

The value of the objective function $\mathcal{O}(\mathcal{P}_i)$ needed by the SA algorithm to design a tactical plan depends on the scheduling method. Some hospitals schedule a patient's treatment when he or she arrives, and do this in the earliest time available. Some others aim to level the use of their resources each time a patient comes. On the other hand, other hospitals first wait to accumulate a group of patients (e.g. patients that arrived a certain day are scheduled at the end of the day) and then schedules the treatment of every patient in the group. Even though the ProaRT method can be applied to many scheduling methods (as long as the constraint by the $V_{g,m}$ variables can be imposed), in this section we present the three methods exemplified above. Before describing each scheduling method in detail, let us introduce some notation.

Each patient $p \in \mathcal{P}_i$ has a known arrival day a_p and a known category $g \in \mathcal{G}$ that defines the number of fractions s_g and the linacs $f_{g,m}$ that can treat him or her. The parameter $b_{p,g}$ gets a value of one if patient p is categorized into g and zero otherwise. We assume a patient can only belong to one category, i.e. $\sum_g b_{p,g} = 1, \forall p$. Furthermore, we consider that all linacs $m \in \mathcal{M}$ have a number of timeslots $\mathcal{T}$, for every day $d \in \mathcal{D}$, in which they can deliver fractions. One timeslot $t \in \mathcal{T}$ corresponds to one patient fraction of any kind. However, as mentioned earlier, during periodic maintenance inspections $q \in \mathcal{Q}$, linacs cannot be used to deliver fractions of radiation to patients. As mentioned earlier, we consider that the complete schedule of these maintenance inspections is known in advance. We define the binary parameter $r_{q,m,t,d}$ to equal one if maintenance inspection q is scheduled in timeslot t at machine m on day d and zero otherwise. With respect to the decision variables, we introduce the binary variable $X_{p,m,t,d}$ which indicates whether patient p is scheduled to receive a fraction in timeslot t at machine m on day d $\left(X_{p,m,t,d} = 1\right)$ or not. We also introduce an auxiliary binary variable $X_{p,d}^{start}$ which indicates if patient p received his or her *first* fraction on day d. As mentioned earlier, decisions are constrained by the tactical plan variables $V_{g,m}$. The relation between these tactical variables $V_{g,m}$ and the patient scheduling variables $X_{p,m,t,d}$ can be seen in Constraint (6):

$$\sum_{g\in\mathcal{G}} \sum_{p\in\mathcal{P}_i} \sum_{t\in\mathcal{T}} b_{p,g} \cdot X_{p,m,t,d} \le V_{g,m} \qquad \forall m, d \tag{6}$$

Finally, for every method, the performance is measured as a weighted (penalized) function of the access time for the patients of the different categories $\mathcal{O}(\mathcal{P}_i)$, as seen in Equation (7):

$$\mathcal{O}(\mathcal{P}_i) = \sum_{g\in\mathcal{G}} \left[\alpha_g \cdot \sum_{p\in\mathcal{P}_i} \left(\underbrace{\sum_d (d - a_p) \cdot b_{p,g} \cdot X_{p,d}^{start}}_{Access\ time\ of\ patient\ p} \right) \right] \tag{7}$$

We now describe in more detail the three operational scheduling methods used as examples at the beginning of this section. Method 1 (Open Access Scheduling) and Method 2 (Balanced Workload Scheduling) are the methods in which patients are scheduled as soon as they arrive, i.e. no grouping. Method 3 (Weekly Optimal Scheduling) on the other hand, groups patients for a week and then schedules them. The methods are described using the general notation from above and with Constraint (6) implicitly introduced.

Open Access Scheduling

This method is based in the common 'first come first served' scheduling rule. In the LCPP, however, a patient that comes first is not necessarily treated earlier in time than a patient that arrives later. This situation might result due to the constraints on the linacs, e.g. the earliest available linac can irradiate the patient that arrived today is fully booked until three days later. This method is an 'online-operational' scheduling one because patients are scheduled as soon as they arrive, one by one (no grouping of patients for a week in order to do a schedule for the next one). A requirement of this method is a set of patients $\mathcal{P}_i$ that is ordered in non-increasing arrival days a_p. All daily fractions from patient p are scheduled in the first available feasible linac m. Please note that the first available linac is determined from the current schedule which consists of all variables $X_{p',m,t,d}$ for patients p' earlier than p in the ordered set $\mathcal{P}_i$. This method tries to schedule patients as soon as possible while filling the first linacs also as soon as possible.

Table 8 - Open access scheduling algorithm:

Open Access Scheduling
Sort all $p \in \mathcal{P}_i$ in non-increasing arrival days a_p.
For $p = 1$ to $\lvert\mathcal{P}_i\rvert$ do
For $d = a_p$ to $\lvert\mathcal{D}\rvert$
For $m = 1$ to $\lvert\mathcal{M}\rvert$ do
If $f_{g\lvert b_{p,g}=1,m} = 1$ then
For $t = 1$ to $\lvert\mathcal{T}\rvert$ do
If $\sum_{p'\neq p} X_{p',m,t,d} + \sum_q r_{q,m,t,d} = 0$ then
If $\sum_g \sum_{p'\neq p} \sum_{t'} \left(b_{p',g} \cdot X_{p',m,t',d}\right) \le V_{g,m}$ then
Set $X_{p,m,t,d'} = 1, \forall d' = \{d, d+1, \dots, d+s_g\}$.
Set $X_{p,d}^{start} = 1$.
Exit Loops t, m, d.
End If.
End If.
End For t.
End If.
End For m.
End For d.
End For p.
Calculate $\mathcal{O}(\mathcal{P}_i)$.

An important remark is that linacs are ordered alphabetically, e.g. A1, A2, B1, B2, etc. The complete algorithm for the 'Open Access Scheduling', including the tactical plan constraint, can be found in Table 8.

Balanced Workload Scheduling

This method is an extension of the 'first come first served' with one additional consideration in comparison to Method 1 (Open Access Scheduling). This method sorts all linacs that are available on the earliest day by non-decreasing number of planned patients. A patient is then scheduled in the first linac of this list, thus scheduling him or her in the earliest available linac that has the least amount of treatments to deliver (i.e. workload). Opposite to the previous method, this method does not fill the first linacs first, but aims to balance the workload among all available linacs (hence the name). For this purpose, we introduce an auxiliary integer variable L_m which indicates the number of patients planned on linac m at a given point in time. We define it as shown in Equation (8). We use the index d' in this equation to remark that this variable is updated every time a patient is planned, and thus changes over the day. Please note that the index d' is not applied in the L_m variable, just in the $X_{p,m,t,d'}$. The complete algorithm for the 'Balanced Workload Scheduling', including the tactical plan constraint, can be found in Table 9.

Table 9 - Balanced Workload scheduling algorithm:

Balanced Workload Scheduling
1. Sort all $p \in \mathcal{P}_i$ in non-increasing arrival days a_p.
2. For $p = 1$ to $\lvert\mathcal{P}_i\rvert$ do
3. For $d = a_p$ to $\lvert\mathcal{D}\rvert$
4. Evaluate L_m according to Equation (8).
5. Sort all $m \in \mathcal{M}$ in non-decreasing L_m.
6. For $m = 1$ to $\lvert\mathcal{M}\rvert$ do
7. If $f_{g\vert b_{p,g}=1,m} = 1$ then
8. For $t = 1$ to $\lvert\mathcal{T}\rvert$ do
9. If $\sum_{p' \neq p} X_{p',m,t,d} + \sum_q r_{q,m,t,d} = 0$ then
10. If $\sum_g \sum_{p' \neq p} \sum_{t'} \left(b_{p',g} \cdot X_{p',m,t',d}\right) \leq V_{g,m}$ then
11. Set $X_{p,m,t,d'} = 1, \forall d' = \{d, d+1, \dots, d+s_g\}$.
12. Set $X_{p,d}^{start} = 1$.
13. Exit Loops t, m, d.
14. End If.
15. End If.
16. End For t.
17. End If.
18. End For m.
19. End for d.
20. End for p.
21. Calculate $\mathcal{O}(\mathcal{P}_i)$.

$$L_m = \sum_{p \in \mathcal{P}_i} \sum_{t \in \mathcal{T}} X_{p,m,t,d'} \qquad \forall m, d' \tag{8}$$

Weekly Optimal Scheduling

In this last method, we consider two significant differences from the previous ones. The first difference is that this is an 'offline-operational' scheduling method as described by the framework of Hans *et al.* (2012). Instead of scheduling a patient's fractions as soon as he or she arrives (as in the previous two methods), this method assumes patients can be 'buffered' for a week and then scheduled. We denote these weekly buffers of patients with $w \in \mathcal{W} | w \subset \mathcal{P}_i$. The motivation for this 'buffering' is that during this time, a patient is being processed in the first steps of the RT process, and then a 'ready to receive fractions' day a_p is known for when the pre-treatment phase ends. The second, and most significant difference, is that this method uses an ILP (integer linear program) to develop an optimal solution for the weekly objective function $\mathcal{O}(w)$ as seen in Equation (9). To model this method as an ILP, we introduce an auxiliary binary variable $X_{p,m}^{linac}$ which indicates whether patient p gets treatment on linac $\left(X_{p,m}^{linac} = 1\right)$. For a week w, the schedule of all previous weeks w' are taken into account by the variables $X_{p,m,t,d} \big| p \in w'$ which act as parameters rather than variables. The ILP formulation of the 'Weekly Optimal Scheduling' (where the index d runs for the days in week w) has the objective:

$$\min \mathcal{O}(w) = \sum_{g \in \mathcal{G}} \left[\alpha_g^{wait} \cdot \sum_{p \in w} \left(\underbrace{\sum_d (d - a_p) \cdot b_{p,g} \cdot X_{p,d}^{start}}_{Access\ time\ of\ patient\ p} \right) \right] \tag{9}$$

subject to the constraints:

$$\sum_g \sum_p \sum_t b_{p,g} \cdot X_{p,m,t,d} \leq V_{g,m} \qquad \forall m,d \tag{10}$$

$$X_{p,m,t,d} \leq f_{g,m} \qquad \forall m,t,d,p,g | b_{p,g} = 1 \tag{11}$$

$$\sum_p X_{p,m,t,d} + \sum_q r_{q,m,t,d} \leq 1 \qquad \forall m,t,d \tag{12}$$

$$\sum_{m,t} X_{p,m,t,d} \leq 1 \qquad \forall p,d \tag{13}$$

$$\sum_{m,t,d} X_{p,m,t,d} = s_g \cdot \sum_d X_{p,d}^{start} \qquad \forall p,g | b_{p,g} = 1 \tag{14}$$

$$\sum_{t,d} X_{p,m,t,d} \leq s_g \cdot X_{p,m}^{linac} \qquad \forall m,p,g | b_{p,g} = 1 \tag{15}$$

$$\sum_{m' \in \mathcal{M} \setminus \{m\},t,d} X_{p,m',t,d} \leq s_g \cdot \left(1 - X_{p,m}^{linac}\right) \qquad \forall m,p,g | b_{p,g} = 1 \tag{16}$$

$$\sum_d X_{p,d}^{start} \leq 1 \qquad \forall p \tag{17}$$

$$\sum_{d'=d}^{d+s_g-1} \sum_{m,t} X_{p,m,t,d'} \geq s_g \cdot X_{p,d}^{start} \qquad \forall p,d,g | b_{p,g} = 1 \tag{18}$$

$$All\ X_{p,m,t,d}, X_{p,d}^{start}, X_{p,m}^{linac} \in \{0,1\} \tag{19}$$

The tactical plan is enforced by Constraints (10). Constraints (11) ensure that a patient is only treated in a machine capable of doing so. The restriction of having a patient treatment if and only if the timeslot in a linac is available (e.g. no other fraction or a maintenance inspection is done at the time) is imposed by Constraints (12). The "one fraction per day" is reflected on Constraints (13). The complete treatment (number of fractions) for the care plan a patient has is ensured with Constraints (14). The set of Constraints (15) and (16) make sure that all the fractions of a patient are assigned to the same linac. Constraints (17) assign the value of the starting day of treatment for a patient. Constraints (18) make certain that, after a patient has started treatment, the remaining fractions are given on consecutive days. Comparable formulations of ILPs for scheduling radiotherapy patients can be found in Conforti *et al.* (2010) and (2011). However, we use the ILP as a mean for designing a tactical plan, i.e. is a part of a larger model rather than the only model. In addition, an ILP can give insights on the optimality gap of previous methods for a weekly schedule.

4.3.3 Statistical Analyzer

The last step of the ProaRT method receives as input all tactical plans x_i's and through a statistical analysis of the $V_{g,m}$ variables generates the best tactical plan x'. Every tactical plan x_i is myopically optimized by the SA for its "sampled" patients i. There might be some samples i, which due to randomness, are very rare realizations of the entire probability distribution (e.g. outliers). Allowing the SA algorithm to obtain one tactical plan x' over all samples can result in a possible bias of this plan towards that specific realization. For this reason, we decide to look at several statistics of each individual $V_{g,m}$ variable in all tactical plans x_i's. We define $\mathcal{A}\left(\{x_1, x_2, \ldots, x_{|\mathcal{I}|}\}\right)$ as the parameterized function used to define x'. In this function, the $V_{g,m}$ variables in x' (denoted as $V_{g,m}^{x'}$) are defined through a weighted average of the mean, median and mode correspondent $V_{g,m}$ in all x_i's (denoted as $V_{g,m}^{x_i}$). We see this definition in Equation (20). Once again, by assigning different weights to the different statistics we can ensure that a possible "rare realization" of the arrival distributions will not have a large impact. A brief discussion on how we defined the weights can be seen in the following sub-section. Finally, the weights constitute the set of parameters $\mathcal{H}^3$ of the ProoART method, as seen in Equation (21).

$$V_{g,m}^{x'} = \frac{h_1 \cdot Mean_{i\in\mathcal{I}}\left(V_{g,m}^{x_i}\right) + h_2 \cdot Median_{i\in\mathcal{I}}\left(V_{g,m}^{x_i}\right) + h_3 \cdot Mode_{i\in\mathcal{I}}\left(V_{g,m}^{x_i}\right)}{h_1 + h_2 + h_3} \quad \forall g,m \qquad (20)$$

$$\mathcal{H}^3 = \{h_1, h_2, h_3\} \qquad (21)$$

4.3.4 ProaRT Parameter Selection

All parameters for ProaRT (i.e. $\mathcal{H}^1, \mathcal{H}^2, \mathcal{H}^3$) are user defined, meaning there is no sub-algorithm determining them. Some parameters are problem dependent (such as are the categories $\mathcal{G}$ and their arrival rates λ_g) and therefore are fixed inputs the user can only enter. On the other hand, the problem independent parameters can be modified as the user wants. These input parameters (such as the number of simulations or samples $|\mathcal{I}|$ and the SA parameters) influence the performance of the ProaRT method (the quality of the tactical plan). The tradeoff on choosing these input parameters is between quality of the solution and computational time. To choose the best values for the ProaRT problem-independent parameters, we carry out a small numerical search considering the problem dependent parameters from the NKI-AVL's RT department. We notice that the SA parameters chosen (see Table 10) were robust enough for all samples $i \in \mathcal{I}$, meaning the algorithm could find a tactical plan x_i that significantly improved the objective function. As explained earlier, the tactical plan developed by ProaRT is related to the way the operational scheduling is done. For the theoretical and practical experiments in the remaining of this thesis, we choose ProaRT's operational scheduling method to be the 'balanced workload' one because it resembles current hospitals scheduling (higher implementation potential) while performing better than the 'open access' and being far less computationally expensive than the 'weekly optimal'. As reported by Vermeulen *et al.* (2009), an approach that improves, but not replace, the current way of scheduling in a hospital has the greatest benefits in flexibility of usage and acceptability. Throughout the remaining of this thesis, for both the numerical experiments and the case study, the aforementioned ProaRT considerations and parameters are used.

Table 10 - Values for the ProaRT problem-independent parameters

Parameter	Value
$\|\mathcal{I}\|$	30 samples
$\tau^{initial}$	120
τ^{final}	90
δ	0.98
κ	200
$\eta^{initial}$	1
$\mathcal{O}(\mathcal{P}_i)$	Balanced workload.
h_1	20
h_2	30
h_3	50

4.4 Theoretical Experiments

As mentioned before, researchers have identified a need for 'in-advance' planning methods for effectively managing the RT capacity. However, not all hospitals which provide RT have the same linac-capacity characteristics or face the same treatment demand, and therefore have the same need for 'in-advance' or tactical planning. In this section, we make a series of theoretical (numerical) experiments to test, under different theoretical circumstances, how well ProaRT works. With these experiments we aim to get insight on when (e.g. large demand, constrained linacs, etc) a tactical plan (designed through the ProaRT method) can be an effective way of managing the RT capacity in a hospital (and thus solving the LCPP) and when does it not make a difference at all. These numerical experiments are based on realistic data gathered from the NKI-AVL's Radiation Oncology department, but are modified to the different theoretical circumstances. Specific experiments for the NKI-AVL are realized in the case study of Chapter 5. Following this introduction to the theoretical experiments, we explain what the experimental configuration in Section 4.4.1. We describe the LCPP settings considered, as well as the simulation setup used for the statistical validity of the results. In Section 4.4.2 we present our hypotheses and the experimental factors (experimental variables) we consider for testing then. We describe what levels (values) we consider in each factor and their motivation. Finally, in Section 4.4.3 we analyze and present the results of these theoretical experiments.

4.4.1 Experiments Setup

We first introduce the problem settings, which are the LCPP parameters that remain constant throughout all the experiments. These LCPP parameters are based in the current situation of the NKI-AVL's RT. We consider demand for treatment to come from 16 categories, i.e. $|\mathcal{G}| = 16$. These categories have fixed 'importance factors' $\alpha_g \forall g \in \mathcal{G}$ as seen in column W1 of Appendix 9. They also have fixed 'number of fractions' $s_g \forall g \in \mathcal{G}$ seen in the same appendix. These categories correspond to the 16 largest care plans (in terms of patient-type and fractionation-scheme) from the NKI-AVL. To deliver the radiation to the patients from these categories, we consider there are eight linacs, i.e. $|\mathcal{M}| = 8$. The time horizon for which we want to minimize the expected (penalized) access-time function is six months, i.e. $|\mathcal{D}| = 130$. The LCPP patient arrival parameters μ_g, σ_g^2 , linac feasibility $f_{g,m}$, and the number of timeslots $\mathcal{T}$ are used in the experimental factors described in the next section, and hence are variable throughout the experiments. To construct a tactical plan x' that solves the LCPP, we use the ProaRT method configured as explained in Section 4.3.4.

In the second place, we introduce the simulation settings we use to guarantee the validity of the conclusions. For every experiment, we construct a tactical plan x' according to the experimental settings and factors. Since this tactical plan is constructed under the stochasticity of the LCPP, its potential improvements are also stochastic. In the interest of giving a better estimate of this improvement, we decide to build confidence intervals (as opposed to point estimates) for the performance. Using the so-called Sequential Procedure, we determine the number of replications to be 1000, for a confidence level of 95% and a maximum relative error allowed of 10%. Furthermore, the simulation we use for the numerical experiments is categorized as a non-terminating one (Law, 2007). This means that the performance must be analyzed when the system has reached a steady state. In our simulation, the initial condition (empty linacs) has an influence on the when the steady state is reached. We use Welch's method to determine the 'warm-up' period, which is the period it takes for the simulation to reach a steady state. This period is estimated to be of 25 days. According to Law (2007), the run lenth should be much larger than the warm-up period in order to be able to better capture the steady state performance indicators. We increase the run length from 130 to 260 days, which makes each simulation a year worth and makes the run length more than 10 times the warm-up period. At last, to assure a proper comparison, we apply the concept of Common Random Numbers to our simulation. Common Random Numbers filter out differences due to variability in stochastic settings. In our simulation, we measure both scheduling with ProaRT's tactical plan and without it over the same set of patients. This is an advantage of a simulated environment, since in reality it is not possible to schedule a patient's fractions in two ways. These sets of patients are randomly generated, and stored for applying the different scheduling methods. For a more detailed explanation on the simulation settings, we refer the reader to Appendix 8.

4.4.2 Experimental Factors

The two main factors that make the LCPP a distinct problem from most of the problems studied in the RT planning literature are the decisions for categories of patients (rather than individuals) and the use of a large set of constrained linacs. As explained in all three previous chapters, effectively managing access times becomes challenging when there is uncertainty in the arrival of patients, they have different priorities for starting treatment according to their category and not all linacs in use are able to treat them. In our formulation of the LCPP, the parameters μ_g, σ_g^2 and $f_{g,m}$ control these challenging characteristics, which we consider experimental variables for our theoretical experiments. An important remark is that we assume arrivals to be Poisson distributed (i.e. $\mu_g = \sigma_g^2 = \lambda_g$) based on the evidence of Appendix 5 and the properties of this distribution, meaning that the interest variable is λ_g. In addition to the two distinctive and patient-related factors mentioned above, we consider the third experimental variable to be the number of timeslots $\mathcal{T}$. This experimental variable is of interest from a management perspective, since it is one which can have potential costs benefits. For instance, experiments might show that reducing the nominal working time while using a tactical plan through ProaRT can achieve the same performance indicator as a nominal working time without this planning method.

Based on the experimental variables described above, we define the three experimental factors we consider most relevant for the development of a tactical plan as follows: *Factor 1: -* Linac feasibility ($f_{g,m}$'s), *Factor 2* - Capacity availability ($\mathcal{T}$) and *Factor 3* - Fraction distribution (λ_g's). For each factor, we consider three levels of the experimental variables as can be seen in Table 11. All the levels identified with an "N" correspond to the normal, current situation of the NKI-AVL. Levels identified with a "C" correspond to lower, or critical, level with respect to the current situation. Levels identified with an "R" correspond to a higher, or relaxed, level with respect to current. The values of the different levels are chosen in such a way that they represent realistic hospital characteristics. A more detailed view of the different levels, and values used for the different experimental variables can be found in Appendix 9.

Table 11 - Experimental factors for the numerical experiments of ProaRT:

Experimental Factor (EF)	ID	Levels	Description of the levels
1. Linac feasibility	L-C L-N L-R	50% 63% 75%	Percentage of the total linacs (on average) from which a category can receive fractions.
2. Capacity availability	T-C T-N T-R	28 timeslots 30 timeslots 32 timeslots	Timeslots available per day per linac.
3. Fraction distribution	F-C F-N F-R	(2x30%, 1x20%, 13x1%) (2x15%, 4x10%, 10x3%) (16x6%)	This is the distribution of patient type – fraction scheme demand among the 16 categories.

We hypothesize a tactical plan will have a higher impact on the critical levels (identified with a C) than the others levels (identified with an N and an R). By a higher impact we mean that the value of the weighted access-time function will be lower than the normal way of working of a hospital. We consider the normal way of working to be the non-tactical, open access scheduling (which is the current practice at many hospitals such as the NKI-AVL). Finally, we define three hypotheses, in order to get insights on the impact of the critical level of each individual factor. These hypotheses can be seen in Table 12.

Table 12 - Hypotheses for the theoretical experiments:

Hypotheses for the theoretical experiment:
A tactical planning and control approach (through the ProaRT method) will have the highest positive impact on the performance of a hospital that: *(H1) has highly constrained linacs,* *(H2) has lowest available capacity,* *(H3) has a not-evenly distributed demand (patient type –fraction scheme).*

4.4.3 Experimental Results

In accordance with the number of experimental factors and levels, we construct a 3^k experimental design. With this design, a total of 27 experiments are carried out. Each experiment consists of 1000 simulated years for three planning and control methods: (1) Open access scheduling, (2) Balanced workload scheduling and (3) Tactical planning through ProaRT. As explained in the simulation setup, the same set of patients (common random numbers) is used for the three methods, for the simulation of a single year. Through our simulation we are able to analyze 81000 years worth of data. Before diving into the analysis of this data, we first introduce a legend in Table 13 which applies for all figures and tables from this subsection. For readability purposes, we divide the results in three parts, each corresponding to one hypothesis. Nevertheless, all statistics from the experiments can be found in Appendix 10.

Table 13 - Legend for results' figures and tables:

Legend for all experiments figures and tables		
Color Coding:	■ Blue ■ Red ■ Yellow	'Open access scheduling' (OAS) 'Balanced workload scheduling' (BWS) 'Tactical plan with ProaRT' (ProaRT)
Naming Convention:	$\underbrace{\ }_{P1}/\underbrace{\ }_{P2}/\underbrace{\ }_{P3}$	The name of each experiment consists of 6 characters in 3 positions. "L" stands for the linac feasibility (factor 1), "T" for the capacity availability (factor 2), "F" for the fraction distribution (factor 3), "C" for the critical level of the factors, "N" for the normal level of the factors and "R" for the relaxed level of the factors.
Line type: (figures only)	———— – – – – – –	Average (point estimate) Confidence interval (bounds)
Objective Function	Z	The objective function is the expected weighted sum of all access times of all patients (i.e. average $\mathcal{O}(\mathcal{P})$ for the 1000 simulated $\mathcal{P}$s)
Relative Improvement	C.I.	C.I. stands for a 95% Confidence Interval. The relative improvement is measured as the absolute difference over the initial value of the objective function.

1. Analysis of hypothesis 1

Our first hypothesis (H1) states that, tactical (in-advance) planning through the ProaRT method has a higher positive impact in those cases where there are highly constrained linacs. In our experiments, highly constrained linacs occur when experimental factor 1 (linac feasibility) is in the critical level (L-C in our notation). To test this hypothesis, we fix the remaining two factors (capacity availability and fraction distribution) in one of their levels.

In Figure 21 we observe the analysis of hypothesis 1 for 'critical levels' of the capacity availability and fraction distribution (factors 2 and 3 respectively). From left to right, we see the linac capacity (factor 1) going from largely constrained to rarely constrained. When largely constrained linacs occur (F-C/L-C/T-C), the improvement of ProaRT with respect to OAS is in the order of 39-39% and when rarely constrained linacs occur (F-C/L-R/T-C), the improvement is in the order of 8-8% (see Table 14). Analogous improvements occur with respect to BWS. Therefore, in 'critical levels', our hypothesis 1 is supported.

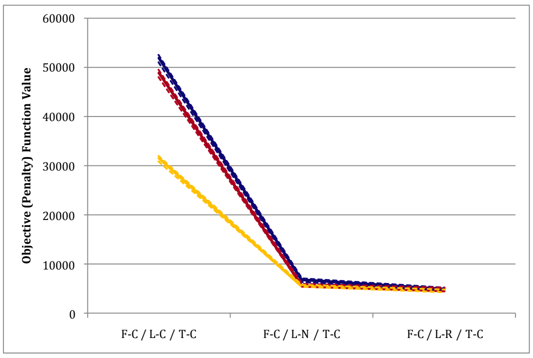


Figure 21 - Hypothesis 1 for critical levels

In Figure 22, we observe now 'normal levels' of the capacity availability and fraction distribution. Again, from left to right, we see the linac capacity going from largely constrained to rarely constrained. When largely constrained linacs occur (F-N/L-C/T-N), the improvement from OAS is in the order of 48-51% and when rarely constrained linacs occur (F-N/L-R/T-N), the improvement is in the order of 41-45%. The improvements from BWS are in lower magnitude and in the opposite direction hypothesized. Thus, in 'normal levels', hypothesis 1 is partly contradicted.

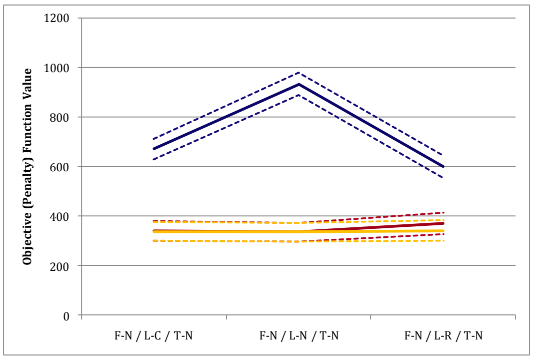


Figure 22 - Hypothesis 1 for normal levels

In Figure 23, we observe the 'relaxed levels' of the capacity availability and fraction distribution. Again, from left to right, we see the linac capacity going from largely constrained to rarely constrained. When largely constrained linacs occur (F-R/L-C/T-R), the improvement from OAS is in the order of 54-58% and when rarely constrained linacs occur (F-R/L-R/T-R), the improvement is in the order of 79-84%. The improvements from BWS are in lower magnitude in the hypothesized direction. Consequently, hypothesis 1 is partly supported in the 'relaxed levels'.

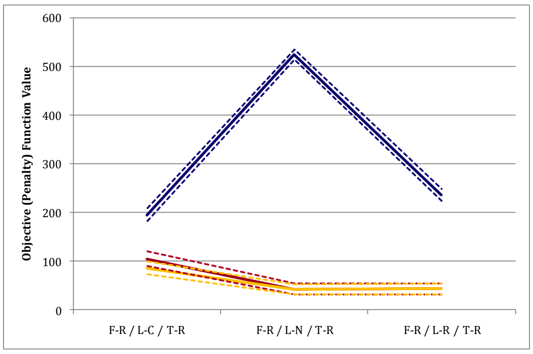


Figure 23 - Hypothesis 1 for relaxed levels

Table 14 - Results for hypothesis 1:

Experiment ID	Objective Function Z (average $\mathcal{O}(\mathcal{P})$)			C.I. Percentual Relative Improvement		
	OAS	BWS	ProaRT	OAS→ BWS	OAS→ProaRT	BWS →ProaRT
C-C/L-C/F-C	51806	48776	31450	[6% , 6%]	[39% , 39%]	[35% , 36%]
C-C/L-N/F-C	6783	5708	5596	[16% , 16%]	[16% , 19%]	[-1% , 4%]
C-C/L-R/F-C	5031	4878	4625	[3% , 3%]	[8% , 8%]	[5% , 6%]
C-N/L-C/F-N	671	341	338	[48% , 50%]	[48% , 51%]	[0% , 2%]
C-N/L-N/F-N	934	337	336	[63% , 65%]	[63% , 65%]	[0% , 0%]
C-N/L-R/F-N	599	371	342	[36% , 40%]	[41% , 45%]	[8% , 8%]
C-R/L-C/F-R	195	105	86	[46% , 47%]	[54% , 58%]	[18% , 18%]
C-R/L-N/F-R	525	43	42	[91% , 93%]	[91% , 93%]	[0% , 3%]
C-R/L-R/F-R	236	43	43	[79% , 84%]	[79% , 84%]	[0% , 0%]

2. Analysis of hypothesis 2

Our second hypothesis (H2) states that, tactical planning has a higher positive impact in those cases where there is low available capacity. By low available capacity we mean that demand is able to fill up (theoretically) 96% of the linacs. In our experiments, this situation is obtained by varying the number of timeslots (experimental factor 2). The setup for the analysis is similar as the one of hypothesis 1.

In Figure 24 we observe the analysis of hypothesis 2 for 'critical levels' of the linac feasibility and fraction distribution (factors 1 and 3 respectively). From left to right, we see the linac availability (factor 2) going from low (28 timeslots – 96%) to high (32 timeslots – 84%). When low linac availability occurs (F-C/L-C/T-C), the improvement is in the order of 39-39% and when the contrary occurs, (F-C/L-C/T-R), the improvement is in the order of 41-42% (see Table

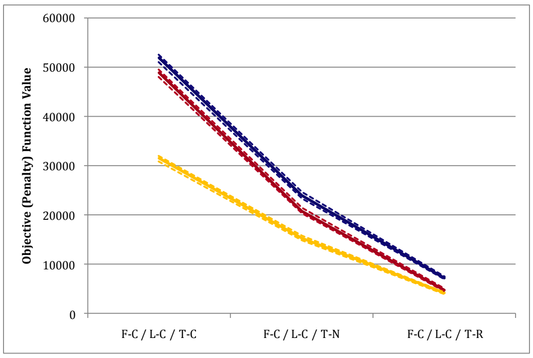


Figure 24 - Hypothesis 2 for critical levels

15). The improvements from BWS are in similar magnitude in the hypothesized direction. For this reason, in 'critical levels', hypothesis 2 is supported.

Figure 25 corresponds to 'normal levels' of the linac feasibility and fraction distribution. Again, from left to right, we see the capacity availability going from low to high. When low available capacity occurs (F-N/L-N/T-C), the improvement from OAS is in the order of 20-21% and when high available capacity occurs in (F-N/L-N/T-R), the improvement is in the order of 90-92%. When compared to BWS, an unique result happens. The impact direction is as hypothesized, but in the low level there is an unimprovement. Thus, in 'normal levels', hypothesis 2 is partly supported.

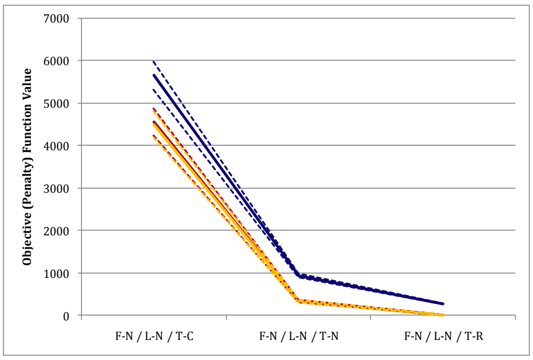


Figure 25 - Hypothesis 2 for normal levels

In Figure 26, we observe the 'relaxed levels' the linac feasibility and fraction distribution. Once more, from left to right, we see the capacity availability going from low to high. When low available capacity occurs (F-R/L-R/T-C), the improvement from OAS is non-existing and when high available capacity occurs in (F-R/L-R/T-R), the improvement is in the order of 79-84%. When compared to BWS, the improvement of ProaRT is simply non existing. For this reason, in 'relaxed levels', hypothesis 2 is completely contradicted.

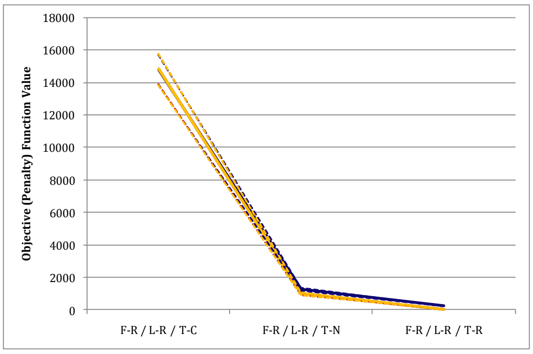


Figure 26 - Hypothesis 2 for relaxed levels

Table 15 - Results for hypothesis 2:

Experiment ID	Objective Function Z (average $\mathcal{O}(\mathcal{P})$)			C.I. Percentual Relative Improvement		
	OAS	BWS	ProaRT	OAS→BWS	OAS→ProaRT	BWS→ProaRT
F-C/L-C/T-C	51806	48776	31450	[6% , 6%]	[39% , 39%]	[35% , 36%]
F-C/L-C/T-N	23995	20861	15364	[13% , 13%]	[36% , 36%]	[26% , 27%]
F-C/L-C/T-R	7147	4775	4162	[33% , 34%]	[41% , 42%]	[12% , 13%]
F-N/L-N/T-C	5649	4552	4497	[19% , 20%]	[20% , 21%]	[1% , 1%]
F-N/L-N/T-N	934	337	336	[63% , 65%]	[63% , 65%]	[0% , 0%]
F-N/L-N/T-R	267	15	19	[94% , 95%]	[92% , 93%]	[-41% , -17%]
F-R/L-R/T-C	14783	14825	14803	[0% , 0%]	[0% , 0%]	[0% , 0%]
F-R/L-R/T-N	1287	1002	1002	[21% , 23%]	[21% , 23%]	[0% , 0%]
F-R/L-R/T-R	236	43	43	[79% , 84%]	[79% , 84%]	[0% , 0%]

3. Analysis of hypothesis 3

Our last hypothesis (H3) states that, tactical (in-advance) planning through the ProaRT method has a higher positive impact in those cases where there is a not-even distribution of demand (patient type – fraction scheme). By not-even we mean that a small number of categories account for the vast majority of the demand. In our experiments, this situation is obtained by varying the arrival of patients in experimental factor 3. The setup for the analysis is similar as the previous ones.

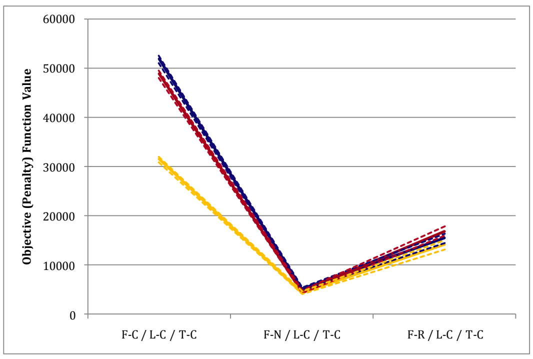


Figure 27 - Hypothesis 3 for critical levels

Figure 27 shows the analysis of hypothesis 3 for 'critical levels' of the linac feasibility and capacity availability (factors 1 and 2 respectively). From left to right, we see the fraction distribution (factor 2) going from not-even to even. When the fraction distribution is not even (F-C/L-C/T-C), the improvement is in the order of 39-39% and when fractions are evenly distributed, (F-R/L-C/T-C), the improvement is in the order of 8-9% (see Table 16). The improvements from BWS are in similar magnitude in the hypothesized direction. For this reason, in 'critical levels', hypothesis 3 is supported.

In Figure 28 we see the 'normal levels' of the linac feasibility and capacity availability. Again, from left to right, we see the fraction distribution going from not-even to even. When there is a not-even distribution of fractions (F-C/L-N/T-N), the improvement from OAS is in the order of 47-49%, as when the fraction demand is evenly distributed (F-R/L-N/T-N), the improvement is in the order of 31-33%. The improvements from BWS are very small, but in the hypothesized direction. As a result hypothesis 3 is also supported in 'normal levels'.

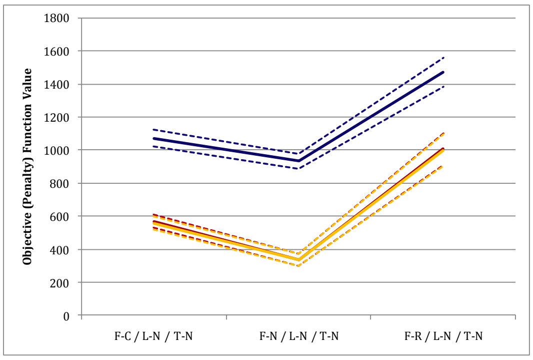


Figure 28 - Hypothesis 3 for normal levels

Figure 29 corresponds to the 'relaxed levels' the linac feasibility and capacity availability. Once more, from left to right, we order the fraction distribution going from not-even to even. When demand is not-even (F-C/L-R/T-R), the improvement from OAS is around 56-65% and when demand is even (F-R/L-R/T-R), the improvement is in the order of 79-84%. When compared to BWS, the improvement of ProaRT is simply non existing. For this reason, in 'relaxed levels', results say the opposite to hypothesis 3.

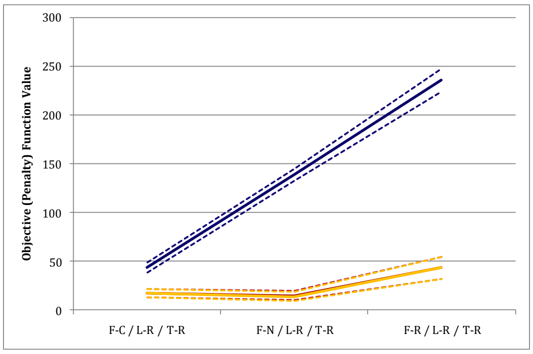


Figure 29 - Hypothesis 3 for relaxed levels

Table 16 - Results for hypothesis 3:

Experiment ID	Objective Function Z (average $\mathcal{O}(\mathcal{P})$)			C.I. Percentual Relative Improvement		
	OAS	BWS	ProaRT	■OAS→■BWS	■OAS→■ProaRT	■BWS→■ProaRT
F-C/L-C/T-C	51806	48776	31450	[6% , 6%]	[39% , 39%]	[35% , 36%]
F-N/L-C/T-C	5174	4615	4445	[11% , 11%]	[14% , 14%]	[3% , 4%]
F-R/L-C/T-C	15478	16917	14161	[-10% , -8%]	[8% , 9%]	[16% , 17%]
F-C/L-N/T-N	1071	568	557	[46% , 48%]	[47% , 49%]	[1% , 2%]
F-N/L-N/T-N	934	337	336	[63% , 65%]	[63% , 65%]	[0% , 0%]
F-R/L-N/T-N	1473	1005	999	[31% , 33%]	[31% , 33%]	[0% , 1%]
F-C/L-R/T-R	43	17	17	[56% , 65%]	[56% , 65%]	[0% , 0%]
F-N/L-R/T-R	139	15	14	[87% , 91%]	[88% , 92%]	[4% , 7%]
F-R/L-R/T-R	236	43	43	[79% , 84%]	[79% , 84%]	[0% , 0%]

4.4.4 Experiments Conclusion

The overall results of the theoretical experiments show that using ProaRT significantly improves the performance of a RT department that uses OAS as its scheduling (planning) method. In all experiments and figures (from the previous section) except one (experiment F-R/L-R/T-C in Figure 26), the yellow line (ProaRT) is lower (better) than the blue line (OAS). The relative improvement (from OAS to ProaRT) can reach up to 93% (F-N/L-N/T-R), situation in which the method can virtually reduce the access times to zero. However, this relative improvement is quite high because the demand/capacity ratio (due to factor T-R) is low (ratio of approximately 84%) and the access time function is already quite low (i.e. ProaRT improves something that is already good). From queueing theory we know that access times explode when the demand/capacity ratio gets closer to 100% (as explained in Section 1.4). In our experiments, the higher this ratio goes is 96% with experimental factors T-C. In this case (in which access times are really large) the highest improvement seen with ProaRT is 39% (F-C/L-C/T-C). In absolute (not relative) terms this is a more substantial result considering the access time function is more than 190 times larger here than the situation of the 93% improvement. To come to the point, ProaRT performs better than OAS for critical, normal and relaxed levels of the important RT factors.

In addition to OAS, we also experiment using a BWS rule. In this case, the results of the theoretical experiments show that using ProaRT improves the performance for some cases, has no significant improvement for others, and even “deteriorates” the performance for some few ones. We observe that ProaRT significantly improves the performance from BWS in those experiments that had highly constrained linacs (L-C), the highest improvement being in the critical levels F-C/L-C/T-C with 36%. In 13 out of the 27 experiments ProaRT had no significant improvements (0-4%). All of these 13 experiments had at least one factor in the normal level. At last, in 3 of the experiments there was a negative improvement (deterioration) in the objective value. These three experiments had the relaxed level of the capacity availability and at least one of the other factors in the normal level. As discussed before, the relaxed level of the capacity availability already performs well in terms of access times (since there is enough capacity). The worst deterioration in the objective value was -4, wether in the critical level the improvement is in the order of 17000. To sum up, ProaRT performs better than BWS for critical levels of linac feasibility and fraction distribution, has no significant improvement for most normal levels and deteriorates the performance for relaxed levels of capacity availability.

In our research motivation (Section 1.3) we draw the attention to the delays that can occur when there is no in-advance planning for RT treatments in *constrained linacs*. In the LCPP definition (Section 3.1) we indicate that, these constraints apply to categories of patients (rather than individual patients) whose *arrival is uncertain* (stochastic) and argue decisions should be done accordingly. We hypothesized that the greater these characteristics (constrained linacs and uncertain arrival of categorized patients) are in a hospital, the worse it is not to plan in advance. In our numerical experiments (Section 4.4), we analyze the soundness of this hypothesis. In these experiments, we label the ‘greater’ state of the characteristics as critical levels. We observe that, when all-but-one characteristics are in a critical level (first figure of each hypothesis analysis of the previous section), the higher the benefits are from in-advance planning when the remaining characteristic goes towards a critical level. For example in Figure 21, where the uncertainty in the arrivals is in its critical level (not-even fraction distribution), the improvement of having an in-advance plan (through ProaRT) increases from 8% to 16% to 39% as the *linac constraints* (linac feasibility) increases from a relaxed to a critical level. Similar results occur in Figure 27, which shows how the *arrival uncertainty* increases its complexity. Therefore, we conclude that there is a larger need for a tactical plan when these aforementioned characteristics increase under a critical level of the other ones. Thus, our hypothesis is sustained by the theoretical results.

4.5 Discussion

The theoretical experiments are by no means exhaustive to all LCPP characteristics. The experiments are meant to give indications on the relation between the problem and the solutions when certain circumstances, or combination of characteristics, occur. In this section, we briefly discuss the different characteristics considered, and not considered, in our theoretical experiments. These characteristics influence the results, and hence the analysis that is done from the experiments. We start by examining the input used for the experiments in Section 4.5.1. We discuss about the level of detail of the chosen input and the limitation of the insights. In Section 4.5.2 we talk about the output from the experiments. We discuss about further analyses that can be done, and considerations that need to be taken into account when formulating conclusions. Finally, in Section 4.5.3 we discuss how the medical preferences (i.e. weights) have an influence on the performance of ProaRT when solving the LCPP.

4.5.1 Factors and Levels

The conclusions that can be obtained from the theoretical experiments are limited by their configuration. The chosen configuration resembles the NKI-AVL's current situation in terms of demand (16 categories) and supply (8 linacs) for RT treatments. A more detailed categorization of the demand is useful for medical purposes due to more individualized treatments for patients. However, from an industrial perspective, when categories are identical in logistical aspects, a more detailed categorization is just making the problem unnecessary complex. A small categorization is also not desirable since then the problem just becomes inexistent. In our experiments, the number of categories remains constant. The factor that varies in our experiments, with respect to the demand, is the 'fraction distribution' of the categories. Fraction distribution is the factor that measures the number of patients of a category times the number of fractions each patient receives. For instance, a category with 5 patients that receive 20 fractions each is 'equally distributed' to a category with 100 patients that receive 1 fraction. This is a logistical characteristic that is important for the amount of capacity (linac time) that a category requires (and hence must be allocated). We consider the number of fractions (e.g. 20, 1) to be constant medical aspects, and therefore vary the number of patients (e.g. 5,100). In the 'normal level' of this factor, 6 out of 16 categories require more than 60% of the capacity. In the 'critical level', 3 out of 16 categories require around 80% of the capacity. In the 'relaxed level', all categories require the same percentage of capacity. The categories that require more capacity are chosen based in the group of 'large 5 cancers' (see Section 2.3). A characteristic we do not consider in our experiments is whether the categories that require more capacity are those that need to wait less (higher importance factor). This can also be a characteristic of interest if, for example, one wants to get insights on the benefits of having a tactical plan for categories with high importance factors and low required capacity.

The other point of discussion with respect to the input factors is from the supply side. Just as we consider the 16 categories to be fixed, we consider 8 linacs to be constant throughout the experiments. One of the main reasons for the proposed solution to the LCPP is the constraints the linacs have. When there are a few linacs, it is not possible to experiment how much of an effect the constraints have (e.g. in 2 linacs there is only two options, to use both or just one). Considering that the factor that varies in our experiments with respect to the supply is the 'linac feasibility' (linac constraints), it is desirable to have a relatively large number of linacs. More into detail, the factor shows how many linacs a category can use (i.e. receive fractions from). In the 'normal level', categories can use 63% (5 out of 8) of the linacs, on average. In the 'critical' and 'relaxed' levels, categories can use on average 50% (4) and 75% (6) respectively. In the normal level, the linacs a category can use correspond to the NKI-AVL linac constraints. For the critical and relaxed levels of this factor, the linacs which a category can use are randomly chosen. A characteristic we do not consider in our experiments is the number of categories a linac can treat. This characteristic can be interesting if, for example, one wants to get insights on which linacs the tactical planning reserves timeslots. Furthermore, this characteristic can control the linacs that are 'all-capable' (can treat all categories) and the 'very constrained' (can treat only a few categories). As in the current situation of the NKI-AVL, it might happen that if a linac can only treat a few categories, most of the fractions of one of those categories are planned at that linac (see Section 2.4). These are some examples of what further insights, and different conclusions, can be obtained with other experimental configurations. We believe that, some of these experimental configurations, which are out of the scope of this thesis, are still interesting to research upon and present them in Section 6.3.

4.5.2 Interaction Effects

The results and conclusions from the analysis of the previous section aim to confirm the experimental hypotheses and answer research question 3 (see Section 1.5). However, in all analyses done, we varied one factor at a time. For example, in the analysis of H1, we observe F and T to have the same value in each graph (only L varies). One can also vary two factors at a time, and get insights on the so-called interaction effect. For example, in Figure 30 we observe a constant L, and the factors F and T varying from a normal to a relaxed level. We observe that BWS (red) performs as good as ProaRT (yellow) and better than OAS (blue) in F-N/L-C/T-R. When F relaxes (from F-N to F-R) and T goes in the opposite direction (from T-R to T-N), not only BWS performs worse than ProaRT, but it also performs worse than OAS. In all analysis done before, BWS always performed better than OAS, except in this one. All results can be found in Appendix 10, from which the interested reader can analyze the interaction effects. We do not include an analysis of these effects in the previous section because (1) they answer different questions than the ones we consider and (2) they are considered higher order interactions (more than 2 levels and 2 factors) and hence are rarely meaningful. Nevertheless, it is important to keep in mind their existence and that they might limit the generalizability of the main conclusions from the previous section.

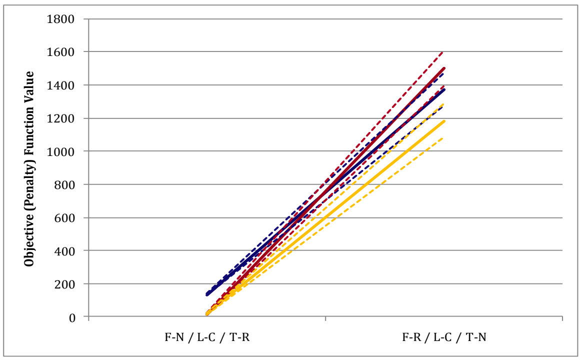


Figure 30 - Interaction effects on the experiments

4.5.3 Weight (penalty) dependence

A more subjective, but very important, point of discussion is the dependence of the approach (and consequently the theoretical results) on the 'importance factors' for the different categories. The proposed method, ProaRT, optimizes the tactical plan according to these 'importance factors'. We believe that the more different the weights are (relative to each other) the higher the impact of ProaRT is on the overall performance. To get an idea on how much the impact of the weights is, we repeat all experiments under a set of 'un-weighted' categories, where all categories' weights are the same, i.e. $\alpha_g = 1 \forall g \in \mathcal{G}$. The results of these experiments can be found in Appendix 11.

In Figure 31 we observe the graph of hypothesis 1 for critical levels looks under un-weighted categories. We see exactly the same pattern in the lines, but a much lower difference from the yellow one to the other ones, meaning a lower impact of planning in-advance through ProaRT. Nevertheless, in Table 17 we see that the results for the critical levels (same analyses done for all hypotheses in the previous section) present a similar tendency, but in much more lower scale. In other words, the hypotheses still hold, but the impact is now smaller. The main conclusion we can get out of these results is that, independent of the weights, the other LCPP characteristics make planning in-advance (through ProaRT) *always a better option* than not doing it. The impact, and therefore the *need to plan in advance,* is much higher as the difference in weights (or medical preferences) increases.

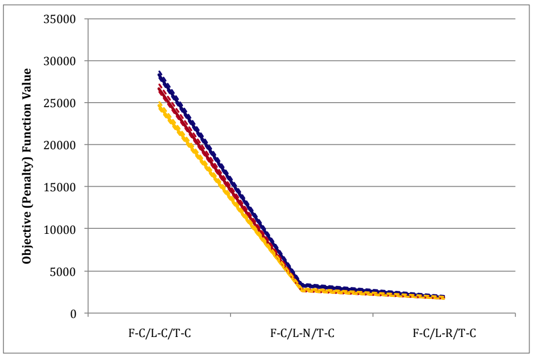


Figure 31 - Hypothesis 1 for critical levels under un-weighted categories

Table 17 - Results of theoretical experiments for 'un-weighted' categories:

Experiment ID	Objective Function Z (average $\mathcal{O}(\mathcal{P})$)			C.I. Percentual Relative Improvement		
	OAS	BWS	ProaRT	■ OAS → ■ BWS	■ OAS → ■ ProaRT	■ BWS → ■ ProaRT
C-C/L-C/F-C	28304	26689	24656	[6% , 6%]	[13% , 13%]	[7% , 8%]
C-C/L-N/F-C	3286	2710	2726	[17% , 18%]	[17% , 17%]	[-1% , 0%]
C-C/L-R/F-C	1861	1791	1791	[4% , 4%]	[4% , 4%]	[0% , 0%]
C-N/L-C/F-N	28304	26689	24656	[6% , 6%]	[13% , 13%]	[7% , 8%]
C-N/L-N/F-N	13021	11323	10533	[13% , 13%]	[19% , 19%]	[7% , 7%]
C-N/L-R/F-N	3821	2538	2681	[33% , 34%]	[30% , 30%]	[-8% , -4%]
C-R/L-C/F-R	28304	26689	24656	[6% , 6%]	[13% , 13%]	[7% , 8%]
C-R/L-N/F-R	1787	1406	1407	[21% , 22%]	[21% , 22%]	[0% , 0%]
C-R/L-R/F-R	3561	3686	3230	[-4% , -3%]	[9% , 10%]	[12% , 13%]

4.6 Summary

In this chapter we mathematically modeled the LCPP and proposed a solution method (ProaRT) based on its characteristics and the guidelines from the previous chapter. Furthermore, we tested the effectiveness of the method with some theoretical experiments and a simulation. More specifically we tested how well ProaRT attains the objective of the LCPP in comparison to other methods under a series of circumstances. The three key points of this chapter are:

- The LCPP is the problem of allocating linac capacity in advance, and to categories of patients, such that the expected access times are minimized for a mid-term horizon while considering all relevant process characteristics.
- ProaRT is a mathematical method that determines, in advance, the maximum linac capacity that can be used by a category of patients per day. In terms of the LCPP description in this chapter, ProaRT outputs a table that gives a threshold on the number of patients from every category that can be treated on every linac, any given day. This table is constructed via a simulation and heuristic algorithm. First, a number of 'samples' of arriving patients are built. Then, a local search heuristic determines a table that achieves the LCPP goals for every specific sample of patients. At last, statistics are applied to all sampled tables and a formula used to merge them into a single, final one.
- The theoretical experiments show that ProaRT significantly achieves lower weighted access times compared to OAS, a typical way of working of hospitals (including the NKI-AVL). Depending on the circumstances, ProaRT can achieve weighted access times that are up to 90% lower than the ones from OAS. When compared to a second way of working, namely BWS, ProaRT achieves, for some circumstances, higher (i.e. worse) weighted access times. This shows that under some circumstances, ProaRT (i.e. planning in advance) might not be relevant. In addition, with our theoretical experiments we tested the hypothesis that motivated this research: the more *constrained* the linacs are and the more *uncertain* the arrival of patients is, the worse it is not to plan in advance. Our numerical results show that as these factors become 'critical' (e.g. patients can be treated in only 50% of the linacs the arrival of 20% of the patients account for 80% of the fractions), the weighted access times are between 8% and 39% lower when having a tactical plan (via ProaRT) than when not having it (using OAS only).

"There is no use talking about the problem unless you talk about the solution."
Betty Williams (1943)

Chapter 5
Case Study at the NKI-AVL

In the previous chapter we consider a number of theoretical situations and show how the ProaRT method *can prevent* delays in the start of radiotherapy (RT). In this chapter, we study the impact this method can have on practical (real-life based) situations from the NKI-AVL. We first review the main characteristics of the demand for radiotherapy treatment and the supply of linacs at the NKI-AVL in Section 5.1. Then, in Section 5.2 we introduce the different cases (questions) we examine, and the methods we use to analyze them. In Section 5.3 we present the results of the access times for each case (answers). More important, we assess the benefits and drawbacks that ProaRT can have when compared to the current way of planning. In Section 5.4 we discuss some important observations about this case study. In Section 5.5 we describe what the conditions for implementing ProaRT are, and what future use can be given to the method. Finally, in Section 5.6 we close with the key points of this chapter.

5.1 Input Data

The NKI-AVL is a large and growing oncology center that diagnoses and treats cancer patients from all over the Netherlands. During the last three years, approximately 13500 new patients arrived to receive radiotherapy. From 4340 patients in 2009 up to 4690 in 2011, the demand for radiotherapy is steadily increasing. In 2012, around 95 new patients arrive for treatment each week, a 5.6% increase on the average of 90 new patients per week from last year. Each patient that arrives is categorized into one out of 60 different care plans by a radiation oncologist. These care plans (CPs) are patient-categories specific to the NKI-AVL's RT department as mentioned in Chapter 2. We reduce the complexity of this case study by considering only 16 CPs, in concordance with Section 2.3.1. Nevertheless, these 16 CPs are representative of the 'demand' at the organization since they account, on a yearly basis, for 80% of the new patients and 90% of the total fractions delivered. Since we consider part of the total demand, we also consider part of the supply (as explained later on). We assume part of the linac capacity not considered to be used to for the remaining care plans (i.e. 20% patients and 10% fractions). For the purpose of this study we consider that all patients from a same CP receive the same number of fractions. The number of fractions for each CP comes from the fractions that the majority of patients (categorized with it) received during 2011 and the first quarter of 2012. We also consider that each CP has a known 'importance factor', which defines how urgent it is to start the treatment of a patient categorized with it. The larger the importance factor of a CP, the shorter a patient categorized with it should wait to start treatment. In other words, low importance factors (e.g. 1) can wait longer than high importance factors (e.g. 3). The importance factors are implicit in the NKI-AVL, e.g. planners know that 'Botmetastasen' should start treatment immediately while 'Prostaat' can wait longer. We quantify this implicit knowledge with experts from the department. All the information about the CPs is shown in Table 18.

Table 18 - Input data for case study at the NKI-AVL:

Care Plan (in Dutch)	Arrival rate (new patients per week)	Fractions per patient	Importance factors	Linac Feasibility							
				A1	A2	A5	B1	B2	B3	B4	B5
Prostaat	4,86	39	1	X	X	X	X		X		X
Mamma Breath Hold	8,48	21	2	X		X	X		X		X
Mamma e- (Okselregio/Parasternaal)	5,03	21	2	X				X		X	
Long > 44 Gy	4,29	24	3	X	X	X	X		X		X
KNO	4,40	23	3	X		X	X		X		X
Mamma	5,86	16	2	X		X	X		X		X
Rectum / sigmoid	2,05	25	2	X		X	X	X	X	X	X
Prostaatloge	1,52	33	1	X	X	X	X	X	X	X	X
Hersenen	1,02	30	3						X		X
Oesophagus	1,15	23	3	X		X			X		
Botmetastasen	25,48	1	6	X		X	X	X	X	X	X
Long AP/PA	2,48	10	3	X		X	X	X	X	X	X
Cervix/Endometrium/Uterus/Ovarium	1,06	23	2	X		X			X		
Hersenen 2vs	4,74	5	3	X		X	X	X	X	X	X
Anus +/- liezen	0,63	33	2	X		X			X		
Blaas	0,80	25	2		X			X	X		

In order to fulfill the growing 'demand' for radiotherapy, the NKI-AVL has a considerable 'supply' of linear accelerators (linacs). In total there are nine different linacs from which eight work continuously (nominal linacs) and one works when the other eight cannot (backup linac). In this case study we consider as the base situation, the situation in which the backup linac only treats patients while one of the nominal linacs is under the weekly maintenance inspection. Unless otherwise stated, this distribution of nominal and backup linacs is considered for each case. Furthermore, technical specifications and other medical considerations forbid some CPs from being treated in some linacs. Some linacs can treat only a few CPs while others can treat almost all of them, as seen in Table 18 where an 'X' denotes that a linac is able to treat a given CP. Demand for radiotherapy is in the form of patient-type and fraction-scheme. In the NKI-AVL, for most patients a fraction lasts one timeslot of 15 minutes. For this reason, we consider the fractions of all CPs to last one timeslot. We measure the supply of linac-time (or linac capacity) in this kind of timeslots. For the purpose of this study, we consider nominal working time to be 30 timeslots per day, instead of 35 that are currently available. We decrease the nominal working time in order to keep the 'demand/capacity' ratio of the NKI-AVL given the reduction to 16 CPs, which is currently around 90%. The 5 timeslots not considered are assumed to be used for the fractions of the excluded CPs, meaning that working time remains unchanged.

Finally, the last characteristic from the NKI-AVL's RT department we introduce is the 'open access scheduling' (OAS). This is the current way of planning and controlling the balance between the demand and supply for RT treatments. In the OAS approach, there is no in-advance assignation of linac capacity to CPs. Instead, linac capacity is assigned individually to every patient, as soon as they arrive. More in detail, all fractions of a new patient are scheduled in the first feasible linac available. This approach seeks to minimize the access time (i.e. time that a patient has to wait before starting treatment) of each individual new patient. However, different types of patients (according to their care plan) have different 'urgencies' for starting treatment (e.g. bone metastases patients require immediate treatment). For this reason, we define *performance* as the weighted sum of access times of all patients, over a period of time, rather than an individual one. The weight of the access time of a patient corresponds to the importance factor of his or her care plan.

5.2 Cases and Methods

The objective of this case study is to look at a small number of practical situations, which we define as cases, and examine what benefits planning the linac capacity in-advance can have. In contrast to the theoretical experiments from Chapter 4, the case study in this chapter does *not* aim to test hypothesis or look for general cause-effect relationships. Instead, our goal is to draw specific-context conclusions which can support management decisions in the NKI-AVL RT department. For this reason, in each case we focus only on one practical factor of interest (e.g. growth in number of patients, increase in the number of timeslots, etc.), and analyze if, for that factor, in-advance planning can improve the access time performance. This performance is scrutinized from all stakeholders' perspectives (i.e. patients, oncologists, management) such that balanced decisions, and thus valid-for-all benefits obtained from planning in-advance for the different cases. Table 19 shows a brief description of each case we study.

Table 19 - Cases analyzed:

Case ID	Situation	Description
1	*Current situation*	In this case we analyze the existing demand-supply presented in Table 18.
2	*Growth in number of patients*	In this case we analyze an increase in the *arrival rate* of patients of 5% and 10%.
3	*Working time*	In this case analyze decreasing and increasing the *nominal working time* 5%.
4	*Old linac replacement*	In this case we analyze replacing one of the existing linacs, thus changing the *linac feasibility*.
5	*New linac acquisition*	In this case we analyze the purchase of a new linac, thus increasing the *linac capacity*.

In order to plan in-advance, we use the ProaRT method. ProaRT is a mathematical method that allocates linac capacity for the medium term, taking into account the characteristics of the supply (i.e. which linacs can treat which CPs) and the characteristics of the demand (i.e. random arrival of patients from a CP, number of fractions, etc.). ProaRT's output is a table that gives the maximum number of patients categorized with a CP that can be planned on a linac, any given day (e.g. no more than 5 'Prostaat' patients in linac 'B1'). The way that day-to-day planning is done is the similar as in the OAS (i.e. a patient's fractions are planned in the earliest available linac) with two main differences being that a patient is planned on the earliest available linac that (1) has less than the number of maximum patients planned given by the ProaRT table and that (2) has the least number of total planned patients for that day. These two differences are two new constraints (with respect to OAS) that ProaRT uses to ensure that the planning that is done will benefit *both* the patient that just arrived *and* the patient that will arrive later in time.

The method we use to investigate the benefits of ProaRT for the different cases is a computer simulation. A computer simulation allows a direct comparison between OAS (the current way of planning) and ProaRT (the proposed way of planning) since the exact same group of simulated patients that was planned (and treated) one way can be 're-planned' (and 're-treated') in the other one. More into detail about the simulation used, we consider the test time (simulation run length) to be of a single year. After one year, treatments (i.e. linac constraints) and demand (i.e. arrival of patients) might change, and thus a new table from ProaRT should be constructed. To obtain a 95% confidence on the performance indicators, we simulate a total of 1000 years (replications) per case. A more detailed explanation about the settings of the simulation (e.g. warm-up, arrival distributions, etc.) and their validity is shown in Appendix 8.

5.3 Results and Analyses

In this section we present, for each case, the results of the simulation and their analyses. We first introduce some general terminology for all cases. The objective value is the main performance indicator we try to minimize. We define the *weighted objective value "Wov"* to be the sum of access times X_i, over all patients i from the n patients during a year, multiplied by their correspondent importance factors w_i. We calculate it by $Wov = \sum_{i=1}^{n} w_i \cdot X_i$. Hence the performance is characterized by a penalty (cost) function of the access time, in which the goal is to lower (minimize) its value. Furthermore, we define the *un-weighted objective value "Uov"* to be the circumstance where all CPs have an importance factor equal to one. We compute it by $Uov = \sum_{i=1}^{n} 1 \cdot X_i$. This un-weighted circumstance is included in the results of each case to analyze the benefits of using ProaRT for a 'strictly equitable' handle of patients (i.e. other stakeholder's perspective). All access times are measured in days. For this reason, the un-weighted objective value shows the exact sum of the access days for all patients in a year. The *expected* objective values (i.e. $\mathbb{E}[Wov]$ and $\mathbb{E}[Uov]$) and *expected* access time statistics (e.g. mean, median) are calculated as the average of the 1000 simulated years for each case. The 95% confidence intervals are built upon the variation observed in this sample of simulated years (frequentist statistics). At last we consider that the user-configuration of the ProaRT method is done according to the suggested settings from Chapter 4.

For readability purposes we use the standards in Table 20 for all figures and tables. Furthermore, when we talk about improvement we refer to the difference between a performance indicator of ProaRT and OAS, i.e. how much lower is the value of the indicator of ProaRT than the one from OAS. We define the relative improvement as the ratio between the improvement and the indicator for the OAS. Finally, the part of a figure indexed with (i) corresponds to the weighted CPs and the one indexed with (ii) corresponds to the un-weighted ones.

Table 20 - Legend for the case study:

Legend for figures and tables of each case's results		
Color Coding:	■ Blue	Current (OAS)
	■ Yellow	Proposed (ProaRT)
Box-Plot Shading:	Striped	1st Quartile to Median
	Solid	Median to 3rd Quartile
Line type in figures:	———	Expected OV
	– – – – – –	Confidence interval OV

5.3.1 Case 1: Current settings

The first case resembles the present-day situation of the NKI-AVL in terms of demand for radiotherapy treatment and supply of linac-time. In this case we estimate how much access time is currently caused due to the linac constraints, the uncertainty of the arrivals and the current way of planning the appointments for fractions. This estimated access time establishes the starting point of comparison to all other cases (e.g. how much will the access time increase in a 10% growth on the number of patients). Furthermore, the comparison is for both the OAS (current) and the ProaRT (proposed) way of planning. We now present the simulation's result for the current situation and the impact ProaRT would have if implemented *immediately*.

Table 21 - Case 1, Numerical results for the current situation:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[889 , 978]	0.24	[378 , 412]	0.24
ProaRT	[299 , 374]	0.05	[103 , 128]	0.05
Improvement	[581 , 613]	0.20	[273 , 287]	0.20
% Improvement	[63% , 65%]	81%	[70% , 72%]	81%

**Expected access time measured as average of all patients and all CPs.*

Currently, the simulation shows there are on average 395 access days per year (un-weighted), which when multiplied by the importance factors of the different patients (weighted), results in a value of 934. If ProaRT would be implemented immediately, we see in Figure 32 (i) that the weighted access days can be reduced to 337 and the un-weighted access days to 115 in Figure 32 (ii). ProaRT is able to reduce the weighted OV from 63% up to 65%, from the one from OAS. Similar relative improvements are obtained in the un-weighted situation, as seen in Table 21. Moreover, we can see that in both situations ProaRT is able to shift the 3rd Quartile below the line of the 1st Quartile of the OAS, meaning that the entire distribution of access times is lowered, not only the expected value. The ProaRT table for this case (i.e. maximum number of patients from a CP that can be planned on a linac) can be seen in Appendix 12.

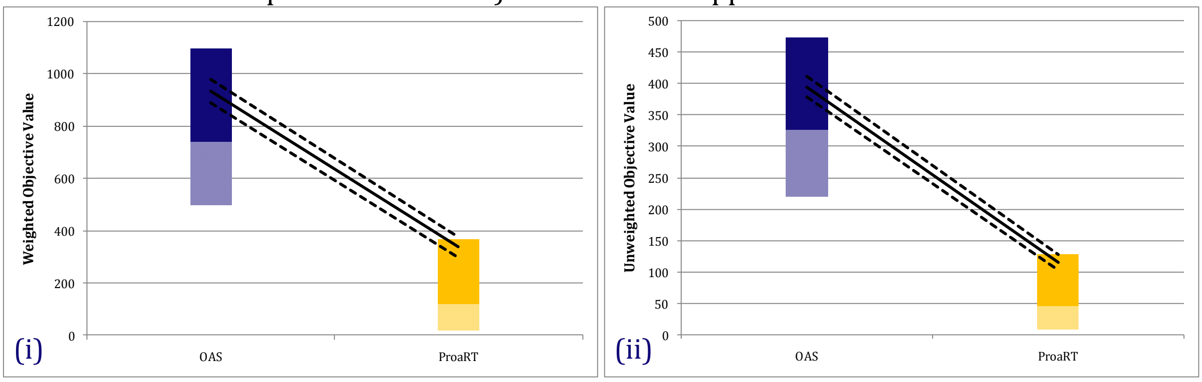


Figure 32 - Case 1, Objective values for the current situation

When taking a closer look at the average access days for all care plans we observe that some of them do not have any access time at all while a few have more than half a day per patient, as seen in Figure 33 (i) and (ii). It is on these latter care plans where ProaRT achieves the largest benefits in access time (e.g. 'Anus+/-liezen'). In Figure 33 (i) and (ii), the three CPs that wait the longest in OAS (blue line) are also the ones that wait the longest in ProaRT (yellow line). Furthermore, the pattern is the same for both weighted and un-weighted graphs, meaning that for the current situation, ProaRT is not dependent on the weights. A deeper discussion about the pattern of the access times per care plan is presented in Section 5.4. For this first case, the main conclusion is that ProaRT can have a positive, significant and large impact for the weighted and un-weighted OVs (relative improvement of 63% and 70% as seen in Table 21) and care plans' access time (0.24 days down to 0.05 days).

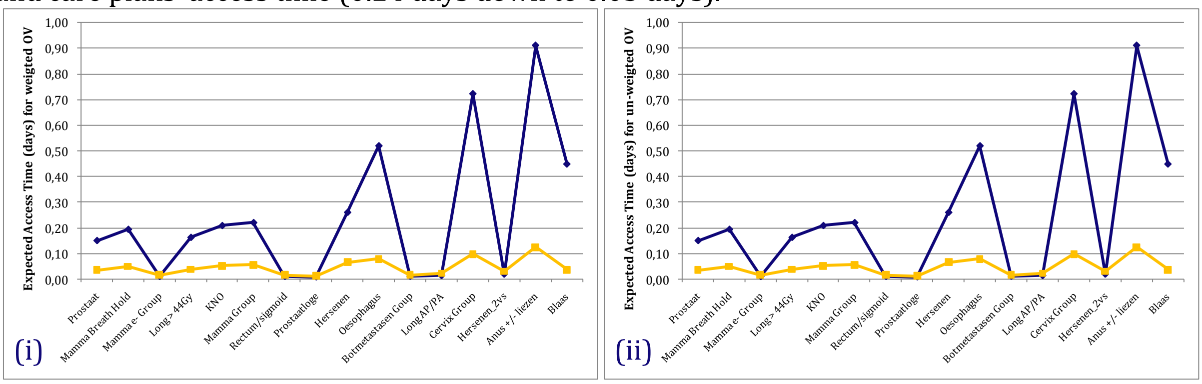


Figure 33 - Case 1, Access times for the current situation

5.3.2 Case 2: Growth in number of patients

The second case we analyze deals with the situation of the growing 'demand'. We analyze the situation when the arrival of patients per week increases 5% (2a) and 10% (2b). These growth bounds are representative to the growth that the NKI-AVL's RT department has experienced over the last years. For this case, the same linacs, number of timeslots and fractionation scheme of the current situation are used. We now present the simulation's result for the aforementioned future situation, which if the trend continues will occur *in one or two years,* and the impact ProaRT would have on it.

Table 22 - Case 2a, Numerical results for a 5% growth in patients' arrivals:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[2854 , 3167]	0.49	[1087 , 1188]	0.49
ProaRT	[1854 , 2149]	0.23	[604 , 696]	0.23
Improvement	[979 , 1038]	0.27	[476 , 498]	0.27
% Improvement	[33% , 34%]	54%	[42% , 44%]	54%

**Expected access time measured as average of all patients and all CPs.*

If there is a 5% growth in the number of patients that arrive for RT and OAS is kept as the chosen way of working, there are on average 1138 access days per year (un-weighted) which account for a weighted objective value of 3011. This is an increment of 743 access days and 2077 weighted-days from the current situation. If ProaRT would be implemented then, the increments would be lower: 255 access days rather than 743 and 1069 weighted-days rather than 2077. However, in this future situation where there is a higher demand, ProaRT is only 33% up to 34% better than OAS in the weighted objective value, as seen in the '% Improvement' row of Table 22. Slightly higher improvements are obtained for the un-weighted OV. In contrast to the current situation, in this growth situation, ProaRT has a lower impact on both OVs (i.e. black lines have a moderate slope in Figure 34 (i) and (ii) rather than the steep one from Figure 32). Furthermore, ProaRT does not shift the entire distribution of access times (i.e. yellow bar is not lower than blue bar in Figure 34 (i) and (ii) as it is in Figure 32). With respect to the objective value, ProaRT would have less relative impact if 'demand grows', but will still achieve significant benefits.

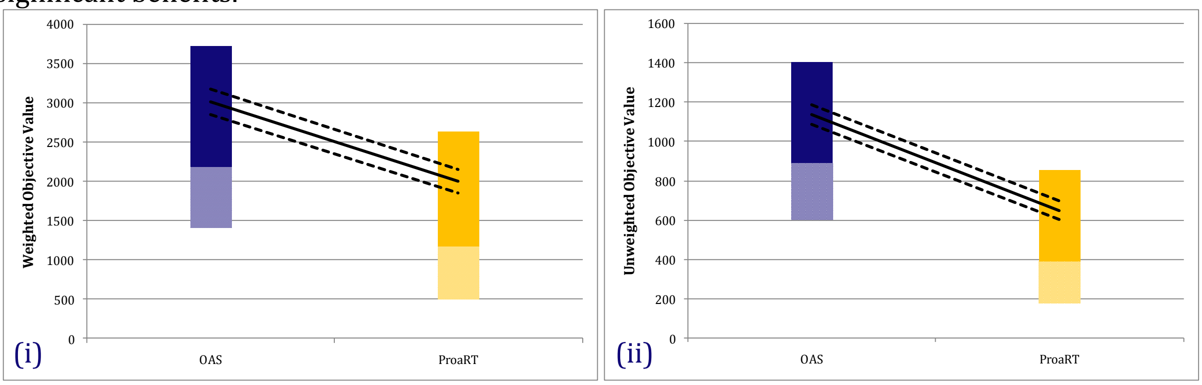


Figure 34 - Case 2a, Objective values for a 5% growth in patients' arrival

The 1138 access days in this growth situation (where there are on average 4032 patients per year) are more substantial than the ones from the non-critical current situation. More into detail about the access time for patients, Figure 35 (i) and (ii) shows that with a 5% growth in the arrival of patients, there are no CPs with zero access time. Furthermore, on the contrary to the current situation (Figure 33), when the demand grows there are more than a few care plans have at least half a day per patient of access time (Figure 35). Just as in the current situation, ProaRT (yellow) has the same line pattern as OAS (blue). An interesting observation in Figure 35 (i) and (ii) is that for the same six CPs as in the current situation (e.g. 'Mamma e- Group', 'Long AP/PA') ProaRT is not able to decrease the expected access time per patient.

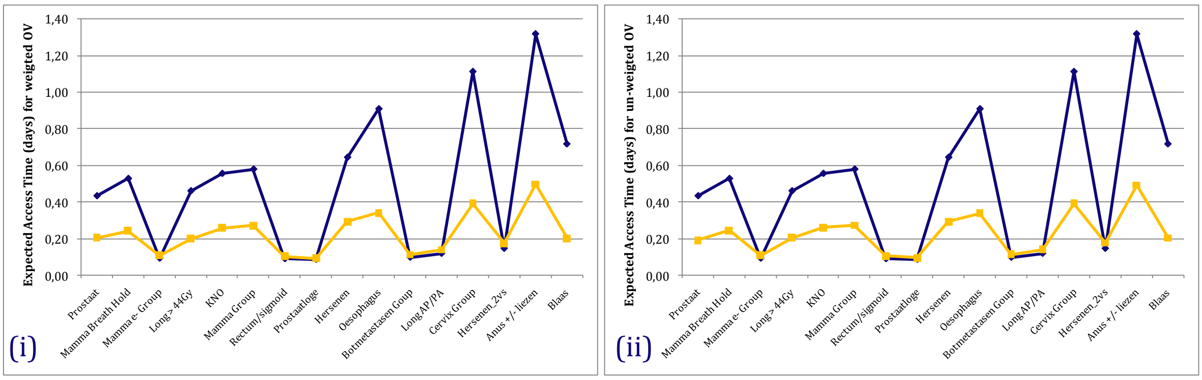


Figure 35 - Case 2a, Access times for a 5% growth in patients' arrivals

For a 10% increment in the arrival rate of patients, the relative improvement of using ProaRT rather than OAS is only 11%, as seen in the lowest row of Table 23. This improvement is lower than the 33% for the '5% growth' and much lower than the 63% for the current situation. Figure 36 shows the same tendency: the ProaRT (yellow bar) is almost the same height as the OAS (blue bar) and the black line is slightly tilted. Furthermore, Figure 37 (i) and (ii) shows that patients from all CPs wait longer than in the previous case, and that ProaRT's improvements are smaller (yellow and blue line are closer). The main conclusion for the second case is that as 'demand' grows, ProaRT is beneficial, but has a smaller impact on the current way of working (11% compared to 33% of the current demand as seen in Table 23 and Table 22 respectively) due to the tight use of capacity (demand/supply ratio of 94% and 98%).

Table 23 - Case 2b, Numerical results for a 10% growth in patients' arrivals:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[13420 , 14989]	1.46	[4358 , 4823]	1.46
ProaRT	[11861 , 13399]	1.14	[3634 , 4089]	1.14
Improvement	[1504 , 1646]	0.32	[708 , 751]	0.32
% Improvement	[11% , 11%]	22%	[16% , 16%]	22%

**Expected access time measured as average of all patients and all CPs.*

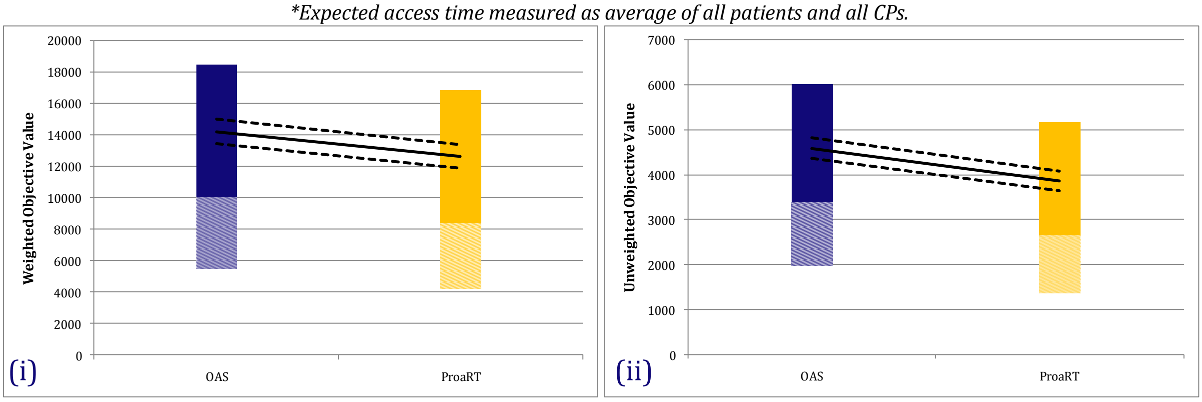


Figure 36 - Case 2b, Objective values for a 10% growth in patients' arrivals

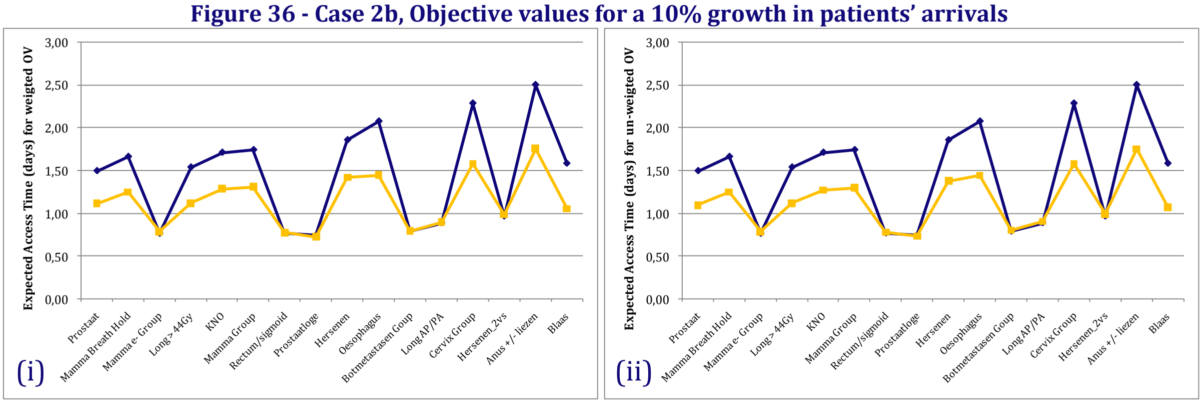


Figure 37 - Case 2b, Access times for a 10% growth in patients' arrivals

5.3.3 Case 3: Working time

The third case we study deals with an important factor from the employees perspective: the working time. We analyze the situation when the nominal working time is reduced (3a) and increased (3b) by 2 timeslots. With respect to the number of timeslots considered representative for the current situation, this represents a 5% change. For this case, the same linacs, weekly arrival rates, and fractionation scheme from the current situation are used. We now present the results for the situation where linac capacity is *tighten* or *eased* by reducing or increasing the working time, respectively.

Table 24 - Case 3a, Numerical results for a 5% reduction in nominal working time:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[5323 , 5974]	0.78	[1874 , 2075]	0.78
ProaRT	[4184 , 4811]	0.50	[1336 , 1527]	0.50
Improvement	[1109 , 1194]	0.29	[529 , 557]	0.29
% Improvement	[20% , 21%]	37%	[27% , 28%]	37%

**Expected access time measured as average of all patients and all CPs.*

If there is a 5% reduction in nominal working time and OAS is kept as the chosen way of working, there is an increment of 1580 access days and 4716 weighted-days from the current situation. An interesting remark is that with this 5% reduction in timeslots, access times are approximately *twice* as much as the ones from 5% increment in patients (see Table 24 and Table 22 respectively). If ProaRT would be implemented in this situation, the increment would be about 20% lower than the one from OAS for the weighted OV. Similar improvements are obtained for the un-weighted OV, as seen in Table 24. Just as when the 'demand' grows (case 2), we observe that when capacity decreases ProaRT's relative improvements are lower than the ones from the current situation. Figure 38 shows this by the yellow bar not being much lower than the blue one, and the black line not very steep. Moreover, Figure 39 shows the same pattern observed in the previous case: ProaRT (yellow) line is able to significantly reduce the access time of those CPs that have the largest average access time per patient in OAS (blue line).

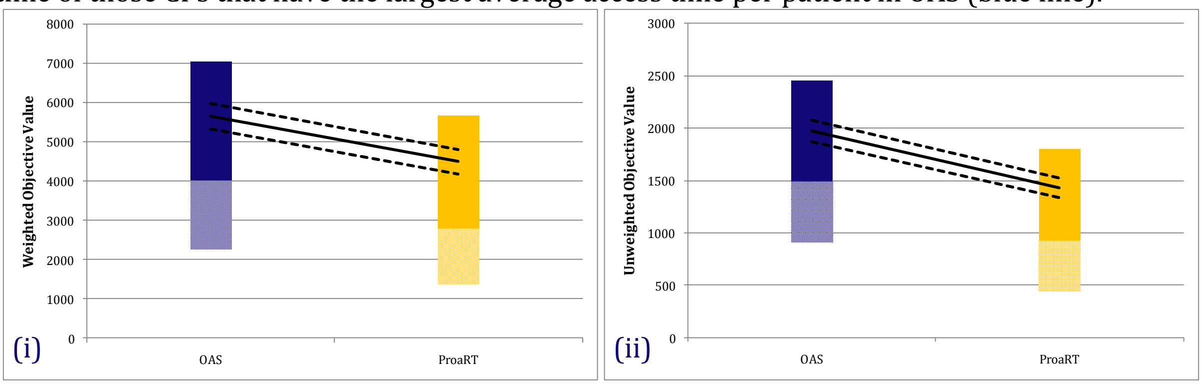


Figure 38 - Case 3a, Objective values for a 5% reduction in nominal working time

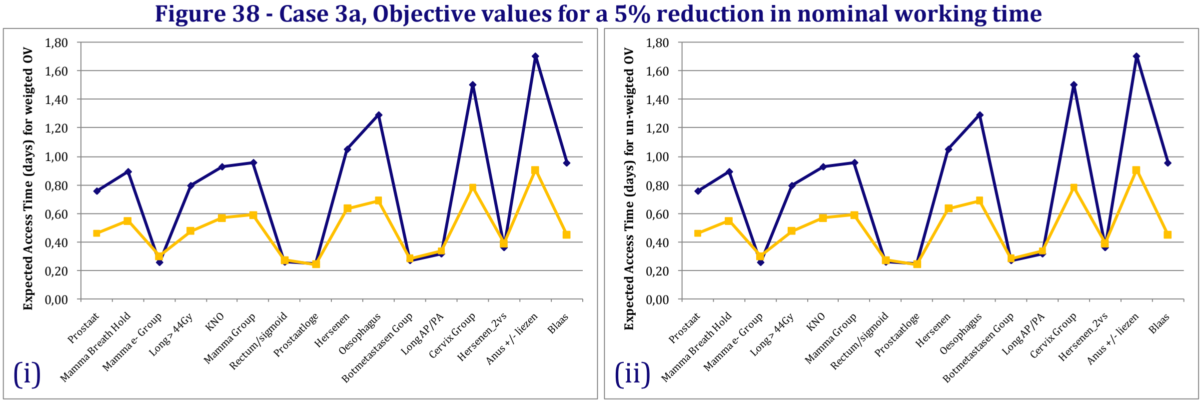


Figure 39 - Case 3a, Access times for a 5% reduction in nominal working time

As expected, if there is a 5% increment in nominal working time (i.e. more capacity) there is a *reduction* of 276 access days and 667 weighted-days from the current situation, when using OAS as the way of planning. On the other hand, the expected OVs from Table 25 show that if ProaRT is implemented in this situation, the access time is almost eliminated (i.e. reduction of more than 90%). Furthermore, Figure 40 shows that not only the expected OV (black line) is decreased, but also the entire distribution (yellow bar) is shrunk to almost zero. Figure 41(i) and (ii) show that, even though the majority of CPs have very low access times per patient in OAS (blue line), ProaRT is able to decrease all of them to an average of zero days (yellow line).

Table 25 - Case 3b, Numerical results for a 5% increment in nominal working time:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[257 , 277]	0.12	[115 , 124]	0.12
ProaRT	[15 , 24]	0.00	[6 , 9]	0.00
Improvement	[240 , 255]	0.11	[108 , 115]	0.11
% Improvement	[92% , 93%]	97%	[93% , 94%]	97%

**Expected access time measured as average of all patients and all CPs.*

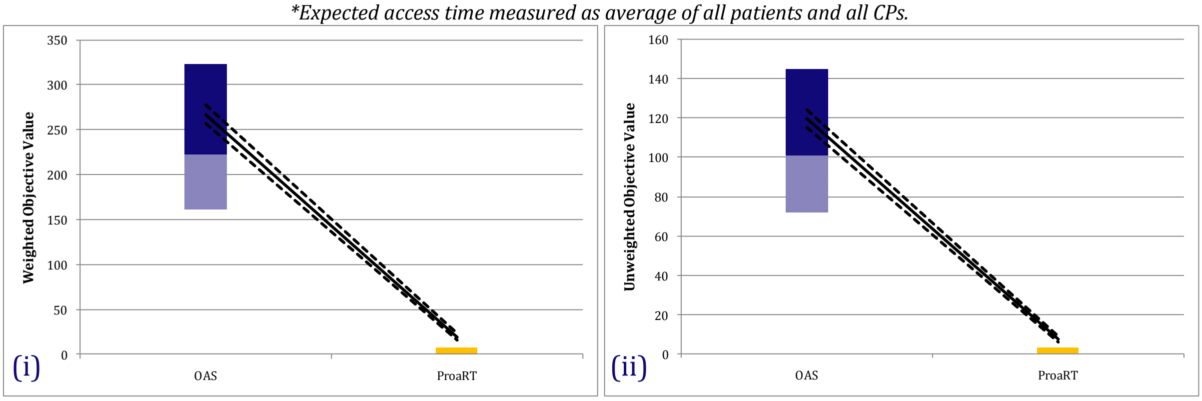


Figure 40 - Case 3b, Objective values for a 5% increment in nominal working time

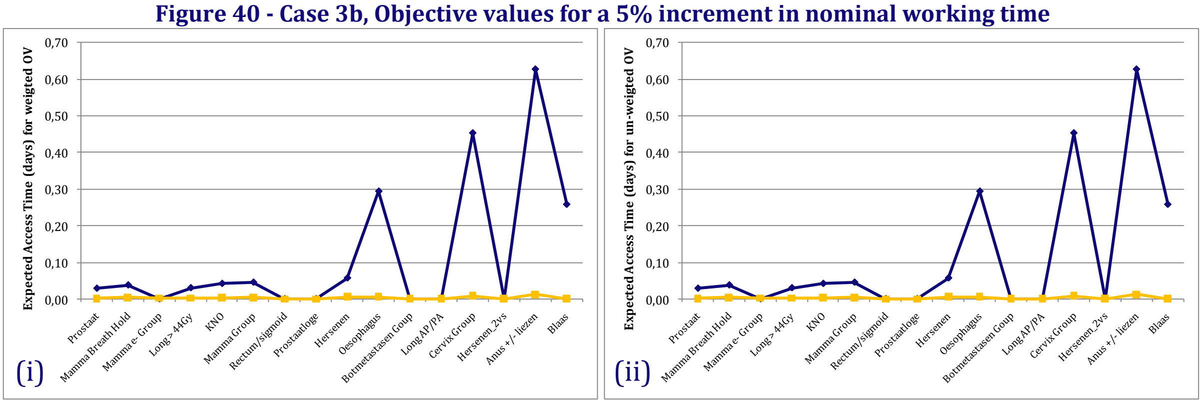


Figure 41 - Case 3b, Access times for a 5% increment in nominal working time

The main conclusion we get from this third case is that the access-time performance is more sensitive to a change in 'supply' (i.e. linac timeslots) than to a change in 'demand' (i.e. number of patients). In case 2a there is a "total-fractions-per-year/capacity" ratio of approx. 94% and an expected weighted OV of 3011 (in OAS). In case 3a where there is a similar demand/supply ratio of approx. 95%, the expected weighted OV is of 5649 (in OAS). These cases account for approximately a 5% change, in the demand and supply respectively, but have a different impact. The ratios of 94% and 95% should, intuitively, have a similar access time function, not a large one as observed. We believe that, due to the *linac constraints*, the performance is more sensible (i.e. the expected weighted OV increases or decreases more) to a change in supply than to a change in demand. As mentioned earlier, in OAS a change in demand had an expected weighted OV of 3011 while a corresponding change in supply had an expected weighted OV of 5649. ProaRT, which always performs better than OAS in these cases, has coinciding observations, supporting the previous conclusion.

5.3.4 Case 4: Old linac replacement

The fourth case we analyze deals with the replacement of an old linac. The NKI-AVL has one spare shielded-room which is continuously used for installing a new linac. Based on this continuous update of technology, we study the replacement of the 'oldest' linac (B4 which dates from 2003) with two possible replacement options: (4a) the oldest linac is replaced with the 'latest' type of linac (A2 from 2011) or (4b) the oldest linac is replaced with a 'highly-capable' type of linac (A1 which can treat 14 out of 16 care plans). For this case we consider the current linac feasibility, the current number of timeslots and a 10% larger arrival rate (which was previously studied in case 2b). We use this increment (which models a two year growth approximately) in order to study the effect during the time when the 'old linac' would stop being used and the replacement one would start. Furthermore, with all the aforementioned settings we can study the effects that having, or not having, a certain type of linac can have on the access time performance. We now present the performance under OAS and ProaRT when *replacing the oldest linac*. In addition, we compare the performance to that of no replacement (i.e. case 2b).

If the 'oldest' linac (B4) is replaced with a linac of the 'latest' type (A2), there is an increment of 743 access days (expected un-weighted OV) and of 5008 weighted days when compared to the no-replacement situation (seen in Table 26 and previous Table 23). This increment in OV is to be expected since a linac of the type of A2 can treat less care plans than a linac of the type of B4. However, under the OAS way of planning, both the replacement and the no-replacement situation have the same expected access time (measured as the average of all patients and all CPs). This apparent 'contradiction' to the increment in the OV is due to a larger number of care plans with similar, closer to average, access times rather than very low and very high as in the no-replacement situation (case 2b). Now, with respect to the ProaRT way of planning, just as the no-replacement situation, ProaRT performs better than OAS. Nevertheless, when compared to the no-replacement situation, the relative improvement between ProaRT and OAS is slightly higher in the weighted CPs than in the un-weighted version. This is the first case in which we encounter this state of improvements, which is due to the linac feasibility and demand. Figure 42 (i) shows that the slightly higher improvement of ProaRT in the weighted CPs is paid with the 'Mamma e- Group' having an access time a little larger than in OAS, i.e. performing worse. Although in Figure 42 (ii) the un-weighted CPs show a relative improvement smaller than the weighted ones, all CPs perform better, or at least equally good, in ProaRT compared to OAS. With this linac replacement, weights influence how ProaRT performs.

Table 26 - Case 4a, Numerical results for replacing B4 with an 'A2-like' linac and 10% growth in arrivals:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[18320 , 20104]	1.45	[5082 , 5584]	1.45
ProaRT	[15384 , 17129]	1.21	[4341 , 4834]	1.21
Improvement	[2873 , 3038]	0.24	[724 , 768]	0.24
% Improvement	[15% , 16%]	16%	[14% , 14%]	16%

**Expected access time measured as average of all patients and all CPs.*

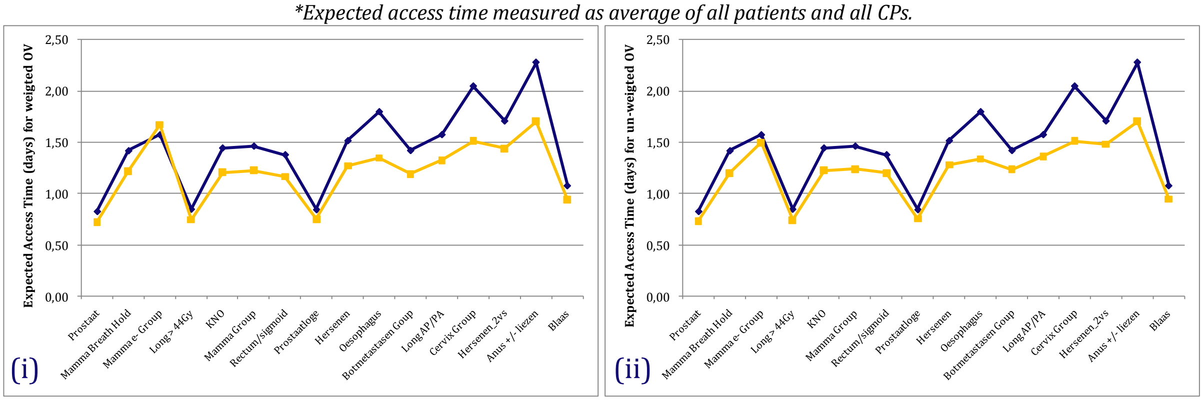


Figure 42 - Case 4a, Access times for replacing B4 with an 'A2-like' linac and 10% growth in arrivals

If the 'oldest' linac (B4) is replaced with a linac of a 'highly-capable' type (A1), the expected OVs for the OAS are equal compared to those when replacing with the 'latest' type (as seen in Table 27 and previous Table 26). In the OAS way of planning, both types of replacement similarly increase the OVs, making it better to not replace the 'oldest' linac at all. However, when ProaRT is used as the way of planning in the simulation, results show the same state of improvement of the previous linac replacement, but in a larger scale. In all previous cases, ProaRT's relative (percentage) improvement was higher in the un-weighted CPs than in the weighted situation. In this 'linac replacement' case, the opposite occurs due to the linac feasibility (i.e. it is the only factor that differs from previous cases). Figure 43 (i) shows that for the weighted OV, ProaRT has a higher improvement (lower yellow bar and steeper black line on the left) than for the un-weighted OV in Figure 43 (ii). Once again, ProaRT's higher improvement comes with the price of the 'Mamma e- Group' having a much worse access time than in the OAS, for the weighted CPs, as seen in Figure 44 (i). A discussion on why this CP is the one whose access time is deteriorated is presented further in this chapter, in Section 5.4. On the other hand, for the un-weighted situation, ProaRT is able to lower *all* access times below their level in OAS.

Table 27 - Case 4b, Numerical results for replacing B4 with an 'A1-like' linac and 10% growth in arrivals:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[18320 , 20104]	1.45	[5082 , 5584]	1.45
ProaRT	[13336 , 14883]	1.28	[4341 , 4835]	1.21
Improvement	[4935 , 5270]	0.17	[723 , 767]	0.24
% Improvement	[26% , 27%]	12%	[14% , 14%]	16%

**Expected access time measured as average of all patients and all CPs.*

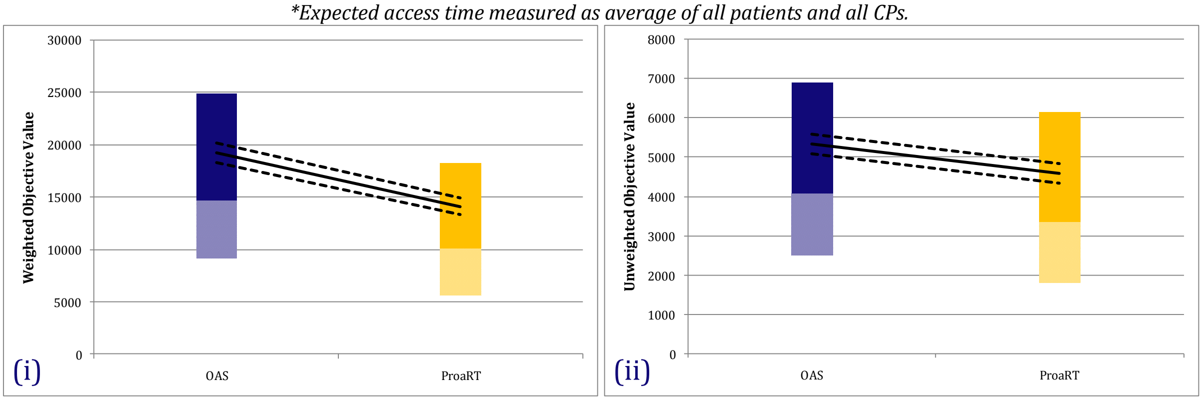


Figure 43 - Case 4b, Objective values for replacing B4 with an 'A1-like' linac and 10% growth in arrivals

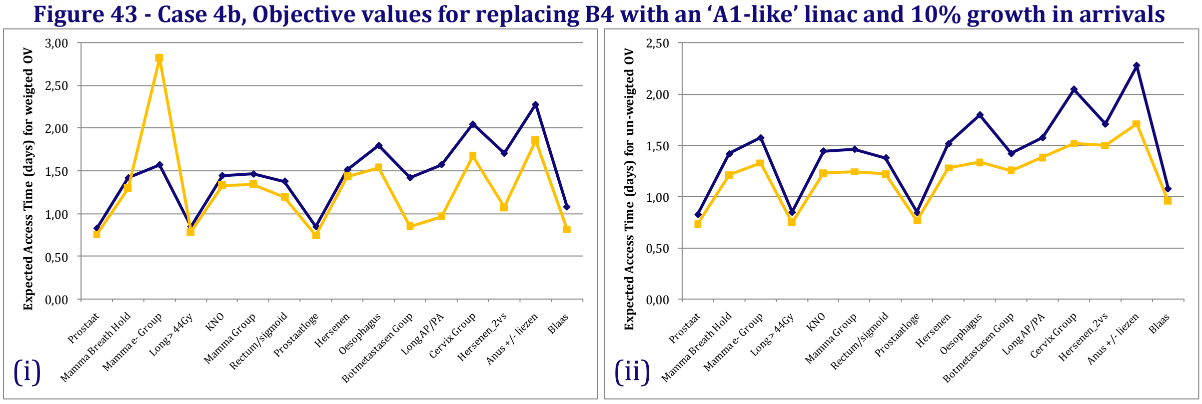


Figure 44 - Case 4b, Access times for replacing B4 with an 'A1-like' linac and 10% growth in arrivals

Finally, in this fourth case, we see how ProaRT can be of support when choosing which linac should replace another one. ProaRT can show differences performance differences that other calculation methods cannot. For instance, in Table 26 and Table 27 we see the same values for the OAS row, showing no difference between linacs A2 and A1 respectively. In the same tables, if we observe the ProaRT row, we do see a difference. What is more important, we observe that for some linac feasibility and demand characteristics, the weights of the care plans influence how much of an equity benefit (for all CPs) ProaRT can achieve. Although A1 performs better than A2 in terms of the weighted objective value, we observe in Figure 44 (i) that there is one CP whose access time worsens. Nevertheless, if the weights are assumed to be correct (and the relative access times to be medically possible) then it can be argued that A1 is a better candidate than A2 to replace B4 due to the differences observed with the ProaRT method.

5.3.5 Case 5: New linac acquisition

In this fifth and last case, we analyze the situation of expanding the capacity. Strictly speaking, acquiring a new linac expands the capacity by 1/8 or 12.5%. However, this new capacity cannot be used by all care plans due to the linac constraints. Similar to Case 4, we study acquiring two types of linacs: the first one (5a) is a linac of type A2, the 'latest type' and the second one (5b) is a linac of type B3, a 'highly-capable type'. Since the new linac means more capacity, increment the demand as well. We study the performance considering a 20% increment in the arrival rates for all care plans in order to observe access times that are significant enough to show differences between the two linacs in question. All other settings remain the same. With this increment in both capacity and demand, the "total-fractions-per-year/capacity" ratio is of approximately 95%, similar to that of case 2a and case 3a. We now present the performance under OAS and ProaRT when *acquiring a new linac*.

We begin by analyzing the case when the 9th linac is of the type of A2. In line with the growth in the number of patients that arrive per year, the expected OVs (which are defined as the yearly sum of all patients of all care plans) in this case are larger than in the previous cases 2a and 3a, which have similar demand/supply ratio, as seen in Table 28. When considering the individual care plan's access time, Figure 46 (i) and (ii) show that the expected access times are, in general, of similar magnitude and pattern (i.e. some care plans half of the average, some more than twice) as in the previous cases with the same demand/supply ratio. This means that with a 9th linac of the type A2, the situation is more of a larger instance of previous ones, rather than a different one. Just as the previous cases, ProaRT performs better than OAS in both weighted and un-weighted situations, with similar relative (percentage) improvements.

Table 28 - Case 5a, Numerical results for adding a 9th linac of the type of A2 and 20% growth in arrivals:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[6357 , 7010]	0,68	[2069 , 2259]	0,68
ProaRT	[4226 , 4844]	0,38	[1267 , 1447]	0,38
Improvement	[2102 , 2196]	0,30	[794 , 820]	0,31
% Improvement	[31% , 33%]	45%	[36% , 38%]	45%

**Expected access time measured as average of all patients and all CPs.*

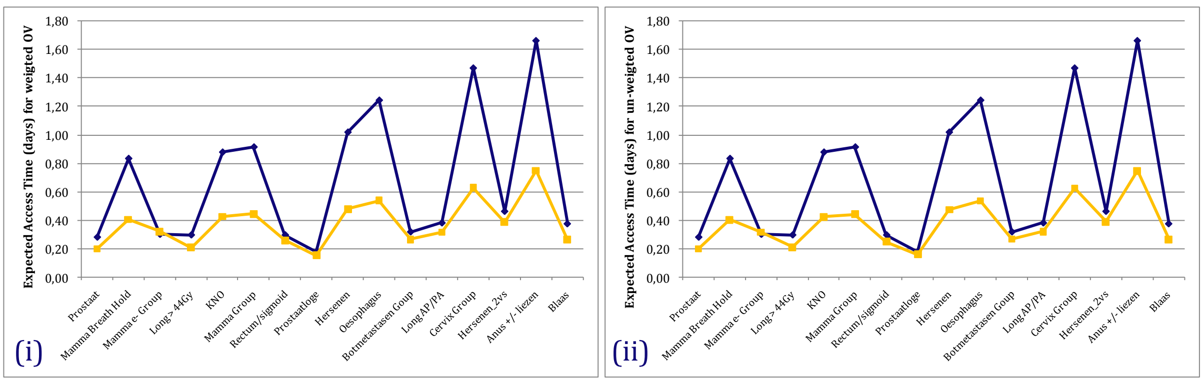


Figure 45 - Case 5a, Access times for adding a 9th linac of the type of A2 and 20% growth in arrivals

When the 9th linac is of the type of B3, the expected OVs in the OAS way of working are much lower than when the 9th linac is of the type of A2, as seen in Table 29. Furthermore, the overall expected access time (average) also decreases and each individual care plan's expected access time is closer to the average, as seen in Figure 46. In this case, we do observe a change in magnitude and pattern of the expected OAS access time when compared to case 2a and 3a. The reason for this case to have the lowest expected OAS access time (of all cases whose fraction/demand ratio is 95%) is that the new linac is able to treat almost all care plans (15 out of 16), allowing the increment in linac capacity to be accessible to almost every patient. On the other hand, this case is also the one where ProaRT improves the least the expected OVs (relative to OAS). There is a smaller difference, compared to other cases, between the two ways of working if B3 is chosen (e.g. expected improvement between 5% and 6% in the weighted CPs as seen in Table 29).

Table 29 - Case 5b, Numerical results for adding a 9th linac of the type of B3 and 20% growth in arrivals:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[3837 , 4437]	0,40	[1245 , 1422]	0,40
ProaRT	[3607 , 4201]	0,31	[1067 , 1239]	0,31
Improvement	[204 , 261]	0,09	[172 , 190]	0,09
% Improvement	[5% , 6%]	23%	[13% , 14%]	23%

**Expected access time measured as average of all patients and all CPs.*

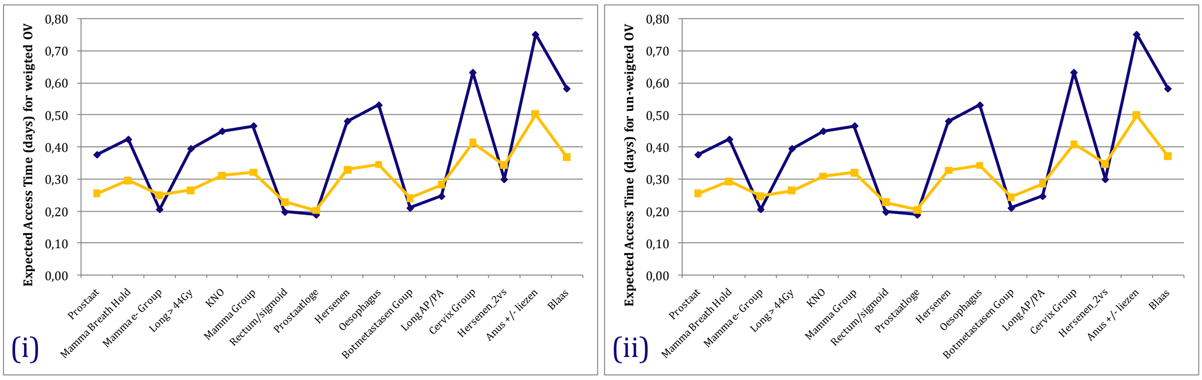


Figure 46 - Case 5b, Access times for adding a 9th linac of the type of B3 and 20% growth in arrivals

Finally, if we were to choose considering OAS as the way of working, the clear choice would be B3. If we were to choose considering ProaRT, the decision would have to be done more carefully and with other considerations, since both linacs access time performance is similar under this way of working. In the theoretical experiments when developing ProaRT, we found that the more constrained a RT department is (i.e. the fewer care plans the linacs can treat), the higher the impact of changing from OAS to ProaRT. In this specific case, ProaRT decreases the access times (with respect to OAS) much more in linac type A2 (which can only treat 4 out of 16 care plans) than in linac type B3 (15 out of 16). The main conclusion in this case is that with ProaRT, two different linacs (one which can treat a few and other which can treat almost all) perform similarly well, thus enabling the decision maker to include and focus on other considerations (such as costs) for the decision.

5.4 Discussion

The general goal of this chapter was to look at a small number of practical situations and examine what benefits could planning the linac capacity in-advance through the ProaRT method have. The general benefit that ProaRT has, in all cases from this chapter, is the significant reduction of the expected objective value, which is the sum of all (weighted) access times of all patients in a year. Depending on the case, these reductions can be large or small (when compared to the current way of working, or OAS). However, when examining the cases from other perspectives and looking into the detail of the results, we observe patterns that pose new questions about the behavior of the performance, in both OAS and ProaRT. In this section we briefly discuss some of these observations and try to answer some of the rising questions.

5.4.1 Importance Factors (Weights)

In all cases from this chapter we present the results of the current importance factors (or weights), seen in Table 18, and which stand for the 'weighted CPs'. In addition, we present the results when all importance factors are set to one, meaning the OV is directly the expected sum of all access days of all CPs, per year (un-weighted CPs). The current way of working, OAS, does not make use of these importance factors, although in reality preferences are done according to them. In the results of the different cases, it is only ProaRT which is influenced by the 'weighted' or 'un-weighted' CPs. In all cases but one (case 4), ProaRT has a higher relative improvement (in the expected OV and with respect to OAS) for the 'un-weighted' care plans compared to the 'weighted' ones. It seems as if better results (for everybody) are obtained if all care plans are equally important rather than differentiated. However, case 4 reveals that this conclusion depends in the linac feasibility and the demand of RT treatments. To illustrate this we will take as an example case 5a (which showed that ProaRT improved more the 'un-weighted' CPs). When adding a 9th linac of the type of A2, but a 30% growth rather than a 20% one, we observe totally different results:

Table 30 - Discussion about weights, numerical results for example situation:

	Weighted Care Plans		Un-weighted Care Plans	
	$\mathbb{E}[Wov]$	E. Access Time*	$\mathbb{E}[Uov]$	E. Access Time*
OAS	[171396 , 177145]	10,70	[48895 , 50536]	10,70
ProaRT	[103017 , 107501]	8,90	[46087 , 47685]	10,17
Improvement	[67572 , 70451]	1,80	[2744 , 2916]	0,53
% Improvement	[39% , 40%]	17%	[6% , 6%]	5%

**Expected access time measured as average of all patients and all CPs.*

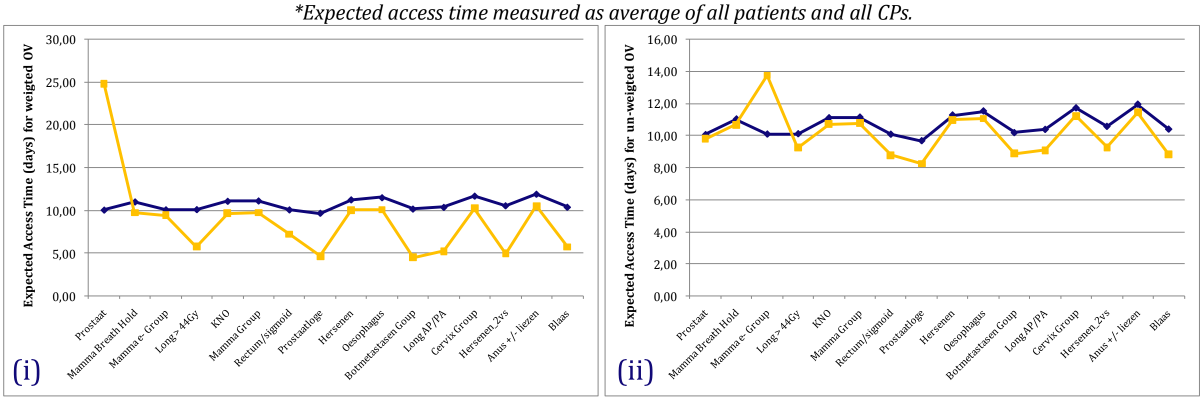


Figure 47 - Discussion about weights: access times for example situation

In this example situation, average demand (patient-type and fractionation-scheme) slightly exceeds supply. From Queuing Theory we know that access times grow infinitely large in this situation. However, since access times are measured for a patient (not the individual fractions which are counted as units of demand) and we consider the average of one year of data, access times do not appear to be infinite, as seen in Table 30. Although this situation would immediately be tackled in reality by increasing capacity, we discuss it to show an extreme situation in the relation between ProaRT and the CPs importance factors (weights). We observe that ProaRT is able to reduce the OVs and the expected access time significantly more in the weighted care plans than in the un-weighted ones. Nevertheless, this comes with a very high price. Figure 47 (i) shows that all care plans' access time (but one) is reduced in the weighted situation. The one that is not reduced ('Prostaat') is more than doubled, since it is 'cheaper' to let them have longer access times than the 'expensive' care plans (e.g. Botmetastasen Group). This is understandable since ProaRT's objective is to minimize the expected weighted sum of access times per year. Strictly speaking, ProaRT achieves its objective; however, the solution is not desirable since the expected access time of one care plan is just unacceptable. Furthermore, in this example situation, having un-weighted care plans is a better solution, but by no means perfect. Figure 47 (ii) shows some care plans whose access time is lower in ProaRT, but also shows that the 'Mamma e- Group' access time in ProaRT is larger than in OAS. With this example we show that the importance factors *determine* how much will ProaRT improve the performance with respect to OAS and also how *realistic* is the solution. Although the situation in this example is not encountered in the majority of cases we study (and hence won't be noticeable in the medium-term future), the implementation of ProaRT in the NKI-AVL should keep in mind the criticality of the weights for the method's solution.

5.4.2 Care Plans - Linac Feasibility

The second discussion point deals with how many linacs are able to treat a care plan. This discussion point arises because, in all cases studied, some care plans appear to always have larger access times than others. To illustrate this discussion point, we will take as example the current situation and an increase in demand (cases 1 and 2 respectively). Figure 48 shows the expected access times for the 16 care plans, where the care plans are ordered in a non-decreasing number of feasible linacs. The general pattern, for the three charts, is that access times decrease as the number of feasible linac increases, which is reasonable since a patient has more linacs to go to. However, the care plans with 3 feasible linacs have both large and low access times when compared to all other care plans. More into detail, Figure 48 shows that the differences between care plans with 3 feasible linacs are larger (almost 2 days) in the case where there is 10% growth. The 3-feasible-linacs care plan with the lowest access time is the 'Mamma e- Group', and the longest one is 'Anus+/-Liezen'. Although they both have 3 feasible linacs, the 'Mamma e- Group' can go to linacs that have a low number of feasible care plans, and the 'Anus+/- Liezen' can go to 3 linacs that can treat almost all other care plans. Hence, there is a larger probability of the latter 3 linacs to be full, compared to the first ones.

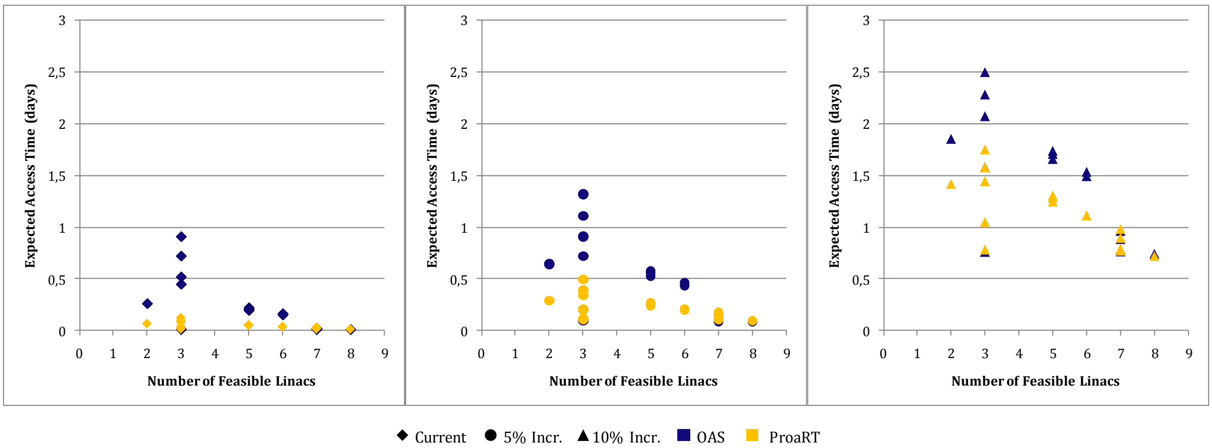


Figure 48 - Detailed view of access times per number of feasible linacs

As seen in cases 4 and 5, and now as illustrated in the previous figures, the linac feasibility is a factor of considerable effect on the behavior of access times, i.e. which care plans waits longer or shorter time. Although ProaRT can be used to cope with this effect of the linac constraints, the linac feasibility and the care plan demand should be carefully studied for long term decisions (as those from cases 4 and 5).

5.5 Implementation

The ProaRT method is a tactical planning method that has to be used at the beginning of every mid-term horizon (e.g. 6 months, 1 year). The output of this methods is a table which is used in the day-to-day scheduling of patients (for the mid-term horizon) as follows: all patient's daily fractions are planned on the earliest available linac that (1) has less than the number of maximum patients (given by the ProaRT table) planned and that (2) has the least number of total planned patients. After the mid-term horizon passed, the method must be executed in order to obtain a new table. In addition, to achieve the benefits of the ProaRT's output, whenever the linac feasibility constraints changes (e.g. new treatments, new equipment, etc.) or whenever there is a significant change in demand (i.e. not due to the normal variation alone) ProaRT should be executed. As explained by van Lent *et al.* (2012), conditions for a successful implementation are related to technical (e.g. data availability, quality of data, simplicity of model, etc.) and process quality factors (e.g. commitment from the user, communication between stakeholders, realistic expectations, etc.). In the NKI-AVL, data availability is not an issue, since an electronic database (MOSAIQ) is kept. Furthermore, ProaRT was programmed as a stand-alone executable file that reads text files (see Appendix 13) which can be generated by MOSAIQ. In addition, all technical factors have been validated and verified with experts from the process and the model has been kept simple to maximize the chance of implementation. On the other hand, planning according to the ProaRT table represents a change (even though small) in the current way of working, and thus requires involvement of the planners. We believe implementation is possible without major efforts or investments at all.

5.6 Summary

In this chapter we analyzed how ProaRT would perform for practical situations, i.e. real-life cases rather than theoretical ones. The different situations, or cases, are based in the NKI-AVL, its characteristics and motivations. We consider the current way of planning at the NKI-AVL to be OAS. For each situation we test for a weighted and an un-weighted circumstance. In the un-weighted one, all CPs are assumed to have an importance factor of 1, meaning that all patients are equally "important" or urgent for starting treatment. The main observations of this case study experiments are:

- Currently, access times from the linac capacity are low: 0.24 days on average for all patients of all CPs. Nevertheless, ProaRT is able to reduce this to 0.05 days (81%). As demand grows (increment in the number of patients that arrive per week), access times also grow and ProaRT's relative improvements reduce. For a 5% and 10% growth in number of patients, ProaRT can reduce access times 54% and 22% respectively.
- Comparing two cases (2a and 3a) we observe that the access-time performance is more sensitive to a change in 'supply' (i.e. linac timeslots) than to a change in 'demand' (i.e. number of patients). In case 2a there is an increment of 5% in the demand. In case 3a there is a reduction of 5% in the supply. In both cases there is a demand/supply ratio of approximately 95%. The expected weighted OV (through OAS) is larger in the change in supply (5649) compared to the change in demand (3011). We believe the change is due to the linac constraints, but further research is necessary to determine if it is not an approximation effect. ProaRT, which performs better than OAS in both cases, has coinciding observations, supporting the previous conclusion.
- The general pattern of the CPs' access times observed in this case study is that they decrease as the number of feasible linacs increase. However, CPs with 3 feasible linacs are the exception, having in some cases both the largest and the lowest access times of all CPs. The 3-feasible-linacs care plan with the lowest access time is the 'Mamma e- Group', and the longest one is 'Anus+/-Liezen'. Although they both have 3 feasible linacs, the 'Mamma e- Group' can go to linacs that have a low number of feasible care plans, and the 'Anus+/- Liezen' can go to 3 linacs that can treat almost all other care plans. Hence, there is a larger probability of the latter 3 linacs to be full, compared to the first ones. When using ProaRT as the planning method, this pattern is less noticeable compared to OAS, but still present.

Chapter 6
Conclusion

In this chapter we summarize the main findings of all previous chapters. We begin by reviewing the objective and motivation with which we worked on this thesis in Section 6.1. Then, in Section 6.2 we briefly outline the answer for each of the research questions posed in the introductory chapter. Finally, in Section 6.3 we provide ideas and directions for future research within the linac capacity planning.

6.1 Thesis Goal

The radiotherapy (RT) process is a complex one, especially when it is done at comprehensive cancer center such as the NKI-AVL. From the entire RT process, our focus was on the linear accelerators (linacs) and the categorized patients that receive treatment from them. In a comprehensive cancer center, new technologies and treatments restrict which linac can treat the different categories of patients. This characteristic, in combination with the uncertainty in the arrival of patients and the different urgencies patients have to begin treatment led us:

Research Goal:

To develop a tactical planning and control methodology for the allocation of linac capacity of a radiotherapy process, to categorized patients, that minimizes the access time of the different categories and maximizes the number of patients treated while taking all process constraints and characteristics.

6.2 Research Answers

Throughout the thesis, an analysis of the RT process at the NKI-AVL, a review of scientific literature, a number of theoretical experiments and a case study helped us developing a methodology that fulfills the goal seen in the previous section. Proactive linac capacity planning with the ProaRT method has been shown, through a series of research questions, to be helpful in preventing delays in the start of radiotherapy. In this section we present the main conclusions we obtained for each question.

1. What is the current situation of the radiotherapy linac capacity and its demand at the NKI-AVL?

Radiation therapy in the NKI-AVL is given using the latest forms of treatments and different, state-of-the-art linacs. Due to the nature of the treatments, and the technology of the linacs, some of them can only treat some patients. There are currently 8 linacs for daily treatments and 1 backup device. Around 95 new patients arrive per week, for a total of more than 4500 per year. Each patient is categorized into a care plan (CP), which determines his or her fractionation scheme. Depending on the CP, a patient can receive from 1 up to 35 daily fractions of radiation. After doing statistical analyses on the electronic database from the department, we concluded that demand (defined as the combination of patient-type and fractionation-scheme) currently requires around 89% of the capacity. Moreover, 16 out of more than 40 CPs account for 80% of the new patients and 90% of the fractions delivered per year. Also, on average a patient can go to 5 out of 8 linacs, but it can vary from 2 up to 7. After interview and meetings with staff from the department, we concluded that there are priorities when scheduling the patients. In addition, the performance (in terms of access times and utilization) is within acceptable levels.

2. What factors and quantitative methods are relevant for planning the radiotherapy linac capacity?

From all the analyses of the current situation of the linac capacity and demand at the NKI-AVL, we concluded the most relevant factors were the *linac constraints* and the *uncertainty in the arrival of patients*. More important, with the insights obtained in Research Question 1, we defined the LCPP and defined which literature would be relevant to review. After a short study of scientific literature about planning the RT linac capacity, we concluded that there was a gap between the strategic studies (which in this case are usually medical oriented and do not include any logistical consideration) and the operational studies (which usually do not include information about the process uncertainties (e.g. future patients). 'Look-ahead' techniques, such as the ones from tactical planning, were used as indication and suggestion by several authors. Furthermore, we derived guidelines as to which quantitative methods were applicable in the RT process (considering all factors and characteristics), from literature on similar processes in healthcare and manufacturing businesses. From the examples studied, we concluded that a single approach (such as mathematical programming or Markov decision processes) is not able to incorporate all necessary factors for tackling the planning problem. Also from the examples, we observed several forms of 'look-ahead' techniques, with the one common aspect of in-advance allocation of capacity to categories (of patients or products) rather than individuals. Allocation of capacity at this level showed the benefit of simplifying the scheduling while attaining the planning objectives of higher levels.

3. What is a useful planning method for radiotherapy linac capacity with NKI-AVL's characteristics?

Based on the guidelines from Research Question 2 we mathematically modeled the LCPP and developed a solution method which we call ProaRT. To achieve the objective of the LCPP, ProaRT determines, in advance, the maximum linac capacity that can be used by a category of patients per day. This proactive allocation can be considered as a planning table that gives a threshold on the number of patients, from each category, which can be treated on every linac on any given day. ProaRT constructs this table via a simulation-and-heuristic approach. In accordance to the examples of Research Question 2, the heuristic approach handles the problems characteristics (e.g. linac constraints, daily fractions of radiation, etc.) and the size of relevant instances (as seen in the data analyses from Research Question 1). The simulation part of the approach handles the uncertainty in the arrivals and the mid-term horizon (for in advance tactical planning). Besides the theoretical guidelines with which ProaRT was built, we carried out a number of theoretical experiments to test the "usefulness" of the method with respect to theoretical (NKI-AVL based) characteristics. The theoretical experiments show that ProaRT significantly achieves lower weighted access times compared to OAS, which is a typical way of working of hospitals and the current way of planning the linac capacity at the NKI-AVL. Depending on the theoretical circumstances, ProaRT could achieve weighted access times that are up to 90% lower than the ones from OAS. In addition, we observed in our theoretical experiments that as the relevant factors from Research Question 2 (the *linac constraints* and the *uncertainty in the arrival of patients*) became 'critical' (e.g. patients can be treated in only 50% of the linacs the arrival of 20% of the patients account for 80% of the fractions) the impact of ProaRT (planning in advance) was higher, i.e. weighted access times were between 8% and 39% lower when having a tactical plan (via ProaRT) than when not having it (using OAS only).

4. What would be the benefits of implementing the proposed planning method for the NKI-AVL?

To analyze the benefits that implementing ProaRT in the NKI-AVL would have, we do a series of experiments (and simulations) of practical (real-life based) situations. Each situation, which we label as a case, uses input data about the current and future linac capacity and demand at NKI-AVL. Benefits from all care plans perspectives are reviewed. Overall, ProaRT performs better in terms of objective function and individual access times than OAS, which is the current way of planning the linac capacity at the NKI-AVL. In the current situation, access times (due to the linac capacity and OAS) are low: 0.24 days on average for all patients of all CPs. In this situation ProaRT is able to reduce this indicator to 0.05 days (81%). However, as demand grows (increment in the number of patients that arrive per week), access times also grow and ProaRT's relative improvements reduce. For a 5% and 10% growth in number of patients, ProaRT can reduce access times 54% and 22% respectively. With respect to each individual CP, in most cases ProaRT reduces, or at least not increases, the access times in a similar manner. However, there are cases, such as replacing B4 with an 'A1-like' linac and 10% growth in arrivals, where ProaRT decreases the average access time over all CPs, but increases one (individual) CP's access time almost twice as much from its original value (in OAS). Another important remark is that in OAS, a general pattern of the access times is observed. In OAS, access times decrease as the number of feasible linacs increase. However, CPs with 3 feasible linacs appear to be the exception. In some cases, the 3-feasible-linacs CPS have both the largest and the lowest access times of all CPs. When using ProaRT as the planning method, an additional benefit is that this pattern is less noticeable, thus leveling all CPs access times (i.e. equity objective).

Finally, the research done in this thesis demonstrates the advantages of planning the linac capacity in advance. More specific, this research shows that allocating a maximum capacity for each care plan in each linac significantly improves the access time of patients when the linacs are constrained and there is an uncertain arrival of patients. Nonetheless, there are still opportunities for more comprehensive models and improved approaches, as seen in the following section.

6.3 Further Research

While answering the research questions, new ideas arose and further questions appeared. In this section we briefly summarize the ideas that have been earlier discussed. We categorized them into two areas of interest: (1) research for the NKI-AVL and (2) research for ProaRT's extensions and improvements.

6.3.1 Research for the NKI-AVL

After carrying on both theoretical and practical experiments, we came with ideas of further research for the NKI-AVL, which can have an impact in accordance to the observations made in the experiments. For instance, further research can be carried on the 'feasibility' of a linac treating a certain care plan. In the ideal world, all patients would be able to go to all linacs, but in reality this is far from true as technologies and human experience are different, and critical, for the success of radiotherapy. Currently, the Clinical Physics and Instrumentation is working on a project of delivering filter-free irradiation. Achieving this project's goal would be of great help, since more linacs would be able to deliver the same treatments, and from the insights of this case study, lower access times would be attained. Furthermore, in the analysis of the current linac situation we observed a differentiation of the 'ideal' and the 'technically feasible' linacs per CP. Further research can be done on how to choose which 'technically feasible' linacs to promote to ideal, or vice versa. These aforementioned research ideas have a logistical impact, but are in the technical and medical domain. Research ideas in the logistics domain can be, for instance, researching about the constraint that a patient should be treated in the same linac for the entire fractionation-scheme. This doesn't necessarily mean plan every fraction in any linac, but rather than just using one, perhaps using two can improve the access times. If moving linac is allowed, then it might be interesting to research how to schedule the maintenance inspections and patients' fractions together. At last, but surely not at least, further research on the tactical (in advance) planning of other resources in the RT process (such as CT scanners, contouring personnel, etc.) can be done such that the entire chain of the process is optimized. This thesis serves as an example on how this kind of planning can be beneficial to attain performance goals.

6.3.2 Research for ProaRT's extensions and improvements

From the literature, the modeling and the experiments, we developed several ideas for future research, both in extensions and improvements of the ProaRT method. Examples of research for extensions include researching the way to incorporate (change) the current assumptions (e.g. same fractionation-scheme for all patients of a category, the discretization of linac capacity in timeslots, etc.). Another extension, in the interest of different stakeholder's perspective, is researching how useful it is to modify the objective function. From the experiments we see cases where some care plans are benefited by ProaRT while some others are not. This brings us to the idea that, if a more equitable access is desired, a term for equity in the objective function or a squaring of the access time variable can be researched upon. Another way for achieving this desire, without modifying the objective function, might be introducing some extra-constraint such as the maximum access time a patient can wait before "cancelled". With respect to the further research on the tactical (in advance) planning of other resources in the RT process (such as CT scanners, contouring personnel, etc.) research can be done to find a way of including these resources in the ProaRT method, or in developing a larger approach that can incorporate ProaRT.

ProaRT is a parameterized simulation-based meta-heuristic whose results depend on the chosen input parameters. For this thesis, a simple numerical search was used to tune these parameters for the NKI-AVL problem settings. However, in the scientific literature there exist methods for *optimal learning* and *simulation optimization* that can provide a base to develop a 'tuning' algorithm for ProaRT's input parameters. With such a tuning algorithm, ProaRT can be guaranteed to deliver the best results possible, independent of the problem settings. Furthermore, ProaRT is a method that can be applied to different forms of operational scheduling, as long as they can have the maximum linac allocation constraint. Further research on scheduling heuristics (such as the balanced workload scheduling) can be done to achieve larger improvements.

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Glossary

In this Glossary we present a list of acronyms, medical and logistical terms used throughout this thesis along with their short explanation.

Access Time	Time that a patient has to wait to begin treatment. In the context of this thesis, the access time is the time in days between the end of the pre-treatment phase and the beginning of the fractions.
Arrival Rate	Rate with which patients arrive to receive treatment, measured in number of new patients of a CP per unit of time (e.g. 25 bone-metastasis patients per week).
Capacity	*See linac capacity.*
Care plan (CP)	Term used to define the type of cancer a patient has and the type of radiotherapy that will be used. It defines how many fractions will a patient receive and which linacs can execute these, among other characteristics.
Category	*See care plan.*
Cone-Beam CT (CB-CT)	Technique for high precision radiotherapy developed in 2004 by the NKI-AVL (The Netherlands Cancer Institute, 2006b). It allows more effective doses on cancerous tissue, while allowing healthy tissue to be less damaged. It uses low-energy X-ray tubes in addition to a silicon flat panel imager. By 2006, 20 linacs around the world had adopted this technology.
CT	*Computed Tomography*
EPID	*Electronic Portal Imaging Devices*
Ideal Linac-CP relationship	The ideal relationship between a linac and a CP denotes that both, technical configuration of the linac and experience of the radiation therapists with a CP, make it preferable to treat that CP in that linac.
Fraction	Session of radiation treatment of a patient.
Instance	An instance is a specific realization of a stochastic input variable(s) from a problem. In the context of this thesis, a problem instance is a random set of patients ready to receive RT.
Linac	*Linear Accelerator*: Machine that accelerates subatomic particles that are used to deliver radiation treatment to a cancer patient.
Linac Capacity	The linac capacity is the amount of fractions a linac can deliver. In the context of this thesis, the linac capacity is the amount of timeslots available per linac.
Metastatic Cancer	Cancer that has spread from the place where it first started to another place in the body.

MRI	*Magnetic Resonance Imaging.*
PET	*Positron Emission Tomography.*
Problem Instance	*See instance.*
Problem Settings	*See settings.*
RT	*Radiotherapy:* the use of high-energy radiation to treat cancer.
Settings	The settings are all the general input parameters of a problem. In the context of this thesis, problem settings are all the parameters of the LCPP described in Section 4.2, i.e. number of CPs, linacs, fractions per CP, etc.
Technically Feasible Linac – CP Relationship	The technically feasible relationship between a linac and a CP denotes that all the technical radiation parameters from a CP can be configured in a linac, but the staff does not have the experience to treat the CP, and hence is not ideal to plan the patient there.

Appendix

1. NKI-AVL's Care Plan Information

ID	Care Plan Name	Average New Pat. Per Week	Std. Dev. Pat. Per Week	Fractions per Patient-Course	Avg. Pat. Per Year	Fractions Per Year	Percentage of Total New Patients	Percentage of Total Fractions Per Year	Feasible Linacs (out of 9)
1	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-	-
19	-	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-	-
21	-	-	-	-	-	-	-	-	-
22	-	-	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-	-	-
25	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-	-
28	-	-	-	-	-	-	-	-	-
29	-	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-	-
33	-	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	-	-	-
36	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	-
38	-	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-	-
40	-	-	-	-	-	-	-	-	-
41	-	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-	-
45	-	-	-	-	-	-	-	-	-
46	-	-	-	-	-	-	-	-	-

*These care plans are combination of various logistically identical sub-care plans.
All information of this table was obtained from the MOSAIQ database "Master Mini-DB" for the year 2011 and the first quarter of 2012. The data was filtered to only Site number 1 and Machines different from "Brachy". All courses and patients are considered.

Appendix 1 - Relevant Care Plan Information

2. Ideal (X) and Technically Feasible (T) Linacs per CPs

ID	Care Plan Name	A1	A2	A4	A5	B1	B2	B3	B4	B5	Total 'X'	Total 'T'
1	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-	-	-	-	-
19	-	-	-	-	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-	-	-	-	-
21	-	-	-	-	-	-	-	-	-	-	-	-
22	-	-	-	-	-	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-	-	-	-	-	-
25	-	-	-	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-	-	-	-	-
28	-	-	-	-	-	-	-	-	-	-	-	-
29	-	-	-	-	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-	-	-	-	-
33	-	-	-	-	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	-	-	-	-	-	-
36	-	-	-	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	-	-	-	-
38	-	-	-	-	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-	-	-	-	-
40	-	-	-	-	-	-	-	-	-	-	-	-
41	-	-	-	-	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-	-	-	-	-
45	-	-	-	-	-	-	-	-	-	-	-	-
46	-	-	-	-	-	-	-	-	-	-	-	-

*These care plans are combination of various logistically identical sub-care plans.
Information is based on the latest version (63) of the 'Logistiek Overzicht' and the care plans selected from Appendix 1. The 'X' represents a linac that is ideal or preferred for treating a CP, and a 'T' represents a linac that can be technically configured to deliver a fraction of radiation for a CP

Appendix 2 - Linacs' Feasible (X) and Technically Possible (T) CPs

3. Percentage of Patients treated in linacs per CP

ID	Care Plan Name	A1	A2	A5	B1	B2	B3	B4	B5
1	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-	-
19	-	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-	-
21	-	-	-	-	-	-	-	-	-
22	-	-	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-	-	-
25	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-	-
28	-	-	-	-	-	-	-	-	-
29	-	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-	-
33	-	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	-	-	-
36	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	-
38	-	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-	-
40	-	-	-	-	-	-	-	-	-
41	-	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-	-
45	-	-	-	-	-	-	-	-	-
46	-	-	-	-	-	-	-	-	-

*These care plans are combination of various logistically identical sub-care plans.
All information of this table was obtained from the MOSAIQ database “Master Mini-DB” for the year 2011 and the first quarter of 2012. The data was filtered to only Site number 1 and Machines different from “Brachy, A3 and A4”. All courses and patients are considered. Differences with the linacs capable of treating can be found due to special treatments for patients of a CP.

Appendix 3 - Percentage of patients assigned to a linac from all patients from a CP

4. CP Fractions delivered per linac

ID	Care Plan Name	A1	A2	A5	B1	B2	B3	B4	B5
1	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-	-
19	-	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-	-
21	-	-	-	-	-	-	-	-	-
22	-	-	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-	-	-
25	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-	-
28	-	-	-	-	-	-	-	-	-
29	-	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-	-
33	-	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	-	-	-
36	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	-
38	-	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-	-
40	-	-	-	-	-	-	-	-	-
41	-	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-	-
45	-	-	-	-	-	-	-	-	-
46	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-

*These care plans are combination of various logistically identical sub-care plans.
All information of this table was obtained from the MOSAIQ database "Master Mini-DB" for the year 2011 and the first quarter of 2012. The data was filtered to only Site number 1 and Machines different from "Brachy, A3 and A4". All courses and patients are considered. Differences with the linacs capable of treating can be found due to special treatments for patients of a CP.

Appendix 4 - Fractions of a CP delivered by a linac

5. Arrival analysis of the 16 largest CPs

With a Chi-Squared Test, we examined the weekly arrivals of the 16 largest from the MOSAIQ database "Master Mini-DB" for the year 2011 and the first quarter of 2012 ($n = 65$). The data was filtered to only Site number 1. With a 95% confidence we do not reject that the arrival of a CP follows a given distribution marked with an "X":

ID	Care Plan Name	Normal	Poisson	Gamma
1	Prostaat	X	-	X
2	Mamma Breath Hold*	-	-	-
3	Mamma e- (Okselregio/Parasternaal)*	X	X	-
4	Long > 44 Gy	-	-	X
5	KNO	-	X	-
6	Mamma*	X	-	X
7	Rectum / sigmoid	-	X	-
8	Prostaatloge	-	-	-
9	Hersenen	-	X	-
10	Oesophagus	-	X	-
11	Botmetastasen*	X	X	X
12	Long AP/PA	X	X	X
13	Cervix/Endometrium/Uterus/Ovarium	-	X	-
14	Hersenen 2vs	X	X	X
15	Anus +/- liezen	-	X	-
16	Blaas	-	X	-

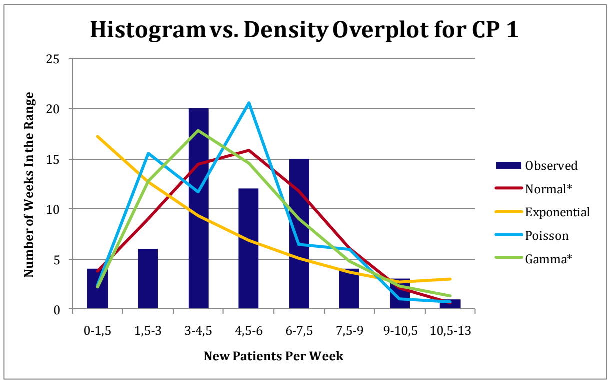
The following table shows the test statistic $\hat{\chi}^2$ for (A) Sturge's rule (table value of $\chi^2_{7,0.95} = 14.07$) and (B) Square-Root Rule (table value of $\chi^2_{8,0.95} = 15.51$) for interval estimation. In this goodness-of-fit test, the null hypothesis H_0 states that the difference between the observed frequencies and the theoretical expectations (from a given distribution) is not significant. If $\hat{\chi}^2 < \chi^2_{k,1-\alpha}$ we conclude the differences are probably due to chance alone.

ID	Care Plan Name	Normal		Poisson		Gamma	
		A	B	A	B	A	B
1	Prostaat	6.31	11.62	32.49	28.62	10.14	18.39
2	Mamma Breath Hold*	15.88	15.77	47.78	46.36	46.27	50.33
3	Mamma e- (Okselregio/Parasternaal)*	10.43	17.09	22.05	3.81	19.86	35.95
4	Long > 44 Gy	46.11	33.50	75.46	21.10	30.20	12.29
5	KNO	16.33	43.47	7.98	6.95	23.09	55.05
6	Mamma*	14.02	25.67	127.44	133.41	7.34	9.78
7	Rectum / sigmoid	42.48	63.95	5.76	5.76	42.88	62.50
8	Prostaatloge	44.88	59.18	36.50	46.40	28.20	36.24
9	Hersenen	63.85	85.86	3.77	3.77	31.39	31.43
10	Oesophagus	70.13	70.44	42.95	1.35	81.88	72.91
11	Botmetastasen*	4.11	4.95	7.82	29.58	3.98	11.55
12	Long AP/PA	6.63	21.18	6.53	6.53	3.61	12.70
13	Cervix/Endometrium/Uterus/Ovarium	93.69	119.02	0.47	36.56	75.92	116.54
14	Hersenen 2vs	14.59	10.51	5.26	8.15	11.18	14.47
15	Anus +/- liezen	126.90	163.83	2.78	29.75	58.42	91.79
16	Blaas	88.94	101.62	38.70	3.87	64.33	60.13

Discussion about the test:

The χ^2 statistical estimator works better as $n \to \infty$. The sample size cannot be extended, since the CPs have changed over the last years. Law (2007) recommends at least 3 intervals and a theoretical number of observations in each interval of at least 5. The theoretical number is dependent on the sample size, and hence our small sample size limits us from more accurate results. Nevertheless the test is used to get an indication about the statistical distribution of the arrivals.

At last, we decide to use a Poisson distribution in our ProaRT tactical model because it is an ideal discrete distribution to describe arrivals (rates) that are independent from each other.



Graphical example of the χ^2 test for the 'Prostaat' CP.

Appendix 5 - Arrival analysis of 16 largest CPs

6. Framework for Healthcare Planning and Control by Hans *et al.* (2012)

Managerial Areas / **Hierarchical Decomposition**

	Medical Planning	*Resource Capacity Planning*	*Materials Planning*	*Financial Planning*
Strategic	Research, development of medical protocols	Case mix planning, capacity dimensioning, workforce planning	Supply chain and warehouse design	Investment plans, contracting with insurance companies
Tactical	Treatment selection, protocol selection	Block planning, staffing, admission planning	Supplier selection, tendering	Budget and cost allocation
Offline Operational	Diagnosis and planning of an individual treatment	Appointment scheduling, workforce scheduling	Materials purchasing, determining order sizes	DRG billing, cash flow analysis
Online Operational	Triage, diagnosing emergencies and complications	Monitoring, emergency coordination	Rush ordering, inventory replenishing	Billing complications and changes

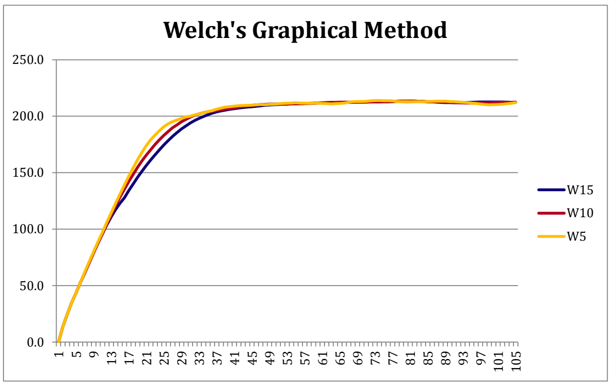
Appendix 6 - Example of Framework for Healthcare Planning and Control applied to a general hospital by Hans *et al.* (2012)

7. Mathematical Notation in LCPP Formulation and ProoART Method

Sets	*Indices*	*Description*
$\mathcal{G}$	g, g'	Categories (care plans)
$\mathcal{M}$	m, m'	Machines (linear accelerators).
$\mathcal{D}$	d, d'	Days in the planning horizon ($\mathcal{D} \subset \mathbb{N}$).
$\mathcal{T}$	t, t'	Timeslots a machine can work during a day ($\mathcal{T} \subset \mathbb{N}$).
$\mathcal{Q}$	q	Maintenance inspections (quality checks).
$\mathcal{I}$	i	Simulations (samples) in the ProaRT method ($\mathcal{I} \subset \mathbb{N}$).
$\mathcal{H}^1, \mathcal{H}^2, \mathcal{H}^3$	-	Sets of input parameters for the ProaRT steps (1,2,3 respectively).
$\mathcal{P}_i$	p, p'	Patients in a simulation i.
Parameter	*Domain*	*Description*
μ_g	$\mathbb{R}$	Mean arrival rate of category g.
σ_g^2	$\mathbb{R}$	Variance of the arrival rate of category g.
s_g	$\mathbb{N} \leq \lvert\mathcal{D}\rvert$	Sessions of radiation treatment (fractions) a patient from category g requires.
α_g	$\mathbb{N}$	Importance factor of a patient of group g (penalty for one day of access time in the objective function).
$f_{g,m}$	$\{0,1\}$	Feasibility of treating patient group g on machine m $(f_{g,m} = 1)$ or not.
r_q	$\mathbb{N}$	Frequency (in days) of maintenance inspection q.
c	$\mathbb{N}$	Number of simultaneous inspections q that can be done at a time.
k_q	$\mathbb{N} \leq \lvert\mathcal{T}\rvert$	Consecutive timeslots maintenance inspection q needs.
λ_g	$\mathbb{R}$	Mean of a Poisson distribution describing the arrivals of category g.
φ	$\mathbb{N} \leq \lvert\mathcal{D}\rvert$	Conversion factor for the arrival of patients.
a_p	$\mathcal{D}$	Arrival day of patient p.
$\tau^{initial}$	$\mathbb{R}$	Initial temperature of the SA algorithm in the ProaRT.
τ^{final}	$\mathbb{R}$	Final temperature of the SA algorithm in the ProaRT.
δ	$(0,1)$	Cooling parameter of the SA algorithm in the ProaRT ($\tau^{next} = \delta * \tau^{previous}$).
κ	$\mathbb{N}$	Number of random changes (Markov chain length) of the SA algorithm in the ProaRT.
$\eta^{initial}$	$\mathbb{R}$	Initial value of the accepting probability parameter of the SA algorithm in the ProaRT.
$b_{p,g}$	$\{0,1\}$	Patient p belongs to group g $(b_{p,g} = 1)$ or not.
$r_{q,m,t,d}$	$\{0,1\}$	Inspection q is done at machine m during timeslot t on day d.
h_1, h_2, h_3	$\mathbb{R}$	Weights in the $\mathcal{A}(\{x_i \forall i\})$ statistical function.
Variable	*Domain*	*Description*
$V_{g,m}$	$\mathbb{N} \leq \lvert\mathcal{T}\rvert$	Tactical variable that indicates how many timeslots from machine m are allocated to category g (maximum number of patients of category g that can be treated in machine m in any day d according to the ProaRT method).
x	$[V_{g,m} \forall g, m]$	Tactical plan (vector of all $V_{g,m}$ variables).
x_i	$[V_{g,m} \forall g, m]$	Best tactical plan for simulation i in the ProaRT method.
x'	$[V_{g,m} \forall g, m]$	Overall best tactical plan (solution given by the ProaRT method).
$\mathcal{F}_g(x)$	$\mathbb{N}$	Total access time function for category g when given a tactical plan x.
$\mathbb{E}^{\mathcal{D}}[\mathcal{F}_g(x)]$	$\mathbb{N}$	Expected total access time function for category g (sum over all expected patients) for planning horizon $\mathcal{D}$ and for a given a tactical plan x.
$\mathcal{O}(\mathcal{P}_i)$	$\mathbb{N}$	Penalized total access time function for a given set of patients $\mathcal{P}_i$ for simulation i in the ProaRT method.
$\mathcal{A}(\{x_i \forall i\})$	x	Statistical weighted function to construct x' given all x_i's in the ProaRT method.
τ	$\mathbb{R}$	Temperature variable of the SA algorithm in the ProaRT.
η	$\mathbb{R}$	Accepting probability variable
$X_{p,m,t,d}$	$\{0,1\}$	Scheduling variable that indicates if timeslot t at machine m is assigned to patient p on day d.
$X_{p,d}^{start}$	$\{0,1\}$	Scheduling variable that indicates the day d in which patient p started the treatment.
L_m	$\mathbb{N}$	Auxiliary variable which indicates the number of patients planned on linac m at a given point in time.
$X_{p,m}^{linac}$	$\{0,1\}$	Auxiliary variable that indicates whether patient p gets treatment on machine m.

Appendix 7 - Notation used in our formulation of the LCPP and ProaRT method

8. Simulation Setup for the Numerical Experiments



The simulation used for both, the numerical experiments and the case study of this thesis, is a non-terminating one. For this reason, we are interested in the steady state performance, which can be estimated only when the system has reached this state. In our simulation, the linacs start empty, which has an influence in the waiting time of the first patients that arrive. In order to determine from which day it is significant to start measuring the performance we applied Welch's graphical method. We follow the procedure and parameters recommended by Law (2007), and obtained the graph to the right. From this graph, it is possible to observe that the system reaches its steady-state around day 25. This value is used for all experiments and simulations for a proper comparison. Furthermore, it is recommended that a simulation run must be much larger than the warm-up period. For this reason, the run length was increased from 6 months (130 days) to 1 year (260 days).

In order to guarantee statistical validity of a simulation, we used a sequential procedure to determine the number of replications (in our case number of simulated years) that are needed to achieve a maximum relative error. With this maximum error allowed, we seek that the confidence intervals have a high probability of containing the real mean of a performance indicator. After sequentially increasing the number of replications from 100 to 1000, we obtained the following table, which indicates the simulation is able to achieve the desired confidence level.

Sequential Procedure Parameter	C1L1T30-M1	C1L1T30-M2	C1L1T30-M2
Sample's average $\bar{X}_n$	913.11	316.30	314.31
Sample's variance S_n^2	423912.96	286392.18	278878.25
Number of replications n	1000.00	1000.00	1000.00
Relative error allowed γ	0.10	0.10	0.10
Confidence interval probability α	0.05	0.05	0.05
Corrected relative error γ'	0.09	0.09	0.09
T-student table value $t_{n-1,1-\alpha/2}$	1.96	1.96	1.96
Estimated relative error $\hat{\gamma}$	0.04	0.10	0.10

Appendix 8 - Simulation setup

9. Overview of Data for Numerical Experiments

This is the input data for the numerical experiments

ID	Categories (care plans) $g \in \mathcal{G}$	Fractions s_g	Average Arrival (Patients Per Week) For a Pois(λ) Distribution						Importance Factor α_g	
			C2 λ	Perc.*	C1 λ	Perc.*	C3 λ	Perc.*	W1	W2
1	Prostaat	39	8.92	32%	4.86	18%	1.75	6%	1	1
2	Mamma Breath Hold*	21	15.50	30%	8.48	17%	3.21	6%	2	1
3	Mamma e- (Okselregio/Parasternaal)*	21	9.21	18%	5.03	10%	3.21	6%	2	1
4	Long > 44 Gy	24	1.54	3%	4.29	10%	2.83	6%	3	1
5	KNO	23	1.58	3%	4.40	9%	2.92	6%	3	1
6	Mamma*	16	2.13	3%	5.86	9%	4.21	6%	2	1
7	Rectum / sigmoid	25	0.75	2%	2.05	5%	2.71	6%	2	1
8	Prostaatloge	33	0.54	2%	1.52	5%	2.04	6%	1	1
9	Hersenen	30	0.38	1%	1.02	3%	2.25	6%	3	1
10	Oesophagus	23	0.42	1%	1.15	2%	2.92	6%	3	1
11	Botmetastasen*	1	9.17	1%	25.48	2%	67.50	6%	6	1
12	Long AP/PA	10	0.88	1%	2.48	2%	6.75	6%	3	1
13	Cervix/Endometrium/Uterus/Ovarium	23	0.38	1%	1.06	2%	2.92	6%	2	1
14	Hersenen 2vs	5	1.71	1%	4.74	2%	13.50	6%	3	1
15	Anus +/- liezen	33	0.25	1%	0.63	2%	2.04	6%	2	1
16	Blaas	25	0.29	1%	0.80	2%	2.71	6%	2	1

*This is the percentage patient-x-fractions out of total patient-fractions.

ID	Category Name	L2								L1								L3							
		1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
1	Prostaat	X	X	X				X	X	X	X	X	X		X		X	X	X		X	X	X	X	
2	Mamma_Breath_Hold_Group			X	X			X	X	X		X	X		X		X	X			X	X		X	X
3	Mamma_e-_(Okselregio/Parasternaal)_Group			X	X			X	X	X				X		X		X	X	X		X		X	X
4	Long_>_44_Gy			X	X	X		X		X	X	X	X		X		X	X		X		X	X	X	X
5	KNO		X	X				X	X	X		X	X		X		X	X	X	X	X	X	X		X
6	Mamma_Group		X		X	X		X		X		X	X		X		X	X	X	X	X	X	X	X	
7	Rectum_/_sigmoid		X	X	X			X		X		X	X	X	X	X	X	X	X	X	X	X	X	X	
8	Prostaatloge	X		X			X		X	X	X	X	X	X	X	X	X	X		X		X	X	X	
9	Hersenen			X	X				X						X		X	X	X	X	X	X	X	X	
10	Oesophagus		X			X	X	X	X	X		X			X			X	X	X		X			X
11	Botmetastasen_Goup	X					X		X	X		X	X	X	X	X	X	X	X			X		X	X
12	Long_AP/PA	X	X				X			X		X	X	X	X	X	X	X				X	X	X	X
13	Cervix/Endometrium/Uterus/Ovarium	X				X	X	X	X	X		X			X			X	X	X		X	X	X	X
14	Hersenen_2vs	X	X			X	X	X		X		X	X	X	X	X	X	X	X	X	X	X	X		
15	Anus_+/-_liezen		X	X		X	X			X		X			X			X			X	X	X	X	X
16	Blaas				X			X	X		X			X	X			X	X		X	X		X	X

This table defines the parameter $f_{g,m}$ for the three levels of the linac feasibility experimental factor.

Appendix 9 - Input data for numerical experiments

10. Statistical Results for Set of Numerical Experiments 1

Each experiment is based on a simulation of 1000 replications and a run length of 1 year (260 days) for the set of penalties (weights) W1. The experiments are labeled with the ID combination of the experimental factors found in Section 4.4. The value in each cell of the following table is the average objective function.

Experiment	Average of M1	Average of M2	Average of M3	Variance of M1	Variance of M2	Variance of M3	Average of Diff. M1-M2	Average of Diff. M1-M3	Average of Diff. M2-M3	Var. of Diff. M1-M2	Var. of Diff. M1-M3	Var. of Diff. M2-M3
F-N/L-N/T-N	934	337	336	524049	368890	365747	597	597	0	65554	65202	454
F-N/L-N/T-C	5649	4552	4497	27527031	25905889	25479929	1097	1151	55	465823	473408	51476
F-N/L-N/T-R	267	15	19	26805	3462	4330	252	248	-4	16413	15167	168
F-N/L-C/T-N	671	341	338	437115	396326	376349	330	333	3	38494	32130	5118
F-N/L-C/T-C	5174	4615	4445	27616642	27432948	25568433	559	729	170	306814	353762	162473
F-N/L-C/T-R	134	16	18	13744	4504	4696	118	117	-2	7234	6779	144
F-N/L-R/T-N	599	371	342	525438	513709	461410	228	257	29	4171	6854	2419
F-N/L-R/T-C	5407	5119	4655	32401442	32626642	24762487	288	752	464	16888	2018734	2035975
F-N/L-R/T-R	139	15	14	9603	6136	5358	124	125	1	1871	2015	52
F-C/L-N/T-N	1071	568	557	672957	410859	397885	503	514	11	68999	73600	2617
F-C/L-N/T-C	6783	5708	5596	24351542	22603641	10554686	1074	1187	113	291774	5898817	5367806
F-C/L-N/T-R	207	46	47	39352	13341	13405	160	159	-1	13242	12967	37
F-C/L-C/T-N	23995	20861	15364	93318503	94151036	46250482	3134	8631	5497	935983	15674033	15876713
F-C/L-C/T-C	51806	48776	31450	154665295	157465496	72193584	3030	20356	17326	930114	26509974	27600040
F-C/L-C/T-R	7147	4775	4162	20604382	16854526	12424620	2371	2985	614	774217	2136478	967128
F-C/L-R/T-N	425	350	345	293507	280405	259970	75	80	5	1951	3243	1531
F-C/L-R/T-C	5031	4878	4625	23948406	23834761	21320801	153	406	253	11765	522797	514718
F-C/L-R/T-R	43	17	17	6733	5492	5492	26	26	0	368	368	0
F-R/L-N/T-N	1473	1005	999	1983422	2284773	2271802	467	473	6	35392	34664	3116
F-R/L-N/T-C	14817	15093	14062	227759723	238203708	219286388	-276	754	1030	574100	690421	894579
F-R/L-N/T-R	525	43	42	27312	31280	30268	482	483	1	5205	4951	153
F-R/L-C/T-N	1371	1498	1183	2468270	3082712	2537671	-127	188	315	91472	39014	58523
F-R/L-C/T-C	15478	16917	14161	233191556	246876727	215457803	-1438	1317	2755	604716	1089795	2062858
F-R/L-C/T-R	195	105	86	44938	58053	47971	90	109	19	6062	4995	1342
F-R/L-R/T-N	1287	1002	1002	2181885	2277108	2278051	285	285	0	12981	13334	575
F-R/L-R/T-C	14783	14825	14803	226329408	232805303	232453270	-41	-19	22	154287	150926	10237
F-R/L-R/T-R	236	43	43	35504	32142	32142	192	192	0	4288	4288	0

The following are the 95% confidence intervals $\left(\bar{X}_n \pm t_{n-1,1-\alpha/2} \cdot \sqrt{S_n^2/n}\right)$ of the data above $\left(n = 1000, \alpha = 0.05, t_{n-1,1-\alpha/2} = 1.96\right)$ for the objective function of the 3 methods and the difference between them. Since common random numbers were used (i.e. the same 1000 sets of patient for each method), a pairwise t-approach analysis can be done for the differences. This means that, if zero is not within the confidence interval, the differences are significant. For example, in experiment C1L1T1 the average difference between M2 and M3 is not significant, however, for experiment C1L1T2 this differences is significant and M3 performs better (is lower) than M2. A negative difference, like the one in the comparison between M2 and M3 in C1L2T3, means that first method compared (M2) performs better.

Confidence Interval for:	Average M1		Average M2		Average M3		Average Difference M1-M2		Average Difference M1-M3		Average Difference M2-M3	
Experiment	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB
F-N/L-N/T-N	889	978	299	374	299	374	581	613	581	613	-1	2
F-N/L-N/T-C	5323	5974	4236	4868	4184	4811	1054	1139	1109	1194	41	69
F-N/L-N/T-R	257	277	12	19	15	24	244	260	240	255	-5	-3
F-N/L-C/T-N	630	712	302	380	300	376	318	342	322	344	-1	7
F-N/L-C/T-C	4848	5500	4290	4940	4131	4759	525	593	692	766	145	195
F-N/L-C/T-R	127	141	12	20	13	22	113	124	111	122	-3	-1
F-N/L-R/T-N	554	644	326	415	300	384	224	232	252	262	26	32
F-N/L-R/T-C	5054	5760	4764	5473	4346	4964	280	296	664	840	375	552
F-N/L-R/T-R	132	145	10	20	9	18	121	126	122	127	0	1
F-C/L-N/T-N	1020	1122	528	608	518	596	487	520	497	531	8	14
F-C/L-N/T-C	6476	7089	5413	6003	5394	5797	1041	1108	1036	1338	-31	257
F-C/L-N/T-R	194	219	39	53	40	54	153	167	152	166	-1	-1
F-C/L-C/T-N	23396	24595	20259	21463	14942	15786	3074	3194	8385	8877	5250	5744
F-C/L-C/T-C	51034	52578	47997	49554	30923	31977	2971	3090	20037	20676	17000	17652
F-C/L-C/T-R	6865	7429	4521	5030	3943	4381	2317	2426	2894	3076	553	675
F-C/L-R/T-N	391	458	317	382	313	377	72	78	76	83	2	7
F-C/L-R/T-C	4727	5335	4575	5181	4339	4912	146	160	361	451	208	297
F-C/L-R/T-R	38	49	13	22	13	22	25	27	25	27	0	0
F-R/L-N/T-N	1385	1560	912	1099	906	1093	456	479	462	485	3	9
F-R/L-N/T-C	13880	15753	14135	16050	13143	14981	-323	-229	703	806	972	1089
F-R/L-N/T-R	514	535	32	54	31	53	477	486	478	487	0	2
F-R/L-C/T-N	1274	1469	1389	1607	1085	1282	-146	-108	175	200	300	330
F-R/L-C/T-C	14531	16426	15941	17892	13250	15072	-1486	-1390	1252	1382	2666	2844
F-R/L-C/T-R	182	209	90	120	73	100	86	95	105	114	17	21
F-R/L-R/T-N	1195	1379	908	1096	908	1095	278	292	278	292	-1	2
F-R/L-R/T-C	13850	15717	13878	15771	13857	15749	-65	-17	-43	5	16	28
F-R/L-R/T-R	224	248	32	54	32	54	188	197	188	197	0	0

Appendix 10 - Statistical data for the set of numerical experiments 1

11. Statistical Results for Set of Numerical Experiments 2

Each experiment is based on a simulation of 1000 replications and a run length of 1 year (260 days) for the set of penalties (weights) W2. The experiments are labeled with the ID combination of the experimental factors found in Section 4.4. The value in each cell of the following table is the average objective function.

Experiment	Average of M1	Average of M2	Average of M3	Variance of M1	Variance of M2	Variance of M3	Average of Diff. M1-M2	Average of Diff. M1-M3	Average of Diff. M2-M3	Var. of Diff. M1-M2	Var. of Diff. M1-M3	Var. of Diff. M2-M3
F-N/L-N/T-N	395	115	115	71414	38075	38079	280	280	-1	13137	12843	106
F-N/L-N/T-C	1975	1432	1432	2622026	2361501	2361958	543	543	0	53691	52573	1072
F-N/L-N/T-R	120	6	8	5240	478	586	114	112	-2	3426	3132	40
F-N/L-C/T-N	284	110	112	55733	37355	37427	174	171	-2	7557	6910	138
F-N/L-C/T-C	1787	1406	1407	2559101	2390402	2378165	380	380	-1	34663	34336	1536
F-N/L-C/T-R	61	5	6	2659	463	492	56	55	-1	1597	1534	10
F-N/L-R/T-N	192	101	101	42249	39569	39430	92	92	0	554	562	6
F-N/L-R/T-C	1548	1416	1409	2581770	2580399	2564217	132	139	7	1206	1312	181
F-N/L-R/T-R	50	4	4	948	462	448	46	46	0	294	295	1
F-C/L-N/T-N	545	280	283	172465	99904	101554	265	262	-4	19522	19059	265
F-C/L-N/T-C	3286	2710	2726	5460243	4987394	5017211	576	560	-15	74445	73425	4874
F-C/L-N/T-R	104	23	24	10646	3491	3665	81	80	-1	3639	3580	16
F-C/L-C/T-N	13021	11323	10533	28284719	28585973	22512036	1698	2488	790	267445	1394998	1260794
F-C/L-C/T-C	28304	26689	24656	47208430	48159821	41876364	1615	3647	2033	267161	1180137	1090215
F-C/L-C/T-R	3821	2538	2681	6091700	4960379	4276243	1283	1140	-143	226680	742042	476894
F-C/L-R/T-N	160	123	123	40053	37661	37366	37	36	0	297	306	20
F-C/L-R/T-C	1861	1791	1791	3410757	3389505	3389738	70	70	0	1391	1396	11
F-C/L-R/T-R	19	6	7	906	694	725	13	12	-1	81	74	5
F-R/L-N/T-N	486	235	235	112434	121383	121431	250	251	0	1694	1699	86
F-R/L-N/T-C	3578	3445	3412	11986017	12384808	12189781	132	165	33	24582	23091	5881
F-R/L-N/T-R	231	10	11	2399	1733	1720	221	220	-1	843	819	20
F-R/L-C/T-N	359	307	271	130065	146087	130890	53	89	36	2419	1741	1116
F-R/L-C/T-C	3561	3686	3230	12092061	12572829	11254053	-125	331	456	18476	42427	68209
F-R/L-C/T-R	67	20	13	2838	2529	1503	47	54	7	463	625	204
F-R/L-R/T-N	342	222	222	117783	115874	115716	120	120	0	876	884	20
F-R/L-R/T-C	3434	3325	3325	11816908	12030624	12022500	109	109	0	5442	5373	290
F-R/L-R/T-R	78	9	9	2313	1620	1582	68	68	0	506	513	2

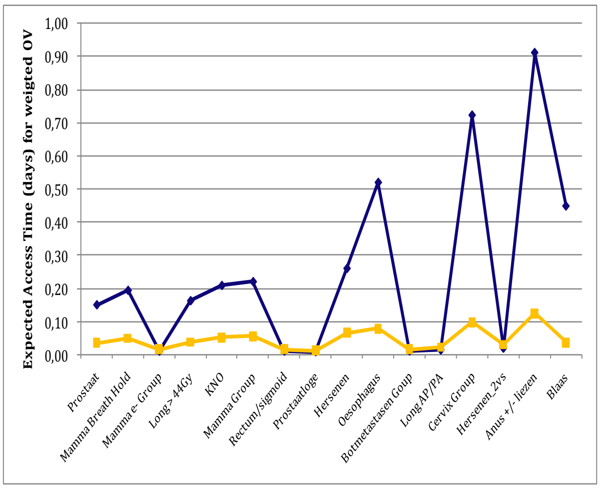
The following are the 95% confidence intervals $\left(\bar{X}_n \pm t_{n-1,1-\alpha/2} \cdot \sqrt{S_n^2/n}\right)$ of the data above $\left(n = 1000, \alpha = 0.05, t_{n-1,1-\alpha/2} = 1.96\right)$ for the objective function of the 3 methods and the difference between them. Since common random numbers were used (i.e. the same 1000 sets of patient for each method), a pairwise t-approach analysis can be done for the differences. This means that, if zero is not within the confidence interval, the differences are significant.

Confidence Interval for:	Average M1		Average M2		Average M3		Average Difference M1-M2		Average Difference M1-M3		Average Difference M2-M3	
Experiment	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB	CI-LB	CI-UB
F-N/L-N/T-N	378	412	102	127	103	128	273	288	273	287	-1	0
F-N/L-N/T-C	1874	2075	1337	1527	1336	1527	528	557	529	557	-2	2
F-N/L-N/T-R	115	124	5	7	6	9	110	117	108	115	-2	-1
F-N/L-C/T-N	269	298	98	122	100	124	168	179	166	176	-3	-2
F-N/L-C/T-C	1688	1886	1311	1502	1312	1503	369	392	368	391	-3	2
F-N/L-C/T-R	58	65	4	7	5	7	54	59	53	58	-1	0
F-N/L-R/T-N	180	205	88	113	88	113	90	93	90	93	0	0
F-N/L-R/T-C	1448	1648	1316	1516	1309	1508	130	134	137	142	7	8
F-N/L-R/T-R	48	52	3	5	3	5	45	47	45	47	0	0
F-C/L-N/T-N	519	571	260	299	263	303	257	274	253	270	-5	-2
F-C/L-N/T-C	3141	3431	2572	2849	2587	2865	559	593	543	577	-20	-11
F-C/L-N/T-R	97	110	20	27	20	28	77	84	76	84	-1	0
F-C/L-C/T-N	12691	13351	10991	11655	10239	10827	1666	1730	2414	2561	720	860
F-C/L-C/T-C	27878	28730	26258	27120	24255	25058	1583	1647	3580	3715	1968	2097
F-C/L-C/T-R	3668	3974	2400	2676	2553	2809	1254	1313	1087	1194	-186	-100
F-C/L-R/T-N	147	172	111	135	111	135	36	38	35	37	-1	0
F-C/L-R/T-C	1746	1976	1677	1905	1677	1905	68	72	68	72	0	0
F-C/L-R/T-R	17	21	4	8	5	8	12	13	12	13	-1	-1
F-R/L-N/T-N	465	507	214	257	214	257	248	253	248	253	0	1
F-R/L-N/T-C	3363	3792	3227	3664	3196	3629	123	142	156	175	28	38
F-R/L-N/T-R	228	235	8	13	9	14	219	223	218	222	-1	-1
F-R/L-C/T-N	337	382	283	331	248	293	49	56	86	91	34	38
F-R/L-C/T-C	3345	3776	3466	3906	3022	3438	-134	-117	318	344	440	472
F-R/L-C/T-R	64	70	17	23	11	15	46	49	53	56	6	8
F-R/L-R/T-N	321	364	201	243	201	243	118	122	119	122	0	0
F-R/L-R/T-C	3221	3648	3110	3541	3110	3541	104	114	104	113	-1	1
F-R/L-R/T-R	75	81	7	12	7	12	67	70	67	70	0	0

Appendix 11 - Statistical data for the set of numerical experiments 2

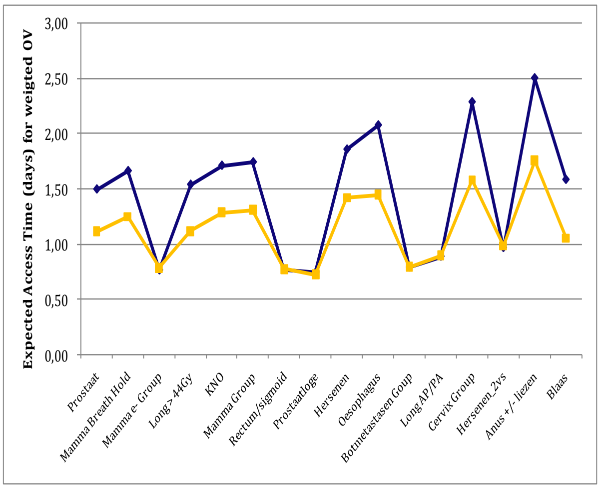
12. Tactical Output for Case Study

For the current situation (case 1):



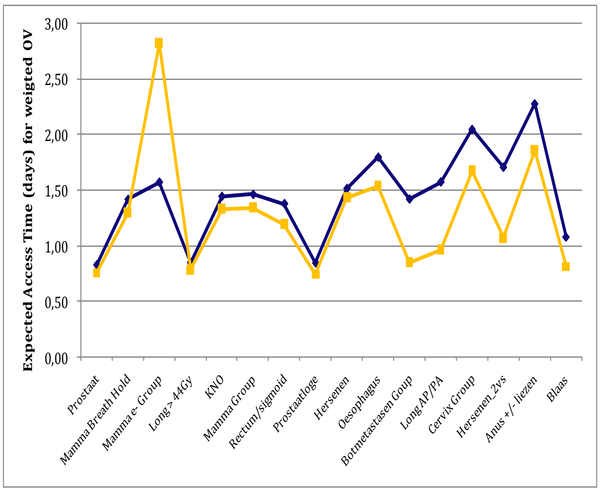
ProaRT table:	A1	A2	A5	B1	B2	B3	B4	B5
Prostaat	19	26	14	11	0	11	0	12
Mamma Breath Hold	15	0	15	14	0	15	0	18
Mamma e- Group	18	0	0	0	20	0	20	0
Long > 44Gy	19	16	7	7	0	12	0	12
KNO	13	0	13	12	0	21	0	15
Mamma Group	8	0	17	18	0	24	0	10
Rectum/sigmoid	12	0	18	15	24	17	22	9
Prostaatloge	6	5	14	16	15	7	16	25
Hersenen	0	0	0	0	0	16	0	16
Oesophagus	17	0	10	0	0	13	0	0
Botmetastasen Goup	14	0	14	6	19	23	9	16
Long AP/PA	18	0	21	15	8	20	11	12
Cervix Group	12	0	17	0	0	13	0	0
Hersenen_2vs	19	0	9	24	22	17	14	16
Anus +/- liezen	16	0	15	0	0	22	0	0
Blaas	0	17	0	0	24	19	0	0

For a 10% increment in arrival of patients (case 2b):



ProaRT table:	A1	A2	A5	B1	B2	B3	B4	B5
Prostaat	16	21	5	9	0	9	0	8
Mamma Breath Hold	21	0	20	16	0	16	0	19
Mamma e- Group	24	0	0	0	14	0	17	0
Long > 44Gy	12	20	13	15	0	16	0	8
KNO	19	0	13	15	0	19	0	19
Mamma Group	17	0	14	23	0	17	0	16
Rectum/sigmoid	15	0	14	14	5	17	15	16
Prostaatloge	10	21	6	15	6	9	16	6
Hersenen	0	0	0	0	0	5	0	19
Oesophagus	12	0	21	0	0	12	0	0
Botmetastasen Goup	8	0	15	10	24	24	13	13
Long AP/PA	19	0	17	23	15	15	6	9
Cervix Group	20	0	20	0	0	21	0	0
Hersenen_2vs	10	0	11	23	21	19	15	11
Anus +/- liezen	9	0	7	0	0	16	0	0
Blaas	0	24	0	0	14	19	0	0

For replacing B4 with type A2 and 10% increase in number of patients (case 4b):

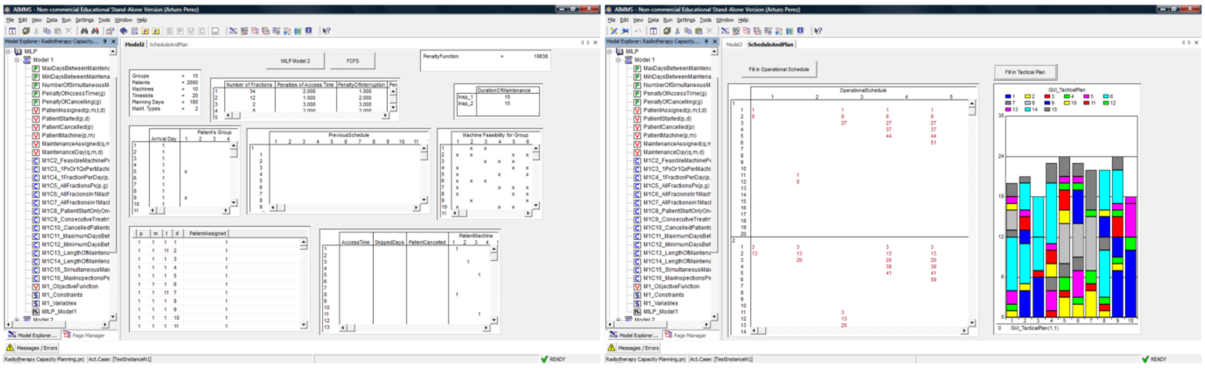


ProaRT table:	A1	A2	A5	B1	B2	B3	B4	B5
Prostaat	12	25	19	6	0	8	25	10
Mamma Breath Hold	7	0	23	14	0	9	0	21
Mamma e- Group	22	0	0	0	6	0	0	0
Long > 44Gy	14	12	12	16	0	15	24	13
KNO	6	0	19	6	0	19	0	14
Mamma Group	15	0	19	20	0	23	0	13
Rectum/sigmoid	11	0	18	17	5	16	0	14
Prostaatloge	17	10	14	16	3	26	14	17
Hersenen	0	0	0	0	0	9	0	16
Oesophagus	16	0	13	0	0	18	0	0
Botmetastasen Goup	10	0	15	20	15	17	0	19
Long AP/PA	16	0	14	19	23	10	0	14
Cervix Group	11	0	5	0	0	15	0	0
Hersenen_2vs	22	0	15	14	18	18	0	8
Anus +/- liezen	11	0	20	0	0	18	0	0
Blaas	0	17	0	0	5	16	8	0

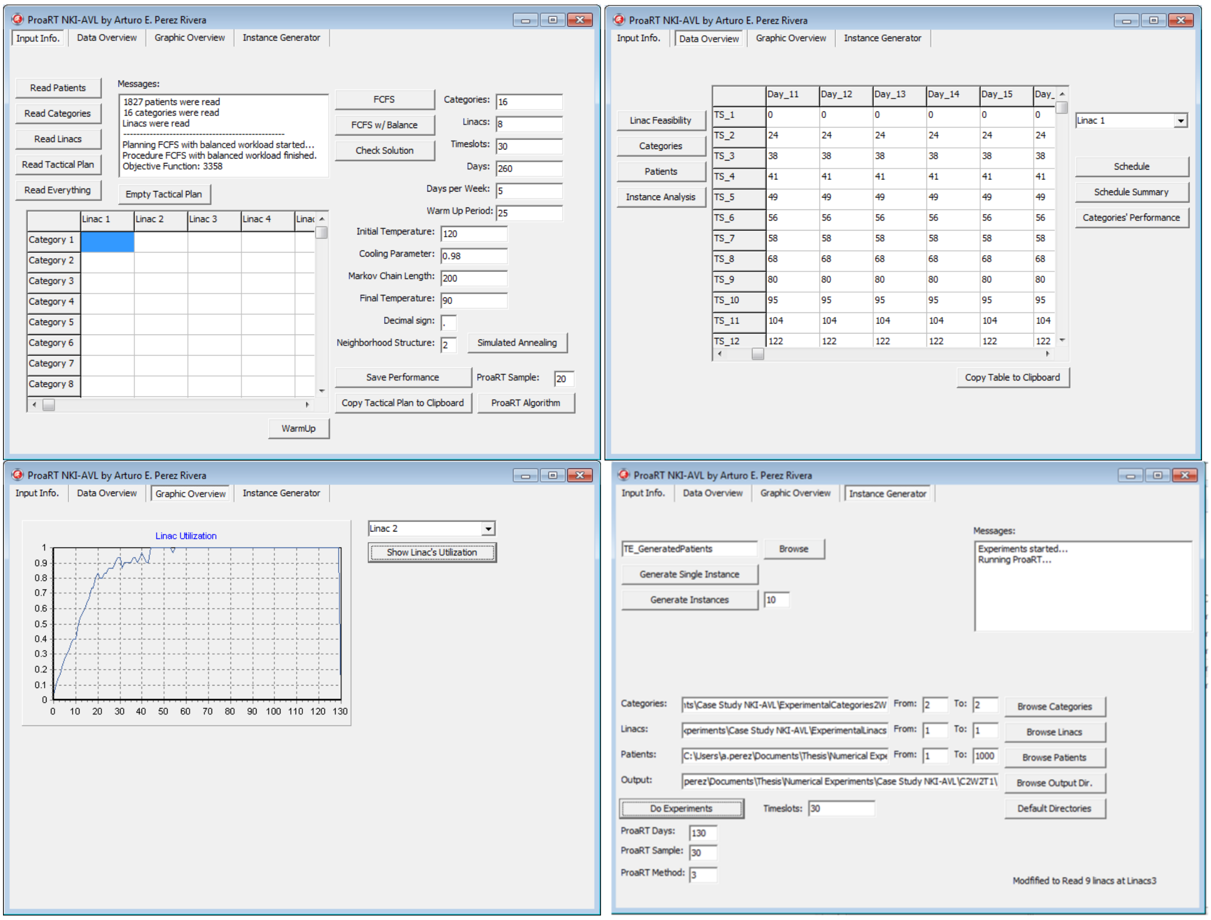
Appendix 12 - Examples of ProaRT output for the case study

13. Developed Software for Models and Algorithms

For the Mixed-Integer Linear Program proposed as an operational scheduling method a test model was developed in the modeling software AIMMS 3.10. Numerical tests with this model showed that it was computationally not feasible for large instances (combination of number of machines, planning days and timeslots). In addition, the software uses 'bulk-instruction' coding, which makes it slower for running meta-heuristics and simulations such as the ones required by the ProaRT method. Nevertheless, for small instances this model achieves optimal solutions for the LCPP operational schedule. These are some screenshots of the application:



For the ProaRT algorithm, and the remaining two operational scheduling methods, Embarcadero Delphi XE2 Version was used. An advantage of this software is that it creates a stand-alone application which can be run in any computer (no installation required). Furthermore, the simulations for the numerical experiments and case study were coded here since the program runs much faster than other simulation packages. For the simulation, an open source random-variables generating code was used. These are some screenshots of the application:



Appendix 13 - Developed applications for the ProaRT Method