Discrete Event Simulation for Prediction of Patient Flow and Capacity in HollandPTC

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Summary

Aim:
Treatment with Proton Beam Therapy (PBT) is highly complex due to a variety of activities integrated into the workflow to ensure treatment quality and patient safety. The effects of changes to the workflow with the intend to scale up a PBT facility are therefore hard to predict. The purpose of this study was to develop a forecasting simulation-based application which could predict the effects of systematic optimisation of the healthcare processes within a PBT facility.

Methods:
A Discrete Event Simulation application was developed which modelled the entire workflow of the PBT facility HollandPTC in Delft. The simulation was validated using real-world historical data. Scenarios were simulated according to a waterfall approach to predict potential capacity bottlenecks. A list of recommended modifications to the current processes was developed which can be used as guidelines towards a systemic increase in capacity.

Results:
The first simulated scenario extrapolated the patient distribution of 2020 to match a target of 600 patients treated. A total number of 475.8 ± 12.67 patients were simulated to be treated. The capacity bottlenecks were caused by retention of the planning resources. The second scenario simulated 556.3 ± 11.97 treated patients. The capacity bottlenecks were caused by too little availability of radiation oncologists. The third scenario simulated 588.3 ± 4.26 patients. The capacity bottlenecks were caused by too little availability of the gantries. The fourth scenario simulated the target: 601.4 ± 7.72 patients.

Conclusion:
In this project, we employed a validated DES simulation to model the in-house workflow of HollandPTC and to make predictions on capacity, throughput, patient flow, and availability of resources. The developed simulation is expected to be applicable to other PBT facilities around the world. The extent to which the simulation is applicable should be further explored.

Contents

List of Abbreviations

CB:	Cone-Beam
CHO:	Chondrosarcomas or Chordomas
CT:	Computed Tomography
CTV:	Clinical Target Volume
DES:	Discrete Event Simulation
GI:	Gastrointestinal
GTV:	Gross Tumour Volume
HL:	Highly Likely
IMRT:	Intensity Modulated Radiotherapy
IQR:	Interquartile Range
KNO:	Head & Neck tumours
LONG:	Lung tumours
LYM:	Lymphomas or hematological tumours
MAM:	Breast tumours
MRI:	Magnetic Resonance Imaging
NEU:	Neurological tumours
NTCP:	Normal Tissue Complication Probability
OAR:	Organs At Risk
OES:	Oesophageal tumours
OOG:	Ocular tumours
PBT:	Proton Beam Therapy
PC:	Plan Comparison
PET:	Positron Emission Tomography
PTC:	Proton Therapy Center
QA:	Quality Assurance
THO:	Tumours in the thoracic area
WHO:	World Health Organisation

Part I

Literature review

Review of available Simulation-Based Optimisation Methodologies for Demand Forecasting and Capacity Planning for a Proton Treatment Facility

J. Eijkenduijn

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1 Introduction

Proton Beam Therapy (PBT) is an emerging radiation treatment modality with a distinct advantage to conventional photon radiation due to the highly localised deposition of energy.[1] This results in a lower dose delivered to the organs at risk compared to photon radiation.[2] These clinical benefits were first described by Robert Wilson in 1946[3] and the past decades of scientific progress led to the improvement of the treatment modality, causing the emergence of numerous PBT facilities globally.[1,2,4] As of December 2020, there are 110 particle therapy facilities worldwide. HollandPTC (Proton Therapy Centre, Delft, The Netherlands) is one of the three facilities located in the Netherlands.[4]

1.1 Proton beam generation

Protons are first accelerated to 250MeV typically by a cyclotron or a synchrotron and subsequently decelerated to therapeutic energies. They are magnetically guided to the treatment room where they enter the treatment nozzle mounted on a rotating gantry. The gantry is then used to aim the beam at the target tissue inside the patient. Optimal directions can be achieved by changing the gantry position and by rotating the couch on which the patients lies.[5] The cyclotron used in HollandPTC serves multiple gantries. The beam is, therefore, directed towards the requested gantry in chronological order or in order of priority. Figure 1 shows the layout of three gantry treatment rooms for PBT.

Figure 1: Layout of three gantry treatment rooms for PBT. Protons are guided from the cyclotron to the gantry. This diagram was developed by HollandPTC

1.2 Therapeutic fields of application

Clinical evidence considering PBT remains limited compared to photon radiation. Cost-effectiveness analyses and clinical trials have proved the value of PBT for multiple different oncological indications.[6] Approvement of PBT based on Randomised Controlled Trials (RCTs), as is conventional, comes with ethical concerns considering the higher radiation toxicity patients get exposed to when treated with photon radiation during an RCT. The Dutch government has, therefore, approved PBT based on a distinction between standard indications and model-based indications defined by Dutch health authorities.[7] Standard indications are described as indications where PBT is the first choice of treatment: intra-ocular tumours, chordoma and chondrosarcoma, and paediatric tumours. Model-based indications were introduced with the purpose to properly select patients who are most likely to benefit from PBT in terms of prevention of side-effects. Subsequently, this approach allows for the validation of the clinical benefits by comparing the PBT plan to the photon plan. To perform patient selection using

a model-based approach, both plans (photon and proton) are made and compared using the difference in Normal Tissue Complication Probability (ΔNTCP). Patients are selected for PBT when their ΔNTCP is high enough and a benefit from PBT can be expected.[7–9] The clinical indications where a model-based patient selection needs to be performed are tumours of the head and neck, mammary glands, lung, prostate, and neurological tumours.[10]

Apart from the standard, and model-based indications, PBT shows potential advantages for the treatment of rectal and anal tumours due to the lower dose to the bladder, bowel and hip joints. It may also have potential advantages for pancreatic, esophageal, gastroesophageal junction, gastric, and hepatobiliary tumours, as it delivers a lower dose to the lungs, small bowel, liver, heart, kidneys and spinal cord, and may also be used for bone and soft tissue sarcomas.[6,11] Tumours situated in the Gastrointestinal (GI) tract, however, remain challenging to irradiate due to the wide penumbra of the proton-beam at higher depths, uncertainties due to air in the GI tract, and radiation-sensitivity of these organs.[5,6]

However, as more clinical trials are being conducted and concluded, and technical challenges resolved, the areas of application and acceptance of PBT increases. It is expected that the need for PBT will, therefore, increase steadily in the upcoming years eventually leading to a shortage in capacity.

1.3 HollandPTC

In the Netherlands PBT has become available in 2018. This year also marked the opening of HollandPTC.[10] In 2013, the Netherlands approved for 2200 patients to be treated annually with PBT in one of the three available Dutch centres.[12] This number is expected to increase as more indications are being considered, both for standard- and model-based indications. Currently, however, HollandPTC is not able to match its part of this expected target, due to limited resources such as personnel and equipment. HollandPTC, therefore, aims to increase its capacity in various ways the upcoming years. The desired increased capacity proves difficult to effectuate due to the complex healthcare processes, research projects, and different treatments all running in parallel. Therefore, it's necessary to provide insight into these processes to determine the cause of possible capacity bottlenecks and to investigate the possible impact of process reformations and improvements, e.g. including evening scheduling or in-room CT scans.

To accomplish this, a forecasting optimisation methodology is needed which is able to model changes in patient-flow, waiting-time, capacity, and resources (personnel, equipment, and facilities), and which is able to predict the effects of systematic optimisation of the healthcare processes within HollandPTC.

1.4 Aim

The aim of this review is to propose a methodology which is most suitable for an analysis of the healthcare processes within HollandPTC. A clear and systematic overview of the available literature on validated simulation-based optimisation methodologies for demand forecasting and capacity planning applied to healthcare processes is provided. This review includes information on the key theoretical concepts and most important advantages and disadvantages of these methodologies.

2 Methods

2.1 Inclusion of papers

The MEDLINE database was searched, and abstracts were screened for eligibility. Papers were of interest when they satisfied three elements. First, the paper had to discuss or describe a clinical process with the goal of optimising capacity or resource utilisation; identifying capacity bottlenecks and increasing throughput or decreasing waiting times; or to increase safety and reliability. All clinical processes were eligible. The paper, secondly, had to have developed, used, or described a statistical, mathematical or simulation-based tool or model to systematically evaluate the clinical process and to gain a detailed insight. The paper, thirdly, had to use this simulation or model to make prediction about hypothetical situations or "what-if" scenarios and had to use these predictions to support policy decisions.
The model should not have been used for

educational purposes, e.g. a patient simulation for the training of nursing staff. Using these elements, the following search query was developed:

(("process assessment, health care"[MeSH Terms] OR "capacity planning"[Title/Abstract]) AND ("model"[All Fields] OR "simulat*"[All Fields]) AND ("predict*"[All Fields] OR "forecast*"[All Fields] OR "future*"[All Fields])) NOT "educat*"[All Fields]*

After initial inclusion, the full texts of the included papers were read and papers were subsequently excluded when they did not describe a validation method and, therefore, did not test their simulation or methodology to substantiate their claims. All validation methods were accepted, e.g. running real, historical data through the simulation to predict established outcomes; using outlier data to evaluate the insecurity of the simulation; applying cross-validation; or, simply, by asking experts if the simulation was reliable according to their expertise.

2.2 Content evaluation

After inclusion of the papers, the content was evaluated to answer the following questions: What simulation or model was used? When was the model applied and is it, therefore, still considered up-to-date? What are the biggest advantages and disadvantages of the model? What field is the model applied to and is that comparable to a PBT centre? What type of software was used and can that be used within HollandPTC, considering its limited resources? Does the model describe and predict complex processes? How reliable and reproducible is this model? Was it tested on a large or small patient population? How was the method validated?

To answer the first questions, information about the methodology, field, time-frame, and software was extracted from the papers and the methodology was categorised.

2.2.1 Categorisation of methodologies

Brailsford et al. (2009)[13] described methodologies as belonging to certain categories based on their underlying theory. Their four major categories were Qualitative Modelling, Statistical Analysis, Statistical Modelling, and Computer Simulation. These categories, their underlying theory, and their advantages and disadvantages are explored in this section.

Qualitative Modelling
Qualitative modelling concerns the representation of continuous processes in a symbolic, graphical manner. This can be done for entire systems (process mapping) or for decisions (cognitive models). Qualitative modelling lays the foundation for quantitative analysis in that it builds a framework which can be built upon. Qualitative models, therefore, form a precursor for the development of quantitative models.[13,14] A qualitative model can be developed easily, but contains little detailed information.

Statistical Analysis
Statistical analysis is the science of data collection and finding trends and patterns.[15] Regression, specifically, is used to find the relationship between two numerical variables. This is done by plotting different outcomes on a scatter plot and finding the line that best describes the average trend of the data. This trend can then be described with a Poisson distributed probability to make prediction of where a new data point could be situated around that line. Regression is easy and fast to calculate, but the biggest disadvantage is that an assumption has to be made on whether two outcomes are related, which leads to the introduction of biases when assuming the relationship within complex systems. The more complex a system becomes, the less correlation is generally observed and the less reliable this method becomes in making accurate predictions.[16]

Statistical Modelling
With statistical modelling, statistical methods are used in combination with qualitative modelling to make more accurate and reliable decisions. Structural Equation Modelling (SEM) is a method where the relationship between steps within a process are described by statistical or mathematical equations. Markov models are comparable to SEM in the sense that every step is described separately, but with Markov models, these relationships are stochastic and described probabilistically.[17] These two methods allow for the description of more complex systems than statistical analysis because all different steps can

be described by different equations, such as linear regression or aggregated means, or by different probabilities. One disadvantage of statistical modelling is that they are very sensitive to the reliability of the underlying assumptions (e.g., if the relationship is linear), which can lead to misleading results.[18–20] Another disadvantage is the sensibility to errors. Errors introduced early in the model are propagated without adjustments. This can lead to undesirable results. Statistical Models, furthermore, need a lot of data to operate reliably. For SEM this data is needed to derive equations which describe the relationship between steps. For Markov models, more data means more accurate probabilities and more accurate predictions.[21]

Computer Simulation

Computer Simulations include Descrete Event Simulation (DES) and Queueing theory. They describe the real, continuous world as a series of discrete events which can occur instantly, are logistically separable and progress through time, causing transitions from one state to another.[22] DES, specifically is largely based on queueing theory, which allows the two to be described together. The biggest advantage of DES is that it allows graphical modelling of complex systems with different entities (inputs: patients) which have a Poisson distributed probability of appearance, just as patients in the real world. The biggest disadvantage of DES is the computational power it requires. The more complex a model becomes, the more processing needs to be done. Furthermore, multiple runs of the simulation have to be performed for the model to be considered robust leading to longer run-times. Another disadvantage when using DES is the need for complex and expensive software.

2.2.2 Applicability-score

To combine most of the remaining questions after categorisation and to provide a clearer overview of the applicability of the included literature, a scoring system was developed by which all content was evaluated. Papers would first be rated on the size of their patient population. HollandPTC aims to increase its capacity towards 600 patients treated per year. Therefore, a patient population size of 500-1000 was deemed applicable, more than 1000+ was better, less than 500 was deemed insufficient.

The papers, subsequently, were scored on reproducibility: did they map out the care processes and did they include the simulation or model by means of screenshots or equations?
Furthermore, the complexity of the model was scored based on the number of different entries, the number of methods compared or used in unison, the number of complex interconnected steps in the process, and the number of "what-if" scenarios predicted.
Lastly, the validation method was rated. Prediction of real, historical data was considered the best validation method, all other methods were considered acceptable. Except when expert's or colleague's opinions were used as validation, this method was considered too subjective and was not assigned any points for validation methodology.

Table 1: Applicability scoring system: papers can get a maximum of 10 points.

Patient population size	0-500	0
	500-1000	1
	1000+	2
Reproducibility	Includes processmapping	1
	Displays model or simulation	1
Complexity	Multiple entries used as input	1
	Compares or describes the use of multiple models	1
	Complex care process with multiple interconnected steps	1
	Predicts multiple "what-if" scenarios	1
Validation methodology	Subjective validation methods	0
	Statistical validation methods	1
	Validation using historical data	2

The scoring system is displayed in table 1. By utilising this scoring system, papers could get a total of 10 points and a clear overview could be created which showed the applicability of the paper's method to HollandPTC.

3 Results

3.1 Inclusion of papers

The initial search of the MEDLINE database resulted in 230 possible papers of which the abstracts were screened. After screening, 197 papers were excluded. Of these 197 papers, 111 did not evaluate a clinical process, meaning that the simulation or statistical model was not used

for capacity prediction, but other indications, e.g. patient outcome prediction based on risk factors or population based disease deposition prediction based on current trends. Another 57 papers did not describe a mathematical model or simulation-based tool. These papers mostly evaluated the clinical process using questionnaires or other subjective methods. A further 25 papers did not make any prediction or did not develop a forecasting tool to evaluate "what-if" scenarios. Three papers did develop a simulation-based tool and evaluated a clinical process, however the tool was not used for the evaluation, but to predict trends in epidemiology. One paper was excluded because it evaluated an educational simulation.

After the first assessment, the full articles were read and another 13 papers were excluded. Five papers were excluded because of similar reasons as in the first screening, but which did not become clear after initial reading of the abstracts. Two papers had no available full text online. Six papers did not validate their methodology in any way and were therefore deemed unreliable and were subsequently excluded.

After completion of the second assessment, 20 papers were included. The full inclusion- and exclusion-process is visualised in figure 2.

Table 2: Distribution of the simulation methodologies and statistical models described in the papers divided per category.

Computer Simulation	12		
		Discrete Event Simulation	10
		Queueing Theory	2
Statistical Analysis	3		
		Regression analysis	3
Statistical modelling	2		
		Markov models	1
		Structural equation modelling	1
Qualitative modelling	3		
		Process mapping	2
		Cognitive modelling	1

3.2 Content Evaluation

Table 3 displays an overview of information extracted from the included papers: the authors, model or simulation methodology used, which category it falls into, year of application, field of application, software used, and applicability-score. The distribution of the methodologies per corresponding category is displayed in table 2. DES was the most used method (n=10). All computer simulation methodologies scored 4/10 or higher on applicability according to the scoring system. All other methods scores lower than 4/10. The software used most in these studies was Arena (n=4), followed by Simul8 (n=3), and MedModel

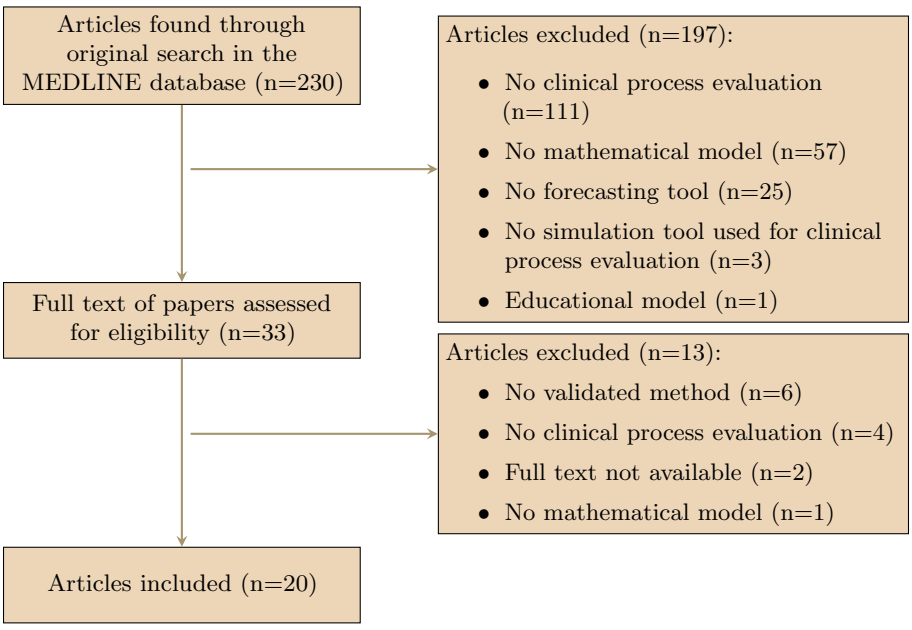

Figure 2: Overview of the selection process

Table 3: Overview of the included papers with information regarding the author, the model or simulation and its corresponding category, year and field of application and software used.

Authors	Model name	Model category	Year	Field	Software	Score
Asaduzzaman M et al.[24]	Queueing theory	Computer Simulation	2006	O&N	None provided	6
Bae KH et al.[25]	Discrete Event Simulation	Computer Simulation	2012	Long Term Care	Simio	7
Baia Medeiros DT et al.[26]	Discrete Event Simulation	Computer Simulation	2016	Mental health and psychiatrics	Simul8	8
Bowers J et al.[27]	Process mapping	Qualitative modelling	2001	New diagnostic and treatment center	Excel	2
Cai H et al.[22]	Discrete Event Simulation	Computer Simulation	2009	Surgery; Independent Clinic; ED	MedModel; Arena; FlexSim; Simul8	10
Ferraro NM et al.[28]	Discrete Event Simulation	Computer Simulation	2013	O&N	MedModel	10
Fontanesi J et al.[29]	Process mapping	Qualitative modelling	2002	Vaccination	OCPE-S and CART	2
Gupta D et al.[30]	Discrete Event Simulation	Computer Simulation	2001	Cardiology	None provided	9
Hung GR et al.[31]	Discrete Event Simulation	Computer Simulation	2005	ED	Arena	4
Kaw N et al.[32]	Structural equation modelling	Statistical modelling	2018	Nursing	R (package mgcv)	2
Luengo-Fernandez R et al.[33]	Regression analysis	Statistical Analysis	2012	Cardiology	None provided	3
Lyon ME et al.[34]	Discrete Event Simulation	Computer Simulation	2019	COVID-19	Simio	4
Monks T et al.[35]	Discrete Event Simulation	Computer Simulation	2013	Stroke	Simul8	9
Nas S et al.[36]	Discrete Event Simulation	Computer Simulation	2017	ED	Arena	4
Olaisen RH et al.[37]	Regression analysis	Statistical Analysis	2013	PC	None provided	2
Roberts RR et al.[38]	Regression analysis	Statistical Analysis	2000	Health acquired infection	None provided	2
Simons PA et al.[23]	Markov models	Statistical modelling	2012	H&N cancer radiotherapy	None provided	3
Steins K et al.[39]	Discrete Event Simulation	Computer Simulation	2006	IC	Arena	5
Takagi H et al.[40]	Queueing theory	Computer Simulation	2011	O&N	None provided	7
Wooldridge AR et al.[41]	Cognitive modelling	Qualitative modelling	2013	PC	Adobe Illustrator	3

Abbreviations: O&N: Obstetrics and Neonatal Care; H&N: Head and Neck; ED: Emergency Department; COVID: Corona Virus Disease; PC: Primary Care; IC: Intensive Care

and Simio (n=2). One paper (Cai et al.[22]) was a case report discussing three different utilisations of DES and described, therefore, multiple fields of application and different software packages.

One study[23] was notably executed within a radiotherapy centre. This study, unfortunately, did not aim to assess similar outcomes as HollandPTC. They redesigned the in-house processes and measured the effects on patient outcomes using an economic Markov model (statistical modelling) and evaluated the cost-effectiveness. This methodology was not in accordance with the demands of HollandPTC and, therefore, scored low on applicability according to the scoring system (3/10).

4 Discussion

This literature review aimed to propose a methodology which is most suitable for an analysis of the healthcare processes within HollandPTC. Of the 20 included papers, DES was applied by 10 papers, which makes this methodology, by far, the most frequently used methodology. This method, subsequently, scored high on applicability the most frequently. DES is, therefore, the most suitable methodology. DES has its disadvantages: large run-times and availability of software. These should be considered when executing DES in subsequent research.

The applicability-score was based on the

demands, wishes and requirements of HollandPTC. A potential confirmation bias exists where the requirements for a potential methodology naturally lead to DES being the most favourable. This is not considered problematic for this literature review because the purpose was to investigate applicable methodologies when specifically keeping the requirements in mind. It is important to note that the applicability-score has to be reconsidered when this literature review is used for different applications.

4.1 Conclusion

This review provided an overview of the available simulation-based optimisation methodologies with the purpose of proposing one methodology which is most applicable to perform an analysis of the healthcare processes within HollandPTC. DES is the most applicable methodology because it allows for the simulation of complex processes, such as the processes within HollandPTC, and because it satisfied the requirements of HollandPTC best.

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Part II

Thesis

Chapter 1: Introduction

Cancer is a leading cause of death worldwide according to the World Health Organisation (WHO)[1]. Radiation therapy is one of the most widely applied treatment modalities against cancer, both as solitary treatment or used in combination with surgery or chemotherapy[2].

Proton Beam Therapy (PBT) is an emerging radiation therapy modality with a distinct advantage over conventional photon radiation due to the highly localised deposition of energy[3]. In selected patients, this results in a lower dose delivered to the Organs At Risk (OAR) compared to photon radiation, potentially resulting in less toxicity[4]. The past decades of scientific progress led to the improvement of the treatment modality, causing the emergence of numerous PBT facilities globally[3–5]. As of December 2020, 110 particle therapy facilities have emerged worldwide. HollandPTC (Proton Therapy Centre, Delft, The Netherlands) is one of three facilities located in the Netherlands[5].

HollandPTC is able to treat multiple types of cancers and facilitates education and research while maintaining high standards of personalised treatment. Treatment with PBT, however, is highly complex due to a variety of activities integrated into the workflow to ensure treatment quality and patient safety. Though HollandPTC intends to scale up its capacity, insight into the workflow, processes and their interactions is insufficient to effectively implement measures to do so. A simulation-based application that can visualise the workflow and make predictions accordingly is therefore desired.

For a complete understanding of the thesis, some elementary knowledge of all aspects of PBT is required. In this chapter, the different aspects of PBT will be discussed. First broadly from a historical, physical, and clinical perspective, followed by a more focused introduction on HollandPTC, culminating in the problem definition. The chapter will conclude by proposing the aim and purpose of the thesis.

1.1 Proton Beam Therapy

1.1.1 Historical background

The field of radiotherapy has seen numerous scientific advances over the past 125 years[4]. It started with the emergence of X-rays used for medical applications in 1895 which became one of the main treatment modalities in the physicians' arsenal against malignancies[6]. The decades after the first application, the modality was greatly improved. The main focus being the reduction of dose to healthy tissue while maintaining prescribed doses to targeted tumours, spearheaded by the introduction of fractionated radiation therapy in the 1920s and 1930s[7]. Advances in imaging, patient setup and the emergence of computerised treatment planning, have led to more precise dose distributions. However, residual dose delivered to healthy tissue remained.

In 1946, Robert Wilson outlined the first clinical benefits of using heavy particle radiation[8]. He discussed that the finite range of these particles could be utilised for precise treatment based on the physics of protons. In the next decade, experiments using proton beams for medical use would be performed, concluding with the first patient treated with PBT in 1954[9]. Further experiments on fractionated dose delivery, biological effects, and different indications would soon follow[10–13].

The first proton therapy facilities opened in Russia, starting in Moscow in 1967, and Japan in 1979 in Chiba[14, 15]. Other countries soon followed in the late 1980s and early 1990s. These facilities were predominantly linked to research institutions and the number of patients treated remained modest. The first hospital-based facility was built in 1990 in California, USA [16], but treatment was still considered experimental. The first commercially viable

equipment became available in 2001 and in-hospital or independent clinics would rapidly appear worldwide during the following years[5].

1.1.2 Background on physics

PBT is a complex treatment modality with numerous facets, expertise, and processes needed for successful treatment. For a complete understanding of the thesis, a broad understanding of all steps within the treatment process is recommended. This section will, therefore, be dedicated to the physics of PBT to enable this broad understanding of the corresponding processes.

Proton accelerators
The two types of machines most commonly used for particle acceleration are cyclotrons and synchrotrons. A cyclotron uses a constant magnetic field with two or four D-shaped electrodes using a constant oscillating voltage to accelerate charged particles. The protons are extracted from a tank of hydrogen in the centre and travel in a circular motion until they exit the cyclotron. They are directed towards the target using strong magnetic fields. This circular motion is where the name is derived from. A synchrotron, on the other hand, uses synchronised increasing magnetic fields to accelerate protons. This synchronisation allows for the acceleration to higher speeds than the cyclotron can achieve. However, the synchrotron needs more area to operate. Synchrotrons are most commonly used in research facilities, such as CERN[17]. A cyclotron is smaller, but cannot accelerate protons to the extremely high velocities that are required for some types of research. A cyclotron, however, can reach common therapeutic velocities (the maximum is in the 230-250 MeV range) and is, therefore, the most commonly used type of accelerator for stand-alone proton treatment facilities, such as HollandPTC[4, 18].

After acceleration, protons are magnetically guided to the treatment room where they enter the treatment nozzle mounted on a rotating gantry. The gantry is then used to aim the beam at the target tissue inside the patient. Optimal directions can be achieved by changing the gantry position and by rotating the couch which supports the patient[19]. The cyclotron used in HollandPTC serves multiple gantries. The beam is, therefore, directed towards the requested gantry in an alternating order or in order of priority. Figure 1.1. shows the layout of three gantry treatment rooms for PBT and one research room.

This nature of beam production and guidance leads to a practical limitation of PBT: the beamtime, i.e. the time the beam is directed towards a target. Beams can only be directed towards one target at a time, meaning that synchronous measurements, research, or treatment is not possible. This adds complexity to logistic planning and scheduling.

The Bragg peak
The difference in dose deposition between photons and protons is shown in Figure 1.2. The thinner line corresponds to the depth-dose curve of X-ray photons in tissue. X-ray photons lose energy during interactions with tissue, but will never lose speed, for their speed is always constant: C (299,792,458 m/s). Photons always have residual energy after leaving the target. Protons, on the other hand, lose speed during interactions with tissue. Eventually, protons will be fully stopped. The thicker line shows the characteristic depth-dose curve of protons called the Bragg peak. This curve shows a buildup of dose in front of the target and a peak at the target where most of the dose is deposited. After the peak, a steep decline in dose is observed as the protons are stopped completely.

Figure 1.1: Layout of three gantry treatment rooms for PBT. Protons are guided from the cyclotron to the gantry. This diagram was developed by HollandPTC

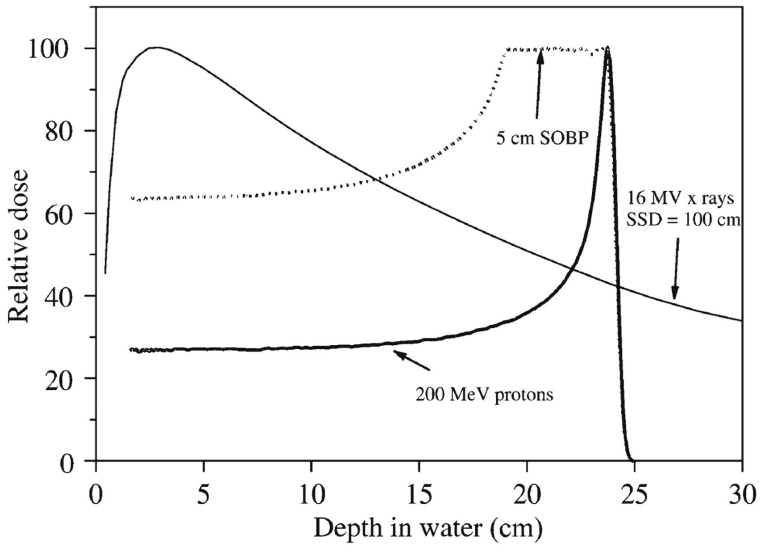


Figure 1.2: Depth-dose curves for a 200 MeV proton beam with a 5 cm spread-out Bragg peak (SOBP), compared with a 16 MV X-ray beam. The curves are normalised in each case to 100 at maximum dose[20].

Some residual dose will be deposited due to scattered protons and expelled particles. This amount of residual dose is dependent on the initial energy of the beam and the depth of the target. More depth leads to more interactions and a more spread-out Bragg peak[4].

It must be noted that this Bragg peak is the predominant advantage of PBT compared to conventional radiotherapy. The Bragg peak allows for precise planning of the dose distribution. However, slight uncertainties, anatomical changes, or movement can lead to a shift in the position of the Bragg peak caused by more or fewer interactions with tissue. This shift can lead to dose being delivered to healthy tissue. Exact and robust planning is, therefore, required.

1.1.3 Robust Planning

Radiotherapy aims to deliver therapeutic doses to tumours while minimising the risk of side effects in healthy tissue. Radiotherapy treatment planning and delivery for both photon radiotherapy and PBT faces uncertainties. The first uncertainty is introduced during the definition of the gross tumour volume (GTV) and Organs At Risk (OAR) caused by the finite resolution of medical images and the fact that imaging modalities are incapable of visualising tumour structures on a microscopic level. Furthermore, patient-specific tissue tolerances and the dose needed for control of the tumour are uncertain[21].

Precise and robust planning is the major challenge in all types of radiotherapy, as mentioned previously. PBT, however, is more sensitive to certain types of uncertainties due to the steep dose fall-off at the distal end. Uncertainties in the planning or dose delivery can have important consequences for the patient. In PBT, these uncertainties are much more prominent compared to conventional radiotherapy because of the more precise dose distribution. In this section, some of the major causes of uncertainties are discussed as well as how the current normal workflow is designed to minimise these uncertainties. Each indication has its specific set of uncertainties and minimisations making the entire workflow more complex.

Uncertainties during PBT planning

Movement

Movement can be defined in two ways: (1) intra-fractional movement (during a single treatment) and (2) inter-fractional movement (between treatments).

Intra-fractional movement can occur because of multiple different causes and each cause is solved differently. General motion of the body during treatment is highly undesirable. This is minimised by fixating the patient to the table or making sure that specific markers on the body are lined up perfectly to in-room laser systems. Fixation of the head and neck is done by the development of a patient-specific mask that precisely fits over the face and secures the entire head. Respiratory movement is caused by the motion of breathing. This specific motion only occurs in tumours located around the thoracic area. The effect can be minimised by adding a margin around the tumour during planning to correct for breathing motion, making sure the entire tumour is always irradiated[22].

Tumours in the eye have a specific problem when it comes to motion. The eye cannot be secured, so the patients have to fixate their gaze to a motionless point.

Inter-fractional movement is partly minimised by the use of the aforementioned mask. Furthermore, a Cone-Beam Computed Tomography (CBCT) scan is made before treatment to evaluate the position of the patient. If uncertainties still arise, a complete CT is made to evaluate the robustness of the plan and to potentially adapt the plan to the new position.

As is apparent, most movement uncertainties are minimised by measures implemented within the workflow to increase the reproducibility of the treatment, limiting the effects ahead of treatment. Adaptive approaches are used when the indication arises. More real-time solutions, such as tracking and repainting, that could increase the accuracy further are not completely integrated into clinical practice yet[22].

Anatomical changes
The anatomy of a patient is not rigid. Changes in body mass, fat percentage, fluid retention, or tumour size can affect the treatment plan. Patients are, therefore, regularly checked and weighed to estimate if anatomical changes occurred and what the appropriate course of action will be. Some patients lose weight during treatment and have to have their plan evaluated. This is done by performing a CT scan and verifying the plan on the new anatomical situation. If the plan is not sufficient, the plan gets adapted and the patient gets treated using the new plan.

Posture
A major uncertainty, similar to anatomical changes, is caused by changing posture. This is similar to inter-fractional movement. During treatment, the skin and tissue below the skin of the patient receives dose (caused by the plateaued build-up region of the Bragg peak) and starts to ache. During treatment, patients are asked to lay motionless for a few minutes. When the initial posture is starting to be too uncomfortable, the plan has to be adapted and the patient has to be treated according to the new plan.

Implants
Uncertainties can be caused by metal implants. These are common around the tumour site, where they were left behind during previous surgery. Tantalum clips, for example, are commonly used to locate the tumour in thoracic, mammary, and ocular tumours[23, 24]. Metal implants, however, attenuate the beam, leading to uncertain dose distributions. Furthermore, these implants can lead to metal streak artefacts on CT images, leading to uncertainties during planning[25]. Most of these uncertainties are minimised by using larger margins around the implant corresponding to protocols during treatment planning. A small portion of patients cannot be treated because too many implants are present or because of the complex location of these implants.

Air gaps
Air creates uncertainties during treatment planning. Air attenuates the beam much less than water, causing a possible underestimation of the dose after an air gap. This is most common in thoracic tumours, due to the lungs. During planning, the algorithms used to calculate the dose distribution take these air gaps into account. During treatment, however, the size of these gaps can change, causing a possible overshoot of dose behind the tumour.

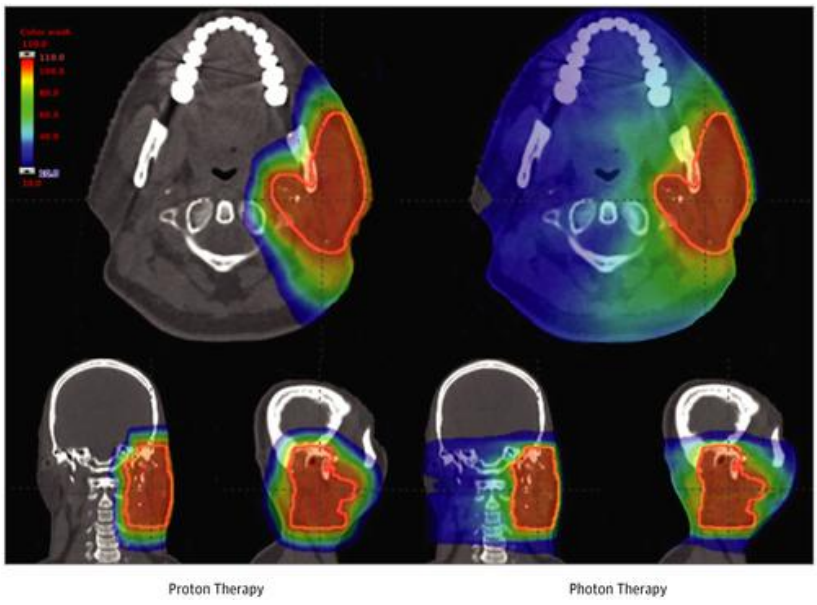


Figure 1.3: Proton (left) vs. Photon (right) therapy dose distributions[26]

Head & neck tumours are especially susceptible to changes in the size of the air gaps because the head & neck region contains a lot of sinuses. During treatment of head & neck tumours, the plan is, therefore, evaluated weekly, thus reducing the associated uncertainties.

All of the discussed uncertainties cause the need for complex robust planning systems. During planning, different structures are delineated: GTV, Clinical Target Volume (CTV), and the OAR. An optimal plan would have CTV coverage of 100% while limiting the dose at the OAR to 0%. In practise, this is not possible and multiple trade-offs have to be made to achieve a clinically acceptable plan. The problem becomes one of optimisation. In treatment planning optimisation systems, the CTV is the target and the OAR are used as constraints. A planning system then calculates numerous scenarios and tries to find the most ideal dose distribution. The planning system furthermore calculates the two least favourable scenarios: the voxelwise minimum (when the least amount of dose is delivered to the CTV) and voxelwise maximum (when the most dose is delivered to the CTV)[27]. These plans are subsequently checked by planning employees, physicians, and physicists to verify the clinical acceptability while ensuring patient safety. Figure 1.3 shows the difference in dose distribution of a proton vs. a photon plan[26].

1.1.4 Clinical Indications

The Dutch government has approved PBT based on a distinction between standard indications and model-based indications defined by Dutch health authorities[28]. Standard indications are described as indications where PBT is the first choice of treatment: intra-ocular tumours, chordoma and chondrosarcoma, and paediatric tumours. For model-based indications, patient selection is performed by comparing proton and photon treatment plans, to select patients most likely to benefit from PBT in terms of prevention of side effects and to determine which treatment gets reimbursement from insurers[29]. Both plans are compared using the difference in Normal Tissue Complication Probability (ΔNTCP). Patients are selected for PBT when their ΔNTCP is above a disease-dependent threshold and a benefit from PBT can be expected[28, 30, 31]. Model-based patient selection needs to be performed for tumours of the head and neck, mammary glands, lung, prostate, and neurological tumours[32].

Apart from the standard and model-based indications, PBT shows potential advantages for the treatment of gynaecological and anal tumours due to the lower dose to the bladder, bowel and hip joints. It may also have potential advantages for pancreatic, oesophageal, gastroesophageal junction, gastric, and hepatobiliary tumours, as it delivers a lower dose to the lungs, small bowel, liver, heart, kidneys and spinal cord, and may also be used for bone and soft tissue sarcomas[19, 33, 34].

1.2 HollandPTC

HollandPTC is one of the three PBT facilities in the Netherlands and opened its doors in 2018[32]. It is an independent clinic with a focus on treatment, education, and research. Currently, eight different types of tumours are treated: head & neck, neurological, hematologic/lymphomas, lung, breast, chordomas, chondrosarcomas, and ocular. In the near future, oesophageal tumours will also be included as new indications[18].

1.2.1 Workflow

Ocular tumours, chordomas and chondrosarcomas are the standard indications treated in HollandPTC, the others indications are all model-based. For these indications, the comparison of the ΔNTCP is done via a Plan Comparison (PC). During a PC a treatment plan is developed based on the CT scan of the referring institute. As much consideration is put into this plan as would be put into a clinical plan. HollandPTC, moreover, considers some model-based indication patients as "Highly-Likely" (HL). The PC plan for HL patients is made using an in-house CT-scan, instead of the CT-scan of the referring institute, because the ΔNTCP is highly likely to be sufficiently high. Considering some patients as HL saves unnecessary imaging steps, speeding up the process. This division between HL patients and non-HL patients adds complexity to the entire workflow.
After a positive PC is acquired, the patient is referred to HollandPTC, where consultations with nurses and physicians are performed, followed by imaging (CT and Magnetic Resonance Imaging (MRI) (if needed)), mask development (if needed), and a Positron Emission Tomography (PET) scan (if needed).
After these intake and imaging steps, HollandPTC starts planning and develops a clinical treatment plan. This step includes numerous verifications, deliberations, and Quality Assurance (QA) steps to ensure an optimal treatment plan and patient safety.

After these steps, the patient is ready to be treated. PBT is performed using fractionated treatment, dependent on the type of tumour and patient characteristics. HollandPTC treats patients five days a week (Monday - Friday). Head & neck patients, for example, need, in general, 35 fractions until completion. These patients, thus, are under treatment for seven weeks[18].

1.2.2 Problem definition

In 2013, the Dutch government approved a total of 2200 patients to be treated annually with PBT in one of the three available Dutch centres[18]. This number is expected to increase as more indications are being considered, both for standard and model-based indications. Currently, however, HollandPTC is not able to match its part of this expected target, due to limited resources such as personnel and equipment. HollandPTC, therefore, aims to increase its capacity in various ways in the upcoming years to be able to treat more patients while maintaining the high quality of personalised treatment, low lead times (time between referral and start of treatment), fast throughput, and ensuring patient safety. The desired increased capacity proves difficult to effectuate because the effects of potential measures and changes to the workflow which would increase capacity are difficult to predict. This makes policy decisions hard to substantiate. It is, therefore, necessary to provide insight into the processes to determine the cause of possible capacity bottlenecks and to investigate the possible impact of process reformations and improvements.

To accomplish this, a forecasting simulation-based application is desired which can model changes in patient flow, throughput, capacity, and resources (personnel, equipment, and facilities), and which can predict the effects of systematic optimisation of the healthcare processes within HollandPTC.

A literature review was performed to determine the most applicable methodology (see Part I) considering the complexity of the workflow within HollandPTC. This review concluded that the methodology called "Discrete Event Simulation" (DES) is the most applicable.

1.3 Aim

The thesis aims to develop a validated DES application that can model the complete workflow of HollandPTC and make predictions on throughput, capacity, lead times, patient flow, and availability of resources. The complete and validated product will be the primary objective of this thesis.

This simulation will subsequently be used to answer the following questions:

"What will be the main causes of capacity bottlenecks when scaling up a proton therapy facility such as HollandPTC?"

"What measures can HollandPTC implement to anticipate these bottlenecks?"

Chapter 2:
Methods

DES was found to be the most applicable simulation methodology for application within HollandPTC (as discussed in Part 1). This project was executed using the typical DES methodology framework described in the literature review by Cai et al.[35]. This framework was modified to fit the scope of the thesis.

The revised framework describes five key steps within the simulation procedure: (1) Data Collection and Analysis, (2) Process Mapping, (3) Base Model Development, (4) Validation, and (5) Scenario Simulation as shown in Figure 2.1. This chapter will first provide background information on DES: theory, terminology, general applicability. The chapter, subsequently, will elaborate on the use of DES within the Thesis according to the revised framework.

Figure 2.1: DES framework as applied in this project, described by Cai et al.[35] and adjusted to fit the scope of the project

2.1 Discrete Event Simulation

Healthcare costs have drastically increased in the last 40 years and healthcare providers have turned to innovative solutions to provide high-quality care at lower costs. DES has risen in popularity because of its ability to aid in decision support for policy design. DES is an operations research modelling and analysis methodology that aids in the evaluation of efficiency and intends to answer "what-if" questions with the goal of improving healthcare systems. DES has been applied to numerous healthcare systems, from emergency rooms to nursing and is widely accepted as a decision support tool because of the large number of studies reported in the literature[36].

In a DES, objects of interest change state at discrete points in time, instead of continuously. The real, continuous world is, therefore, described as a series of discrete events which are logically separable and progress through time[35, 37].

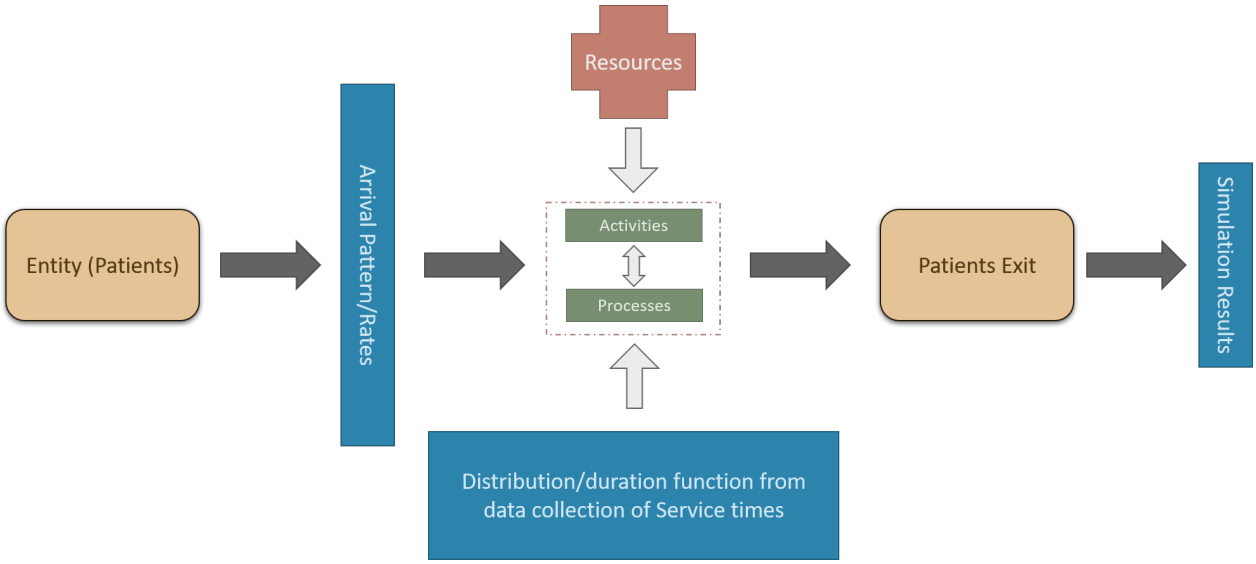


Figure 2.2: Elements of an example DES as described by Cai et al.[35]

2.1.1 Terminology

Table 2.1 describes the DES terminology in the context of its application within HollandPTC.

Table 2.1: DES Terminology in context of HollandPTC

Entity	Entities are the objects of interest moving through the simulation: the patients.
Attribute	Entities possess certain attributes. These influence how the entity behaves within the simulation. An attribute could be, for example, the type of tumour the patient is diagnosed with. An attribute can be altered by events.
Priority	Entities possess a certain amount of priority. This amount determines how the system behaves. High priority entities will get served first. The amount of priority can be altered by events.
Event	Events manipulate the entities. An event can range from simple, e.g. a queue, to complex, e.g. a probability-based interaction including resources and delays. Events happen instantaneously and succeed each other chronologically.
Resources	Resources are the assets for events to occur. These are personnel, equipment, and facilities such as gantries.
Queue	A queue acts as a buffer for entities to accumulate. It releases entities the moment they can progress.
Server	A server "serves" the entity in some way. A server can hold or alter an entity. A server has a service time and a capacity. Each different step in the workflow of HollandPTC can be described as a server.
Delay	Delays can only hold an entity for a specific amount of time. Within HollandPTC, delay describes the necessary time between events until patients can progress to the next step.

2.1.2 Key elements of applying DES

The fundamental elements for using DES in a healthcare setting were described in a literature review by Cai et al. (2019)[35]. These elements are summarised in Figure 2.2. The entities enter the simulation via specific intervals or arrival patterns. These can be modified according to a specific situation. Within the simulation, entities are subjected to activities and processes which determine how the entities will flow through. These activities are dependent on the availability of resources and probabilistic or fixed service time durations. The entities then exit the simulation and the results can be analysed.

2.2 Data collection and analysis

In this first step of the framework, the present situation was assessed. An accurate overview of the current processes was fundamental for an accurate simulation. All activities that the patient had to perform or that had to be performed by personnel for the patient to complete their carepath were investigated and information was acquired regarding activity duration (service time), involved tumour types, location within the carepath, the time between activities (delay), and involved resources.

Data collection was executed using three techniques: extraction, measurements, and inspection. Extraction meant the data collection from electronic medical records from the year 2020 (Neo ZIS|EPD, MI Consultancy), process sheets of 2020 (Microsoft Excel (2018) Microsoft Corporation), or planning software based on 2021 (ARIA Oncology Information System, 1999-2021 Varian Medical Systems).
Measurements were performed on the time duration of certain activities by the researchers and colleagues in the period between January 2021 and May 2021. When extracted and measured data disagreed, the measured data were accepted as true, in consultation with personnel.
During inspection, the execution of activities was observed in the period between January 2021 and May 2021 and interviews with personnel were conducted to verify the extracted or measured data. Inspection was never applied without corresponding extraction or measurements.

In addition to the information regarding the individual activities, process information was extracted from the aforementioned process sheets and planning software, regarding the following topics:

- the distribution of patients between tumour types
- the number of adaptations versus evaluations
- the number of premature terminations of the process
- the distribution of fractionation schemes

2.3 Process mapping

During this step, a pictorial representation of the in-house carepath and workflow was developed. This process map was the foundation of the logic behind the simulation. The process map was developed based on the carepaths defined in ARIA (ARIA Oncology Information System, 1999-2021 Varian Medical Systems) and the experiences of personnel. These carepaths were up-to-date in March 2021. The process map was created using draw.io (2005-2021 diagrams.net).

2.4 Base model development

The third step was the programmatic implementation of the collected data and process map into a base model using a programming environment: Simulink (MATLAB, (2020). R2020b. Natick, Massachusetts: The MathWorks Inc.). Simulink is a graphical programming environment for modelling, simulating and analysing continuous or discrete systems. The extension SimEvents (R2020b) provided the needed DES engine and component library.

A custom application was developed in MATLAB using App Designer: the HPTCapp. This application allowed users to manipulate the simulation and analyse results. Not all features, functionalities, and components of the simulation and the application will be discussed. For more in-depth information on the HPTCapp, see the Dutch user manual on page 58. This thesis will primarily elaborate on the functionalities necessary for a complete understanding of the performance, applicability, and relevance.

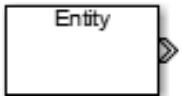
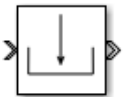
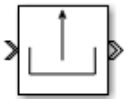
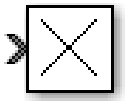
There are eight different tumour types defined within HollandPTC. These were all given three or four letter codes based on their Dutch names. The eight different tumour types and their corresponding codes are: Head & neck tumours (KNO); Neurological tumours (NEU); Lung tumours (LONG); Lymphomas (LYM); Oesophageal tumours (OES); Mammary tumours (MAM); Chordomas and Chondrosarcomas (CHO); and ocular tumours (OOG).
The seven different types of employees were similarly given codes based on their Dutch titles. The seven different types of employees and their corresponding codes are: Nursing Specialist (ZC); Medical Imaging and Radiation-specialist (MBB); Radio-Therapeutic (Radiation) Oncologist (RTO); Clinical Physicist (KF); Dose Planner (DPL); Medical Secretary (MS); and Clinical Physical Worker (KFM).

2.4.1 Simulation components

An overview of the most frequently applied SimEvents and Simulink blocks is provided in Table 2.2 on page 27.

The variables service time, amount of delay, switching criterion, resource amount, and type of resource are non-adjustable variables based on the collected data and the developed process map. Service time can be a constant value or can be based on an input signal.
When the time to perform an activity was considered constant by personnel or measured to be almost non-varying, the service time was set to a constant value. When the time to perform an activity had a relatively high variance, it was modelled using a normal distribution around the mean time, the input signal was randomly generated around that mean based on the extracted or measured standard deviation. More complex service time distributions were simulated using custom-built mathematical input functions.

Table 2.2: Overview of the SimEvents and Simulink components

Icon	Name	Variables	Explanation
	Entity Generator	• Arrival Rate • Attribute • Priority	This block generates Entities (patients). Entities are assigned certain attributes (e.g. the tumour type). The attribute defines how the entity flows through the simulation and what activities the entity will be subjected to. The number of priority defines the rate at which entities get served. The arrival rate defines the interval between generated entities and can be varied according to user input.
	Entity Queue	-	The queue holds entities while they are unable to progress. Entities are released when possible. All queues within the simulation are set to FIFO: First In First Out and have a limitless capacity. Information regarding the number of entities in the queue is later used to calculate capacity bottlenecks.
	Entity Server	• Service Time	A server describes an event. Service time, the time to perform an activity (as discussed in Section 2.2) can be constant or variable, dependent on an input function. Certain activities can modify the attributes of entities to redefine their pathway.
	Entity Transport Delay	• Amount of delay	This block retains entities for a specific, indicated amount of time. This block simulates the standard minimum wait times between activities.
	Entity Input Switch	-	The input switch merges entity flows.
	Entity Output Switch	• Switching criterion	The output switch separates entity flows based on the switching criterion. This separation can be done probabilistically; based on a signal input; or based on entity attribute. Separation based on attribute is used, for example, to guide entities through their corresponding carepath based on their tumour type.
	Entity Replicator	-	This block duplicates entities. This is used to guide entities through non-chronological or parallel activities, or to extract intermediate information.
	Resource Pool	• Resource amount	This block defines an available resources within the simulation.
	Resource Acquirer	• Type of resource • Amount acquired	This block withdraws resources from the pool based on the type and the amount defined by the data analysis.
	Resource Releaser	-	This block returns the withdrawn resources to the pool.
	Entity Terminator	-	This block destroys entities. Information regarding the number of entities arrived can be used for further analysis and is the main output of the simulation.

The simulation, furthermore, contains variables that are adjustable by the user. These variables determine the simulation time, the number of resources, the arrival rate of entities, and process parameters such as the percentage of HL patients and opening hours. These variables are included in the HPTCapp (for more information about these adjustable variables, see the manual on page 58). The simulated time frame (simulation time) includes a warm-up period. This is a short extension of the simulation time to allow the simulation to reach a steady-state and produce more narrow confidence intervals. Warm-up periods of 0.05 years were used in all simulation runs.

In addition to adjustable and non-adjustable variables, flow probability distributions were implemented based on the extracted process information of 2020: the number of adaptations versus evaluations, the number of premature process terminations, and the distribution of fractionation schemes. These distributions described the probability that an entity would follow a certain path or the number of times an entity would undergo a certain activity.

2.4.2 Output, outcomes, and calculations

The primary output of the simulation was the arrival of entities at an Entity Terminator (see Table 2.2). The Entity Terminator outputs a time vector and a corresponding vector describing the number of patients that arrived at that point in time. Three of these Entity Terminator points are incorporated within the simulation. This means that information about entities was extracted at 3 points within the simulation. These three points of measurement are: (1) Before the simulation (pre-intake); (2) right before the first irradiation (pre-treatment); and (3) right after the last irradiation, after completion of the carepath (post-treatment).

With these three points of measurement, calculations were performed to determine primary and secondary outcome values. Primary outcomes were the number of patients starting treatment (for each tumour type); the number of patients treated (for each tumour type); and the number of early terminations of the process. As a secondary outcome, the lead times (times between pre-intake and pre-treatment) were calculated.

As a tertiary outcome value, information on queue lengths was extracted. All Entity Queues and Resource Acquirers output a time vector and a corresponding vector describing the number of patients waiting in the queue at that time point. Using a user-adjustable threshold, the activities with a queue length above that threshold are visualised. This functionality was used to determine the capacity bottlenecks, i.e. the activities where patients accumulated leading to HollandPTC not being able to treat all referred patients. The queue length threshold should be adjusted according to the simulated situation. While simulating high numbers of patients, queues are naturally longer without this being caused by accumulation due to inefficient processes. While simulating 500 patients or less, a queue length of 10 can be considered unnatural accumulation. While simulating more than 500 patients, an unnatural queue length should be closer to 25 patients.

2.5 Validation

The simulation was validated to determine the correctness and to ensure that it accurately represented the real situation. Validation was performed using three methods: (1) face validation, (2) internal validation using real-world data and extremes, (3) and external validation using historical data.

During face validation, involved employees were guided through the simulation steps to confirm the logical succession. Furthermore, the simulation and the application were presented to all employees to confirm the logic and applicability.

During internal validation, at first, extreme values were simulated to test whether the simulation would operate as expected. Extremely high values (1000 patients per tumour type) were expected to cause the simulation to stall due to the accumulation of patients. Extremely low values (0 patients per tumour type) would cause no patients to pass the points of measurements, causing null outcomes.
Internal validation, secondly, was performed by simulating the historical data which was used to build the simulation. Table 2.3 shows the input values per adjustable variable for this validation. The simulation time was set to 1.05 years to account for the warm-up period of the simulation. The simulation was run ten times and the outcome values were extracted and calculated. The average simulated outcome values were then compared to the extracted real outcome values. The similarity between the primary outcome values(number of patients pre-treatment and post-treatment) was calculated by examining whether the real outcome value fell within the Confidence Interval (CI) of the simulated range using $\alpha = 0.05$.
Secondary outcome value similarity was examined by comparing the lead time Interquartile Ranges (IQRs) of both the real and the simulated data using boxplots.

Table 2.3: Input values per adjustable variable for the internal validation using historical data and for the external validation using historical data from September to December 2019 and January to June 2021

Process variables				Resources				Referred patients per year			
	2020	2019	2021		2020	2019	2021		2020	2019	2021
Simulation time [h]	9109	3470	4338	ZC	2	1	2	KNO	113	114	133
HL [%]	6	0	20	RTO	4	4	3	NEU	90	75	82
Hours worked per day	5	4	5	MBB	11	6	10	LONG	21	0	22
				KF	4	4	4	LYM	4	3	20
				DPL	3	2	2	OES	0	0	0
				MS	2	2	2	MAM	99	51	98
				KFM	4	4	4	CHO	14	18	18
				Computers	5	4	5	OOG	33	0	53

Tertiary outcome values were compared qualitatively. No data on the real capacity bottlenecks were available. Employees were, therefore, asked about what activities they expected to be the biggest bottleneck throughout the simulated time frame. This subjective outcome was then compared to the simulated capacity bottlenecks to verify whether they agreed. All queue length thresholds were used to extract accumulation and a queue length ≥ 10 was considered to be unnatural accumulation.

Finally, external validation was performed using historical data other than data from 2020. Two time frames were simulated: 2019 from September to December and 2021 from January to June. These time frames were chosen because the healthcare processes were comparable to 2020 and because of availability of data. Table 2.3 shows the input values per adjustable variable for both time frames. The simulation time was, again, set to 1.05 year to account for the warm-up period of the simulation. The simulation was run ten times and the outcome values were extracted and calculated. Similarity calculations were performed identically to the internal validation.

2.6 Scenario simulation

To answer the questions posed in Section 1.4, predictions on future scenarios were made. As discussed earlier, HollandPTC has set a target to treat 600 patients in the upcoming years and is interested in how this can be effectuated. Scenarios were simulated according to a waterfall approach. In the first scenario, the number of referred patients in 2020 was extrapolated to match the target of 600 patients treated, while the resources, HL percentage, and hours worked remained the same as in 2021. These values were set to the same values as in 2021 because this better described the near future. Early terminations were taken into account and corrected for, using the distributions extracted from the 2020 data. The number of patients used as input is described by Equation 1 and was rounded to the nearest five. Table 2.4 shows the input values per adjustable variable for this scenario.

$$N_{TumorType} = \frac{600 \cdot f_{TumorType}}{1 - P_{term}} \cdot t_{sim} \tag{1}$$

Where $N_{TumorType}$ is the referred number of patients used as input of the simulation, $f_{TumorType}$ is the fraction of that tumour type, P_{term} is the probability of early termination, and t_{sim} is the simulation time (1.05).

Table 2.4: Input values per adjustable variable for the first scenario simulation

Process variables		Resources		Referred patients per year	
Simulation time [h]	9109	ZC	2	KNO	590
HL [%]	20	RTO	3	NEU	195
Hours worked per day	5	MBB	10	LONG	15
		KF	4	LYM	15
		DPL	3	OES	15
		MS	2	MAM	260
		KFM	4	CHO	10
		Computers	5	OOG	65

The output was examined and information on capacity bottlenecks was extracted. A resolution to arisen capacity bottlenecks was simulated in the next scenario. This was repeated until 600 patients were simulated to be treated and all queues lengths were < 25 patients. The simulation time for all scenarios was set again to 1.05 years to account for the warm-up period. All predictive simulations were run ten times and corresponding CI's were calculated.

Using this method, a list of recommended modifications to the current processes was developed which can be used as guidelines towards a systemic increase in capacity.

Chapter 3:
Results

This chapter will discuss the results using the same structure as the framework described in Chapter 2. The Base Model Development step did not generate presentable results, for the DES model itself is the result. Instead, this chapter presents the collected data and designed process map on which the simulation is based as well as the results of the validation and predictions.

3.1 Data Collection and analysis

The information regarding the individual activities (name, involved tumour type, service time (means and standard deviations), amount of delay, involved resources, server capacity, and method of acquisition) is displayed in Table A.1 (Appendix A, page 47).
Most activities have a resource dependent capacity, meaning that as many activities can run in parallel as there are available resources. Constant service times only display their mean time value. Normally distributed service times also include their standard deviation. For delineation, a custom-build input signal was developed which described the real situation using Equation 2:

$$t = \frac{\ln(|N(\mu,\sigma^2)|)}{3} + 3 \tag{2}$$

Where $N(\mu,\sigma^2)$ is a Poisson distributed random number generator with $\mu = 1$ and $\sigma = 0.5$.

OES tumours have not been treated yet. Therefore, no data on this tumour type could be included. However, this is a tumour type that will be treated in the near future and was necessary to include in the simulation development for an accurate prediction of future scenarios. This tumour type is similar to the LONG and LYM pathways. Chordomas and Chondrosarcomas are rare and their pathways are very similar. These are also described together.

Table 3.1 shows, per tumour type, the percentage of patients whose plan had to be adapted and the percentage of patients who were excluded from the process prematurely. Table 3.2 shows the distribution of the locations where early termination of the process was observed. Table 3.3 shows the distribution of the fractionation schemes per tumour type. Within the simulation, these percentages determined how patients would flow through the simulation.

The probability of a second plan adaptation is only applicable to those who already had a first plan adaptation. Patients following the OOG pathway did not need plan adaptations and did not experience premature termination of the process.

The most common reason for early termination was a negative PC. Other reasons included personal preference of the patient, logistic problems, unexpected complications, COVID-19 related, and other, not well-documented reasons.

3.2 Process mapping

The process map is displayed in Figure B.1 (Appendix B, page 53). LONG, LYM and OES tumours are described together under an overarching tumour type: Thoracic tumours (THO), because their carepaths and logistics are similar.

Table 3.1: Distribution of adaptation and termination probabilities between tumour types

	Probability of first plan adaptation [%]	Probability of second plan adaptation [%]	Probability of premature termination of the process [%]
KNO	23.3	14.3	68.9
NEU	1.32	0.00	18.2
LONG	25.0	0.00	65.0
LYM	33.0	0.00	50.0
MAM	12.6	0.00	19.3
CHO	13.3	50.0	23.5

Table 3.2: Locations within the process map where early termination of the process was observed and the probability of early termination at that location

Location within the process map	Probability [%]
Before PC	22.0
After PC	73.0
After delineation	3.2
After planning	1.6

Table 3.3: The different tumour types and their distribution between fractionation schemes within HollandPTC. The number on the left is the possible number of fractions. The number on the right describes the distribution within that specific tumour type.

KNO		**NEU**		**LONG**		**LYM**		**MAM**		**CHO**		**OOG**	
28	5%	25	5%	24	17%	15	45%	15	54%	35	100%	4	100%
33	3%	28	61%	25	33%	18	55%	20	37%				
35	92%	30	14%	30	50%			22	5%				
		33	20%					25	3%				
								30	1%				

3.3 Validation

Face validation confirmed the simulation's logic and applicability. No alterations were suggested and the simulation was approved to be compatible with the current processes. Internal validation using extreme values led to the expected outcomes and error messages included in the manual on page 58.

Table 3.4, 3.5, and 3.6 show the comparison of the simulated means to the real data of the primary outcome values of the validation on historical data of 2020, 2019, and 2021 respectively. In the internal validation of 2020, KNO (pre- and post-treatment) and NEU (post-treatment) were overestimated while MAM (pre- and post-treatment) was underestimated. OOG had little variation and outputted the same value consistently. Totals and early terminations were correctly simulated according to the internal validation.
In the external validation of 2019, KNO was overestimated while the other tumour types were within the CI or marginally deviated from the CI. Totals and early terminations deviated by the same amount as KNO.
In the external validation of 2021, NEU and OOG were overestimated both pre- and post-treatment. The OOG tumour type was simulated with little variation, similar to 2020. The totals and early terminations were, likewise, overestimated.

In general, small patient groups tend to deviate more proportionally: a deviation of three patients for the LYM group for example corresponds to a 270% deviation, while three patients is not considered a large deviation in general.

Figure 3.1a, 3.1b, and 3.1c show the boxplots of the secondary outcome values of the three validation runs: the lead times. Simulated lead times were consistently simulated and their medians were all around 10 days. Real lead times had a higher mean, more variation and more outliers at the high end. The real data of 2020 has the most outliers of the three situations and the data of 2019 had the largest range. The IQR of the simulated data from 2020 deviated slightly from the IQR of the real data of 2020. The IQR of the simulated data from 2019 deviated more from the IQR of the real data. The IQR of the simulated data of 2021 was within the IQR of the real data.

The expected bottlenecks in 2020 were reasoned to be the DPL activities. The simulation predicted the treatments and PC to be the largest bottlenecks (threshold ≤ 5 entities). The expected bottlenecks in 2019 were reasoned to be the DPL activities and the MRI Planning. The simulation predicted the treatments to be the largest bottlenecks (threshold ≤ 5 entities). The expected bottlenecks in 2021 were reasoned to be the DPL activities. The simulation predicted the Plan Team Meeting and the Delineation to be the largest bottleneck (threshold ≤ 5 entities).

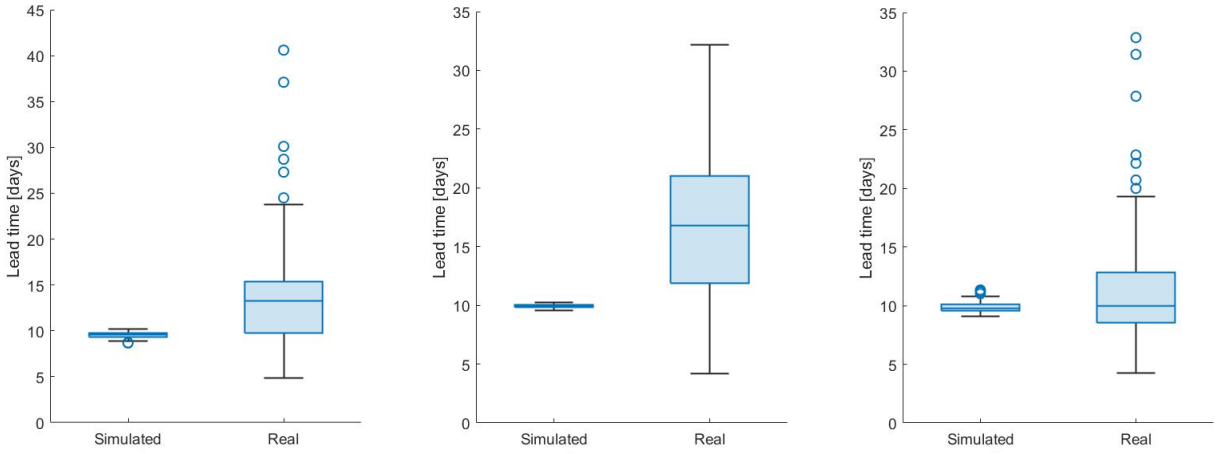


Figure 3.1: Boxplots of the lead times of the three validation runs: (a) 2020, (b) 2019, (c) 2021. The left plot is the simulated data and the right plot is the real data.

3.4 Scenario Simulation

Scenario simulation was performed according to a waterfall approach where the mean total numbers of patients treated were calculated and capacity bottlenecks of ≥ 25 were extracted until an average of 600 patients were simulated to be treated with all queue lengths < 25.
According to this system, four scenarios were simulated as displayed in table 3.7. This table shows the scenario title, description and difference to the previous scenario, mean total patients treated with corresponding CI, extracted capacity bottlenecks with the corresponding threshold, and possible cause of that bottleneck.

Table 3.4: Primary outcomes of the internal validation using historical data of 2020. A positive deviation indicates an overestimation, a negative deviation indicates an underestimation

	Simulated [mean ± CI]	**Real [n]**	**Deviation [n(%)]**	**Real within CI [yes/no]**
KNO pre-treatment	34.2 ± 2.4	30	4(14)	No
NEU pre-treatment	72.7 ± 1.9	72	1(1)	Yes
LONG pre-treatment	6.2 ± 1.1	8	-2(23)	No
LYM pre-treatment	1.8 ± 0.5	2	-0(10)	Yes
MAM pre-treatment	81.2 ± 2.7	86	-5(6)	No
CHO pre-treatment	10.4 ± 1.0	10	0(4)	Yes
OOG pre-treatment	33.0 ± 0.0	33	0(0)	Yes
Total pre-treatment	239.5 ± 5.7	241	-2(1)	Yes
KNO post-treatment	30.0 ± 2.2	26	4(15)	No
NEU post-treatment	66.5 ± 1.5	61	6(9)	No
LONG post-treatment	5.4 ± 1.1	8	-3(33)	No
LYM post-treatment	1.3 ± 0.6	2	-1(35)	No
MAM post-treatment	76.4 ± 2.7	81	-5(6)	No
CHO post-treatment	9.2 ± 1.0	9	0(2)	Yes
OOG post-treatment	33.0 ± 0.0	33	0(0)	Yes
Total post-treatment	221.8 ± 4.7	220	2(1)	Yes
Early termination	141.2 ± 5.7	139	2(2)	Yes

Table 3.5: Primary outcomes of the external validation using historical data of 2019. A positive deviation indicates an overestimation, a negative deviation indicates an underestimation

	Simulated [mean ± CI]	**Real [n]**	**Deviation [n(%)]**	**Real within CI [yes/no]**
KNO pre-treatment	13.2 ± 1.2	7	6(89)	No
NEU pre-treatment	24.8 ± 1.7	25	-1(0)	Yes
LYM pre-treatment	0.2 ± 0.2	0	0(0)	Yes
MAM pre-treatment	16.4 ± 0.8	16	0(2)	Yes
CHO pre-treatment	4.8 ± 0.9	6	-1(20)	No
Total pre-treatment	59.4 ± 2.2	54	5(10)	No
KNO post-treatment	9.7 ± 1.2	4	6(143)	No
NEU post-treatment	18.5 ± 1.3	16	3(16)	No
LYM post-treatment	0.2 ± 0.2	0	0(0)	Yes
MAM post-treatment	13.8 ± 0.7	14	-0(1)	Yes
CHO post-treatment	3.5 ± 0.8	4	-1(13)	Yes
Total post-treatment	45.7 ± 2.7	38	8(20)	No
Early termination	49.8 ± 2.3	54	-4(8)	No

Table 3.6: Primary outcomes of the external validation using historical data of 2021. A positive deviation indicates an overestimation, a negative deviation indicates an underestimation

	Simulated [mean ± CI]	**Real [n]**	**Deviation [n(%)]**	**Real within CI [yes/no]**
KNO pre-treatment	19.0 ± 1.9	17	2(12)	No
NEU pre-treatment	30.7 ± 1.1	23	8(33)	No
LONG pre-treatment	3.6 ± 0.8	1	3(260)	No
LYM pre-treatment	4.2 ± 0.8	1	3(320)	No
MAM pre-treatment	36.6 ± 1.0	38	-1(4)	No
CHO pre-treatment	7.1 ± 0.7	6	1(18)	No
OOG pre-treatment	25.0 ± 0.0	19	6(32)	No
Total pre-treatment	126.2 ± 2.5	105	21(20)	No
KNO post-treatment	13.8 ± 1.2	14	-0(1)	Yes
NEU post-treatment	24.6 ± 1.5	15	10(64)	No
LONG post-treatment	2.6 ± 0.7	0	3(-)	No
LYM post-treatment	3.7 ± 0.9	1	3(270)	No
MAM post-treatment	31.4 ± 0.9	30	1(5)	No
CHO post-treatment	5.2 ± 0.7	1	4(420)	No
OOG post-treatment	23.8 ± 0.4	19	5(25)	No
Total post-treatment	105.1 ± 2.1	80	25(31)	No
Early termination	71.5 ± 2.7	79	-8(9)	No

Table 3.7: Scenario prediction according to a waterfall approach where 1 begets 2, 2 begets 3, and 3 begets 4. The possible cause of the capacity bottlenecks is resolved in the subsequent scenario leading to new bottlenecks with new possible causes. After four scenarios, an average of 600 patients is treated with no capacity bottlenecks remaining with a queue length above or equal to 25.

	Scenario short description	**Description**	**Simulated mean ± CI**	**Capacity bottlenecks + threshold [n]**	**Cause**
1.	Extrapolated	The scenario described in Section 2.5. Where the patient distribution of 2020 was extrapolated to match a target of 600 patients treated. Resources remained the same as in 2021.	475.8 ± 12.67	PC; Plan Comparison Team Meeting; Delineation; Plan Team Meeting. Threshold = 100	Planning resources are retained for too long
2.	Faster Planning	Planning processes sped up according to the new experiences of the DPL employees with an upgrade of the planning software (service time differences are displayed in table A.3 in appendix A). Faster processes led to less retaining of resources.	556.3 ± 11.97	Plan Comparison Team Meeting; Delineation; Plan Team Meeting. Threshold = 100	Too few RTO employees available to execute all delineations and are therefore also not available to participate in the team meetings.
3.	Additional RTO	Extra full-time physician hired to allow for more delineations to be performed (number of RTO = 4 instead of 3)	588.3 ± 4.26	Treatments. Threshold = 25	Too little availability of gantries.
4.	Evening hours	Opening hours are extended to 21:00 with four hours more available for healthcare purposes (hours worked per day = 9 instead of 5)	601.4 ± 7.72	No capacity bottlenecks with threshold = 25.	-

Chapter 4: Discussion

In this chapter, the most important aspects of this research project are discussed. First, we discuss the findings and explain interpretations, followed by the implications: what is the scope of applicability and what can we learn from the results? Next, the limitations of this project will be discussed. Then, we will explain the reasoning behind the applied methodology, discuss the revisions, and provide commentary on decisions. Furthermore, recommendations for future projects are provided, split up into technical improvements to the simulation and a vision for the future. Lastly, the added value of a Technical Medicine Graduate will be briefly substantiated.

4.1 On the results

4.1.1 On the validation

Expert validation and internal validation using extremes both confirmed the simulation's logic. During validation with extremes, capacity bottlenecks arose at the appropriate activities and no alterations were suggested.

The primary outcome values for both internal and external validations were, in general, predicted with little deviation. Generally, small groups of patients were predicted with high proportional deviations, caused by small variations in the real world, e.g. more or fewer patient referrals and accepted PCs. The simulation does not take these real-world random variations in patient referral into account. For tumour types with larger patient cohorts, this random variation has little effect, as the deviation it causes is proportionately small. In smaller patient cohorts, on the other hand, this random variation leads to a proportionately larger deviation while the deviation in absolute patient numbers is still small. These larger deviations in small patient cohorts were, therefore, accepted.

The internal validation of 2020 predicted correct totals and early termination rates. KNO, NEU and MAM however had high deviations. This is partially clinically explained by inconsistent HL percentages. The HL percentage was set to a constant value during the simulation, while this percentage was not consistent for all tumour types in clinical practice. MAM patients were generally more likely to be treated according to the HL pathway and KNO patients were less likely to be treated according to the HL pathway. This means that KNO patients experienced more early terminations due to negative PCs. Furthermore, some MAM patients are treated two times due to tumour tissue being present in both breasts. The simulation does not consider these separately, leading to an underestimation. Lastly, treatment of NEU patients was put on hold later in 2020. These patients were treated in 2021 instead of 2020, leading to an overestimation of the post-treatment NEU patients in the simulation.

The external validation of 2019 did not predict the totals and early terminations correctly and KNO was largely overestimated. This can also be clinically explained. In 2019, KNO patients experienced more negative PCs due to different ΔNTPC guidelines. More patients were therefore referred for photon therapy instead of PBT leading to a higher number of early terminations and lower totals.

The external validation of 2021 predicted the KNO and MAM patients with little deviation. In 2021, NEU patients experienced more early terminations due to negative PCs than expected (25% negative PCs compared to 18% in 2020). The deviation of the OOG tumour type can be explained by the disproportionate referral of OOG patients during that period. The simulation inputs entities with consistent time intervals. When referral in the real world is disproportionate, a deviation is observed. At the start of 2021 (January until March), only 11 OOG patients were referred for PBT while later in the year (April until June) this number increased to 33. Several OOG patients did therefore not finish their treatment at the cutoff point of the simulation which led to a high overestimation. This same disproportionate referral was the case, to a lesser extent, for the LYM, LONG and CHO patients.

The boxplots of the secondary outcome values, the lead times, generally show a consistent simulation of the lead time around a median of 10 days. Real-world data is, unsurprisingly, less consistent. Simulated lead times IQR deviated from the real IQR in 2020 and 2019. This is partly explained by the fact that measurements on service time were performed in the period between January 2021 and May 2021, and thus the prediction of the lead times more accurately represents the situation in 2021. The planning software, which was used to extract standard delays, likewise, more accurately represents the situation of 2021. This software version was chosen for the extraction of the lead times because firstly, these values represent the current processes more closely, allowing for more accurate predictions. Secondly, previous versions were almost unattainable.
The delays in 2019 were higher due to HollandPTC still being a young facility. The deviation in lead times in 2020 is further explained by peaks in the number of referred patients which was observed in both winters of that year (January until March and November until December). This led to processes being executed more slowly.
The delays and service times are not expected to change in the upcoming year, suggesting that the simulation can accurately predict lead times according to the current situation.

The reasoned and simulated capacity bottlenecks did not coincide. This was to be expected because no true capacity bottlenecks, as defined in Section 2.3.2, were observed during the validation time frames. The healthcare processes, although sometimes feeling inefficient, have always been efficient enough to treat all referred patients.

From the validation runs, we can conclude that the simulation accurately predicts the real-world data considering the clinical explanations for the observed deviations. When examining the output of the simulation, it needs to be recognised that the simulation inputs patients according to consistent time intervals. This is not an accurate representation of the world, where patient referral is inconsistent. Furthermore, the inconsistent HL percentages should be considered when interpreting individual totals. Moreover, lead time predictions are reliable when simulating 2021 and onward.

4.1.2 On the predictions

The four simulated scenarios show the activities where capacity bottlenecks will arise in the near future and what measures HollandPTC can implement to prevent them to allow systematic growth towards 600 patients treated per year. The first bottleneck will arise in the PC due to the long duration of the planning activities. An upgrade of the dose planning upgrade is needed which allows for faster and more efficient execution of these dose planning steps. This upgrade has been implemented at the point of writing. This happened in March of 2021 and the difference in time to execute the dose planning steps was used in the prediction. HollandPTC is already noticing the initial effects of this upgrade, although the effects are minimal due to startup problems. When the new software is used optimally within the workflow, the outcome values of the first prediction are expected to become visible.
The second bottleneck will arise during the delineation and team meeting activities, due to a shortage of radiation oncologists. HollandPTC needs to employ one additional full-time radiation oncologist. This should relieve the workload which will arise due to additional delineations and necessary team meetings. This is especially needed after full integration of the novel OES pathway which requires specialised expertise and more distribution of the workload.

The last bottleneck is expected to be caused by a limitation in the gantry availability. Evening opening hours or weekend opening hours should be considered to prevent this. Extended opening hours will lead to more availability of the gantries and thus the treatment of more patients. Evening opening hours, or weekend opening hours, is the only way to relieve this resource, except for the construction of another gantry, which is not realistic.

The previous simulated scenarios led to the simulated treatment of 600 patients with queues smaller than 25 patients. Queues higher than 10 patients remained. These queue lengths were considered "natural" for this project, but the activities where these queues arise teach us about potential bottlenecks in the far future or after unforeseen setbacks. Activities where queues higher than 10 patients but lower than 25 patients arose were: The PC, PC meetings, and the treatments. The bottlenecks at the PC and PC Meetings are caused by an insufficient number of resources. This can be negated by employing more DPL and RTO personnel and investing in more Computers. Another possibility to relieve these resources is investing in methods for DPL and RTO employees to perform more activities in parallel.
The capacity of the treatments can only be increased by extending the opening hours beyond 21:00 or including more of the weekends. The maximum capacity of the gantries, therefore, leads to an eventual inescapable capacity plateau.

4.2 Implications

This project aimed to develop a validated DES application that can model the complete in-house workflow of HollandPTC and to provide suggestions toward a systematic capacity increase. The simulation allowed for a low-cost method to substantiate policy decisions without compromising real-world patient safety by denial of care due to insufficient capacity or resources. With the use of the HPTCapp, simple situational variations can be simulated, such as different case mixes, peaks in the number of patient referrals, the employment of personnel, investment in more equipment, or extended opening hours. The HPTCapp was developed to make these simple alterations easier to implement because these alterations are expected to be the most commonly applied. More complex situations can be simulated outside of the HPTCapp by altering the simulation itself. More in-depth knowledge of the simulation design is required to accomplish this. Complex situations are, for example, alterations to the processes, such as changing the delays or the service times, or a temporary loss of personnel due to illness. The user manual includes a part on complex alterations.

4.2.1 Model Complexity

The simulation remains a simplification of the real-world processes and can never fully encompass its full complexity. This is both a weakness and a strength. The weakness is that outcomes should never be accepted at face value and should always be interpreted within the situational context. For example: during the external validation of 2019 we found unexpected results which were clinically justified by different ΔNTCP guidelines during that time frame. Predictions should therefore always be interpreted with caution because multiple different factors can cause the result to deviate from the prediction. The simplicity is a strength because it enables the interpretation of isolated scenarios and quantification of individual policy changes, excluding real-world variation. Simulating multiple scenarios separately can give insight into how these scenarios interact in the real world, assisting in the understanding of real-world complexity.

The simulation and the accompanying application apply to the in-house processes until June of 2021. It remains applicable while the processes remain similar within the boundaries discussed previously. Radical changes to the processes, i.e. the introduction of new tumour pathways, the introduction of a new type of employee, or the rearrangement of the workflow, cannot be directly implemented in the simulation. For the simulation of these types of radical changes, a completely new simulation design is needed, for it reshapes the entire carepath developed in step 2: Process Mapping.
Furthermore, the simulation is meant to predict long term outcomes of policy changes (half a year or more). It is not able to simulate short term developments in patient referrals. Simulating situations from a week-to-week basis is, therefore, not reliable.

4.2.2 Generalisation

The simulation is not only applicable to the in-house processes of HollandPTC but can also be used in other centres with minimal modifications. Within the Netherlands, two other PBT facilities are operational: Maastro in Maastricht and UMCG Protonentherapiecentrum in Groningen. Maastro and UMCG protonentherapiecentrum are both independent clinics that offer PBT for multiple different indications. The workflow of these centres is comparable to HollandPTC because they execute the same general steps (intake, PCs, QA, etc), employ the same kind of personnel, and utilise the same kind of equipment. PCs for model-based indications are mandated by the Dutch governments, thus, all Dutch centres will have a comparable workflow. Differences arise when comparing the tumour types which are treated in each centre. Maastro and UMCG both already treat oesophageal tumours and UMCG also includes paediatric tumours in its list of indications. HollandPTC is, furthermore, the only centre treating ocular tumours[38, 39]. The simulation and the accompanying application can, therefore, be used by these centres except for the paediatric pathway. When implementing the simulation in these centres, the number of resources (number of gantries specifically), the delays and service times, and the maximum capacity of the activities should be carefully adjusted to the in-house situation.

Because the simulation was based on the process including the mandated PC for model-based indications, this simulation is not applicable outside countries where PCs are not an essential part of the workflow, such as the USA[40]. The Netherlands and Denmark are, currently, the only countries that utilise the ΔNTCP model for the PC for model-based indications as a standard part of the workflow[41, 42]. Treatment of standard indications (intra-ocular tumours, chordoma and chondrosarcoma, and paediatric tumours) can be simulated in other centres around the world because this workflow excludes PCs and is comparable to the Dutch workflow[40, 43].

4.2.3 Similar Projects/Studies

This project differs from similar studies where the workflow of a PBT facility was evaluated using statistical or computational methods. One study[44] evaluated the treatment workflow and applied Markov Modelling to improve patient admission policies. They solely modelled the treatment and did not consider all other aspects of the process. They also left out waiting times and delays. Furthermore, Markov Modelling is a statistical approach to decision support and cannot simulate the full complexity of the processes and utilisation of resources. For this, DES is a superior methodology. Another similar study[45] developed a Monte Carlo simulation in MATLAB to simulate throughput and waiting times of a PBT facility in the UK. They simulated multiple treatment rooms that shared a common proton accelerator, comparable to HollandPTC, and validated their model against data for the MD Anderson Cancer Centre. They showed agreement between the model and the data from the clinical centre and were confident in its use as a predictive tool. Their simulation, however, only modelled the treatment. A Monte Carlo approach was appropriate for this study. However, Monte Carlo simulations cannot easily model dynamic, event-driven processes. Here, DES is a superior methodology. Their developed model, however, could be a useful addition to our simulation and their predictions on stochastically driven throughput could be of value to HollandPTC.

4.3 Limitations

This project has some limitations. Firstly, the validity of the simulation was evaluated using historical data from September to December of 2019 and January to June of 2021. The number of patients treated in the smaller tumour pathways was very low, which led to a relatively high proportional deviation in the validation. Small differences in the real-world processes, which led to one patient being treated more or less, had a larger proportional effect on the amount of deviation. The predictions of small patient cohorts are, thus, unreliable. A similar limitation is that the non-adjustable variables were primarily based on process data of 2020. Here, small deviations in the smaller patient cohorts could have led to a systemic deviation. Eventually, the non-adjustable variables such as early termination, the number of plan adaptations and specific tumour dependent service times of these smaller tumour pathways should be reconsidered based on larger patient cohorts.

Secondly, the capacity bottleneck extraction functionality, which was used to determine the tertiary outcome values, was not properly validated. Ideally, this functionality should have been validated on historical data, similar to the primary and secondary outcome values. This was, however, not possible, because no patients were refused treatment after referral in the researched time frames. Treatment of patients was put on hold in 2020 (see the explanation of the deviation of the post-treatment NEU patients in Section 4.1.1). This, however, did not lead to the accumulation of patients to an extend which would influence the real-world situation and become measurable. For this project, the validity of the tertiary outcome value was assumed based on the validity of the primary and secondary outcome values. This functionality has to be evaluated when more data on capacity bottlenecks becomes available.

The validation and prediction runs were performed using a continuous patient input with the purpose to simplify the processes without taking into account the variability in patient referral rates. This led to the outcomes being purely caused by the in-house processes instead of factors outside of the control of HollandPTC. This, however, is not a completely realistic estimation of the real world. More realistic simulation runs including variable arrival rates may generate more realistic outcomes.

The software upgrade was implemented in March of 2021. This means that in the external validation of 2021, there were three months where this upgrade was not operational and three months where it was. The times to execute the dose planning activities did, however, not largely differ due to start-up difficulties in that time frame. We chose to include these three months to simulate more patients and make the validation of the historical data of 2021 more reliable. As input for the simulation, we calculated the average number of resources throughout this time frame.

Although the use of MATLAB and Simulink in this project was substantiated (see Section 4.1), some practical limitations remain. Firstly, MATLAB is not a free software outside of academic use. For the continuation of this project, HollandPTC has to own a licence, a computer with the installed software, and someone with the know-how and skills to operate the program. This is further required for the implementation of complex alterations to the simulation. The user manual is meant to assist in this, but the manual cannot encompass all possible complex alterations to the simulation.
Another limitation in the use of Simulink and MATLAB as a programming environment is that Simulink is not intended to be used for healthcare processes and the toolbox SimEvents is more generally used to simulate industries. Although no real problems arose while using Simulink, simulating complex patient flows proved to be difficult. Other software packages have more built-in functionalities which assist in the allocation of resources and design of complex patient pathways. The practical advantages of using Simulink, however, outweighed these limitations.

4.4 On the methodology

In this project, we used DES to simulate the in-house processes of HollandPTC. DES allows for the description of activities as separate events and to simulate patient throughput, resource utilisation and make predictions accordingly. The substantiation of the decision to utilise DES in this project is provided in the literature review of Part I, where the value of DES compared to other process analysis methodologies was shown. DES was applied most frequently in studies with similar research questions. DES was further considered a superior methodology compared to other proposed methods because it allows for the simulation of complex processes of large, mixed patient cohorts, it is easy to understand and reproduce due to the visual programming of the steps in the carepath, and it allows for prediction making and decision support. The disadvantage described in the literature, i.e. the large run time and computational requirements, proved minimal disadvantages during this project.

The standard methodology of DES development described by Cai et al.[35] was revised to fit the scope of this project. Two steps from the original framework were removed in the revised framework: "Result Analysis" and "Design Decisions". "Result Analysis" was integrated with the steps "Validation". In the original framework, "Validation" was included in the "Base Model Development" step. For this project, however, this step was considered separately to emphasise this step. "Scenario Simulation" was added as an additional step in the revised framework for the same reason. In the "Design Decisions" step, key findings of the simulation are used to substantiate policy decisions and redesign the process according to the result. For this project, this step was removed, for the responsibility of this step lies with the management of HollandPTC.

For programmatic development of the simulation in the "Base Model Development" step, MATLAB and Simulink were used as the programming language. There are multiple simulation packages available on the market with a focus on healthcare, such as Arena, SIMUL8, MedModel, and Simio, as discussed in the literature review of Part I. None of the included studies in this review used Simulink. The main reasons to use Simulink in this project were both practical convenience and similarity to other software packages. We were interested in a cheap (preferably free) software package with little to no learning curve, allowing the focus of the project to be on the actual simulation development, not the mastering of a new software package. The free MATLAB and Simulink licences provided by the TU Delft allowed for the low-cost development of the simulation and previous experience with Simulink provided an advantage in the familiarisation with the programming environment. Because none of the reviewed literature used Simulink for their simulation development, the comparability of the programming environment to other software packages had to be confirmed. Free trials of the most frequently applied software packages in the literature (Arena and Simul8) were requested. The similarity was confirmed by evaluating whether the software packages offered similar design components, how resource utilisation was managed, and whether entity flow was comparable for a simple model.

4.5 Recommendations

Two types of recommendations will be discussed in this section. Firstly, there are alterations to improve the simulation and application. Secondly, there is a vision for the future and possible next steps for this research project.

4.5.1 Improvements to the simulation

Several alterations can improve the simulation to make it more complete. These alterations were outside of the scope of this project because the current simulation functioned to answer the specific research question of this thesis. However, the alterations discussed in this section can make the application more applicable to different research purposes.

This simulation used a continuous patient input to evaluate potential capacity bottlenecks at maximum capacity for a uniform arrival pattern of entities. A realistic entity generation functionality built into the application simulates the arrival of patients according to a predictable peak in referrals once a year. This "realistic" functionality closely represents the arrival patterns in 2020. However, it does not fully represent all possible arrival patterns. This functionality can be expanded to include multiple peaks per year. Different tumour types can have different peaks in referrals. This functionality should, furthermore, be expanded to allow for multiple peaks at different times in the year for different tumour types.
Another way to make this functionality more realistic is by making the time between the generation of entities (dt) random according to a Poisson distribution. This introduces more uncertainty in the simulation by making the peak in patient referral unpredictable.

In this project, we were predominantly interested in the total number of patients treated and the lead time for

all tumour pathways. In practice, this lead time is different per tumour type. The OOG pathway, specifically, is completely different from the other pathways. The lead times per pathway should therefore be visualised separately to analyse the effects of specific measures on tumour-specific lead times.

A resource that was not included in this project was beamtime. Beamtime, as discussed in Chapter 1, is the time the proton beam is directed at a target. The availability of the beamtime communicates information on the efficiency of cyclotron use. With the inclusion of this resource, a more in-depth understanding of the efficiency of all processes using the cyclotron can be developed, both healthcare and non-healthcare related e.g. research and maintenance. To implement beamtime in the simulation, the treatment step should be split up into smaller steps, including patient positioning, image matching, and irradiation. The irradiation step then acquires the beam. For this project, this resource was excluded because the resource "Gantry" was sufficient for the simulation of the healthcare processes by itself.

Although the follow-up steps were included in the carepath developed during Process Mapping, these steps were excluded from the simulation. The reason being that in the current processes, follow-up is not performed by a standardised pathway. The delay between the end of treatment and follow-up can be many months and sometimes it is performed in person and sometimes telephonically. These uncertainties would introduce unnecessary complexity to the simulation while only being a small part of the entire process. It was therefore considered disproportionately complex compared to the added value to the process and excluded. Follow-up requires additional resource utilisation of the radiation oncologist and has, therefore, a small influence on the availability of this resource. For a complete simulation of the healthcare processes, follow-up should be included in a way that accurately represents the uncertain real-world situation.

Lastly, the simulation developed in this project did not include any information on costs. Although the DES methodology is not a conventional method to perform a healthcare costing analysis, the simulation can aid in the quantification of resource use and predict future cost items after growth. The prediction of resource use and accompanying costs is more substantiated and reliable than the extrapolation of current costs to a larger patient population. To accomplish this, first, the current in-house costs should be systematically analysed and allocated per resource.

4.5.2 Future perspective

As discussed previously, this project aimed to predict the total number of patients and saw lead time as the secondary outcome. Switching this priority and setting lead time as primary outcome value could lead to a new perspective on efficiency that can generate other activities to come up as lead time bottlenecks. The focus would be on the efficiency of the activities with the largest delays and service times (such as the intake, Dry Runs, DPL Activities, and Delineation) instead of resource use and waiting times.

The simulation and the accompanying application should be used by employees to simulate a variety of different situations. From temporary employee shortage to changing the non-adjustable variables or simulating complicated entity arrival rates. Furthermore, applicability to other PBT centres should be explored. As discussed before, the simulation is expected to apply to all Dutch PBT centres. However, the extent to which it is applicable should be investigated. After the efficacy of the HPTCapp and the accompanying simulation to other PBT facilities is demonstrated, the simulation and application can be further developed into a wide-scale deployable product. PBT facilities around the world can then evaluate their in-house situation and investigate specific targets for capacity increase. In the far future, this product can thus be used by all PBT facilities to investigate how to treat more patients.

4.6 Added value of the Technical Physician (Personal Opinion)

This project could not have been done without the knowledge of all processes within HollandPTC. Clinical knowledge was required on how correct PBT is performed, what role the physicians and other clinical staff have, what patients experience, and how activities are executed. Thinking about the efficiency of activities without losing sight of patient well-being and safety was necessary. As a technical physician, I have had the opportunity to observe all different types of personnel with all clinical activities and to experience all facets of the treatment. This proved essential for the development of a complete and correct simulation, for the process sheets and planning software proved insufficient for the complete description of the real-world processes. Furthermore, medical knowledge was required to completely understand the complexity of the most time-consuming activities: delineation and planning. I had the opportunity to execute these activities myself, to experience why these activities are so time-consuming and to think about how these limitations could be overcome.

Previous technical knowledge about proton physics was a major advantage at the start of the project. It was possible to start up quickly and it was fairly easy to integrate into the team because I was already familiar with some of

the jargon. Knowledge about physics was essential to understand the corresponding steps in the processes, just as with the clinical knowledge. Understanding the corresponding process steps was essential for the development of an accurate simulation.
Another technical advantage was my previous experience with MATLAB and Simulink. These programming environments were a staple in our curriculum. This experience led to the fast development of a working prototype that could be extensively built upon. The development of the application was, eventually, the way to ensure usability.

This, combined with the scientific experience in the execution of research projects gained in the past years, enabled a scientific and statistical approach to facilitate the development of a validated simulation with demonstrated applicability. Collaboration with the board and staff of HollandPTC allowed for the translation of their policy and clinically driven requests to an application that described reality and generated useful outcomes for decision support.

In summary, being a jack-of-all-trades enabled me to provide the needed expertise and know-how to set up this project and work from a request to a product. This was only possible for someone with both a clinical and technical background.

4.7 Conclusion

In this project, we employed a validated DES simulation to model the in-house workflow of HollandPTC and to make predictions on capacity, throughput, patient flow, and availability of resources.
With this DES simulation, we found potential causes of capacity bottlenecks and provided suggestions for how these bottlenecks can be prevented.

The developed simulation is expected to be applicable to other PBT facilities around the world with mandated PCs for model-based indications with minor alterations. The developed products can be used by other PBT facilities to evaluate their in-house workflow and to investigate their specific targets for capacity increase. The extent to which the simulation is applicable should be further explored.

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Part III

Appendix

Chapter A:
Tables

Table A.1: Overview of the activities within the care trajectories with corresponding information on involved tumour types, service time, delay, involved resources, capacity and method of acquisition.

Activity	KNO	NEU	LONG	LYM	OES	MAM	CHO	OOG	Mean Service Time [h]	σ Service Time [h]	Delay [h]	Resources	Max Capacity[1]	Data Acquisition Method
Import KNO[2]	x								0,17	NA	24	DPL; Computer	Computer	I; M
Import NEU[2]		x							0,17	NA	24	DPL; Computer	Computer	I; M
Import THO[2]			x	x	x				0,50	NA	24	DPL; Computer	Computer	I; M
Import MAM[2]						x			0,17	NA	24	DPL; Computer	Computer	I; M
Image Registration KNO[2]	x								0,00	NA	0	DPL; Computer	Computer	I; M
Image Registration NEU[2]		x							0,00	NA	0	DPL; Computer	Computer	I; M
Image Registration THO[2]			x	x	x				0,50	NA	0	DPL; Computer	Computer	I; M
Image Registration MAM[2]						x			0,00	NA	0	DPL; Computer	Computer	I; M
Delineation KNO[2]	x								0,17	NA	0	DPL; Computer	Computer	I; M
Delineation NEU[2]		x							0,17	NA	0	DPL; Computer	Computer	I; M

[1] Capacity is often resource dependent. When that is the case, the resource which determines the max capacity is displayed, otherwise the overall max capacity is provided.
[2] Subactivity of "DPL Plan Comparison" within the process map

Delineation THO[2]			×	×	×				0,50	NA		0	DPL; Computer	Computer	I; M
Delineation MAM[2]						×			0,17	NA		0	DPL; Computer	Computer	I; M
Plan Development KNO[2]	×								0,17	NA		0	DPL; Computer	Computer	I; M
Plan Development NEU[2]		×							0,33	NA		0	DPL; Computer	Computer	I; M
Plan Development THO[2]			×	×	×				0,17	NA		0	DPL; Computer	Computer	I; M
Plan Development MAM[2]						×			0,17	NA		0	DPL; Computer	Computer	I; M
Optimisation KNO[2]	×								6,00	NA		0	Computer	Computer	I; M
Optimisation NEU[2]		×							6,00	NA		0	Computer	Computer	I; M
Optimisation THO[2]			×	×	×				8,00	NA		0	Computer	Computer	I; M
Optimisation MAM[2]						×			12,0	NA		0	Computer	Computer	I; M
Spotfilter KNO[2]	×								0,00	NA		0	Computer	Computer	I; M
Spotfilter NEU[2]		×							2,00	NA		0	Computer	Computer	I; M
Spotfilter THO[2]			×	×	×				4,00	NA		0	Computer	Computer	I; M
Spotfilter MAM[2]						×			6,00	NA		0	Computer	Computer	I; M
Evaluation KNO[2]	×								2,00	NA		0	Computer	Computer	I; M
Evaluation NEU[2]		×							2,00	NA		0	Computer	Computer	I; M
Evaluation THO[2]			×	×	×				2,00	NA		0	Computer	Computer	I; M
Evaluation MAM[2]						×			4,00	NA		0	Computer	Computer	I; M
Evaluation and Input Aria[2]	×	×	×	×	×	×			0,05	NA		0	DPL	DPL	I; M
DPL Approval	×	×	×	×	×	×			0,17	NA		2	RTO	RTO	E; I
Plan Comparison Team Meeting	×	×	×	×	×	×			0,17	NA		2	2 RTO; KF; DPL	1	E; I
DPL MBB Verification	×	×	×	×	×	×			0,50	NA		2	DPL	DPL	E; I
DPL Verification	×	×	×	×	×	×			0,50	NA		4	KF	KF	E; I
OZP Preparation	×	×	×	×	×	×			0,08	NA		0	MS	MS	E
Phone Consultation ZC	×	×	×	×	×	×	×	×	0,25	NA		24	ZC	ZC	E; I; M
Outpatient Clinic ZC 30 min	×	×	×	×	×	×	×		0,83		0,08	24	ZC	ZC	E; I; M
First Outpatient Clinic	×	×	×	×	×	×	×	×	0,58		0,02	0[3]	RTO	RTO	E; I; M
Pathway Verification	×	×	×	×	×	×	×	×	0,08	NA		1	MS	MS	E
Outpatient Clinic ZC 15 min								×	0,25	NA		0	ZC	ZC	E; I; M
Positioning Meeting	×	×	×	×	×	×	×		0,25	NA		0	2 MBB; RTO; KF; CT	1	E; I
Dry Run THO[4]			×	×	×				0,25	NA		0	2 MBB; CT	CT	E; I
IV Cannulation	×	×	×	×	×		×		0,25	NA		0	2 MBB; CT	CT	E; I
Mask	×	×							0,50	NA		0	2 MBB; CT	CT	E; I
Positioning Meeting OOG[5]								×	0,25	NA		0	2 MBB; RTO; KF; Parel	1	E; I
4DCT Planning			×	×	×				0,75	NA		0	2 MBB; CT	CT	E; I
CT Planning	×	×				×	×		0,50	NA		0	2 MBB; CT	CT	E; I
MRI Planning	×	×					×		1,50		0,08	0	2 MBB; MRI	MRI	E; I
Dry Run MAM[6]						×			0,50	NA		0	2 MBB; CT	CT	E; I
Simulation OOG								×	1,25	NA		0	2 MBB; RTO; Parel	Parel	E; I

[3]The OOG pathway has a 24h delay
[4]Is combined with "Dry Run MAM" as one activity "Dry Run" in the process map
[5]Is combined with "Positioning Meeting" as one activity in the process map
[6]Is combined with "Dry Run THO" as one activity "Dry Run" in the process map

Image Processing OOG								×	0,50	NA		1[7]	2 MBB; 2 RTO	RTO	E; I
PET CT Preparation	×		×	×	×				0,50	NA		24	2 MBB; PETCT	PETCT	E; I
PET CT Injection	×		×	×	×				1,00	NA			2 MBB; PETCT	PETCT	E; I
PET CT Planning	×		×	×	×				0,50	NA			2 MBB; PETCT	PETCT	E; I
Fusion PET CT	×		×	×	×				0,25	NA		1	2 MBB; DPL; PETCT	PETCT	E; I
Image Processing	×	×	×	×	×	×	×		0,25	NA		1	MBB; DPL	DPL	E; I
Delineation	×	×	×	×	×	×	×	×	1,00[8]		0,50	1	2 RTO	RTO	E; I
Delineation Verification	×	×	×	×	×	×	×		0,25	NA		0	2 RTO	RTO	E; I
DPL OOG								×	2,00	NA		0	2 DPL	DPL	E; I; M
Dry Run NEU		×							0,50	NA		24	DPL	DPL	E; I
Aperture Milling								×	1,00	NA		24	KFM	KFM	E; I
Data Preparation[9]	×	×	×	×	×	×			0,17	NA		1	DPL	DPL	E; I
Highly Likely Export[9]	×	×	×	×	×	×			0,17	NA		1	MS	MS	E
Highly Likely Plan Import[9]	×	×	×	×	×	×			0,17	NA		24	MS	MS	E
Import KNO[10]	×								0,33	NA		0	DPL; Computer	Computer	I; M
Import NEU[10]		×							0,33	NA		0	DPL; Computer	Computer	I; M
Import MAM[10]						×			0,17	NA		0	DPL; Computer	Computer	I; M
Import CHO[10]							×		0,33	NA		0	DPL; Computer	Computer	I; M
Image Registration KNO[10]	×								0,25	NA		0	DPL; Computer	Computer	I; M
Image Registration NEU[10]		×							0,25	NA		0	DPL; Computer	Computer	I; M
Image Registration MAM[10]						×			0,17	NA		0	DPL; Computer	Computer	I; M
Image Registration CHO[10]							×		0,25	NA		0	DPL; Computer	Computer	I; M
Plan Development KNO[10]	×								0,17	NA		0	DPL; Computer	Computer	I; M
Plan Development NEU[10]		×							0,50	NA		0	DPL; Computer	Computer	I; M
Plan Development MAM[10]						×			0,17	NA		0	DPL; Computer	Computer	I; M
Plan Development CHO[10]							×		0,17	NA		0	DPL; Computer	Computer	I; M
Optimisation KNO[10]	×								24,0	NA		0	Computer	Computer	I; M
Optimisation NEU[10]		×							18,0	NA		0	Computer	Computer	I; M
Optimisation MAM[10]						×			18,0	NA		0	Computer	Computer	I; M
Optimisation CHO[10]							×		32,0	NA		0	Computer	Computer	I; M
Spotfilter KNO[10]	×								6,00	NA		0	Computer	Computer	I; M
Spotfilter NEU[10]		×							2,00	NA		0	Computer	Computer	I; M
Spotfilter MAM[10]						×			6,00	NA		0	Computer	Computer	I; M
Spotfilter CHO[10]							×		48,0	NA		0	Computer	Computer	I; M
Evaluation KNO[10]	×								6,00	NA		0	Computer	Computer	I; M
Evaluation NEU[10]		×							4,00	NA		0	Computer	Computer	I; M
Evaluation MAM[10]						×			4,00	NA		0	Computer	Computer	I; M
Evaluation CHO[10]							×		6,00	NA		0	Computer	Computer	I; M
Evaluation and Input Aria[10]	×	×				×	×		0,50	NA		0	DPL; Computer	Computer	I; M

[7] Delay pulsates periodically to 24h

[8] Service time is variable over time using the formula: $t = \frac{\ln(|N(\mu,\sigma^2)|)}{3} + 3$

[9] Belongs to HL pathway

[10] Subactivity of "DPL Standard 3D IMRT" within the process map

Import THO[11]			×	×	×			0,50	NA		0	DPL; Computer	Computer	I; M
Image Registration THO[11]			×	×	×			0,50	NA		0	DPL; Computer	Computer	I; M
Plan Development THO[11]			×	×	×			0,25	NA		0	DPL; Computer	Computer	I; M
Optimisation THO[11]			×	×	×			18,0	NA		0	Computer	Computer	I; M
Spotfilter THO[11]			×	×	×			6,00	NA		0	Computer	Computer	I; M
Evaluation THO[11]			×	×	×			6,00	NA		0	Computer	Computer	I; M
Evaluation and Input Aria[11]			×	×	×			0,50	NA		0	DPL; Computer	DPL	I; M
DPL MBB Verification	×	×	×	×	×	×	×	0,50	NA		2	DPL	DPL	E; I
DPL Approval	×	×	×	×	×	×	×	0,17	NA		3	RTO	RTO	E; I
IGPT Protocol Notation	×	×	×	×	×	×	×	0,17	NA		0	RTO	RTO	E; I
Phone Consultation ZC	×	×	×	×	×	×	×	0,25	NA		1	ZC	ZC	E; I
Dry Run OOG								1,00	NA		48	MBB: RTO	RTO	E; I
Plan Processing	×	×	×	×	×	×	×	0,50	NA		24	DPL	DPL	E; I
Plan Processing Verification	×	×	×	×	×	×	×	0,25	NA		2	DPL	DPL	E; I
Plan Team Meeting	×	×	×	×	×	×	×	0,17	NA		0	2 RTO; KF; DPL	1	E; I
DPL Verification	×	×	×	×	×	×	×	0,50	NA		4	KF	KF	E; I
QA Plan Development	×	×	×	×	×	×	×	2,00	NA		2	KF	KF	E; I
QA Plan Measurement	×	×	×	×	×	×	×	0,50		0,25	4	2 KFM; Gantry	Gantry	E; I; M
QA OOG								2,00	NA		4	2 KFM; Parel	Parel	E; I
QA Plan Verification	×	×	×	×	×	×	×	0,50	NA		4	KF	KF	E; I
Treatment Approval	×	×	×	×	×	×	×	0,17	NA		4	KF	KF	E; I
KNO Treatment	×							0,50		0,08	24	3 MBB; Gantry	Gantry	E; I; M
NEU Treatment		×						0,33		0,08	24	3 MBB; Gantry	Gantry	E; I; M
LONG Treatment			×					0,50		0,08	24	3 MBB; Gantry	Gantry	E; I; M
LYM Treatment				×				0,50		0,08	24	3 MBB; Gantry	Gantry	E; I; M
OES Treatment[12]					×			0,50		0,08	24	3 MBB; Gantry	Gantry	
MAM Treatment						×		0,50		0,08	24	3 MBB; Gantry	Gantry	E; I; M
CHO Treatment							×	0,42		0,08	24	3 MBB; Gantry	Gantry	E; I; M
OOG Treatment								1,00	NA		24	3 MBB; Parel	Parel	E; I; M
Consultation During Treatment RTO	×	×	×	×	×	×	×	0,25	NA		0,25	RTO	RTO	E; I
Dental Hygienist[13]	×							0,25	NA		0	-	1	E
Dietician[13]	×							0,25	NA		0	-	1	E
Approvement Treatment Summary								0,17	NA		0	KF	KF	E; I
Mask	×	×						0,50	NA		0	2 MBB; CT	CT	E; I
CT Repetition	×	×				×	×	0,25	NA		0,25	2 MBB; CT	CT	E; I
CT 4D Repetition			×	×	×			0,50	NA		0,75	2 MBB; CT	CT	E; I
Image Processing	×	×	×	×	×	×	×	0,50	NA		1	DPL	DPL	E; I
Plan Evaluation	×	×	×	×	×	×	×	0,50	NA		4	DPL	DPL	E; I
Delineation	×	×	×	×	×	×	×	1,00[8]		0,50	24	2 RTO	RTO	E; I
DPL Approval	×	×	×	×	×	×	×	0,17	NA		3	RTO	RTO	E; I

[11] Subactivity of "DPL 4D" within the process map
[12] Based on the LYM and LONG trajectories
[13] No resource defined because of the self-contained activity

Import KNO[14]	0,33	NA	0	DPL; Computer	Computer	I; M
Import NEU[14]	0,33	NA	0	DPL; Computer	Computer	I; M
Import THO[14]	0,50	NA	0	DPL; Computer	Computer	I; M
Import MAM[14]	0,17	NA	0	DPL; Computer	Computer	I; M
Import CHO	0,33	NA	0	DPL; Computer	Computer	I; M
Image Registration KNO[14]	0,25	NA	0	DPL; Computer	Computer	I; M
Image Registration NEU[14]	0,25	NA	0	DPL; Computer	Computer	I; M
Image Registration THO[14]	0,50	NA	0	DPL; Computer	Computer	I; M
Image Registration MAM[14]	0,17	NA	0	DPL; Computer	Computer	I; M
Image Registration CHO[14]	0,25	NA	0	DPL; Computer	Computer	I; M
Plan Development KNO[14]	0,17	NA	0	DPL; Computer	Computer	I; M
Plan Development NEU[14]	0,50	NA	0	DPL; Computer	Computer	I; M
Plan Development THO[14]	0,25	NA	0	DPL; Computer	Computer	I; M
Plan Development MAM[14]	0,17	NA	0	DPL; Computer	Computer	I; M
Plan Development CHO[14]	0,17	NA	0	DPL; Computer	Computer	I; M
Optimisation KNO[14]	24,0	NA	0	Computer	Computer	I; M
Optimisation NEU[14]	18,0	NA	0	Computer	Computer	I; M
Optimisation THO[14]	18,0	NA	0	Computer	Computer	I; M
Optimisation MAM[14]	18,0	NA	0	Computer	Computer	I; M
Optimisation CHO[14]	32,0	NA	0	Computer	Computer	I; M
Spotfilter KNO[14]	6,00	NA	0	Computer	Computer	I; M
Spotfilter NEU[14]	2,00	NA	0	Computer	Computer	I; M
Spotfilter THO[14]	6,00	NA	0	Computer	Computer	I; M
Spotfilter MAM[14]	6,00	NA	0	Computer	Computer	I; M
Spotfilter CHO[14]	48,0	NA	0	Computer	Computer	I; M
Evaluation KNO[14]	6,00	NA	0	Computer	Computer	I; M
Evaluation NEU[14]	4,00	NA	0	Computer	Computer	I; M
Evaluation THO[14]	6,00	NA	0	Computer	Computer	I; M
Evaluation MAM[14]	4,00	NA	0	Computer	Computer	I; M
Evaluation CHO[14]	6,00	NA	0	Computer	Computer	I; M
Evaluation and Input Aria[14]	0,50	NA	0	DPL; Computer	Computer	I; M

NA: Not Applicable; E: Extracted; I: Inspected; M: Measured; OZP: ; IGPT: Image Guided Proton Therapy; IMRT: Intensity Modulated Radiotherapy

[14] Subactivity of "DPL Plan Adaptation" within the process map

Table A.3: Differences in planning process service times after implementation of a software upgrade in march 2021. The faster service times are implemented in the simulation for the prediction of scenario 2 of the predictions.

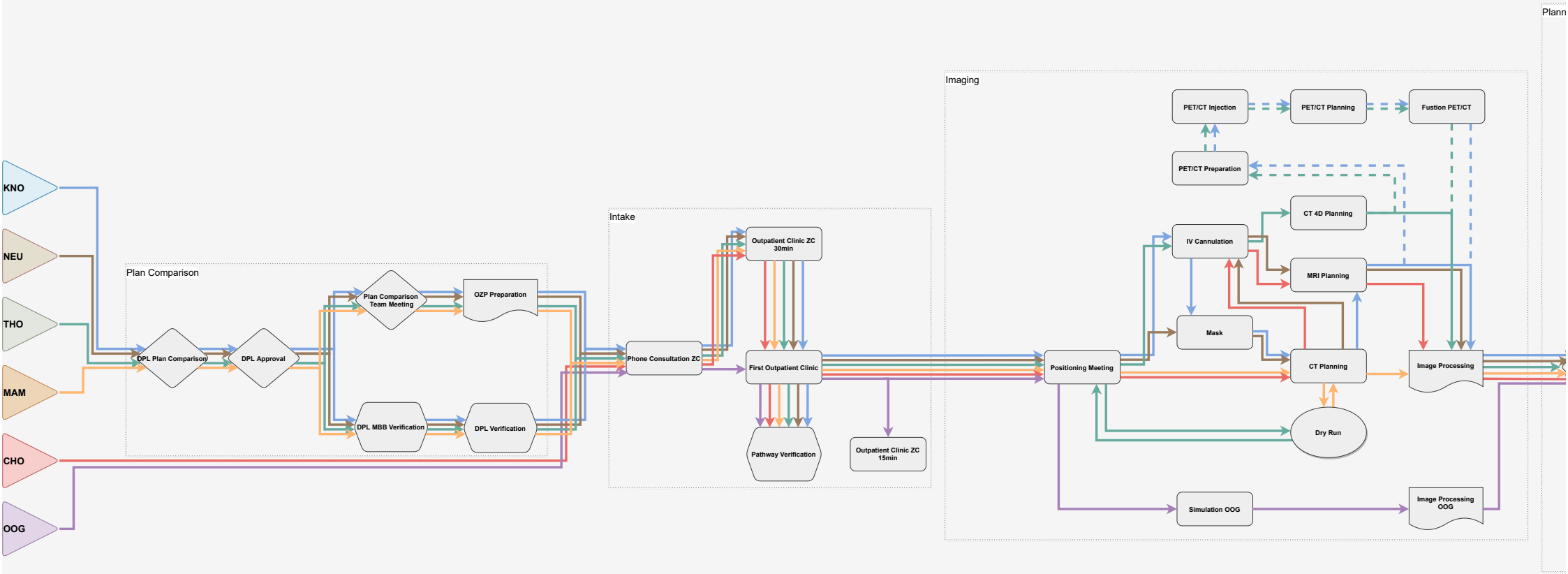
Activity	**Old Service Time [hours]**	**New Service Time [hours]**
Plan Comparison		
Optimisation KNO	6,00	9,00
Optimisation NEU	6,00	6,00
Optimisation THO	8,00	8,00
Optimisation MAM	12,0	12,0
Spotfilter KNO	0,00	0,00
Spotfilter NEU	2,00	0,00
Spotfilter THO	4,00	0,00
Spotfilter MAM	6,00	0,00
Evaluation KNO	2,00	0,05
Evaluation NEU	2,00	0,05
Evaluation THO	2,00	0,50
Evaluation MAM	4,00	0,17
Clinical Plan		
Spotfilter KNO	2,00	0,00
Spotfilter NEU	6,00	0,00
Spotfilter THO	6,00	0,00
Spotfilter MAM	6,00	0,00
Spotfilter CHO	48,0	0,00
Evaluation KNO	6,00	0,05
Evaluation NEU	4,00	0,17
Evaluation THO	2,00	1,00
Evaluation MAM	4,00	0,05
Evaluation CHO	6,00	0,17
Plan Adaptation		
Spotfilter KNO	2,00	0,00
Spotfilter NEU	6,00	0,00
Spotfilter THO	6,00	0,00
Spotfilter MAM	6,00	0,00
Spotfilter CHO	48,0	0,00
Evaluation KNO	6,00	0,05
Evaluation NEU	4,00	0,17
Evaluation THO	2,00	1,00
Evaluation MAM	4,00	0,05
Evaluation CHO	6,00	0,17

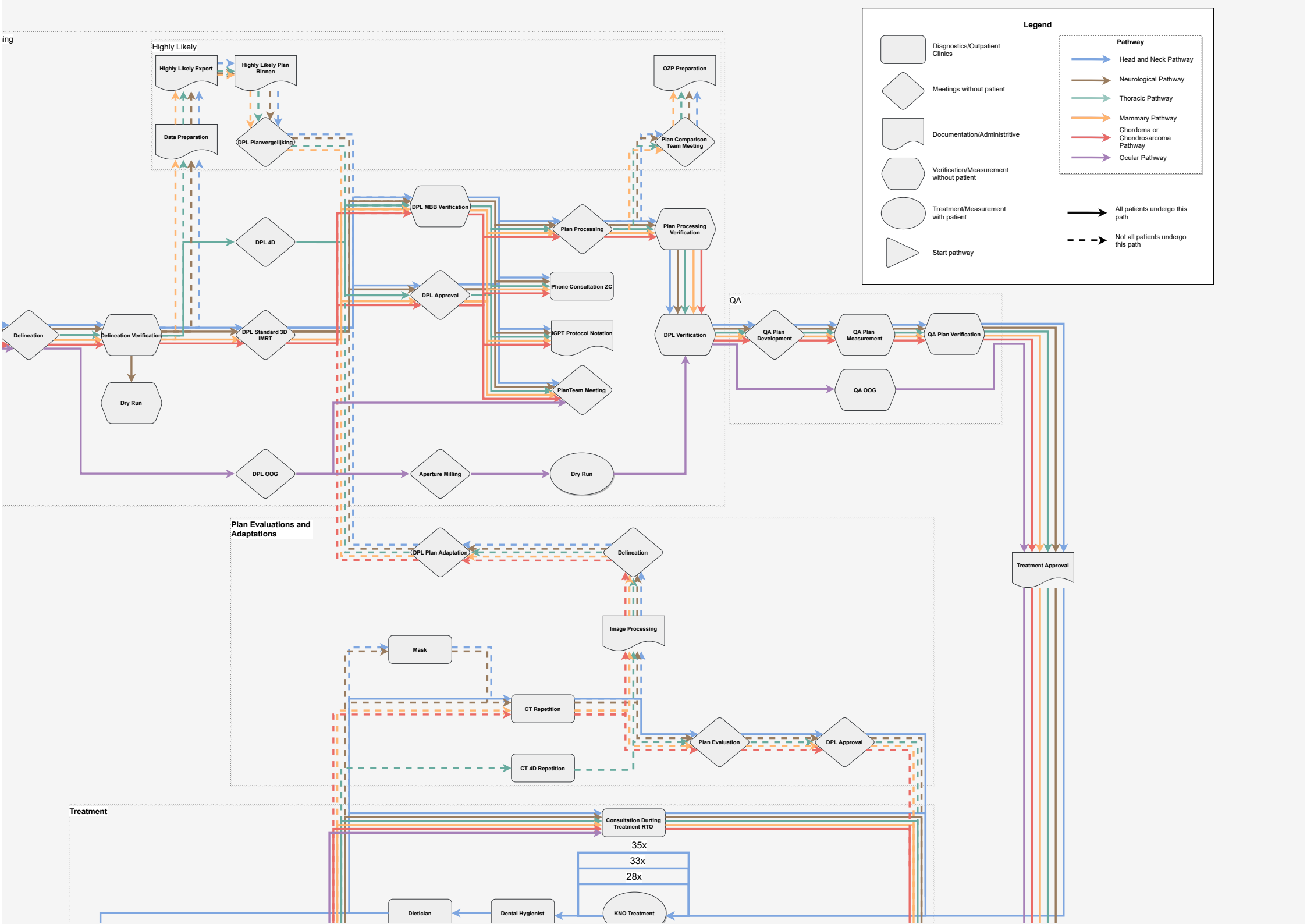
Chapter B:
Process map

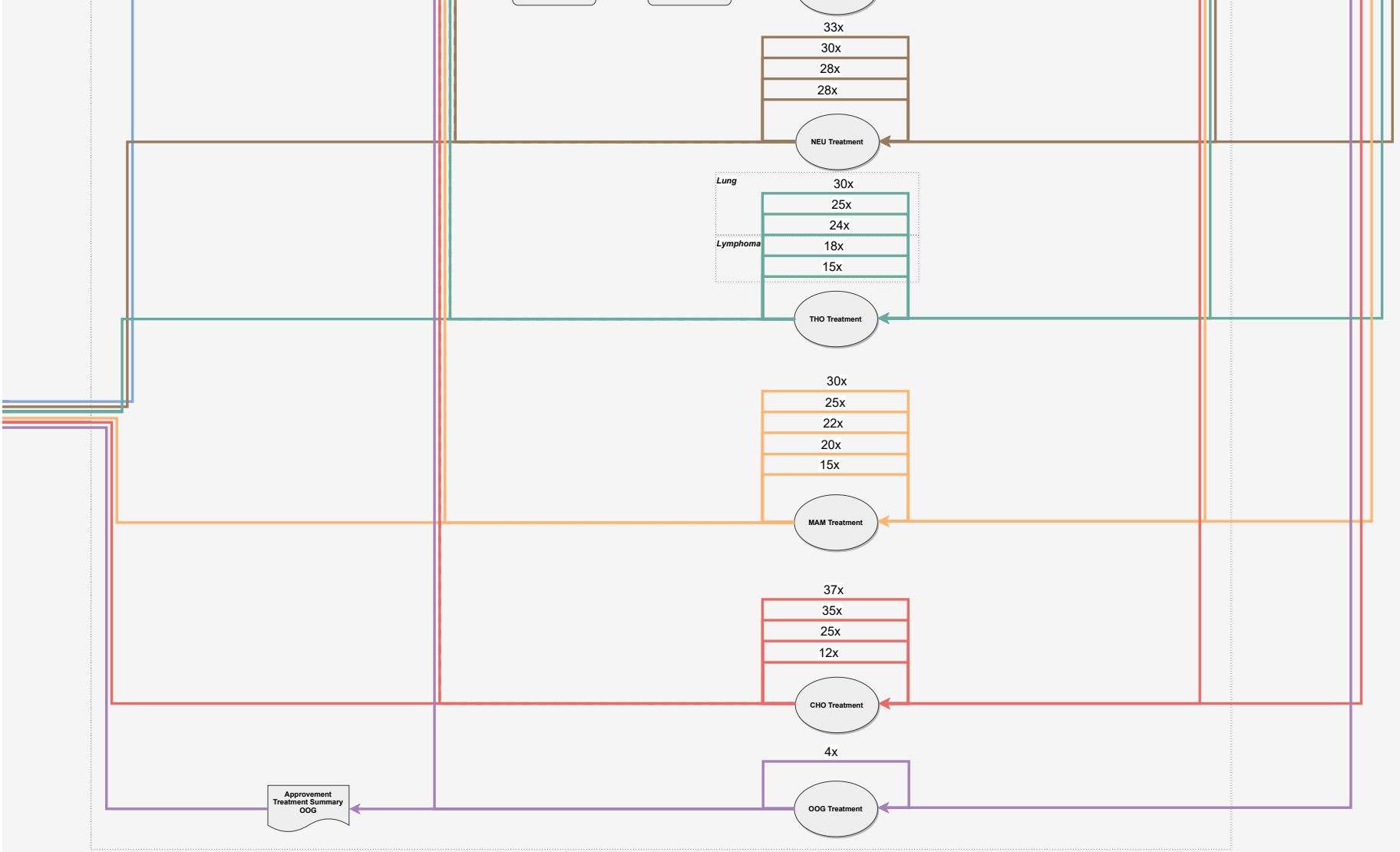
See next page.

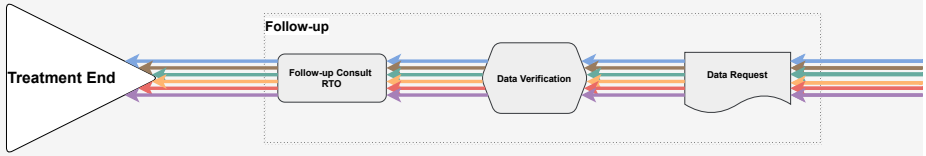
The complete file can be found at:
`https://repository.tudelft.nl/`

Figure B.1


KNO
NEU
THO
MAM
CHO
OOG
Plan Comparison
DPL Plan Comparison
DPL Approval
Plan Comparison Team Meeting
OZP Preparation
DPL MBB Verification
DPL Verification
Intake
Phone Consultation ZC
Outpatient Clinic ZC 30min
First Outpatient Clinic
Pathway Verification
Outpatient Clinic ZC 15min
Imaging
Positioning Meeting
PET/CT Injection
PET/CT Planning
Fustion PET/CT
PET/CT Preparation
CT 4D Planning
IV Cannulation
MRI Planning
Mask
CT Planning
Image Processing
Dry Run
Simulation OOG
Image Processing OOG
Plann


Legend
Diagnostics/Outpatient Clinics
Meetings without patient
Documentation/Administritive
Verification/Measurement without patient
Treatment/Measurement with patient
Start pathway
Pathway
Head and Neck Pathway
Neurological Pathway
Thoracic Pathway
Mammary Pathway
Chordoma or Chondrosarcoma Pathway
Ocular Pathway
All patients undergo this path
Not all patients undergo this path
Highly Likely
Highly Likely Export
Highly Likely Plan Binnen
Data Preparation
DPL Planvergelijking
OZP Preparation
Plan Comparison Team Meeting
DPL MBB Verification
DPL 4D
DPL Approval
Plan Processing
Plan Processing Verification
Phone Consultation ZC
GPT Protocol Notation
PlanTeam Meeting
Delineation
Delineation Verification
DPL Standard 3D IMRT
Dry Run
DPL OOG
Aperture Milling
Dry Run
DPL Verification
QA
QA Plan Development
QA Plan Measurement
QA Plan Verification
QA OOG
Treatment Approval
Plan Evaluations and Adaptations
DPL Plan Adaptation
Delineation
Image Processing
Mask
CT Repetition
CT 4D Repetition
Plan Evaluation
DPL Approval
Treatment
Consultation Durting Treatment RTO
35x
33x
28x
KNO Treatment
Dental Hygienist
Dietician


33x
30x
28x
28x
NEU Treatment
Lung
30x
25x
24x
Lymphoma
18x
15x
THO Treatment
30x
25x
22x
20x
15x
MAM Treatment
37x
35x
25x
12x
CHO Treatment
4x
OOG Treatment
Approvement Treatment Summary OOG


Follow-up
Treatment End
Follow-up Consult RTO
Data Verification
Data Request

Chapter C:
Manual

See next page.

HPTCapp

Werkinstructies

Joep (J.) Eijkenduijn

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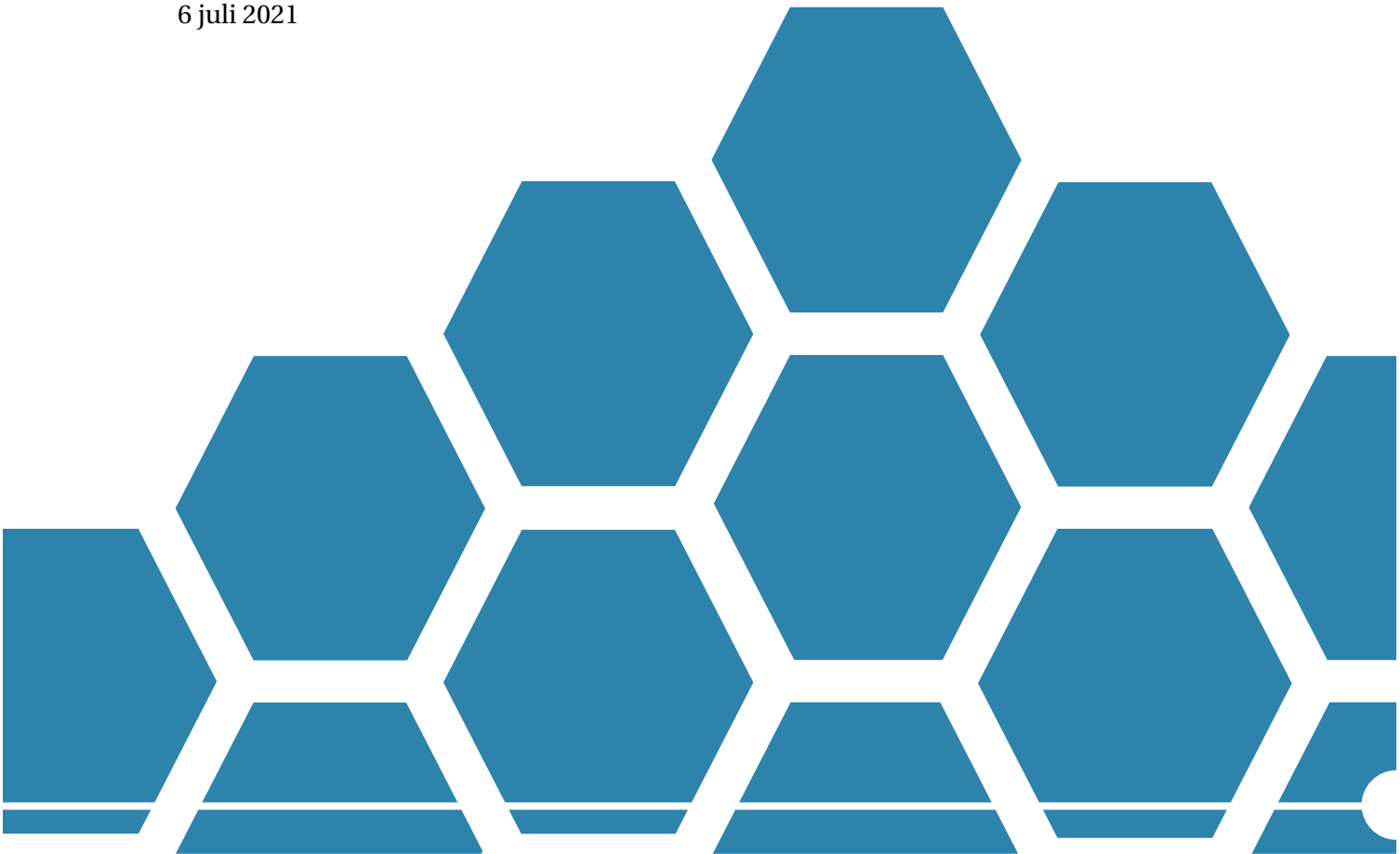
Master thesis project

TU Delft, Erasmus MC, LUMC

HollandPTC

6 juli 2021



Inhoudsopgave

Hoofdstuk 1

Algemeen

1.1 Introductie

Welkom, dit zijn de werkinstructies voor het zelfstandig toepassen van de *HPTCapp*. Deze handleiding is bedoeld voor medewerkers van HollandPTC die de *HPTCapp* willen gebruiken om onderbouwde keuzes te kunnen maken op het gebied van beleid, kliniek, of uit pure nieuwsgierigheid. In deze handleiding wordt stap voor stap uitgelegd hoe gegevens ingevuld moeten worden, hoe de gegenereerde data geïnterpreteerd moet worden, en hoe je complexere aanpassingen kan maken. Deze handleiding gaat niet in op de wiskunde achter de simulatie of waarom bepaalde keuzes zijn gemaakt. Voor deze onderbouwing, lees het thesis document behorende bij het volledige project.

Om deze handleiding goed te begrijpen moet je bekend zijn met de processen binnen HollandPTC en een globale kennis hebben van de carepaths gedefinieerd in Aria.

Het programma is bedoeld om voorspellingen te doen op het gebied van doorstroomtijden, capaciteitsontwikkelingen en beschikbaarheid van ruimtes en medewerkers. Deze voorspellingen kunnen gebruikt worden ter onderbouwing van beleidsmatige beslissingen. Het programma is gebaseerd op de carepaths uit begin 2021. Houd er rekening mee dat na grote herzieningen van de processen het programma niet meer betrouwbaar werkt.

In deze handleiding gaan we in op het algemene gebruik, van input tot output; hoe gegevens geïnterpreteerd moeten worden; hoe eventuele complexere aanpassingen gedaan kunnen worden aan de simulatie zelf; en wat er gedaan moet worden bij bepaalde foutmeldingen.

1.2 Technische achtergrond

De simulatie is gebaseerd op een simulatietechniek genaamd Discrete Event Simulation (DES). DES benadert een continu proces als een serie discrete handelingen (Events). Deze discrete evenementen komen voor op een specifiek tijdpunt en beïnvloeden het volledige systeem. Het proces wordt bewandeld door individuele voorwerpen genaamd Entities. Deze Entities bevatten een eigenschap (Attribute) en een prioriteit (Priority). Deze Attributes en Priorities beïnvloeden hoe het systeem omgaat met de Entities. Tijdens een events kan een Entity worden veranderen, vastgehouden, afgeremd, gedupliceerd, of vernietigd.

In de toepassing van de zorgprocessen binnen HollandPTC zijn patiënten de Entities. De belangrijkste Attribute van de patiënt is de tumorsoort. De Priority wordt bepaald door hoeveel fracties de patiënt al gehad heeft. Immers, als de behandeling eenmaal gestart is, kan deze niet zomaar gepauzeerd worden. De Events zijn de stappen in het zorgproces, bijvoorbeeld: Consult, Behandeling, QA Meten, etc.

De simulatie maakt ook gebruik van gebruiksmiddelen (Resources). Dit zijn essentiële onderdelen die nodig zijn om een handeling uit te voeren. De Entity houdt deze resource vast tot de handeling, of keten handelingen, is voltooid.
Binnen HollandPTC hebben we drie Resources gedefinieerd: (1) Personeel, (2) ruimtes, (3) overige apparatuur. Voorbeeld: Bij een behandeling in de Luit moeten 3 MBB medewerkers en een Gantry ruimte worden ingezet; bij een consult is een Radiotherapeutisch Oncoloog nodig; bij de zorgketen masker-CT-infuus zijn 2 MBB'ers en de CT ruimte nodig; voor een dosisplanning is een DPL medewerker en een DPL computer nodig.
Wanneer deze resources niet beschikbaar zijn wordt de Entity vastgehouden tot de benodigde Resources vrijkomen, waarna het proces wordt vervolgd.

Wanneer Entities worden vastgehouden, ontstaat er in het proces een wachtrij (Queue). Door het achterhalen waar Queues ontstaan, kunnen we bepalen waar in het proces zich knelpunten voor gaan doen en waardoor dit komt.

1.3 Benodigdheden

Om de simulatie correct te kunnen uitvoeren is een computer nodig waarop MATLAB R2020b is geïnstalleerd. Tevens zijn de volgende packages nodig:

- Curve Fitting Toolbox™
- SimEvents®

Contactgegevens

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Hoofdstuk 2

Stap-voor-stap gebruik

De simulatie is gebaseerd op de carepaths van begin 2021 (januari - maart), zie bijlage 1. Het is mogelijk om onderscheid te maken tussen oesophagus, lymfoom en long patiënten in plaats van thorax.

2.1 Algemene waarschuwingen

⚠ Pas nooit iets aan in de simulatie of de code van het programma zonder dat deze handleiding daar expliciet instructies toe geeft.

⚠ De runtijd van de simulatie is afhankelijk van de complexiteit van de input: lengte simulatietijd, ingevoerde aantallen en een realistische input. Pas niet teveel in één keer aan om de simulatietijd behapbaar te houden

⚠ De runtijd is ook afhankelijk van alle lopende achtergrondprocessen. Sluit dus zoveel mogelijk applicaties eerst af voor gebruik.

⚠ Start altijd heel MATLAB opnieuw op nadat de simulatie vastgelopen lijkt te zijn.

⚠ Complexe berekeningen kunnen een paar minuten duren, wacht daarom 5 minuten voor het herstarten van MATLAB.

⚠ Bij het afsluiten van de simulatie zal er gevraagd worden of de wijzigingen moeten worden opgeslagen. Het programma past variabelen aan in de simulatie, hierdoor ontstaat deze melding. Als er alleen gebruik is gemaakt van het programma, sla dan de simulatie niet opnieuw op.

2.2 Opstart

Om het programma op te starten moet een computer gebruikt worden waarop MATLAB is geïnstalleerd en de bijbehorende licentie is geactiveerd. Voor meer informatie over het opstarten en activeren van MATLAB en Simulink, ga naar: `https://nl.mathworks.com/support.html?s_tid=gn_supp`.

Ga naar de map `xxx` en open het bestand genaamd `HPTCapp_ProgramV1.mlapp`. Er openen nu **twee** vensters:

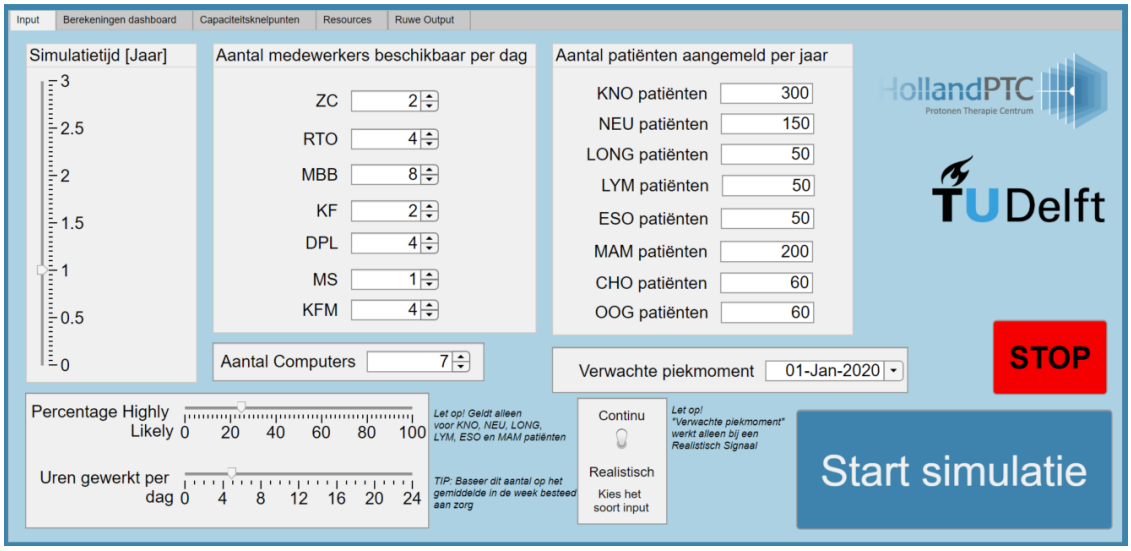
1. Het programma: dit is het belangrijkste gebruikersonderdeel. Hier kun je de meeste situaties simuleren. In veel gevallen is het dus prima de andere programma's met rust te laten.
2. MATLAB zelf: Dit is het hoofdvenster van de software die we gebruiken om de simulatie en het programma uit te voeren. Dit hoef je niet te gebruiken (TIP: links onderin dit venster geeft MATLAB aan wat hij aan het doen is. In de meeste gevallen staat hier "`Ready`". Bij het opstarten van de simulatie en het programma staat er "`Initializing`", tijdens het runnen van een simulatie staat er "`Busy`". Hier kun je snel zien of het al mogelijk is van start te gaan.).

Wacht tot alles volledig is opgestart.

2.3 Inputscherm

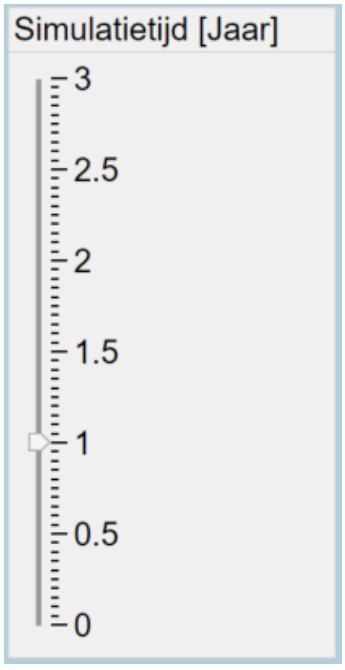
Het inputscherm is het eerste tabblad van het programma wat direct in beeld komt nadat het programma is opgestart. Hier kan je als gebruiker de verschillende variabelen aanpassen die invloed hebben op de simulatie. In deze sectie worden alle onderdelen apart toegelicht.
Het is erg belangrijk dat de input klopt. Als hier fouten of onzorgvuldigheden in zitten, is de output niet betrouwbaar.

De simulatie werkt met veel random number generators (RNG). Sommige inputs fungeren dan ook meer als richtlijnen dan harde eisen.



Simulatietijd

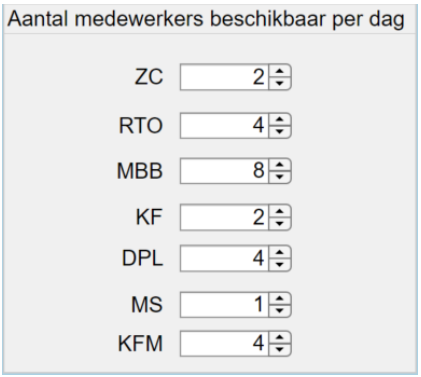
Dit is de exacte tijd dat de simulatie gerund wordt. Hij staat standaard op 1 jaar. Het minimum is 0 jaar en het maximum 3.



⚠ LET OP: De simulatie heeft tijd nodig om een "steady state" te bereiken. Dit heet de "warm-up periode". Als je exact een realistisch jaar wilt simuleren, simuleer dan 1.05 jaar om ruimte te geven voor 0.05 jaar warm-up.

⚠ LET OP: Simulatietijd is **de belangrijkste** variabele die de totale runtijd beïnvloed. Als je snel resultaten wilt, houd dit getal dan laag. Simulatietijden van meer dan 2 jaar duren meer dan 5 minuten.

Aantal medewerkers beschikbaar per dag



Het aantal medewerkers is het gemiddelde aantal dat beschikbaar was gedurende de simulatietijd. Voor een realistische simulatie is het aangeraden dit getal te berekenen uit historische gegevens. Als er uitval heeft plaatsgevonden wat mee gesimuleerd moet worden, ga dan naar sectie 3.2.2.

Er is geen limiet aan hoe hoog deze getallen kunnen worden. Het getal kan niet negatief worden. Een realistische simulatie heeft wel een minimum aantal medewerkers nodig.

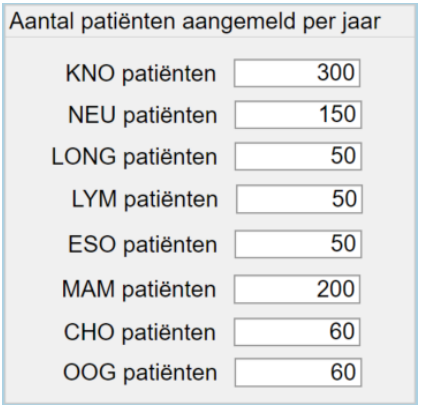
Uitleg afkortingen, plus minimum nodig voor realistische simulatie:

ZC	Verpleegkundig Conslent Oncologie	1
RTO	Radiotherapeutisch Oncoloog	2
MBB	Medische Beeldvormings- en Bestralingsdeskundigen	3
KF	Klinisch Fysicus	1
DPL	Dosisplanner	1
MS	Medisch Secretariaat	1
KFM	Klinisch Fysisch Medewerker	2

Aantal patiënten aangemeld per jaar

Het aantal patiënten per jaar die aangemeld worden door verwijzende instituten is vrij te variëren. Er zijn 8 tumorlijnen gedefinieerd in de simulatie:

KNO	KNO tumoren, passend bij het KNO zorgpad
NEU	Neurologische tumoren, passend bij het Neuro zorgpad
LONG	Long tumoren, passend bij het thorax of long zorgpad
LYM	Lymfoom tumoren, passend bij het thorax of lymf zorgpad
OES	Oesophagus tumoren, passend bij het thorax zorgpad
MAM	Mamma tumoren, passend bij het Mamma zorgpad
CHO	Chordomen of Chondrosarcomen, passend bij het CH zorgpad
OOG	Oogmelanomen, passend bij het Oog zorgpad



Het aantal patiënten kan globaal of exact zijn, afhankelijk van het soort input (Realistisch of Continu). Zie "soort input"voor meer informatie.

⚠ LET OP: Er staat specifiek "Patiënten **aangemeld**". De Simulatie houdt rekening met uitval gedurende het proces, denk aan negatieve planvergelijkingen,

afhaken van de patiënt, of overlijden.

De uitvalpercentages zijn constant en gebaseerd op de data uit 2020 en ervaringen van de medewerkers. De uitvalpercentages zijn als volgt:

KNO	70%
NEU	20%
LONG	65%
LYM	50%
OES	60%
MAM	20%
CHO	25%
OOG	0%

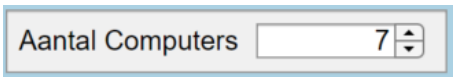
Houd bij het invoeren van het aantal aangemelde patiënten dan ook rekening met de uitvalpercentages en de warm-up tijd. Als je 100 behandelde KNO patiënten per jaar wilt simuleren moet je dus $\frac{100}{1-0.7} \times 1.05 \approx 350$ patiënten invoeren.

Er zit geen limiet aan hoe hoog deze getallen kan worden. Het getal kan niet negatief worden.

⚠ LET OP: Als je korter dan een jaar wilt simuleren moet je bij het invullen van het aantal patiënten aangemeld per jaar nog steeds het aantal per jaar invullen. Dus: bij simulatie van een half jaar waarin 50 KNO patiënten zijn behandeld, moet je bij aangemelde patiënten $\frac{50}{1-0.7} \times 1.05 \times \mathbf{2} \approx 350$ patiënten invoeren

Aantal Computers

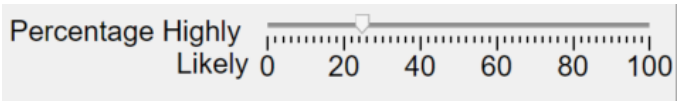
Het aantal computers gaat over de hoeveelheid beschikbare computers voor de DPL medewerkers. Dit is een gemiddeld getal gedurende de simulatietijd en staat standaard op het (op de tijd van schrijven) maximale getal: 7.



Er zit geen limiet aan hoe hoog dit getal kan worden, het getal kan niet negatief worden.

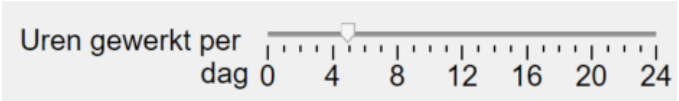
Percentage Highly Likely

Dit percentage bepaald globaal hoeveel patiënten in de simulatie behandeld worden volgend de HL carepaths.
Dit houdt in dat ze sommige stappen van de simulatie later doorlopen en sommige stappen helemaal niet. Dit percentage staat standaard op 25%, gebaseerd op data uit 2020.



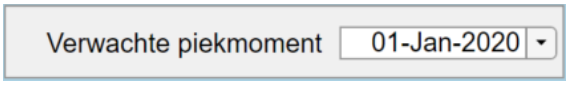
⚠ LET OP: Dit getal is alleen van toepassing op de tumorlijnen KNO, NEU, LONG, LYM, OES en MAM. De tumorlijnen CHO en OOG werken niet met Highly Likely.

Uren gewerkt per dag



Het aantal uren gewerkt per dag bepaalt wanneer patiënten worden doorgelaten in de simulatie. Het kan gezien worden als een openingstijden functie. Hier wordt een gemiddeld getal ingevuld die per dag besteed is aan zorg over de simulatietijd. Hij staat standaard op 5 uur. Dit getal is gebaseerd op een negenurige werkdag van een zorgmedewerker die 4 uur per dag besteedt aan scholing, administratie, intercollegiaal consult, pauze en laakbaarheid. Bij aanpassen van dit getal hoort met deze factoren rekening gehouden te worden voor een realistische simulatie.

Verwachte piekmoment



Onder "Verwachte piekmoment- is het mogelijk een dag in het jaar te kiezen. Deze dag wordt door de simulatie genomen als piekmoment. Dit houdt in dat er een golf zichtbaar wordt in het aantal gegenereerde patiënten. Hij staat standaard op 1 januari 2020, zonder specifieke reden. De kalender loopt vanaf 2018 t/m het einde der tijden. 2018 is gekozen als startjaar, gezien in dit jaar HollandPTC geopend is.

⚠ LET OP: Deze functie werkt alleen als het knopje "Kies het soort input" is omgeschakeld naar "Realistisch".

Soort input

De "Kies het soort input"knop bepaalt hoe de simulatie omgaat met het aantal aangemelde patiënten.

Continu

Bij een continue input is het aantal aangemelde patiënten exact: $\frac{n}{8675} = n_h$. Met n: ingevuld aantal patiënten per jaar aangemeld, 8675: het aantal uren in een jaar, en n_h: aantal patiënten gegenereerd per uur.

Realistisch

Bij een realistische input worden patiënten gegenereerd met een random tijdsinterval tussen twee patiënten. Deze tijdsintervallen zijn globaal afhankelijk

van het "verwachte piekmoment". Rondom het piekmoment worden de tijdsintervallen tussen twee patiënten gemiddeld korter, buiten dit piekmoment wordt dit tijdsinterval gemiddeld langer.

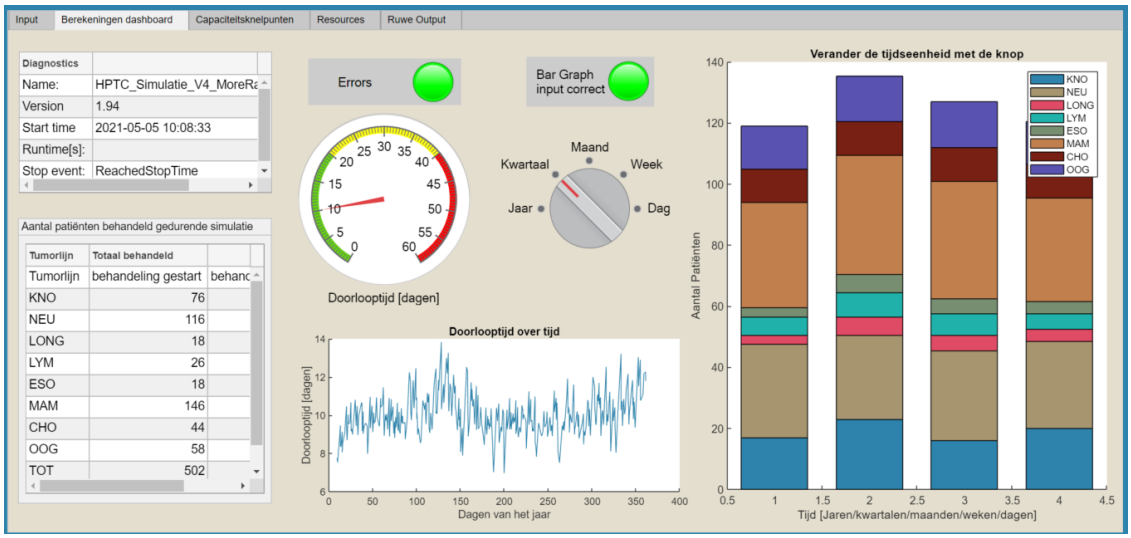
Start en stop knop

Met deze knoppen wordt de simulatie gestart of gestopt. Door op "Start Simulatie" te klikken wordt alle input in de simulatie geladen, worden resultaten gewist en wordt de simulatie gerund. MATLAB zal doorgaan met runnen tot er een eindpunt is bereikt, tenzij "STOP" wordt ingedrukt in de tussentijd. De STOP-knop werkt niet direct, maar het kost een paar seconden voor de STOP-knop om de hele simulatie af te sluiten. De STOP-knop zal in de meeste situaties niet nodig zijn. Gebruik deze knop dan ook alleen als je merkt dat je een fout gemaakt hebt bij het invoeren van inputgegevens en niet wil wachten tot de simulatie klaar is.

⚠ LET OP: Na het indrukken van de STOP-knop worden nog wel berekeningen uitgevoerd gebaseerd op hoever de simulatie is gekomen en worden voorgaande berekeningen verwijderd. Zorg dus dat data uit voorgaande simulaties goed is opgeslagen.

⚠ LET OP: Na het indrukken van de START-knop zal eerst de simulatie geïnitialiseerd worden. Gedurende deze tijd werkt de STOP-knop niet. Wacht dus een paar seconden na indrukken van de START-knop om de STOP-knop in te drukken.

2.4 Berekeningen dashboard



Berekeningen dashboard na simuleren van de input aangegeven in sectie 2.3

Het berekeningen dashboard is het tweede tabblad van het programma. Klik hiervoor op de desbetreffende tab naast input. Nadat de simulatie is gestart zullen hier de belangrijkste resultaten verschijnen. In deze sectie worden alle onderdelen apart toegelicht.

Diagnostics tabel

De diagnostics tabel is een tabel waar de gebruiker zich niet vaak over hoeft te bekommeren. Als de simulatie goed loopt en er geen errors zijn, zal deze niets bijzonders weergeven.

Diagnostics	
Name:	HPTC_Simulatie_V4_MoreRandomandD…
Version	1.94
Start time	2021-05-05 10:27:27
Runtime[s]:	148.8030
Stop event:	ReachedStopTime

Deze tabel geeft weer:

- De naam van het gebruikte Simulink model
- Het versienummer van het model
- De tijd en datum dat de simulatierun gestart is
- De totale runtijd van de simulatie
- De reden waarom de simulatie is gestopt

Als alles goed gaat staat bij "Stop event": "ReachedStopTime". Na indrukken van de STOP-knop komt hier "StopCommand"te staan.

Aantal patiënten behandeld tabel

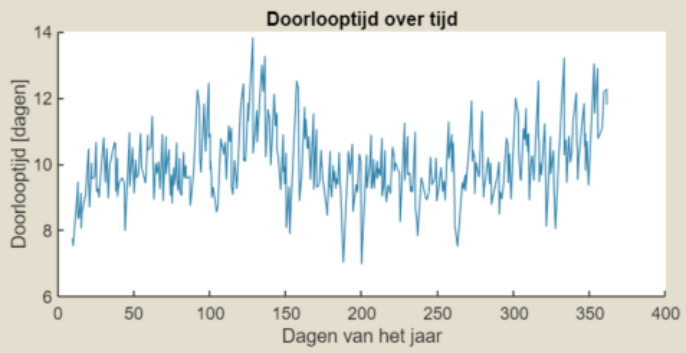
Deze tabel laat het aantal patiënten waarvan de behandeling is gestart en waarvan de behandeling is voltooid zien, genomen over de gehele ingevoerde simulatietijd. Hij geeft van alle tumorlijnen deze informatie, evenals totale aantallen. Hiernaast geeft hij ook het aantal patiënten weer waarvan het proces gestopt is door uitval.

Aantal patiënten behandeld gedurende simulatie

Tumorlijn	Totaal behandeld	
Tumorlijn	behandeling gestart	behandeling voltooid
KNO	84	73
NEU	109	98
LONG	17	15
LYM	27	25
ESO	18	16
MAM	149	132
CHO	46	38
OOG	58	57
TOT	508	454
Uitval		351

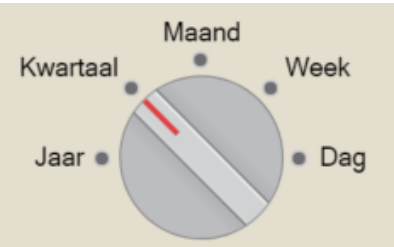
Doorlooptijden (grafiek en metertje)

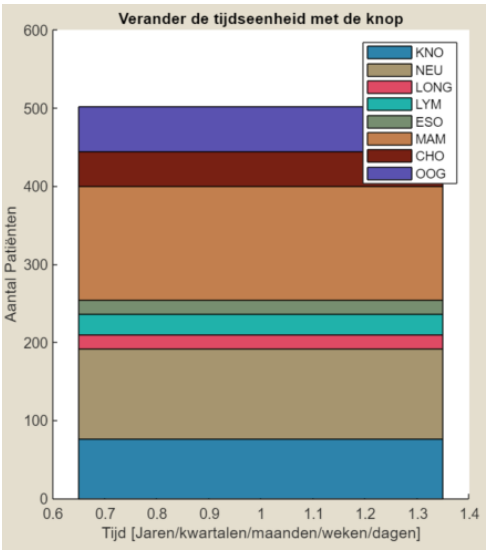
Deze meter en grafiek geven informatie over de doorlooptijden. De meter geeft het gemiddelde weer en de grafiek geeft de doorlooptijden aan over de gehele simulatietijd. Doorlooptijd is gedefinieerd als de tijd tussen de start van het proces en de start van de behandeling. Deze tijd is aangegeven als meest variabel. Immers, wanneer de behandeling is gestart, lopen de processen volgens het fractioneringsschema.



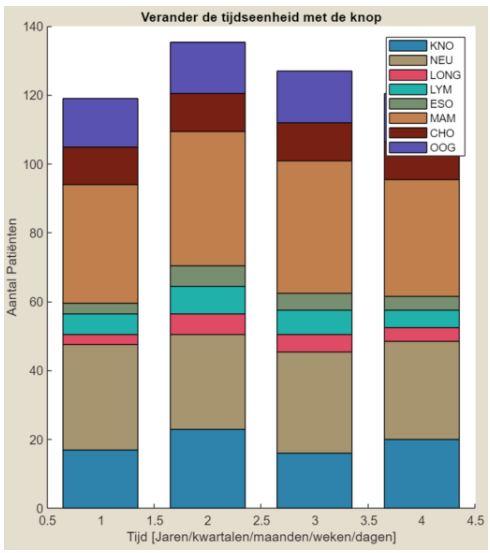
Staafgrafiek

De staafgrafiek geeft de hoeveelheid patiënten weer waarvan de behandeling is gestart per tijdseenheid. De tijdseenheid is te veranderen door middel van de draaiknop. Op pagina 15 staan verschillende configuraties van de staafdiagram, afhankelijk van de stand van de draaiknop.

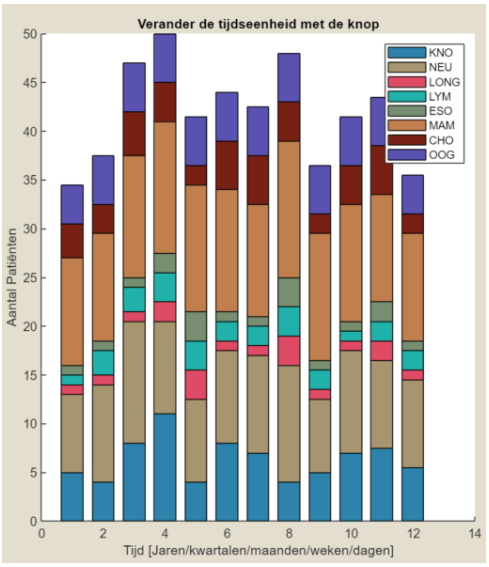




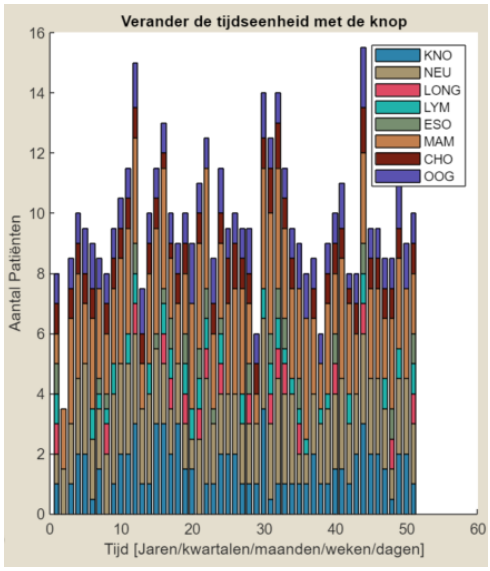
(a) *Knop staat op "Jaar"*



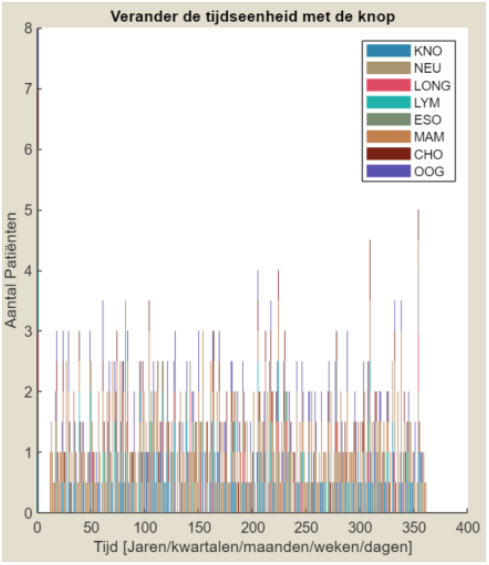
(b) *Knop staat op "Kwartaal"*



(c) *Knop staat op "Maand"*



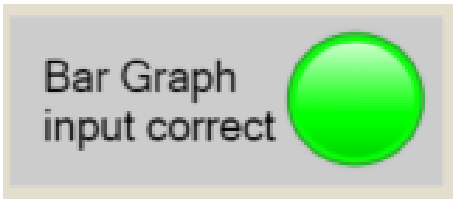
(d) *Knop staat op "Week"*



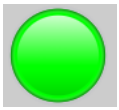
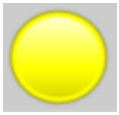
(e) *Knop staat op "Dag"*

Staafdiagrammen in verschillende configuraties

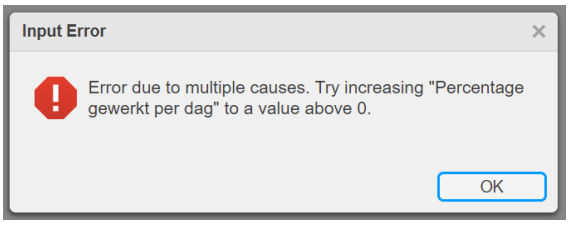
Bar Graph Lamp
Dit lampje dient als ondersteuning bij de staafdiagram. Als er iets in de berekeningen van de aantallen fout gaat wordt het lampje rood. Over het algemeen gebeurt dit alleen wanneer de simulatie zelf niet meer klopt. Wanneer dit gebeurt, start dan de simulatie opnieuw op of herstart een oudere versie. Mocht dit niet werken, neem dan contact op met de ontwikkelaars.



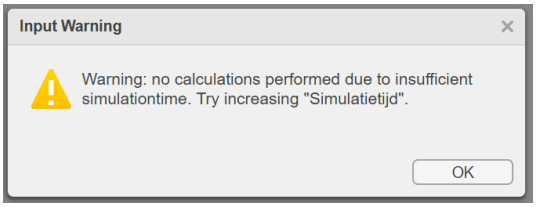
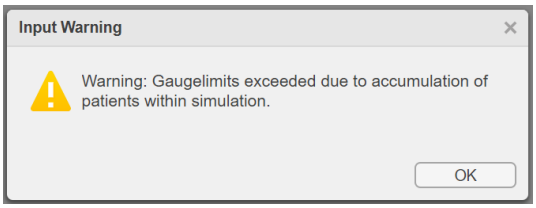
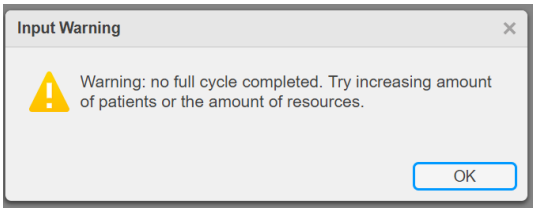
Errors
Het errorlampje kan drie kleuren worden:

Kleur	Betekenis
	Alles is in orde
	Waarschuwing: de simulatie heeft gedraaid, maar de output is niet logisch/niet betrouwbaar
	Error: de simulatie heeft niet gedraaid

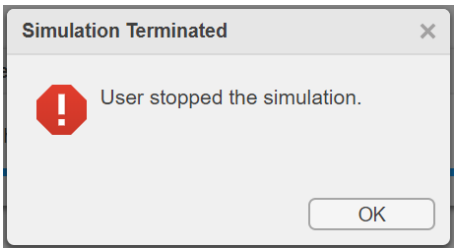
Input Errors

Error bericht	Uitleg
	het programma heeft de simulatie niet kunnen starten omdat de simulatie niet geopend is. Open het bijbehordende .slx (Simulink model) bestand.
	Deze error ontstaat doordat er ergens in de simulatie door 0 gedeeld wordt. Waarschijnlijk is de "uren gewerkt" slider de boosdoener. Verhoog dit getal naar een waarde boven 0. Als dit niet werkt, controleer de andere input waarden.

Input Warnings

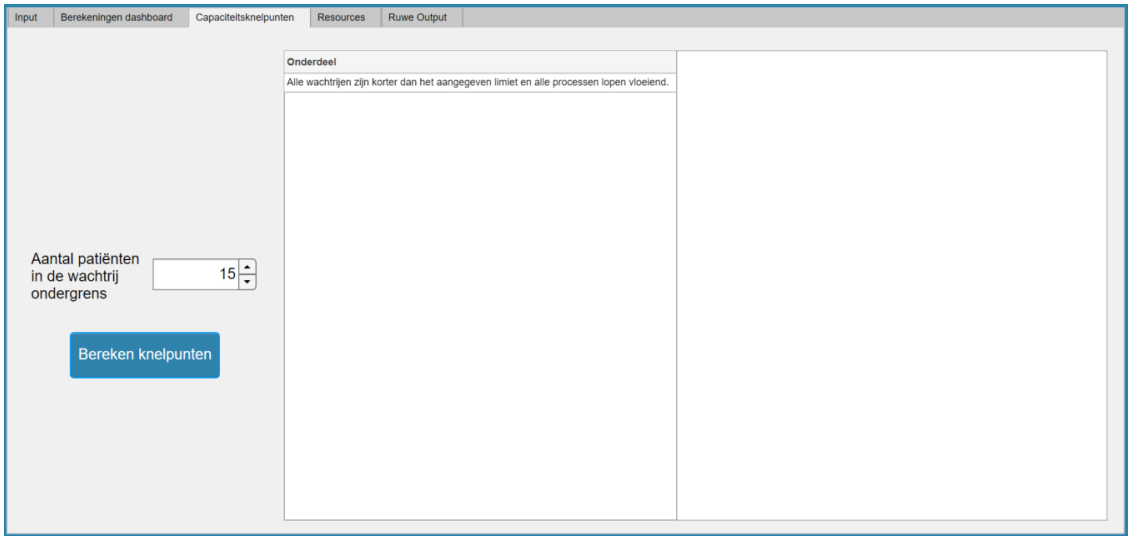
Error bericht	Uitleg
	De simulatie heeft geen berekeningen opgeleverd omdat de simulatietijd te kort was. Verhoog de simulatietijd.
	Berekeningen kunnen niet goed worden uitgevoerd omdat patiënten zich ophopen in de simulatie. Dit is op te lossen door de knelpunten op te lossen door bijvoorbeeld het aantal Resources te verhogen.
	Geen enkele patiënt heeft een behandeling voltooid. Dit kan twee oorzaken hebben: (1) Geen enkele patiënt heeft de simulatie doorlopen. Oplossing: verhoog het aantal patiënten in de input. (2) Alle patiënten lopen vast in de simulatie. Oplossing: Verhoog het aantal Resources.

Overig

Error bericht	Uitleg
	Gebruiker heeft op de STOP-knop ingedrukt

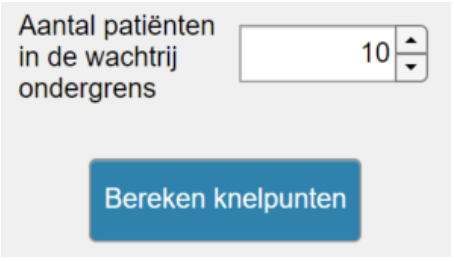
Voor ongedocumenteerde errors, neem contact op met de ontwikkelaars.

2.5 Capaciteitsknelpunten



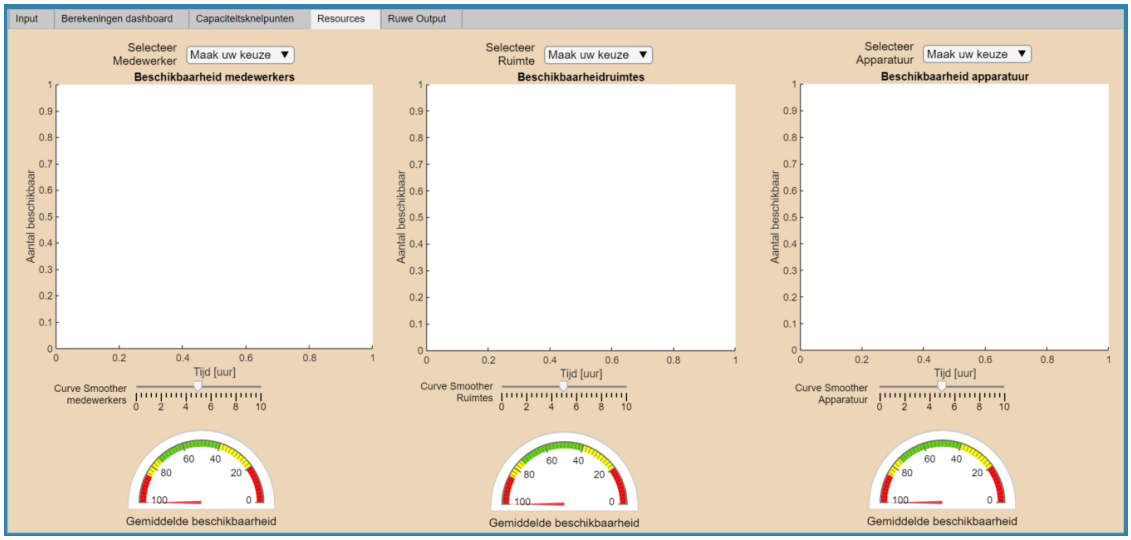
Knelpunten tabblad na simuleren van de input aangegeven in sectie 2.3

Het Capaciteitsknelpunten tabblad is het derde tabblad van het programma. Klik hiervoor op het desbetreffende tab naast het berekeningen dashboard. Nadat de simulatie is gestart, is dit tabblad te gebruiken om te achterhalen waar mogelijke knelpunten zullen ontstaan. Het programma berekent de lengte van alle wachtrijen van alle activiteiten in de simulatie. Hoe efficiënter het proces loopt, hoe kleiner deze wachtrijen over het algemeen zijn. Een hoge wachtrij betekent dan ook dat patiënten zich ophopen in de simulatie: een capaciteitsknelpunt.



Het scherm aan de rechterkant van het tabblad geeft de mogelijke knelpunten weer. Hier wordt aangegeven welke activiteit het knelpunt bevat, bij welk onderdeel binnen het zorgproces deze activiteit hoort en wat mogelijke oplossingen zijn.
Er is één variabele die aangepast kan worden: de "wachtrij ondergrens". Deze variabele geeft aan wat voor wachtrijlengte "geaccepteerd" wordt. Hoe kleiner dit getal, hoe meer activiteiten als "knelpunt"worden gezien. Deze worden dan na het indrukken van de knop "Bereken knelpunten" weergegeven op het scherm. Door dit getal geleidelijk aan te verhogen, is het mogelijk te bepalen waar de grootste problemen zich gaan voordoen.
Wat voor ondergrens reëel is, is afhankelijk van de simulatie parameters en het vraagstuk.

2.6 Resources



Het Resources tabblad is het vierde tabblad van het programma. Klik hiervoor op het desbetreffende tab naast het knelpunten tabblad. Er zijn drie grafieken weergegeven. Eén per soort Resource: personeel, ruimtes en apparatuur.

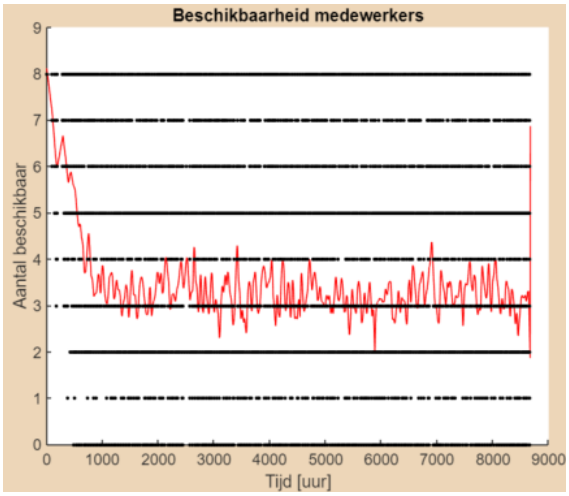
Dit tabblad bevat 4 onderdelen per Resource: (1) het keuzemenu, hieruit is het mogelijk om een Resource te selecteren per soort. (2) De beschikbaarheid grafiek, waarover later meer. (3) De Curve Smoother slider, deze wordt gebruikt om de rode trendlijn meer of minder egaal te maken. (4) Het Gemiddelde beschikbaarheid metertje, waarin het gemiddelde percentage beschikbaarheid is weergegeven.

Het keuzemenu

Het is mogelijk om per Resource een specifiek onderdeel uit te kiezen. Dit is opgesplitst in de drie verschillende soorten. De keuzes zijn:

Personeel	Ruimtes	Apparatuur
MBB	Gantries	Computers
RTO	Parel	
DPL	CT	
KFM	MRI	
ZC	PET-CT	
KF		
MS		

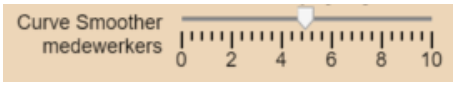
Bezetting grafiek



Deze grafiek laat de beschikbaarheid van de gekozen Resource zien. De zwarte stippen is de exacte beschikbaarheid voor de gekozen Resource op een specifiek tijdspunt. Deze begint altijd op het maximaal aangegeven aantal Resources in de input tab en zal rondom een "steady-state"blijven schommelen.
De rode lijn geeft de trend van de zwarte punten weer. Deze lijn is dan ook een benadering van de steady-state.

Interpretatie van de grafiek
Deze grafiek kan goed gebruikt worden om te achterhalen of de Resources optimaal benut worden. Over het algemeen geldt: hoe hoger de lijn van de steady-state, hoe meer Resources er beschikbaar zijn. Dit houdt in dat er teveel Resources zijn voor de gevraagde taken. Hoe lager de lijn van de steady-state, hoe minder Resources beschikbaar zijn. Dit betekent dat er een tekort is aan deze Resource. Dus, hoe groter de kans dat deze Resource leidt tot een capaciteitsknelpunt.
Er moet gestreefd worden naar een steady-state rond het midden van de grafiek: Resources zijn niet inactief/nutteloos en ook niet overwerkt/uitgeput.

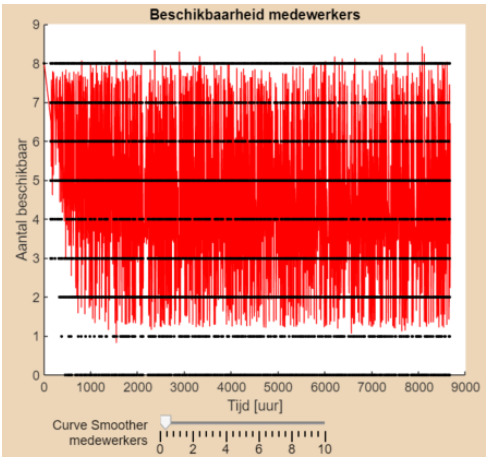
Curve Smoother slider



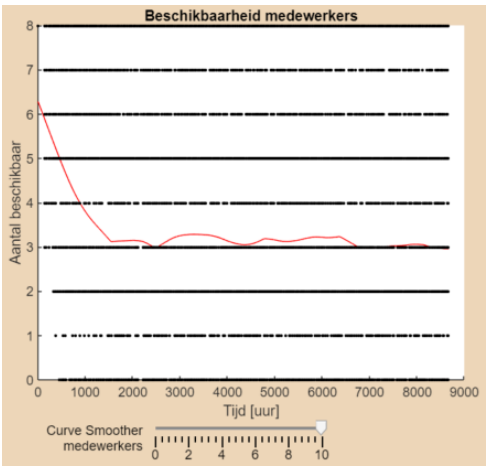
Deze slider kan gebruikt worden om de trendlijn af te vlakken. Hij gaat van 0 (geen afvlakking) tot 10 (maximale afvlakking) en hij staat standaard op 5 (middelmatige afvlakking). Een lagere afvlakking laat een duidelijkere trend zien: het wordt goed zichtbaar hoe de verdeling van de Resource precies is. Een hogere afvlakking brengt de lijn meer in de buurt van de steady-state. Het figuur op de volgende pagina laat de grafiek zien met de twee uiterste sliderwaarden.

Gemiddelde beschikbaarheid metertje

Deze meter geeft de gemiddelde beschikbaarheid weer als percentage van de maximale beschikbaarheid. 100% betekent dat de volledige Resource altijd beschikbaar is, 0% betekent dat de volledige Resource maximaal uitgeput is.



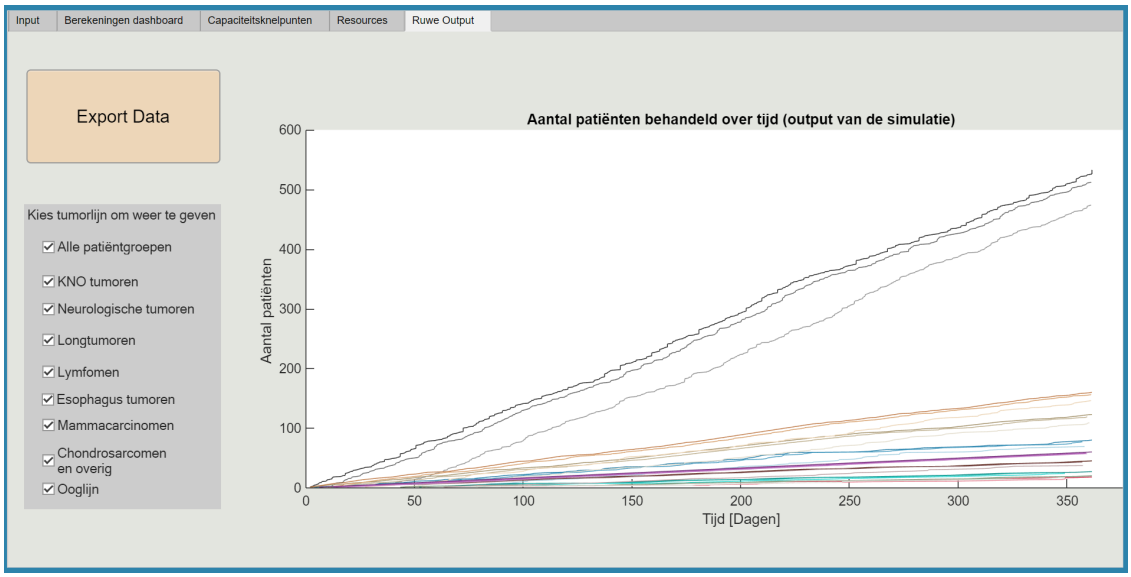
(a) *Slider staat op 0.5*



(b) *Slider staat op 10*

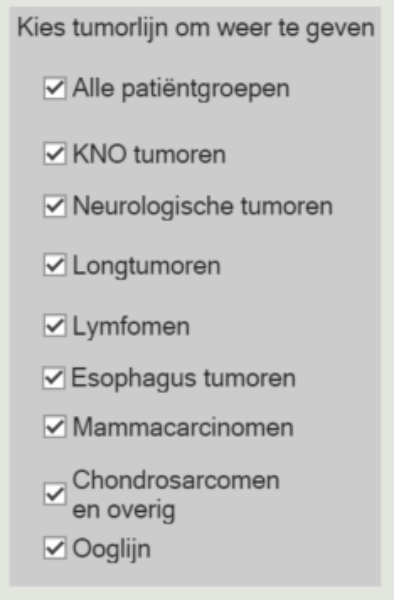
De kleuren geven aan welk gebied ideaal
is: rondom het midden. Een te hoge beschikbaarheid is onwenselijk, gezien dit waarschijnlijk komt door een ophoping van patiënten ergens in de simulatie waardoor de Resource niet aan bod komt. Een te lage beschikbaarheid is ook niet wenselijk, gezien dit inhoudt dat er een Resource schaarste ontstaat, wat leidt tot capaciteitsknelpunten.

2.7 Ruwe Output



Ruwe Output tabblad na simuleren van de input aangegeven in sectie 2.3

Het Ruwe Output tabblad is het laatste tabblad van het programma. Hier hoef je als gebruiker, over het algemeen, niets mee te doen. Klik voor het bereiken van het Ruwe Output tabblad op het desbetreffende tab naast het Resources tabblad.
In de figuur wordt de directe output van de simulatie weergegeven. Er zijn drie momenten dat er informatie over de entities wordt onttrokken: (1) Voorafgaand aan de intake, wanneer patiënten nog geen enkele activiteit hebben ondergaan. (2) Vlak voor de behandeling, direct na de QA. (3) Na voltooiing van de behandeling.
In de figuur staan een aantal oplopende grafieken. Per tumorlijn zijn er drie grafieken zichtbaar, één per meetmoment. Tevens is hier ook een totaal grafiek meegenomen.



Iedere keer als een patiënt een meetmoment passeert gaat de grafiek een stapje omhoog. De figuur laat voor alle tumorlijnen (en de totalen) per meetmoment zien hoeveel patiënten op welk tijdstip het meetmoment gepasseerd hebben. Met de vakjes aan de linkerkant is het mogelijk bepaalde tumorlijnen aan of uit te zetten. De tijd tussen het eerste meetmoment en het tweede meetmoment is de doorlooptijd.

Dit tabblad bevat ook een knop waarmee de data geëxporteerd kan worden. Na indrukken van deze knop verschijnt er een

Excel bestand in dezelfde map met de naam `ExportedDataSheet.xls`. Hierin staat alle informatie over de totalen, doorlooptijden en beschikbaarheid van middelen die aangegeven zijn in het Resources tabblad.

Hoofdstuk 3

Complexe aanpassingen

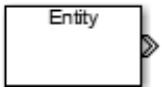
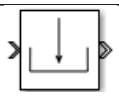
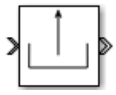
⚠ Belangrijk: sla de simulatie eerst op onder een andere naam voordat je aanpassingen doet, pas deze naam ook aan in de code van het programma (lees sectie 3.2.1 voor instructies over hoe dat moet

3.1 Uitleg Simulink

Simulink is een blok-diagram programmeeromgeving, te gebruiken voor het ontwerpen van modellen. Simulink vormt een grafische weergave met blokken die door de gebruiker aangepast kunnen worden. Binnen Simulink maken wij specifiek gebruik van een toolbox genaamd "SimEvents". Deze toolbox is specifiek ontworpen om Discrete Event Simulations mee te ontwerpen en uit te voeren.

SimEvents blokken

De simulatie maakt gebruik van blokken om evenementen, wachtrijen, processen, patiëntstromen, en gebruik van middelen weer te geven. De volgende blokken worden het meest gebruikt en zijn het belangrijkst om globaal te begrijpen voordat aanpassingen aan de simulatie worden gemaakt.

Icoon	Naam	Uitleg
	Entity Generator	Dit blok genereert Entities (patiënten). De Entities krijgen een prioriteit en een set "Attributes": Tumortype (welke tumorlijn ze gaan bewandelen), DryRun (of ze een DryRun hebben gehad), Behandeld (hoeveel behandelingen zijn geweest), HighlyLikely (ja of nee), Planadaptatie (of ze geadapteerd worden) en Uitval (ja of nee). Het blok onder dit blok bepaald hoeveel Entities er per tijdseenheid gegenereerd worden gebaseerd op de hoeveelheid aangemelde patiënten, aangegeven in het programma.
	Entity Queue	Dit blok houdt Entities vast als hun pad geblokkeerd is (als er een Entity in de weg staat). Entities worden meteen losgelaten zodra dat kan. Alle queues binnen de simulatie staan op FIFO (First In First Out) en hebben een oneindige capaciteit. Uit de queues wordt informatie onttrokken over hoeveel Entities er per tijdseenheid inzitten, hoeveel er vertrokken zijn, en wat de gemiddelde wachttijd is. De informatie over hoeveel patiënten er per tijdseenheid in een queue bevinden wordt later gebruikt voor de berekeningen van de capaciteitsknelpunten (zie sectie 2.5).
	Entity Server	Dit blok omschrijft de handelingen of Events. Het blok heeft twee belangrijke variabelen: (1) servicetijd, (2) capaciteit. De capaciteit van alle blokken binnen de simulatie staat op 1 (tevens, we kunnen maar 1 patiënt per keer een activiteit laten doorlopen). De servicetijd varieert afhankelijk van de activiteit. Bepaalde blokken voeren ook nog een aanpassing aan de attribute van de Entity door. Het behandel-serverblok, bijvoorbeeld, telt iedere keer als een Entity passeert 1 op bij zijn attribute "Behandeld".
	Entity Transport Delay	Dit blok houdt Enitities vast voor een specifieke tijd. Dit simuleert de tijd die standaard tussen activiteiten zit. Alle Delay blokken hebben een oneindige capaciteit.
	Entity Input Switch	Deze switch voegt de stromen van Entities samen.
	Entity Output Switch	Deze switch splitst de Entity stromen weer. Dit kan op verschillende manieren, maar de meest gebruikte is gebaseerd op "Tumortype". Dit blok, samen met de Input Switch, zorgen ervoor dat de Entities hun juiste carepath bewandelen. De andere veelgebruikte splitsingsmethode is gebaseerd op een kansfunctie. Dit gebeurt bijvoorbeeld bij het bepalen van uitval of de hoeveelheid Highly Likely's.
	Entity Replicator	Dit blok dient voor het dupliceren van Entities. Er komt 1 Entity in en er gaan er 2 uit. Dit wordt gebruikt om tussentijdse informatie te onttrekken of activiteiten te simuleren die parallel aan elkaar lopen.
	Resource Pool	Dit blok staat los van het gehele proces en bepaalt welke middelen er beschikbaar zijn. Deze zitten zogezegd in het zwembadje. Andere blokken kunnen hier middelen uit onttrekken en weer terug stoppen. De hoeveelheid Resources wordt bepaald via het inputscherm van het programma. Informatie over de hoeveelheid beschikbare Resources wordt gebruikt voor de beschikbaarheids berekeningen omschreven in sectie 2.6.
	Resource Acquirer	Dit blok onttrekt Resources uit de Resource Pool. Per activiteit verschilt welke Resources en hoeveel er onttrokken worden. Dit blok fungeert tevens als queue met onbeperkte capaciteit.
	Resource Releaser	Dit blok geeft de onttrokken Resources weer af aan de Resource Pool.
	Entity Terminator	Dit blok "vernietigt" Entities. Informatie over hoeveel patiënten er in dit blok zijn aangekomen wordt onttrokken en vormt de primaire output van de simulatie waar bijna alle berekeningen mee worden uitgevoerd.
	Scope	Dit blok is een visueel hulpmiddel. Het laat zien hoe de datastromen eruit zien die dit blok passeren.

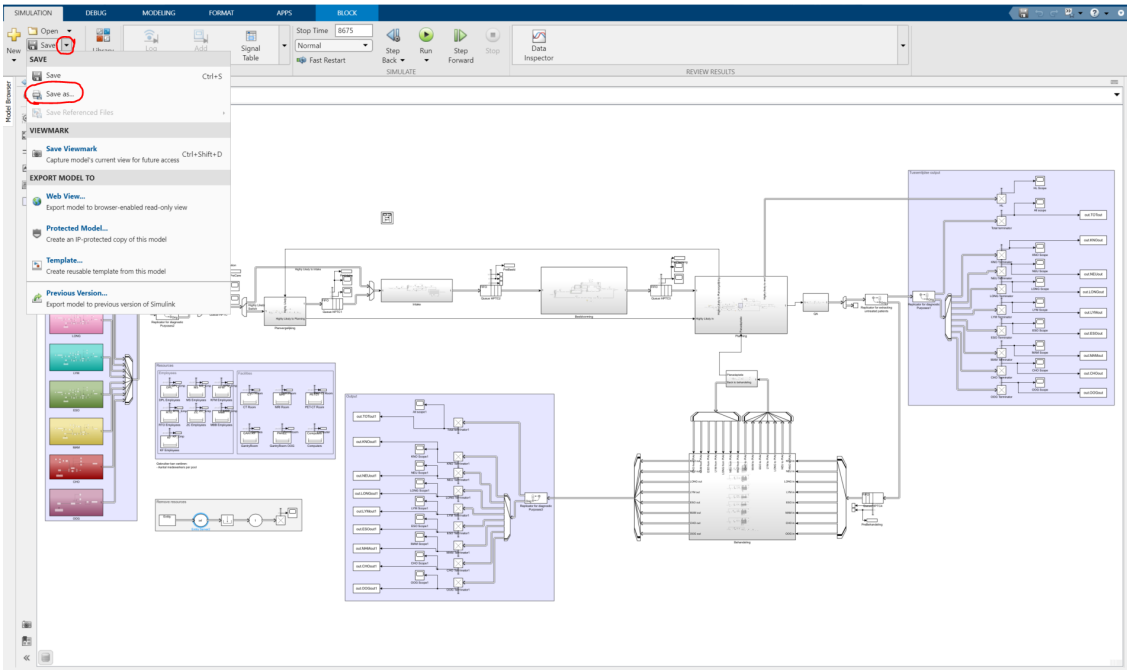
3.2 Aanpassingen doorvoeren

3.2.1 Programma opslaan onder andere naam

⚠ Voer altijd eerst deze stappen uit voordat je aanpassingen maakt aan de simulatie of het programma. Dit moet gebeuren om te waarborgen dat de originele simulatie nog naar behoren blijft werken.

⚠ De gebruikte afbeeldingen kunnen een beetje verschillen van het uiteindelijke product. Kom je er niet uit, neem contact op met de ontwikkelaars.

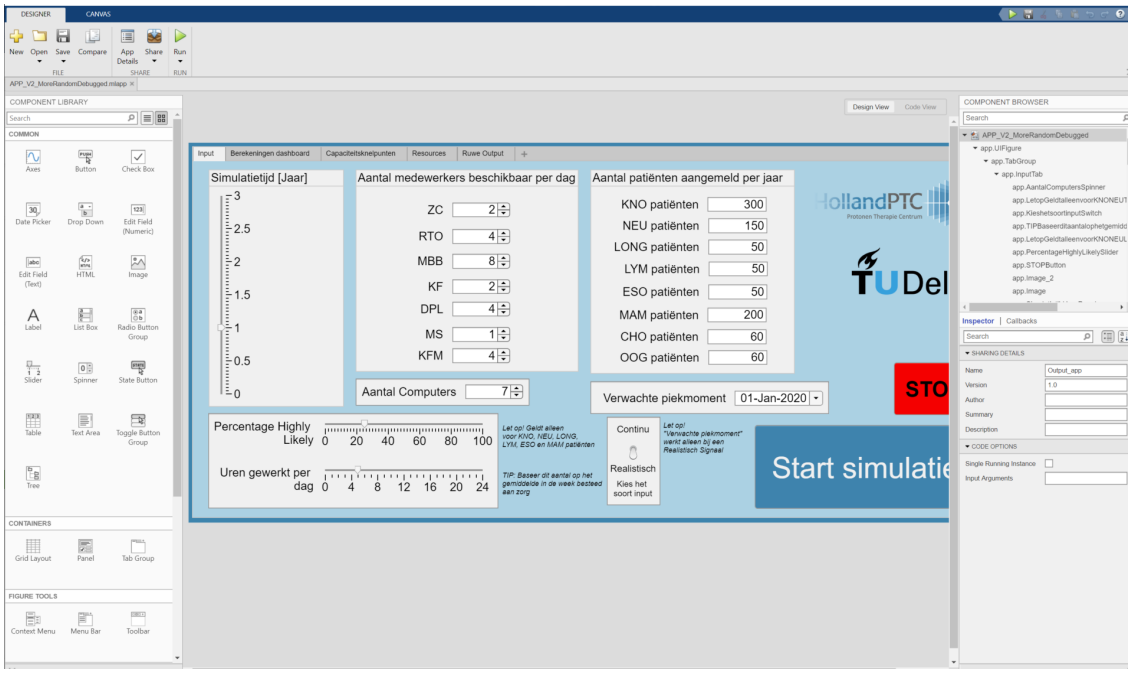
1. Ga naar de simulatie omgeving in Simulink en ga naar het tabblad "SIMULATION". Klik hier op het pijltje rechts van de "Save" knop en kies "Save as". Sla de simulatie op onder een andere naam. Doe dit in de vorm `HPTCapp_SimulationVX_JouwAanpassing.slx`.



Save As in Simulink

2. Ga naar het MATLAB hoofdvenster en dubbelklik op het .mlapp bestand in het venster "current folder".

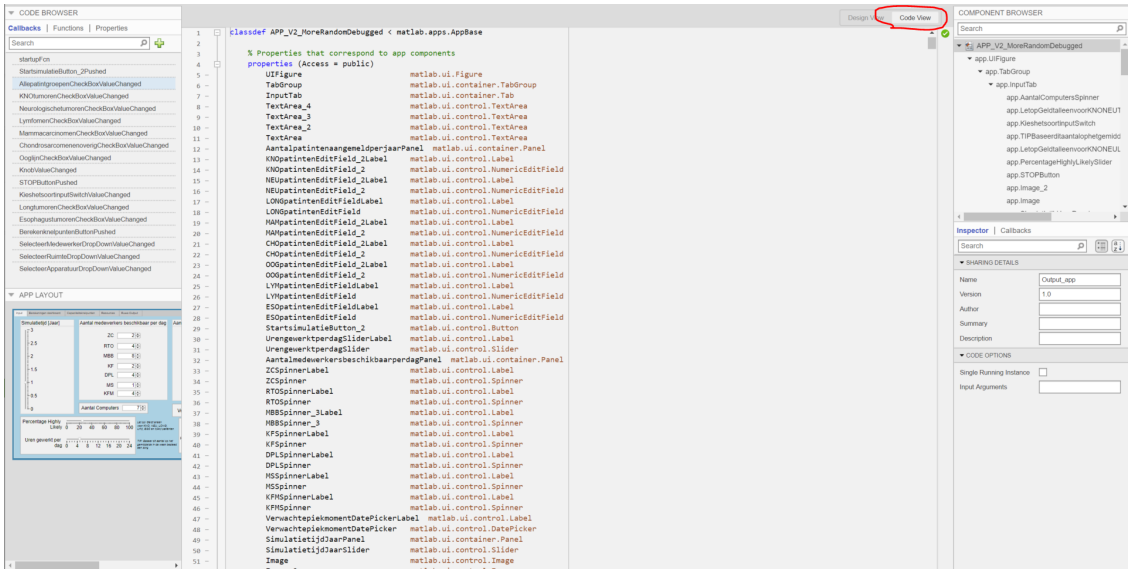
De appdesigner omgeving start nu op.



Appdesigner omgeving

3. Sla het programma onder een andere naam op door onder het "Save" knopje op het pijltje te klikken. Kies "Save as". Doe dit in de vorm: `HPTCapp_ProgramVX_JouwAanpassing.mlapp`

4. Klik op het knopje "Code View" in de rechterbovenhoek van het hoofdvenster.



Code View omgeving

5. Scrol door naar lijn 340 en vervang wat tussen de aanhalingstekens staat (`YourFileName.slx` in het voorbeeld) achter "`app.mdl =`" door jouw gekozen

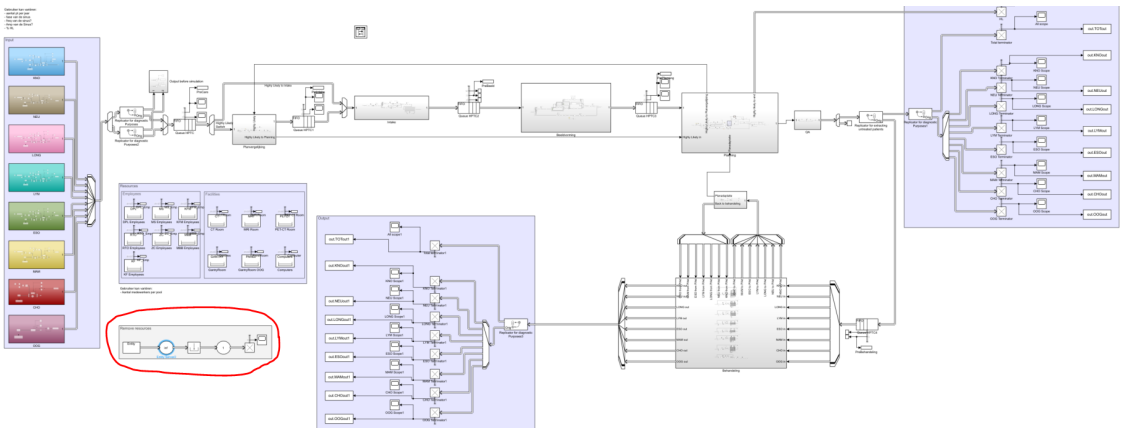
naam van de simulatie als bepaald in stap 1. Zorg ervoor dat de enkele aanhalingstekens blijven staan en dat de bestandsnaam wordt opgevolgd door het `.slx` bestandsformat.

```
338         % Code that executes after component creation
339         function startupFcn(app)
340             app.mdl = 'YourFileName.slx'; % Vul hier de bestandsnaam in
341         end
342
```

3.2.2 Uitval van Resources

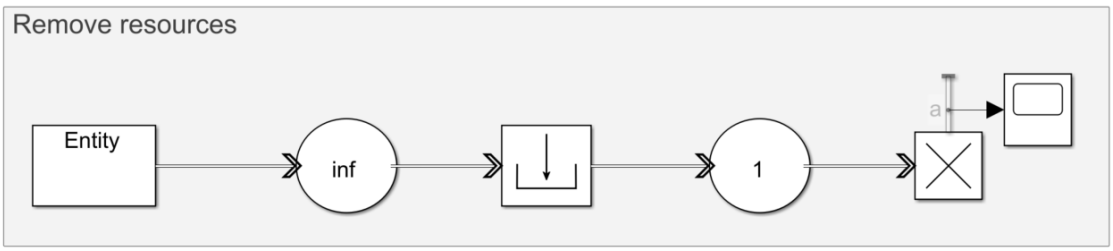
Het is mogelijk om uitval van Resources (Gantry in onderhoud, ziekte van medewerkers, etc) te simuleren. Hiervoor is een apart onderdeel in de simulatie gebouwd. Als voorbeeld nemen we de hypothetische uitval van de Luit door onderhoud voor 1 week in mei 2020. We willen het effect van deze uitval op het gehele jaar simuleren. Dit doen we door de volgende stappen uit te voeren:

1. Open de simulatie in Simulink en ga naar het losstaande onderdeel `Remove Resources`.



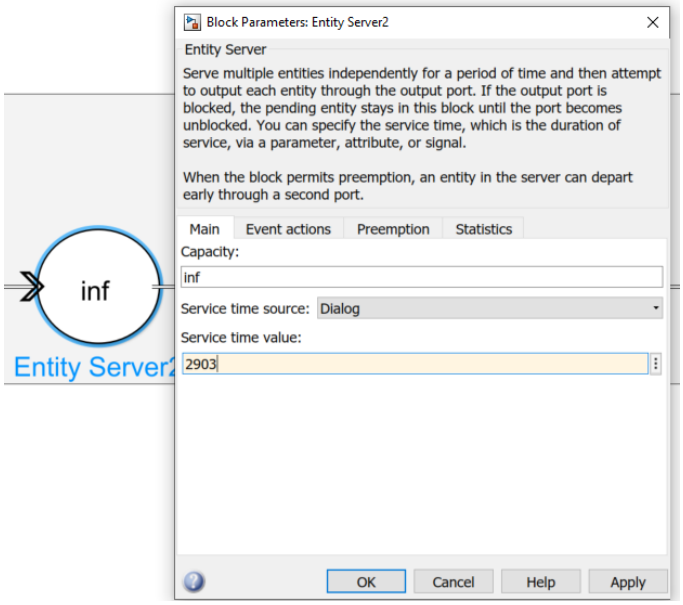
Locatie van het "Remove Resources" blok

Hier zien we een systeem met 6 blokken: een Entity Generator, een Entity Server met oneindige capaciteit, een Resource Acquirer, een Entity Server met een capaceit van 1 en een Entity Terminator met Scope.



Het Remove Resources systeem, met van links naar rechts: Entity Generator, Entity Server met oneindige capaciteit, Resource Acquirer, Entity Server met enkele capaceit, Entity Terminator met Scope.

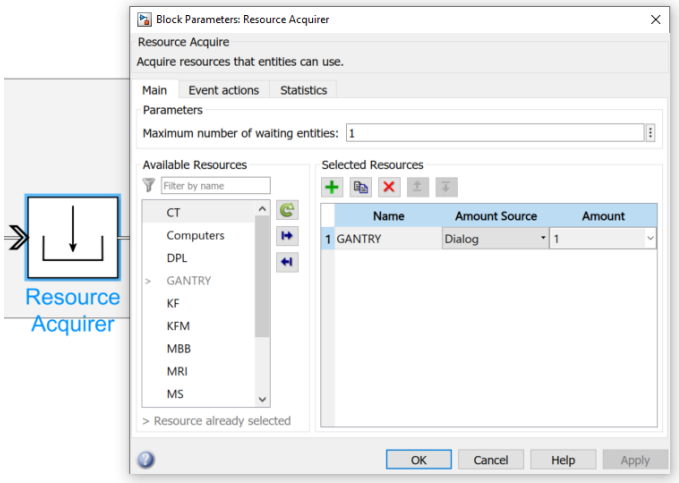
2. Ga naar de eerste Entity Server. Hier moeten we de servicetijd aanpassen. Deze staat standaard op een extreem hoge waarde (1000000) waardoor dit hele subsysteem, onder normale omstandigheden, geen invloed heeft op het totale proces. De servicetijd moet worden ingevuld in uren. Als servicetijd kiezen we de tijd tussen de start van de simulatie (1 januari 2020 in ons voorbeeld) en de start van de uitval (1 mei 2020 in ons voorbeeld). In ons voorbeeld is dit 2903 uur.



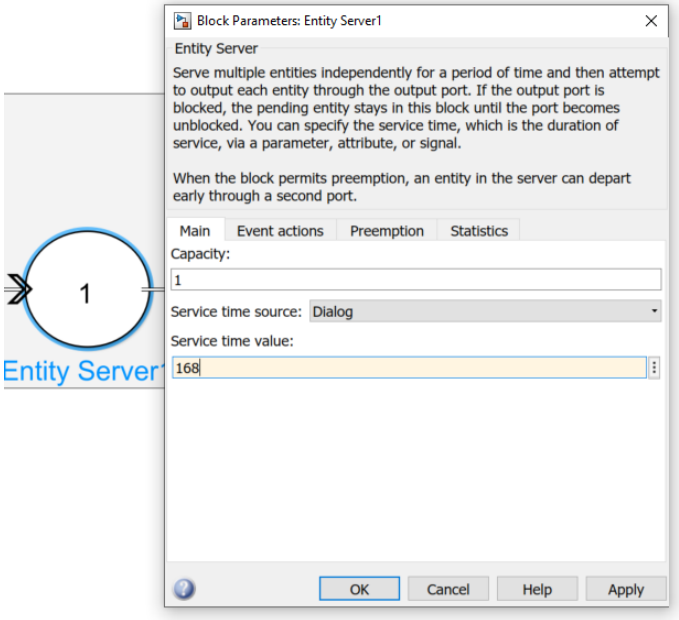
TIP: ga naar deze website voor een snelle berekening van het aantal uren: `https://www.kalender-365.nl/bereken/periode-tussen-twee-datums.html`

3. Ga naar de Resource Acquirer en pas hier de onttrokken Resources aan. In ons voorbeeld onttrekken we 1 Gantry uit het systeem, maar dit kan zo uitgebreid worden gemaakt als je wilt. Door alle medewerkers te onttrekken zou je

bijvoorbeeld tijdelijke sluiting kunnen simuleren.



4. Ga naar de tweede Entity Server. Hier moeten we ook de servicetijd aanpassen. Deze staat standaard ook op een extreem hoge waarde. Deze kun je hoog laten staan wanneer je een permanente uitval wilt simuleren. Bijvoorbeeld: wat is het effect van een permanente halvering van het aantal medewerkers na 3 maanden. Deze Entity Server zorgt er dan voor dat de aangegeven Resources permanent onttrokken blijven. In ons voorbeeld willen we dit tijdelijk houden (1 week). Hiervoor moeten we het aantal uur invoeren bij Service time dat de Resources onttrokken moeten blijven: 1 week = 168 uur.



5. Sla de simulatie op en herstart het programma. Run de simulatie en controleer de resultaten.

3.2.3 Aanpassen van kansverdelingen

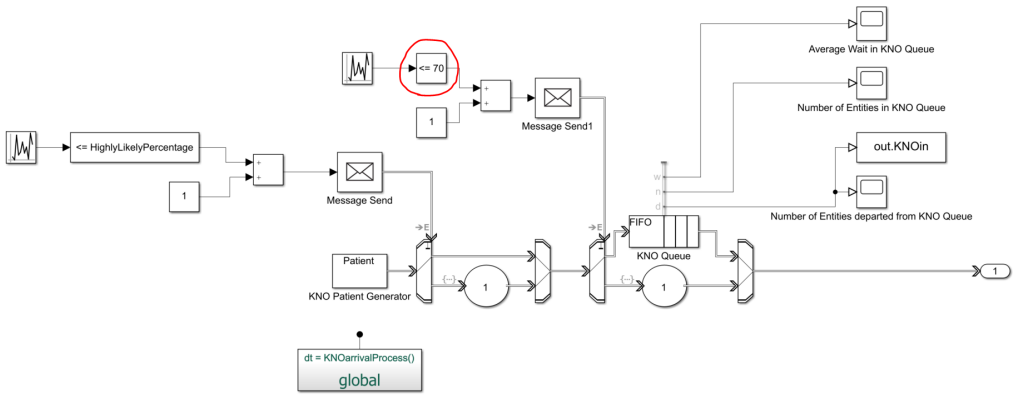
In deze sectie wordt uitgelegd hoe de standaard kansverdelingen kunnen worden aangepast. Deze kansverdelingen worden voor drie situaties gebruikt: (1) uitval van patiënten gedurende het proces, (2) hoeveelheid die het Highly Likely traject bewandelt en (3) de patiënten die een planadaptatie krijgen tijdens het behandelproces. Deze kansen zijn gebaseerd op het digiboard van 2020 en toepasbaar op data uit 2019 en 2021. Deze getallen hoeven dan ook alleen aangepast te worden als daar duidelijke aanleiding toe is.

Uitval

De uitvalpercentages per tumorlijn zijn als volgt:

KNO	70%
NEU	20%
LONG	65%
LYM	50%
ESO	60%
MAM	20%
CHO	25%
OOG	0%

Om één van deze getallen aan te passen ga in de simulatie in Simulink naar het blok die het subsysteem van de desbetreffende tumorlijn bevat. Deze staan bij input. Ga naar het omcirkelde blok passend bij het blok aangegeven in onderstaande afbeelding.

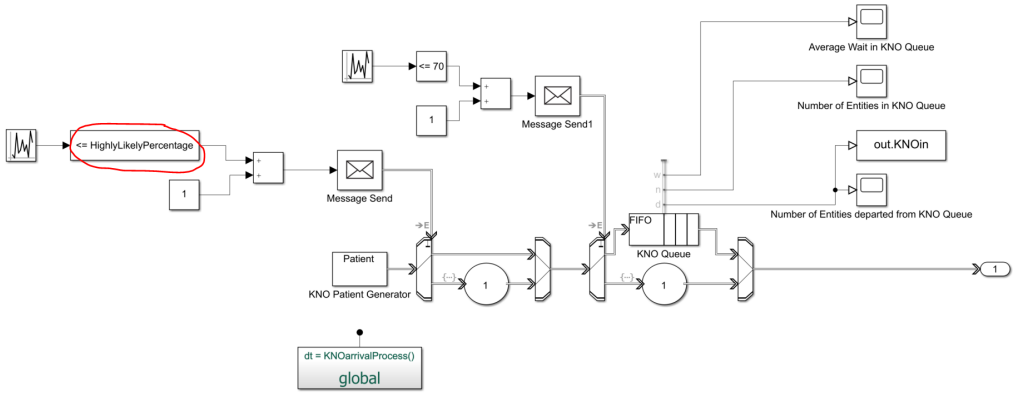


Pas de constante waarden in dit blok aan naar het gewenste percentage.

Highly Likely

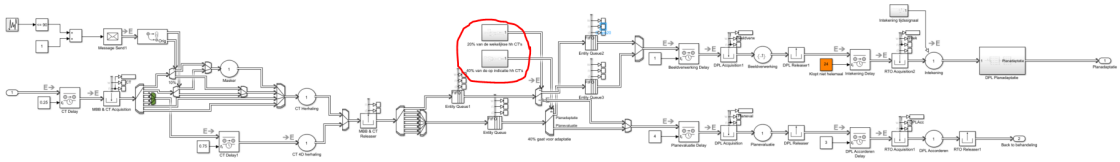
Het Highly Likely percentage is constant voor alle tumorlijnen waarvoor dit geldt. Zoals omschreven in sectie 2.3 is deze te varieren via het programma.

Mocht het nodig zijn om een specifiek percentage per tumorsoort in te vullen, ga dan binnen het blok die het subsysteem van de desbetreffende tumorlijn bevat naar het omcirkelde blok passend bij het blok aangegeven in onderstaande afbeelding.

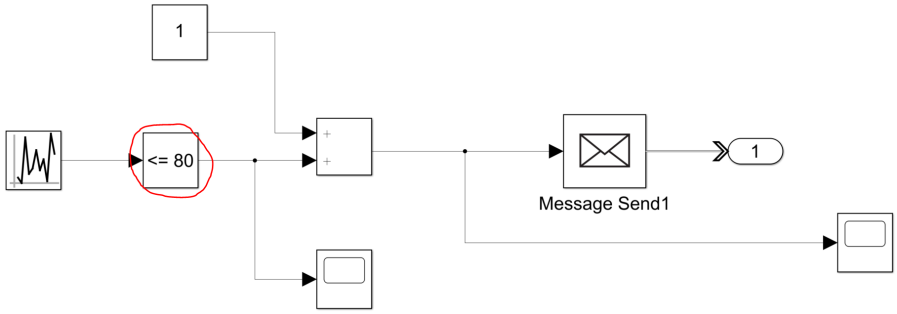


Planevaluaties

De percentages patiënten waarvoor het plan geëvalueerd wordt, wordt verwerkt in het subsysteem `Planadaptatie/Planevaluatie` boven het blok `Behandeling`. In dit blok vinden we twee andere subsystemen die de percentages evaluaties vs. adaptaties bepalen. Deze zijn rood omcirkeld in de afbeelding hieronder.



Binnen deze blokken is weer eenzelfde soort constante te vinden zoals omschreven in de secties hierboven. Zie afbeelding hieronder.



Door deze constante aan te passen wordt het percentage waarvoor geëvalueerd wordt aangepast. De andere patiënten krijgen een planadaptatie.

⚠LET OP: het bovenste blok geldt alleen voor KNO patiënten, gezien deze wekelijks geëvalueerd worden. Voor alle andere indicaties, gebruik het onderste van de twee aangegeven blokken.

⚠LET OP: de percentages gaan over het percentage waarvoor er geëvalueerd wordt. Het percentage planadaptaties is dan ook 100 - het ingevulde getal.

Hoofdstuk 4

Validatie en toepasbaarheid

4.1 Samenvatting validatie

Gedurende het project van Joep is de simulatie gevalideerd op data uit 2020, 2019 en 2021. Voor de de volledige informatie over de validatie, inclusief uitgebreide verklaring over de getallen, zie de thesis.

De belangrijkste uitkomsten die handig te zijn om in gedachten te houden bij de toepassing van de simulatie zijn:

- De simulatie is niet sterk in het simuleren van kleine groepen patiënten. Bij tumorlijnen van 5 of minder patiënten wijkt hij proportioneel veel af.
- Er zit lichte variatie in de uitkomsten per simulatie run. Run de simulatie dan ook een aantal keer en bepaal gemiddeldes om variatie te minimaliseren.
- De OOGlijn is erg stabiel en bevat weinig tot geen variatie. De OOGlijn kan dan ook gebruikt worden om op te sturen. Als deze consistent een juiste uitkomst geeft, zit de rest waarschijnlijk ook in de buurt.
- De simulatie houdt geen rekening met verschillende Highly Likely percentages per tumorlijn. Deze zijn in praktijk wel verschillend. Houd dit in het achterhoofd bij het interpreteren van de resultaten.
- De doorlooptijden zijn toepasbaar op 2021 en daarna.
- De capaciteitsknelpunten functie is niet goed gevalideerd. Dit komt doordat er nooit grote knelpunten zijn geweest waardoor historische validatie niet mogelijk was. We gaan ervan uit dat deze goed werkt, gezien de correcte validatie met de andere uitkomst waarden.

4.2 Toepasbaarheid

De simulatie en de HPTCapp zijn toepasbaar op de processen van HollandPTC tot aan juni 2021. Ze blijven toepasbaar zolang de processen niet drastisch ver-

anderen. Grote veranderingen aan de processen zoals het invoeren van een nieuwe tumorlijn (anders dan de OES lijn), de introductie van een nieuw soort medewerker en het omgooien van de carepaths kunnen niet gemakkelijk geïmplementeerd worden in de simulatie. Hiervoor zal een nieuw simulatie opzet nodig zijn.
De simulatie is bedoeld om lange termijn uitkomsten en beleidsveranderingen van een halfjaar of meer te simuleren. Het is niet geschikt voor korte-termijn ontwikkelingen in verwijzingen of piekmomenten. Het simuleren van situaties van week tot week is daarom niet betrouwbaar en wordt afgeraden.

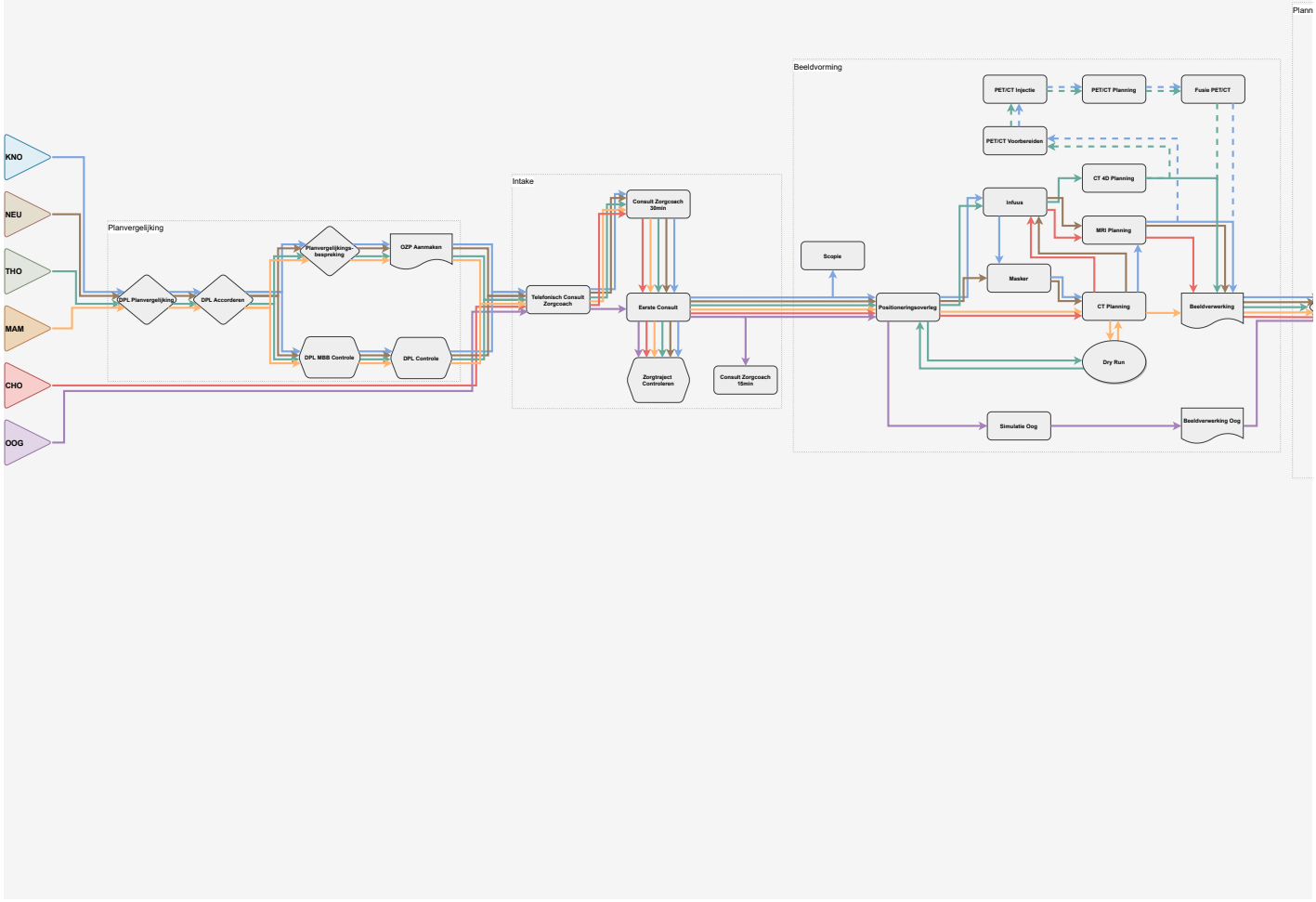
De simulatie is niet alleen toepasbaar op de processen van HollandPTC, maar kan ook worden ingezet in andere centra in Nederland met minimale aanpassingen. Beide centra in Nederland (Maastro en UMCG) hanteren een vergelijkbaar zorgproces, inclusief intake, beeldvorming, planvergelijkingen, QA, etc). Ze hebben hetzelfde soort medewerkers in dienst en gebruiken vergelijkbare apparatuur.
Het verschil tussen deze centra en HollandPTC zit hem in het soort tumoren die behandeld worden. Maastro behandelt ook prostaatkanker en behandelt geen borst- en oogtumoren met protonen. UMCG behandeld ook kinderen en is al gestart met het behandelen van oesophagus patiënten. UMCG behandeld ook geen oogtumoren. De simulatie en de HPTCapp kunnen dan ook gebruikt worden met uitsluiting van de pediatrie en prostaat tumorlijnen. Tevens moet er rekening gehouden worden met de hoeveelheid beschikbare middele en de specifieke service tijden, delays en maximale capaciteit per activiteit van deze twee centra.

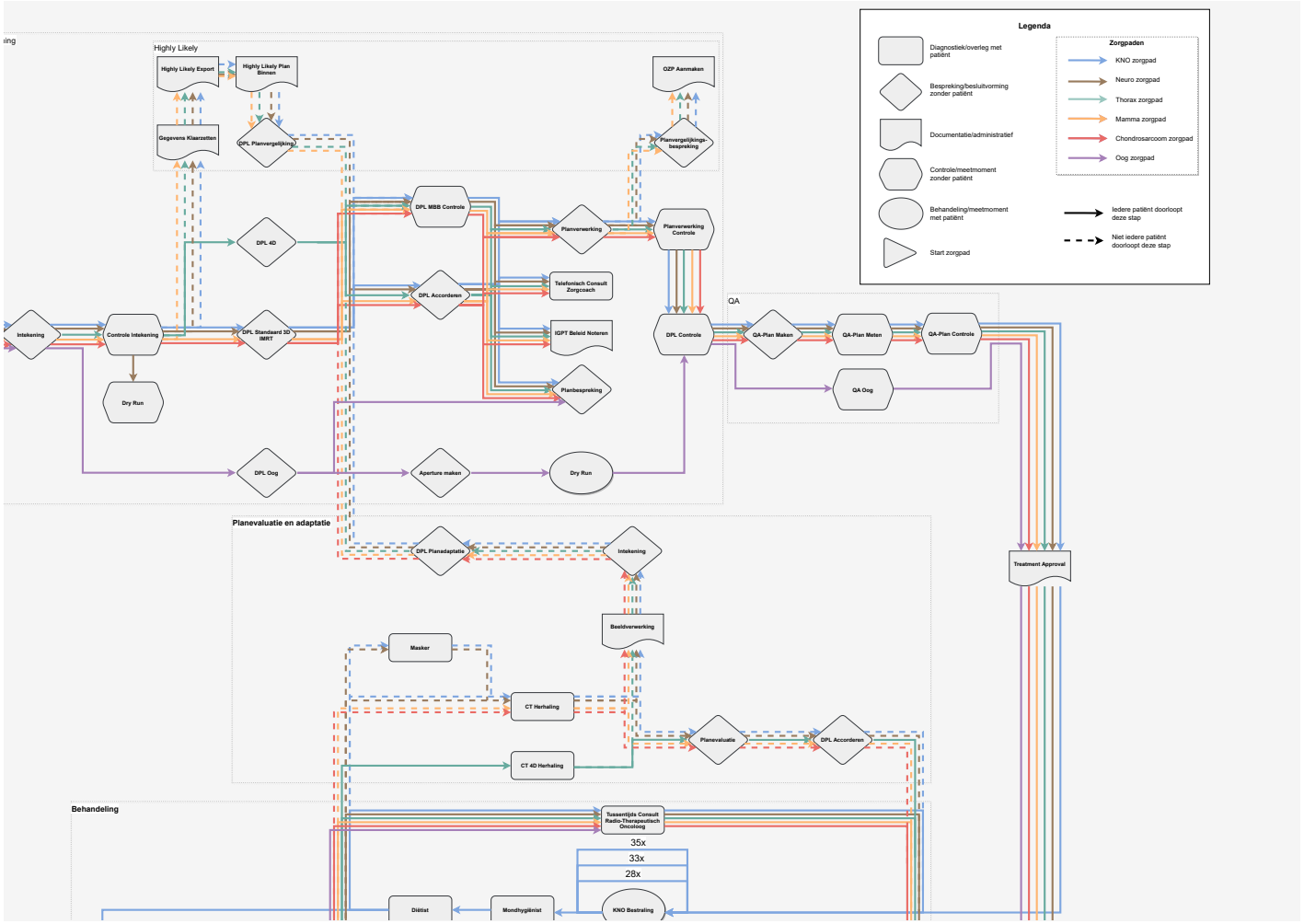
Gezien de simulatie gebaseerd is op de verplichte planvergelijking voor model-based indicaties in Nederland, is de simulatie niet van toepassing op landen waar de planvergelijking geen essentieel onderdeel is van het proces. Standaardindicaties (oogtumoren, chordomen, chondrosarcomen en tumoren bij kinderen) kunnen wel in andere landen gesimuleerd worden, gezien deze tumorlijnen geen gebruik maken van een planvergelijking.

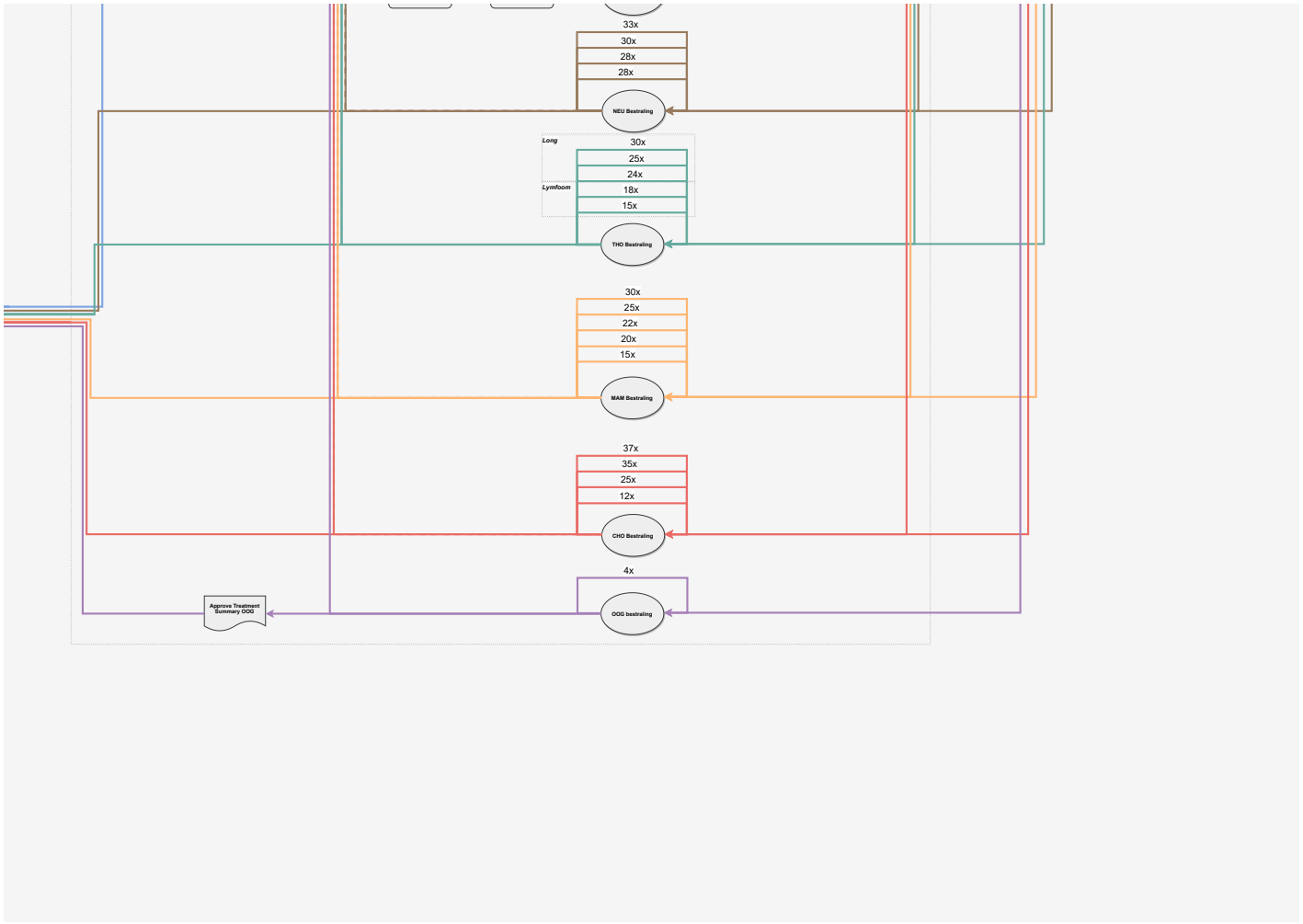
Hoofdstuk 5

Bijlage

5.1 Bijlage 1: Carepath


KNO
NEU
THO
MAM
CHO
OOG
Planvergelijking
DPL Planvergelijking
DPL Accorderen
Planvergelijkings-bespreking
OZP Aanmaken
DPL MBB Controle
DPL Controle
Intake
Telefonisch Consult Zorgcoach
Consult Zorgcoach 30min
Eerste Consult
Zorgtraject Controleren
Consult Zorgcoach 15min
Beeldvorming
Scopie
Positioneringsoverleg
PET/CT Injectie
PET/CT Planning
Fusie PET/CT
PET/CT Voorbereiden
CT 4D Planning
Infuus
MRI Planning
Masker
CT Planning
Beeldverwerking
Dry Run
Simulatie Oog
Beeldverwerking Oog


Legenda
Diagnostiek/overleg met patiënt
Bespreking/besluitvorming zonder patiënt
Documentatie/administratief
Controle/meetmoment zonder patiënt
Behandeling/meetmoment met patiënt
Start zorgpad
Zorgpaden
KNO zorgpad
Neuro zorgpad
Thorax zorgpad
Mamma zorgpad
Chondrosarcoom zorgpad
Oog zorgpad
Iedere patiënt doorloopt deze stap
Niet iedere patiënt doorloopt deze stap
Highly Likely
Highly Likely Export
Highly Likely Plan Binnen
Gegevens Klaarzetten
DPL Planvergelijking
OZP Aanmaken
Planvergelijkings-bespreking
DPL 4D
DPL MBB Controle
DPL Accorderen
Planverwerking
Planverwerking Controle
Telefonisch Consult Zorgcoach
IGPT Beleid Noteren
Planbespreking
Intekening
Controle Intekening
DPL Standaard 3D IMRT
Dry Run
DPL Controle
QA
QA-Plan Maken
QA-Plan Meten
QA-Plan Controle
QA Oog
DPL Oog
Aperture maken
Dry Run
Treatment Approval
Planevaluatie en adaptatie
DPL Planadaptatie
Intekening
Beeldverwerking
Masker
CT Herhaling
CT 4D Herhaling
Planevaluatie
DPL Accorderen
Behandeling
Tussentijds Consult Radio-Therapeutisch Oncoloog
35x
33x
28x
KNO Bestraling
Mondhygiënist
Diëtist


33x
30x
28x
28x
NEU Bestraling
Long
30x
25x
24x
Lymfoom
18x
15x
THO Bestraling
30x
25x
22x
20x
15x
MAM Bestraling
37x
35x
25x
12x
CHO Bestraling
4x
OOG bestraling
Approve Treatment Summary OOG


Follow-up
EINDE BEHANDELING
FU HC Radio-Therapeutisch Oncoloog
Gegevens Controleren
Gegevens opvragen