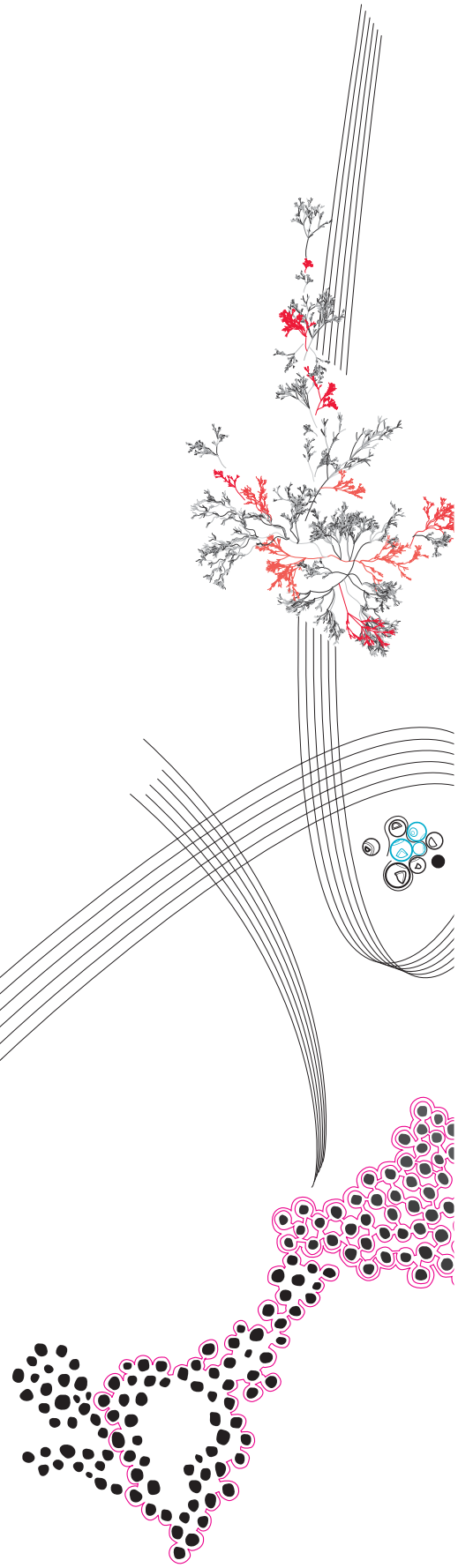

BSc Thesis Industrial Engineering & Management

Innovation Focus Areas for Cervical Cancer Brachytherapy Treatment in Academic European Hospitals

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Supervisor: Daniela Guericke, Gréanne Leeftink & Ate Loonstra

March, 2023

Department of Industrial Engineering & Management
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UNIVERSITY OF TWENTE.

Preface

I would like to thank Elekta for giving me this opportunity. It taught me a lot. For that I would especially like to thank, Dirk Binnekamp, Ate Loonstra, and Jesse Smits from Elekta. They gave me a lot of support, feedback, and also of course fun times. Without their team, I could not have done it!
In addition, I would like to thank Gréanne Leeftink, my supervisor at the University of, Twente for her support and feedback and for helping me get on the right track at the start of my thesis.
Lastly, I would like to thank Stijn de Jong and again Dirk Binnekamp. Knowing that I was not the only one who had to wake up at 05.30 AM gave me the strength to get out of bed. Also, the amazing 'gezellige' car rides, with amazing music, made the long trips from Veenendaal to Twente and vice versa bearable.

Innovation Focus Areas for Cervical Cancer Brachytherapy Treatment in Academic European Hospitals

Lena de Kraker*

March, 2023

This thesis is intended for my supervisors, Gréanne Leeftink and Daniela Guericke. This thesis will present what I have done for my assignment during module 12 as part of the Industrial Engineering and Management educational program at the University of Twente.

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Abstract

Recently a Dutch academic hospital reported that the average cervical cancer brachytherapy [CCB] treatment takes 8 hours and 55 minutes. This is longer than expected and medically necessary. Therefore this treatment brings much patient inconvenience, and should thus be lowered. Medical companies are willing to invest more in innovations to lower the length of this treatment time. However, there is relatively little data available to tell what the focus areas for innovation within these treatments should be.

In this research, we look into CCB treatments to identify the main focus areas of possible innovation. We survey academic hospitals within Europe. In this survey, we asked hospitals for more information on the [self-reported] time spent during the treatment steps. Using these survey results, we identify the accompanying costs per sub-step, based on the Dutch reimbursement system.

Six hospitals in the Netherlands, Germany, and Austria replied to this survey. The average overall treatment time is 7.6 hours. We identified the following steps and accompanying average times: 1. Pre-Operative Preparation [48 min], 2. Applicator Insertion (116 min), 3. Imaging for Treatment planning [39 min], 4. Treatment Planning (162 min), 5. Treatment Delivery [71 min], and 6. Applicator Removal (19 min).

In particular, the time spent on the sub-steps: Needle Insertion, Imaging for Planning, and Plan Optimization is relatively long compared to the other sub-steps. Needle Insertion takes 25 minutes on average. This is 5.5% of the overall treatment time. Imaging for Treatment Planning takes 39 minutes on average. This is 8.5% of the overall treatment time. Lastly, the step Plan Optimization takes 37.5 minutes on average. This is 8.2% of the overall treatment time.

Furthermore, using initial numbers from te Netherlands we identify the costs for the overall process currently. This is €4397.90. Besides, we look into the new costs if a certain innovation takes place that would adjust a sub-step, and we visualize this by using a spreadsheet simulation. An innovation that would decrease the time spent on Needle Insertion by 40%, decreases the costs by €322.98 per treatment. An innovation that would decrease the time spent on Imaging for Treatment Planning by 40%, decreases the costs by €6.44 per treatment. And if the time spent on Plan Optimization decreases by 40%, the costs per treatment decreases by €12.14. Therefore, we conclude that from a financial perspective, the Needle Insertion sub-step should be the area to focus on for future innovations.

Keywords: cervical cancer, brachytherapy, improvement, innovations, workflow

Contents

Glossary

BPMN Business Process Modeling Notation.

CCB Cervical Cancer Brachytherapy.

ESGO European Society of Gynecological and Oncology.

ESP European Society of Pathology.

ESTRO European Society for Radiotherapy and Oncology.

FIGO A classification system specifically used for cervical cancer. More information can be found in Appendix A.2.

MEDLINE The world's largest medical database [MedlinePlus, 2023].

MPSM Managerial Problem-Solving Method created by Hans Heerkens and Arnold van Winden.

OR Operation Room.

QA Quality Assurance.

SLR Systematic Literature Review.

TNM A classification system for malignancies. It is primarily used in the solid tumors for forecasting of the cancer development. Besides it allows for better information sharing and research across populations. The system is based on assessing the tumor, regional lymph nodes, and distant metasis [Rosen and Sapra, 2022]. More information can be found in Appendix A.1.

1 Introduction

This chapter gives a general introduction to cervical cancer and its treatment methods in Section 1.1, and more details on brachytherapy in Section 1.2. The brachytherapy treatment method is also the main focus of this research. Besides, this chapter gives more information on Elekta in Section 1.3, which is one of the main providers of brachytherapy equipment in the world, and they also support this research. Lastly, the problem statement and research questions for this research will be given in Sections 1.4 and 1.5.

1.1 Cervical cancer

Cervical cancer is the ninth most occurring type of cancer [excluding non-melanoma skin cancer] among women in Europe. It is estimated that in Europe every year 58,169 women are diagnosed with the disease, of which 25,989 women die
[HPV Information Centre, 2021]. In Europe, cervical cancer patients are treated according to the ESGO-ESTRO-ESP guidelines for cervical cancer treatment. In these guidelines, the general staging is done by combining FIGO and TNM classification. A treatment plan is made based on the results of this staging [ESGO/ESTRO/ESP, 2018]. More information on the staging can be found in Appendices A.1 and A.2.
The standard treatment of locally advanced cervical cancer uses a combination of radio- and chemotherapy. Both external beam radiation and brachytherapy are used for the radiotherapy part of this treatment [The EMBRACE Collaborative Group, 2018]. Appendix A.3 provides more information on different treatment plans for each stage.

1.2 Brachytherapy

In this research, we focus on brachytherapy treatment. Brachytherapy is a form of radiation therapy for treating tumors using a radioactive source. It is often used for the treatment of small and locally advanced cancer. During a brachytherapy treatment, a radioactive source is brought near to the tumor. The source delivers high doses of ionizing radiation to the area close to it. This radiation damages the cells surrounding the source. Since cancerous cells are more sensitive to radiation than healthy tissue, tumors can be destroyed while bigger parts of healthy tissues survive [American Cancer Society, 2014]. The big advantage of brachy- over external beam therapy is that the source delivers the radiation closer to the targeted cancerous tissues. The radiation does not have to travel through the healthy tissue anymore, which prevents damage to this healthy tissue. Besides, the ionizing radiation transferred from the radioactive source in brachytherapy reduces exponentially when increasing the distance from the source to the target [Crownover et al., 1999]. In other words, most of the impact of the ionizing radiation is given to the cells surrounding the source only. Thus, the damage can be delivered very precisely. This is also the reason that in brachytherapy the radiation dose can be much higher, which results in fewer fractions needed compared to for example external beam radiation.
One of the disadvantages of brachytherapy is that during the treatment the applicator and or needles are inserted into the patient's body. Therefore, the patient needs general or local anesthesia, during the treatment. In addition, as stated before it is not always possible to use brachytherapy for every type of cancer. Examples of brachy treatable malignancies are cervix, endometrium, prostate, skin, and breast cancer
[Prostate Cancer UK, 2022].

1.3 Elekta

One of the main providers of brachytherapy equipment in the world is Elekta. They have initiated this project because they want to improve the brachytherapy treatment. They want to understand how their products are currently utilized when treating cervical cancer following the EMBRACE protocol [Appendix B] in order to prioritize areas for future innovations. The problems their customers encounter and the problems encountered in the literature for cervical brachytherapy treatments are given in Appendix B.

1.4 Problem Statement

Vliet-Perez et al [2022] found that the average procedure time of one brachytherapy treatment in an academic hospital in the Netherlands for cervical cancer is 8 hours and 55 minutes. In contrast, Toita et al [2018] showed that in Japan the average procedure time for cervical cancer brachytherapy treatments in all types of hospitals is 2 hours and 27 min. These times differ much from each other. This difference suggests that especially in European academic hospitals the procedure times for cervical cancer brachytherapy are relatively long and thus that the process is inefficient. This could eventually lead to the procedure being too expensive. Currently, there is little literature available on the costs of this process. These insights lead to the following action problem:

The cervical cancer brachytherapy treatments are organized inefficiently in terms of time and money in European academic hospitals.

The reality is that the cause(s) of the long and inefficient brachytherapy treatment is unknown. The goal of this research is to map out the actual workflows of cervical cancer brachytherapy procedures in European academic hospitals to find these causes. That is, to map out each bigger step and sub-step, and identify their respective duration, required equipment, involvement of staff, and associated costs. In order, to identify the [sub-]steps in which innovations that would increase the speeds or ease, would have the most impact on costs and/or time.

1.5 Research questions

This research is conducted according to the Managerial Problem-Solving Method [MPSM]. The next step in this method is determining the knowledge gaps for the research. These knowledge gaps lead to the knowledge questions for the research. We derived the following main research question from the action problem that was established in 1.4:

What should be the focus area for innovations in cervical cancer brachytherapy treatments in European academic hospitals?

To help answer the action problem, several knowledge problems must be solved first. These are the sub questions. Per phase of the MPSM one or two knowledge questions will be answered [Heerkens and van Winden, 2021]. These questions are listed below.

The sub questions for this research are:

1. What are the current actual workflows of brachytherapy treatment for cervical cancer in academic hospitals in Europe? [Answered in Chapter 3, by means of literature review and a quantitative survey]
   (a) What are the guidelines for cervical cancer treatment in European academic hospitals?
   (b) How are these [sub-]steps currently being employed in European academic hospitals?
   (c) How long do these sub-steps take and what personnel is needed for each step?
2. What [sub-]steps relatively take the most time? [Answered in Chapter 3 by means of a analysis of the survey results]
3. How can innovations in the sub-steps from question 1b be evaluated regarding costs and time? [Answered in Chapter 3 by using the spreadsheet simulation]
4. What should be the focus area for innovations in cervical cancer brachytherapy treatments in European academic hospitals? [Answered in Chapter 4]

2 Methodology

We use different methodologies to collect and analyze the data. Firstly, we identify the guidelines in European academic hospitals for cervical cancer brachytherapy treatment by conducting a systematic literature review [Explained in Section 2.1]. Then we look into the actual workflows in academic hospitals in Europe by sending out a survey [Explained in Section 2.2]. Lastly, we create a spreadsheet simulation to answer question 3 [Explained in Section 2.3].

2.1 Method for gathering data guidelines

To answer question 1a, we perform an SLR [Systematic Literature Review]. Using the SLR, we want to discover if there is a general guideline in European academic hospitals that hospitals use to base their treatment procedures on. If this is the case, these guidelines can be used as a stepping stone for creating the survey [Section 2.2] and spreadsheet simulation [Section 2.3].
We choose an SLR as the method for the collection of the guideline data, since it will be based on all academic hospitals in Europe in general. If we for instance look into the rules of a single hospital and derive general guidelines from this single observation, the guideline found, might not be applicable in another hospital. To ensure that the data for the SLR is reliable and suitable to the question, we use the PubMed database. This database is created specifically for biomedical research. It contains literature from the database MEDLINE, life science journals, and medical online books [PubMed, 2023]. The result of the SLR can be found in Section 3.1.

2.1.1 Deliverables

In Chapter 3, we show the result of the SLR. The main deliverable is a general workflow for the cervical cancer brachytherapy treatment according to the EMBRACE-II Protocol in Section 3.1. This workflow will be depicted in the BPMN [Business Process Modeling Notation] language. This deliverable is the answer to question 1a.

2.2 Method for gathering data from hospitals

To answer question 1b and 1c, we send out a survey to seven European academic hospitals. The general survey design can be found in Figure 1.

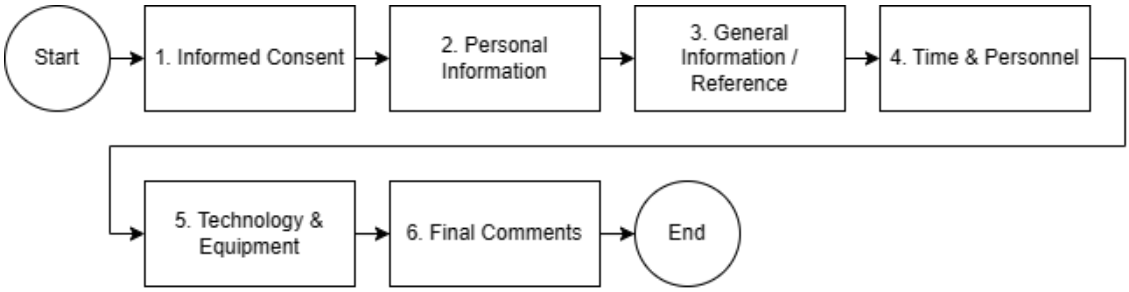

Figure 1: General Survey Design

The survey starts with 1. Informed Consent. If the respondent does not give informed consent the survey will stop. After giving informed consent, the survey continues with 2.

Personal Information. In this part, more information on the respondent's profession and experience is asked. We only include respondents that are clinical physicists [More on this in Section 2.2.2]. Next, the survey continues to 3. General Information / Reference. In this part, there are questions on the protocol that hospitals use. Besides, it is also asked if hospitals use real-time imaging. Real-time imaging is not in the standard EMBRACE protocol [See Section 3.1.3]. However, some hospitals could already be using it. After this the survey continues with the questions on 4. Time & Personnel. More on this later. Then, the survey continues with 5. Technology & Equipment. In this part, more information on for example the imaging modalities is asked. We only include hospitals that use MRI imaging modalities [See Section 2.2.2]. Lastly, there is room for final comments. Here respondents can add general comments about cervical cancer brachytherapy practices in their hospital.

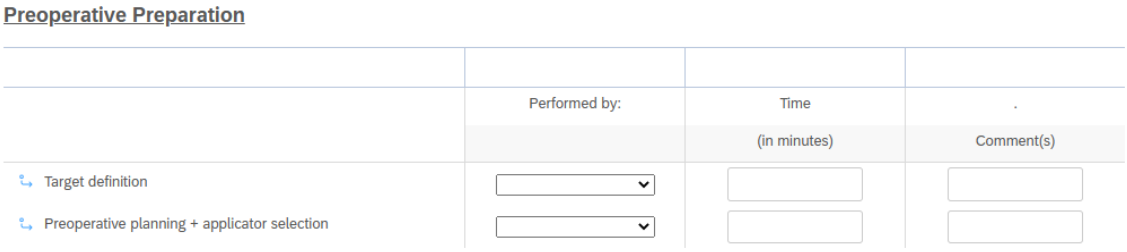

FIGURE 2: Example Question 4. Time & Personnel

In general, we use 2. Personal Information, 3. General Information / Reference, and 5. Technology & Equipment for determining for each hospital if they fall within the in- and exclusion criteria [See Section 2.2.2]. Besides, we use 4. Time & Personnel mostly to answer the questions 1b,1c, and 2 Furthermore, the answer to these questions will help us answer question 3, and later also question 4. An example of a question asked in 4. Time & Personnel is depicted in Figure 2. Appendix C has an overview of all questions asked in the survey.

In order to make it easier for the respondent to understand the questions in 4. Time & Personnel, we asked the question following the chronological structure of the procedure based on the EMBRACE II protocol [Section 3.1.3]:

1. **Pre-Operative Preparation**
   In this step, the preparation for the operation takes place. The initial plan is created, in which the target is defined and the applicator that should be used is chosen.

2. **Applicator Insertion**
   In this step, the operation starts. The patient is positioned and anesthetized. The applicator and needles [needles are sometimes used to reach deeper parts of the tumor] will be positioned according to the plan made in the previous steps. Lastly, the applicator will be fixated in the patient. This is done to prevent movement of the applicator in between the imaging and treatment delivery step.

3. **Imaging for Planning**
   In this step, a new MRI [since this is one of the inclusion criteria] image is made of the patient. This picture is used to make a new radiation plan in the next step.

4. **Treatment Planning**
   In this step, the image of the previous step is used for treatment planning. The applicator, organs at risk, and needle[s] are reconstructed in the picture. The plan made in step 1 is reviewed and optimized with this new information. This new plan will be evaluated by another doctor. Next, the dose summation will be calculated. This is done, to ensure that the patient does not receive too much radiation when the brachytherapy procedure takes place in combination with external beam therapy. Lastly, the final plan is approved one more time by the same doctor.

5. **Treatment Delivery**
   In this step, the treatment takes place. The patient will be brought to a brachy suitable room. In this room the implant [applicator & needles] is connected to the afterloader. Then everything will be checked one final time by the doctor[s]. And lastly, the execution takes place.

6. **Applicator removal**
   After the treatment delivery took place, the implant [applicator & needles] will be removed from the patient.

2.2.1 Self-administered quantitative survey

We choose to use a quantitative survey for collecting the data from the European academic hospitals, since we need many data points from subjects all over Europe. Collecting this data by observations would be too time consuming. Besides, we also need to know the averages of the treatment and thus also information about past experiences. Hence, observations are again not a suitable option [Schindler, 2019].
Eventually, we use a self-administered survey. A self-administered survey is designed to be completed without an interviewer. It is a highly structured list of questions, that have to be filled in by the participant [Schindler, 2019]. We chose for a self-administered survey, because:

- It allows contact with otherwise inaccessible partners [Schindler, 2019]. We want clinical physicists to fill in this survey. Clinical physicists have varying working days. They either have no time during a day, or a lot of time, if for example a treatment is unexpectedly canceled. The self-administered survey makes it possible for the clinical physicist to fill out the survey when they have time and not at a set moment.
- It allows expended geographic coverage without increasing costs [Schindler, 2019]. As stated before, we wanted to investigate the workflow in European academic hospitals. Therefore, we need to send the survey out to many countries within Europe. Using a self-administered survey eases this process.
- Minimal staff is required [Schindler, 2019]. We simply did not have much staff available to visit all centers and ask all questions. Therefore, sending out the self-administered survey was the best option.
- The self-administered survey is more anonymous [Schindler, 2019]. When validating our survey clinical physicists had concerns about the anonymity of the survey results. They stated that making treatment processes of individual hospitals public could result in less financial support for brachytherapy. Hence, the self-administered survey with anonymized results [See 2.3] would be the best option.

Besides all these advantages, also some concerns arise when using a self-administered survey. Below is a description of the concerns that arose and how we try to overcome them:

- Computer security is more important [Schindler, 2019], especially in this case were the results have to be anonymized. We used Qualtrics, which is a verified good survey tool to keep personal data safe [University of Twente, 2023].
- There is no probing for explanation [Schindler, 2019]. The respondent fills in the self-administered survey alone, thus there is no way to ask for more information on a question. We try to overcome this by validating and reviewing the survey many times. We did this by firstly reviewing the survey within Elekta. We start with the validation, and thus we ensured that the questionnaire really measured what we wanted to know [Story et al., 2019]. After this validation, we sent out the pilot version to two clinical physicists from two independent academic centers in Europe. They gave us extensive feedback. We used this feedback to make the final version of the survey, that was sent out to other hospitals.
- The chances of a low response rate are relatively high compared to other research approaches [Schindler, 2019]. One of the reasons this happens, is because many surveys end up in the junk folder. To overcome this, we sent out the survey via a contact person within Elekta, who has a good relationship with the European academic hospitals that were sampled for this survey. We also hoped that the familiar name would increase the response rate.

2.2.2 In- and exclusion criteria

We set certain in- and exclusion criteria to ensure that the results are comparable. These criteria are:

- The hospital must be academic and have an MRI-based brachytherapy treatment [these hospitals usually have the most standardized protocols, which makes them more comparable].
- The hospital must be German or Dutch. We chose for Germany, since this is the largest country in Europe. And we chose the Netherlands, since we know people within these hospitals. Therefore, we could receive feedback on the survey, or go to the hospitals for more information on their answers. Besides, taking only German and Dutch hospitals, makes them more comparable in terms of protocols and costing. In the future, hospitals from other countries should be added to the data pool, to make the research more reliable.

2.2.3 Deliverables

In Chapter 3, we show the results of the survey in different ways. Firstly, we show an 'average' cervical cancer brachytherapy workflow based on the survey results in the BPMN [Business Process Modeling Notation] language in Section 3.2. In this model, we clearly depict the time and (sub-)step carried out. Besides, it will also be clear which profession is performing the step. Thus, this deliverable is the answer to question 1. Furthermore, we statistically analyze the result found in the 4. Time & Personnel questions [For an example question see 2]. We depict this with the use of a graph with box plots per sub-step. Besides, we analyze the data's skewness to determine the reliability of the data. These deliverables can again be found in Section 3.2, and answer question 2.

2.3 Method for determining the costs and time after innovations

Lastly, we build a spreadsheet simulation to analyze the survey results. The spreadsheet simulation makes it possible to present the time and costs saved by innovations in certain sub-steps. The costs taken into account are labor, OR [Operation Room], and MRI costs.

2.3.1 Labor Costs

The labor costs tell how much the staff performing the treatment costs. The labor costs per treatment are calculated by adding all labor costs per sub-step. Per sub-step the labor costs are calculated with the formula below:

$$Labor\ costs_{Sub-step} = Salary_{Profession} * Sub-step\ Time_{Profession} * 1.3,$$

for Profession = {Anesthesiologist, Nurse, Physicist, Radiation Oncologist, and Radiation Therapist}

For salary we use the values in table 1 [Nationale Beroepen Gids, 2023]. For sub-step time per profession we use the information from the survey results [See section 3.2]. Note that these results are only based on the profession performing the step, and not the supporting/additional personnel. Hence, the actual labor costs are probably higher. Lastly, we multiply these costs with 1.3. We do this multiplication to also cover the indirect labor costs [Ondernemen met personeel, 2023].

Profession	Salary
Anesthesiologist	€47.89/hour
Nurse	€18.98/hour
Physicist	€37.36/hour
Radiation Oncologist	€47.89/hour
Radiation Therapist	€19.05/hour

Table 1: Wages per Profession

The labor costs in the spreadsheet simulation are depicted as in Figure 3. On the left, the labor costs per sub-step can be found. The pie charts in the middle show the labor costs per step and per profession, to see where the most improvement can be done in terms of personnel costs. More information on how the spreadsheet simulation works can be found in Appendix D.

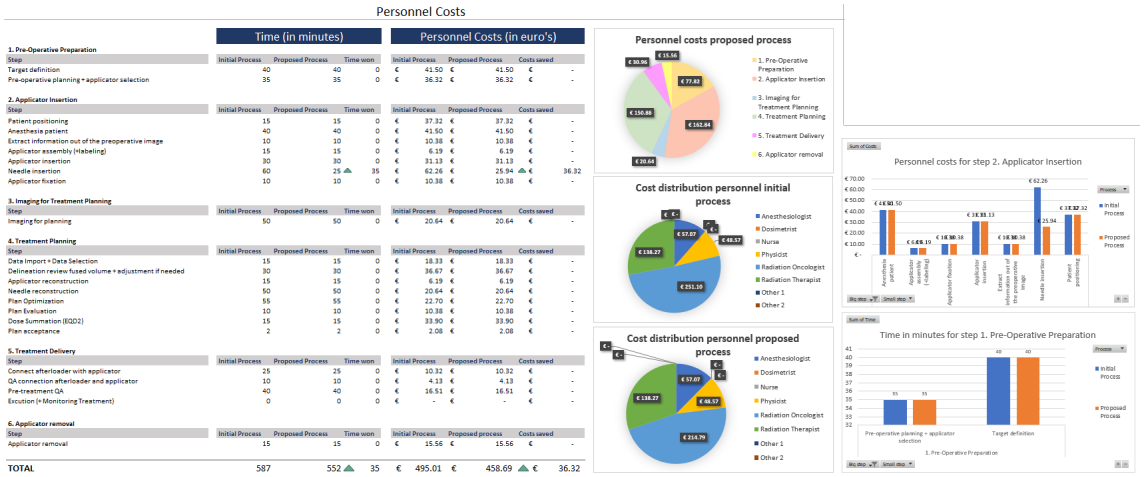

FIGURE 3: Personnel costs in the spreadsheet simulation

2.3.2 OR costs

The OR costs tell how much the OR time costs per treatment. Per treatment these costs are calculated with the formula below:

$$OR\ costs = OR\ costs\ per\ minute * Total\ OR\ Time$$

After consulting a clinical physicist and searching on the internet, we established €31.50 per minute for the OR costs [New Compliance, 2020]. For the total OR time, we add the times for the sub-steps: Patient positioning, Anesthesia patient, Extract information out of the preoperative image, Applicator assembly (+labeling), Applicator insertion, Needle insertion, and Applicator fixation, since these are the sub-steps in which the patient is in the OR room. In the spreadsheet simulation this is depicted together with the MRI costs as Facility costs [See Figure 4].

Facility Costs

Facility	Initial Process	Proposed Process	Time won / Costs saved
1. OR			
OR Time	180	145 ▲	35
OR Costs	€ 5,670.00	€ 4,567.50 ▲ €	1,102.50
2. MRI			
MRI Costs	€ 380.00	€ 380.00 €	-

FIGURE 4: Personnel costs in the spreadsheet simulation

2.3.3 MRI costs

The MRI costs tell the MRI imaging costs per treatment. We used the reimbursement costs for one MRI image to determine these cost. The costs for one MRI scan is thus

€380 [Zorgproducten NZa, 2023]. The MRI costs are depicted in the spreadsheet simulation as shown in Figure 4.

2.3.4 Spreadsheet simulation adaptability

Before creating the spreadsheet simulation we took the following factors into account, regarding adaptability:

- Prices will fluctuate over time. To make the spreadsheet simulation valid for a longer time, we made it possible to adjust the wages and the MRI & OR costs in the spreadsheet simulation. This will also increase the external validity.
- Different personnel might perform certain steps. To overcome the possible invalidity of the spreadsheet simulation we made it possible to adjust the profession[s] performing a step. Besides, we also added two extra staff members called Other 1 and Other 2. If a new role starts playing a part in the process, this profession can be added using Other 1 or 2.
- If something has to be changed, it must be easy to change within the spreadsheet simulation. Therefore, we chose to develop the spreadsheet simulation in Excel. Almost everyone will have access to Excel. Besides, nearly everyone knows how to use it.

The spreadsheet simulation user guide can be found in Appendix D.

3 Results

The results in this chapter are divided over different sections. Firstly, we look into the guidelines for cervical cancer treatment in European academic hospitals [See Section 3.1]. Then, we look into the survey results [See Section 3.2]. And lastly, we look for potential points of improvements [in other words, decreasing the time and costs] for the cervical cancer brachytherapy treatment in European academic hospitals, using the spreadsheet simulation [See Section 3.3].

3.1 Guidelines for cervical cancer treatment in European academic hospitals

3.1.1 ESGO, ESTRO and ESP guidelines for cervical cancer patients

The ESGO [European Society of Gynecological and Oncology], ESTRO [European Society for Radiotherapy and Oncology] and ESP [European Society of Pathology] made a general guideline on how cervical cancer patients should be treated in Europe [ESGO/ESTRO/ESP, 2018]. In these guidelines, it is stated that for some cases brachytherapy is recommended. More information on in which state brachytherapy is recommended is in Section A.3. The guidelines also state that image-guided brachytherapy is recommended in these cases. Image-guided brachytherapy is brachytherapy based on imaging of the affected tissue. This imaging should preferably be done by using MRI. Alternative imaging modalities are CT and ultrasound. Since this research will focus on academic hospitals, we only consider MRI-based procedures. In this section, we will look into the equipment [Section 3.1.2] and the workflow recommended [Section 3.1.3].

3.1.2 Equipment

Firstly, we look into the equipment that is needed to perform a brachytherapy procedure. We do this, to make the protocol for the brachytherapy treatment itself, easier to understand. The equipment used in a brachytherapy treatment is an afterloader, transfer tubes, and an applicator. A simplified overview of this equipment can be found in Figure 5. The afterloader [left in the picture] contains the radioactive source. Via the transfer tubes [gray lines] this radioactive source is brought to the applicator. The applicator [right] is inside the patient. Here the source is held still on the dwell positions according to the treatment plan made. The applicator in the figure is just one of the numerous ones made [Elekta, 2022].

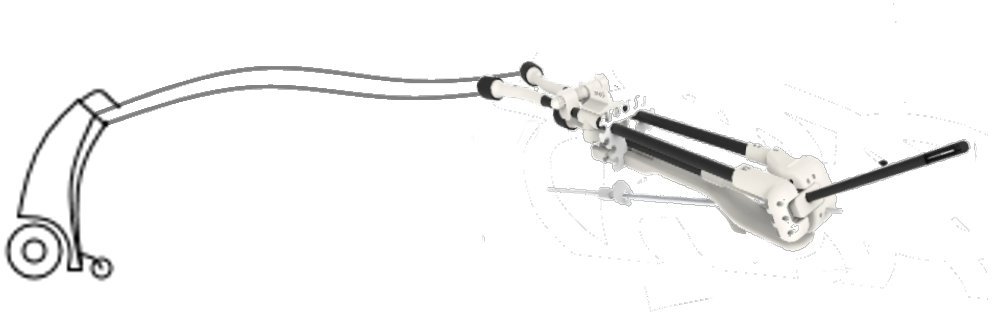

FIGURE 5: Example of equipment used for cervical cancer brachytherapy treatments

3.1.3 EMBRACE II protocol guidelines workflow

The EMBRACE studies [More information in Section B.1] have a big impact in the field of brachytherapy. The protocol based on these studies is designed in association with the ESTRO and improved the clinical outcome for cervical cancer brachytherapy treatment towards its optimum. Hence, the most recent EMBRACE protocol [EMBRACE II] is also the framework for most workflows in European academic hospitals [the EMBRACE Collaborative Group, 2022]. The current workflow according to the EMBRACE II protocol can be found in Figure 6.

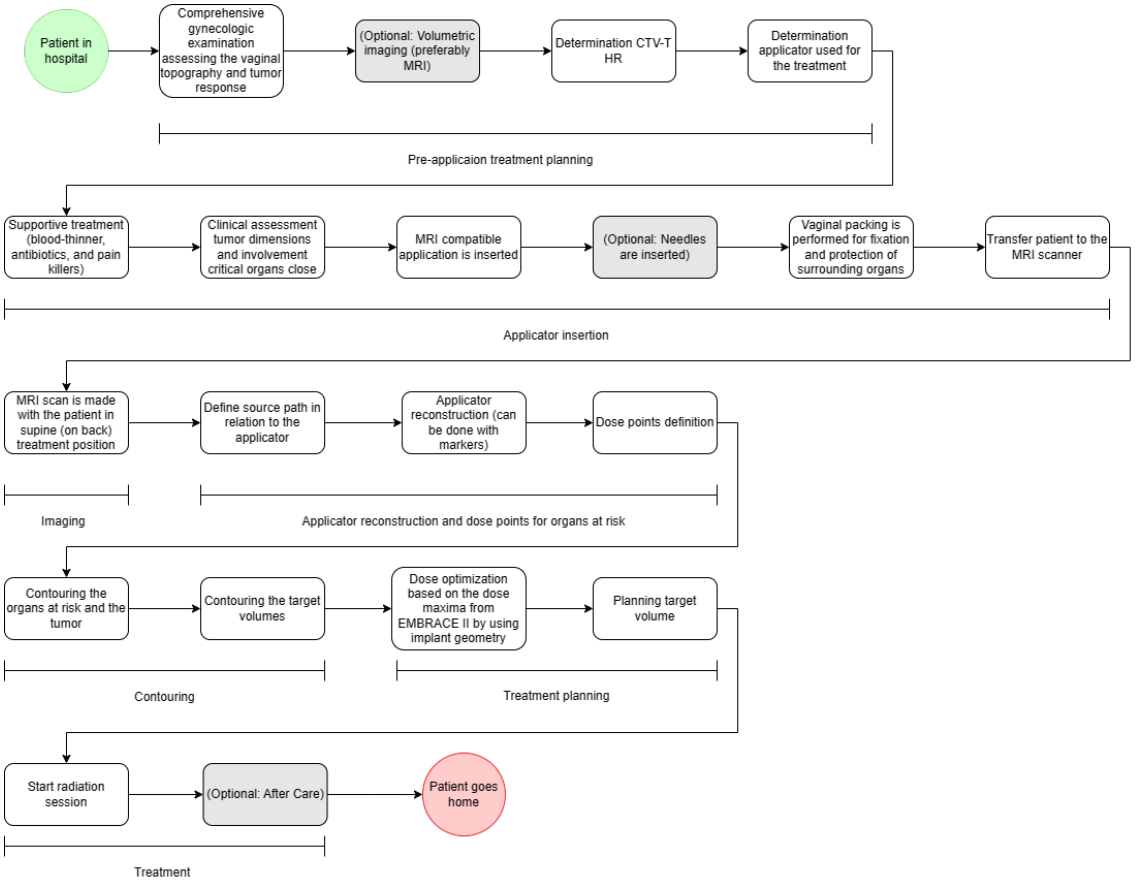

FIGURE 6: Workflow cervical cancer brachytherapy treatment according to EMBRACE-II protocol

The phases performed in this workflow are:

1. *Pre-application planning*
   In this phase, an initial planning is made to determine the applicator that should be used. Having a pre-application planning allows tailoring the applicator to the problem.

2. *Applicator insertion*
   In this phase, the applicator is inserted. Before inserting the applicator, supportive treatment is given. Blood-thinning medicines [for decreasing the chance of thrombosis in the lower body caused by the operations], antibiotics (for decreasing

the chance of infection) and painkillers are given to the patient according to their individual needs. The applicator is also fixated inside the patient in this step, to ensure the least movement of the applicator after the imaging step and thus more precise results.

3. *Imaging*
   In this phase, imaging takes place in order to make an official planning for the treatment later on. This phase always happens again for every treatment, unless an implant is used for the application insertion.

4. *Applicator reconstruction and dose points for organs at risk*
   The applicator is reconstructed in the image made in phase 3. Also, the dose points are determined. These are the points where the radioactive source stops.

5. *Contouring*
   The organs at risk and the tumor are drawn into the image made in phase 3. The organs at risk for cervical cancer brachytreatment are the bladder, rectum, sigmoid, and bowel loops

6. *Treatment planning*
   The final treatment plan is made.

7. *Treatment*
   The treatment takes place.

3.2 Survey results

In total, six European academic hospitals responded to the survey. Four out of the respondents were from German academic hospitals, one was from a dutch academic hospital, and one was from an Austrian academic hospital. Please note that we added the two survey validations to the data pool as well.

3.2.1 Times per sub-step

The average times per sub-step can be found in Table 5. The numbers in front of the sub-steps imply what step [See Section 2.2] the sub-step is part of. In step 1. Pre-Operative Preparation the sub-steps take around 23 minutes. Important to note is that the patient is not part of the process yet. Therefore this time can be considered as less important, and thus not too long. In the next step, 2. Applicator Insertion, it can be seen that the step needle insertion especially takes relatively long here [5.5% of the overall treatment time]. Besides, it is important to note that the patient is under anesthesia during this step. The longer a patient is under anesthesia, the higher the risks of complications [Routh et al., 2008]. Step 3. Imaging for Planning also takes relatively long [8.6% of the overall treatment time]. This is the case because all included hospitals work with an MRI. Making an MRI scan takes longer than making a CT scan [van Beek and Hoffman, 2008]. However, when using MRI instead of CT diagnostic accordance improve significantly [Luo et al., 2020].
The first thing that stands out in step 4. Treatment Planning, is the time for the sub-step delineation review fused volume & adjustment if needed [7.0% of the overall treatment time]. From survey replies, we could not conclude what the reason for the relatively long delineation time was. Besides, the needle reconstruction takes relatively long [6.6% of the overall treatment time]. In step 5. Treatment Delivery, the execution

[5.5% of the overall treatment time], and pre-treatment QA [Quality assessment] [4.4% of the overall treatment time] take longer compared to the other steps. Lastly, the applicator is removed in step 6. Applicator Removal. In steps 4, 5, and 6 the patient is not under anesthesia anymore.

3.2.2 Accuracy survey results

To identify the accuracy of the procedure times for each sub-step, we made box plots of the times. The box plots can be found in Figure 7.

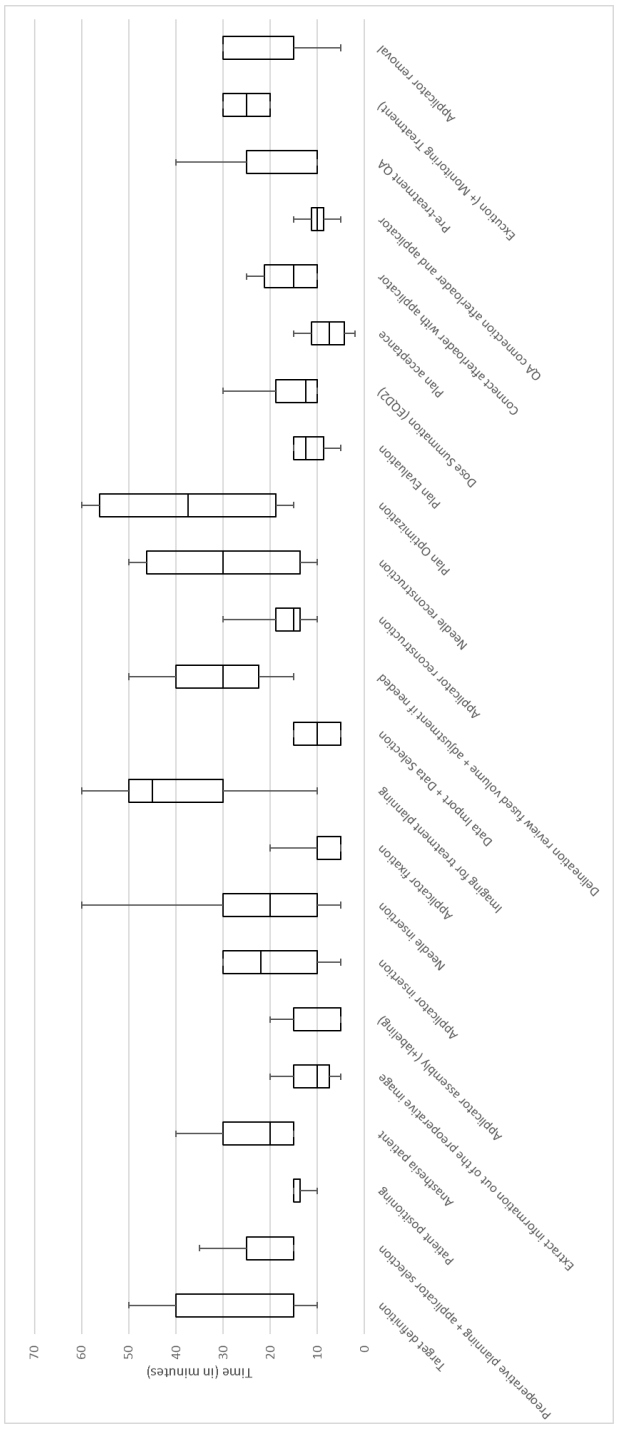

FIGURE 7: Box Plots Times Spent Per Sub-Step Cervical Cancer

The boxplots show the minimum, first quartile, median, third quartile, and maximum of each sub-step's time. Besides looking into the box plots, we also conclude more about the accuracy of our data, by looking into the skewness and median of the times per sub-step. The skewness and median are both in Table 6. A right-skewed step means that more respondents were relatively faster than the average in this sub-step. A left-skewed sub-step means that most respondents were relatively slower than the average. As can be seen in the box plots [Figure 7] and Table 6, the following sub-steps: Target definition, Preoperative planning & applicator selection, Applicator fixation, Pre-treatment QA and Applicator removal are very right-skewed. Future research should clarify the reason for this right-skewness. Most likely, the reason is either that some respondents have a different process design, which results in a faster process, or that the skewness is caused by too few data points.
The sub-steps: Applicator Assembly (& Labelling) and Applicator Fixation are very left-skewed. From this we conclude that most respondents were relatively slower than the average in these sub-steps. Again, future research should discover the reason for this skewness.

3.2.3 Profession performing each sub-step

The average profession performing the sub-steps can be found in Table 7. This profession is determined by taking the profession that was filled in the most by the respondents. Some sub-steps had varying results, many different professions were filled in by respondents in these sub-steps. In particular, the profession Nurse for sub-step Patient Positioning and the profession Radiation Oncologist for the sub-step Applicator Fixation, were both only filled in by 33.3% of the respondents. The reason for the varying results could be that the guidelines per country vary. Furthermore, it could also be due to the few data points. Future research should determine the reason for these variations.
We establish an average workflow based on the average time spend and profession per sub-step. For the sake of the readability, we moved this workflow to Appendix F.

3.3 Potential areas for innovation

Lastly, we score the possible innovations in terms of costs saved and time won. We do this by filling in the average workflow [Appendix F] as the initial situation, and the situation with the innovation, as the proposed situation in the spreadsheet simulation. For the personnel and facility costs, we fill in the values found in Section 2.3. The total costs for the initial process are €4397.90 per treatment according to the spreadsheet simulation [See Figure 8].

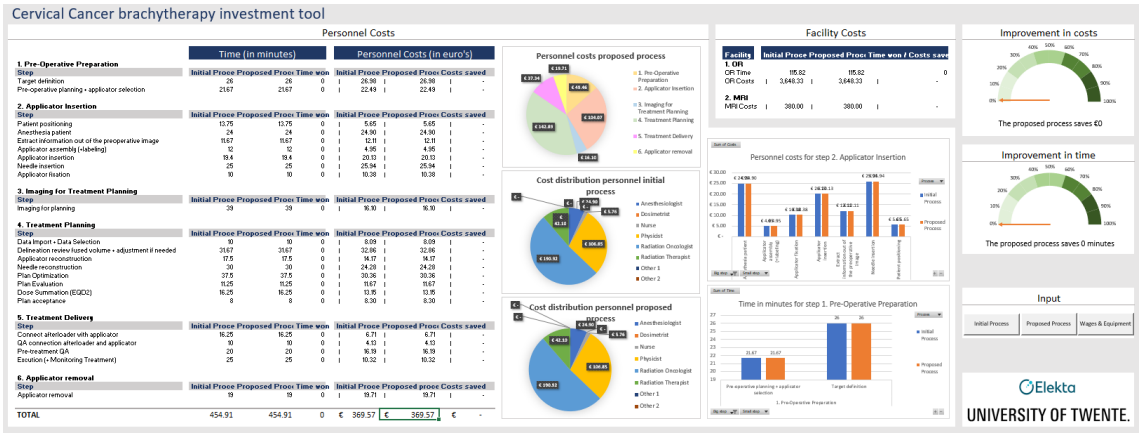

FIGURE 8: Initial situation based on survey results in the spreadsheet simulation

We decided to test the effect of possible innovations on the overall treatment times and costs by testing the effect of innovations on the sub-steps that took the longest according to the survey results [Section 3.2]. We do this by testing the effect of a 40% decrease in the time needed in these sub-steps. Note that this is just an example, an experiment with a decrease of for example 20% in time would also be possible. Besides, doing an experiment in which the profession performing the sub-step changes is also possible. We select the sub-steps for this experiment, that take on average at least 25 minutes [5.5% of the overall treatment time] in the survey results. Therefore, the selected sub-steps are Target Definition, Needle Insertion, Imaging for Treatment Planning, Needle Reconstruction, Plan Optimization, and Execution. Before testing possible innovations in these sub-steps, we excluded some of these sub-steps for various reasons:

- Target Definition, because the skewness in this result was large [see Table 6]. Therefore, there should be collected more data on this sub-step first, before pricing it.
- Needle Reconstruction, because it was performed in a similar sub-step as Plan Optimization by the same profession. The effects would be similar to innovation in the Plan Optimization sub-step. And since the Plan Optimization sub-step took longer than the Needle Reconstruction sub-step, we decide to test that instead.
- Execution, because the high average time in this sub-step, mostly has to do with the radioactive source having to be in a certain spot for a certain time. Innovation in this part is most likely not/limited possible.

Therefore, the sub-steps we use in this experiment are Needle Insertion, Imaging for Treatment Planning, and Plan Optimization.

3.3.1 Needle Insertion

Firstly, we change the time spent on the sub-step Needle Insertion from 25 to 15 minutes [decrease of 40%] in the proposed situation in the spreadsheet simulation. The personnel costs saved per treatment are €10.38 [See Figure 9].

2. Applicator Insertion

Step	Initial Process	Proposed Process	Costs saved
Patient positioning	€ 5.65	€ 5.65	€ -
Anesthesia patient	€ 24.90	€ 24.90	€ -
Extract information out of the preoperative image	€ 12.11	€ 12.11	€ -
Applicator assembly (+labeling)	€ 4.95	€ 4.95	€ -
Applicator insertion	€ 20.13	€ 20.13	€ -
Needle insertion	€ 25.94	€ 15.56 ▲	€ 10.38
Applicator fixation	€ 10.38	€ 10.38	€ -

FIGURE 9: Personnel costs when the time spent on the sub-step Needle Insertion decreases 40%

Besides, the facility costs will go down with €315 per treatment [See Figure 10].

Facility Costs

Facility	Initial Process	Proposed Process	Time won / Costs saved
1. OR			
OR Time	115.82	105.82 ▲	10
OR Costs	€ 3,648.33	€ 3,333.33 ▲	€ 315.00
2. MRI			
MRI Costs	€ 380.00	€ 380.00	€ -

FIGURE 10: Facility costs when the time spent on the sub-step Needle Insertion decreases 40%

Therefore, the total costs will go down with €322.98 per treatment [See Figure 11]. Especially the decrease in the facility costs is remarkable. The reason for this is that the OR costs are relatively high compared to the personnel costs. Again, please note that the supporting personnel is not added in this simulation, and thus that the personnel costs are likely higher than is stated in the spreadsheet simulation. Nonetheless, the OR costs will most likely still have the most impact.

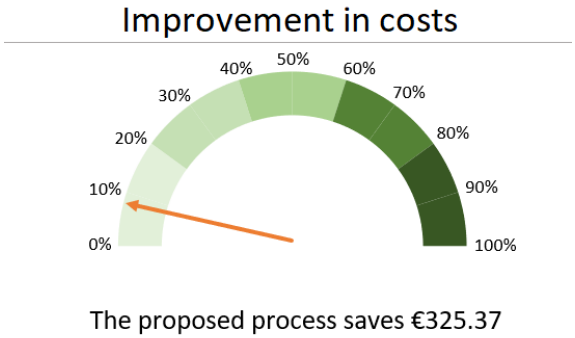

FIGURE 11: Improvement in costs when the time spent on the sub-step Needle Insertion decreases 40%

3.3.2 Imaging for Treatment Planning

Next, we change the time spent on the sub-step Imaging for Treatment Planning from 39 to 23.4 minutes [decrease of 40%] in the proposed situation in the spreadsheet simulation. The personnel costs saved per treatment are €6.44 [See Figure 12].

3. Imaging for Treatment Planning

Step	Initial Process	Proposed Process	Costs saved
Imaging for planning	€ 16.10	€ 9.66	€ 6.44

FIGURE 12: Personnel costs when the time spent on the sub-step Imaging for Planning decreases 40%

The facility costs will not change since the OR time does not change. Therefore, the total costs will go down with €6.44 per treatment [See Figure 13]. This innovation has noticeably less effect on the overall treatment costs, compared to the innovation on the Needle Insertion. The reason for this is that there is no change in the OR costs. Again, we see the big effect of the OR costs on the overall treatment costs.

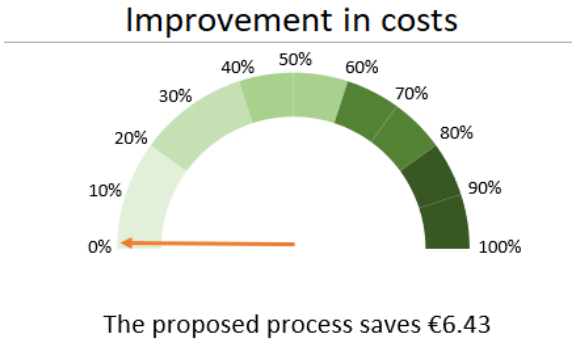

FIGURE 13: Improvement in costs when the time spent on the sub-step Imaging for Planning decreases 40%

3.3.3 Plan Optimization

Lastly, we change the time spent on the sub-step Plan Optimization from 37.5 to 22.5 minutes [decrease of 40%] in the proposed situation in the spreadsheet simulation. The personnel costs saved per treatment are €12.14 [See Figure 14].

4. Treatment Planning

Step	Initial Process	Proposed Process	Costs saved
Data Import + Data Selection	€ 8.09	€ 8.09	€ -
Delineation review fused volume + adjustment if needed	€ 32.86	€ 32.86	€ -
Applicator reconstruction	€ 14.17	€ 14.17	€ -
Needle reconstruction	€ 24.28	€ 24.28	€ -
Plan Optimization	€ 30.36	€ 18.21	€ 12.14
Plan Evaluation	€ 11.67	€ 11.67	€ -
Dose Summation (EQD2)	€ 13.15	€ 13.15	€ -
Plan acceptance	€ 8.30	€ 8.30	€ -

FIGURE 14: Personnel costs when the time spent on the sub-step Plan Optimization decreases 40%

The facility costs will again not change, since the OR time does not change. Therefore, the total costs will go down with €12.14 per treatment [See Figure 15]. Again, we can see the link between the OR time and the overall treatment costs.

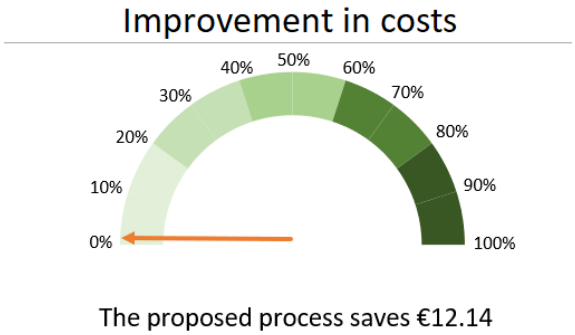

FIGURE 15: Improvement in costs when the time spent on the sub-step Plan Optimization decreases 40%

In conclusion, in this experiment, innovation in the sub-step Needle Insertion would have the biggest impact on the overall treatment costs. The main reason for this is that it lowers the high facility costs, and in particular the high OR costs, compared to the other potential areas innovations. Therefore from a financial perspective, innovation has the highest impact in step 2. Applicator Insertion and especially in the sub-step Needle Insertion.

4 Conclusion & Recommendations

4.1 Conclusion

In this research, we focused on identifying the areas of innovation for cervical cancer brachytherapy treatments within European academic hospitals. From this focus area, we established the following main question:

What should be the focus area for innovations in cervical cancer brachytherapy treatments in European academic hospitals?

To answer this question we designed a quantitative survey that asked out the times spent on each [sub-]step. The step and sub-step structure in the survey were based on the EMBRACE-II protocol. In total, six European academic hospitals responded to the survey. Four out of these respondents were German, one was Dutch, and one was Austrian.

The average overall treatment time from these respondents was 7 hours and 35 minutes. This is a bit lower than the expected average treatment time of 8 hours and 55 minutes, as established by Vliet-Perez et al. [2022] in Dutch academic hospitals. More on the limitations of the data in this research can be found in Section 4.3.

Looking further into the survey results, we found that in particular the sub-steps Target Definition, Needle Insertion, Imaging for Treatment Planning, Needle Reconstruction, Plan Optimization, and Execution took relatively long [over 25 minutes, which is 5.5% of the overall treatment time]. We tested the effect on the costs if innovations would be done in these sub-steps. We excluded the sub-steps Target Definition, Needle Reconstruction, and Execution for this experiment due to unreliable data, or no innovation possibilities [see Section 3.3]. We did this cost-analysis by using a spreadsheet simulation we built in Excel [See Figure 16]. This spreadsheet simulation calculates the personnel and facility costs per cervical cancer brachytreatment.

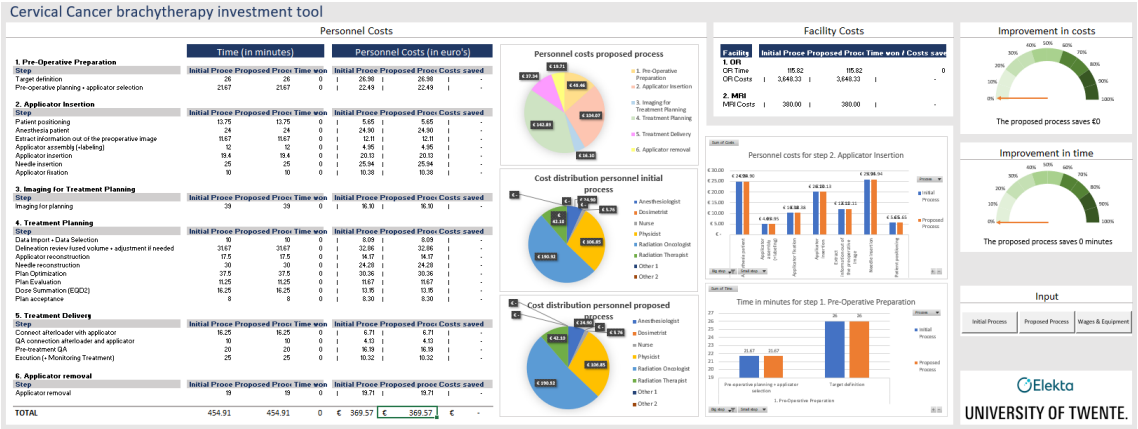

FIGURE 16: The spreadsheet simulation

In this spreadsheet simulation, we added the initial situation, based on the survey results. We decreased the time spent on each sub-steps mentioned above by 40%. Eventually, the decrease in the sub-step Needle Insertion had the biggest impact on the costs. The reason for this was that the OR time went down in this step the most, and the OR costs play

the biggest role in the overall costs for the cervical cancer brachytherapy treatment.

This research has thus shown that especially the sub-steps Target Definition, Needle Insertion, Imaging for Treatment Planning, Needle Reconstruction, Plan Optimization, and Execution are focus areas for innovation. In particular, the sub-step Needle Insertion should be a focus area for innovation, since this will also have the most impact on the overall costs.

4.2 Recommendation Elekta

From the preliminary outcome, the investment by Elekta should be made in innovations for the Needle Insertion sub-step. However, we advise Elekta to do more research first, since the selection of this innovation area is only based on a small data set. More information on the limitations of this research can be found in Section 4.3. Besides, we also advise Elekta to look into other segments of the market. Academic hospitals are only a small part of their customers. Looking into non-academic hospitals and the problems encountered there has even more impact on all their customers.
Besides we also encountered some other issues with Elekta during our research, these were:

- When visiting one of the hospitals, they told us that the software crashes quite often. Looking more into this by for example analyzing crash reports is advised.
- We had relatively few responses to the send-out survey. We advise Elekta to be selective when sending out surveys to customers, since the number of previous surveys may have an impact on the number of responses on a new survey [Porter et al., 2004].

4.3 Research limitations

As stated before this research has some limitations, these are:

1. The conclusion is based on a relatively small data pool. As discussed in 3.2.2, the little available data resulted often in a large skewness in the resulted times found. More respondents could decrease this skewness and increase the reliability of the results.
2. The survey only asked for the professions performing each sub-step. We did not ask about additional or supporting personnel that is present during each sub-step. To make a more accurate cost analysis, this information should be added.
3. The equipment costs are not taken into account in the cost analyses. To increase the accuracy of the cost analysis this should be added to the model.
4. The waiting times in between sub-steps are not taken into account. To increase the accuracy of the cost analysis this should be added to the model.

Thus, to increase the reliability further research should be done to increase the number of respondents. Besides, to increase the accuracy of the costs analysis the information from limitations 2-4 should be researched as well.
Furthermore, future research could be done on why the steps found in the preliminary data take relatively long. This will also give more insight into what the innovations should improve exactly within the step. Lastly, we did not take quality into account in

this research. In further research, this could also be added, because a faster treatment, does not always mean a better one.

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-1-AE27$CLongtermChart1_2$X1_-1-AE27$CLongtermChart1_3$X2_
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A Staging and Treatment Guidelines

In the EMBRACE-II protocol the TNM and FIGO staging are used together to determine a treatment plan for the patient.

A.1 TNM Staging

TNM staging is a general way to categorize all types of tumor cancer. It tells something about three factors. Firstly, the letter T stands for the size or direct extent of the primary tumor [National Cancer Institute, 2023]. For brachytherapy use this is important, since this determines whether the tumor can be accessed. Besides, sometimes if a tumor is too big, brachytherapy cannot work. This is the case since brachytherapy gives off very locally distributed radiation. If the tumor is too big, the radiation will simply not reach the whole tumor. The second letter N stands for the degree of spread to the lymph nodes [National Cancer Institute, 2023]. Cancer usually spreads through the body through the lymphatic system. For this reason, in cases were the degree of spread to the lymph nodes is high. It might be needed to do more intensive radiation therapy. The last letter is the letter M. It stands for the presence of distant metastasis [National Cancer Institute, 2023]. This again is an influence for the type of therapy chosen. For example, if there are metastasis to distance organs, one may choose to use immunotherapy next to radiation therapy.

A.2 FIGO Staging

FIGO staging is used to categorize all types of cervical cancer. It has four main stages which describe the degree of spread. The description of each stage can be found in Table 2 [Merz et al., 2020].

Stage	Description
I	The cancerous tissue is completely limited to the cervix.
II	The tumor is not limited to the cervix and infiltrates 2/3 of the vagina or the parametria
III	The tumor infiltrates the lower 1/3 of the vagina or the pelvic wall. Or there are pelvic and/or retroperitoneal lymph node metastases.
IV	The tumor must at least infiltrate the wall layers of the bladder and/or rectum to the the tumor tissue must infiltrate the wall layers of the bladder and/or rectum to the mucosa. Or there should be distant metastases.

Table 2: Overview of the four stages in cervical cancer FIGO staging

A.3 Treatment plan distribution

Both the TNM and FIGO staging are used to determine an actual treatment plan for the patients. In Table 3 there is an overview given of the recommended therapies according to the TNM and FIGO staging, based on the ESTRO, ESGO and ESP guidelines for management of patients with cervical cancer [ESGO/ESTRO/ESP, 2018]. Besides it tells the frequency of the staging for all cervical cancer patients in Europe [Monk et al., 2022].

T Category	FIGO staging	Frequency	Recommended Treatment Next To Surgery
TX			
T0			
T1	I	55%	
T1a	IA	20%	
T1a1	IA1	16%	No use of radiotherapy
T1a2	IA2	4%	Radiotherapy or chemoradiotherapy is recommended
T1b	IB	35%	
T1b1	IB1	29%	Radiotherapy or chemoradiotherapy is recommended
T1b2	IB2	6%	Chemoradiotherapy and brachytherapy are the preferred treatments
T2	II	20%	
T2a	IIA	5%	
T2a1	IIA1		Radiotherapy or chemoradiotherapy is recommended
T2a2	IIA2		Chemoradiotherapy and brachytherapy are the preferred treatments
T2b	IIB	15%	Chemoradiotherapy and brachytherapy are recommended
T3	III	10%	
T3a	IIIA		Chemoradiotherapy and brachytherapy are recommended
T3b	IIIB		Chemoradiotherapy and brachytherapy are recommended
T4	IV	15%	
	IVA		Chemoradiotherapy and brachytherapy are recommended to prolong life
	IVB		

Table 3: Recommended therapies according to the TNM & FIGO staging and accompanying staging frequencies

B More information cervical cancer brachytherapy treatments

In this Appendix, more background information on cervical cancer brachytherapy treatments will be given. Besides it will tell more about the problems encountered by clients in these treatments.

B.1 EMBRACE studies

There are already several researches done on the optimization of treating cervical cancer. One of the most high-impact researches done to optimize the clinical outcome for cervical cancer are the EMBRACE studies, conducted by the GEC-ESTRO GYN working group. The precursor EMBRACE studies [RetroEMBRACE and EMBRACE I] demonstrated that clinical outcomes related to the dose prescription and techniques used. The perfect combination of techniques that were found in the RetroEMBRACE study were external beam radiation, MRI, radiotherapy, and chemotherapy. The EMBRACE I study optimized the dose prescriptions in brachytherapy for this combination of therapies [the EMBRACE Collaborative Group, 2022]. And the most recent EMBRACE study, the EMBRACE II study, optimized these dose prescriptions again using the newest brachytherapy and external beam radiation techniques. The EMBRACE II study is conducted quite recently. Final side effects and survival rates for this type of research can only be seen after a few years. Thus, the complete proof that the new doses contribute to better long-term clinical outcomes is not there yet. However, so far, the short-term outcomes look promising [The EMBRACE Collaborative Group, 2018].

B.2 Current patient experience brachytherapy

At present, it is not clear what steps are performed during a cervix cancer treatment in different hospitals. Besides it is not clear how these steps are performed. Recently, there was research conducted by multiple researchers, including S.van Vliet – Perez (Erasmus University), presented at ESTRO 2022 on cervical cancer patient's brachytherapy experience using the EMBRACE II protocol [van Vliet-Perez et al., 2022]. This research maps out the patient's experiences and time-action analysis during the brachytherapy treatment execution. It was found that the patient's average total procedure time is 8 hours and 55 minutes. In particular, the waiting time before the actual brachy treatment itself was relatively long. Specifically compared to the times needed for other steps in the process. The patients had to wait on average for 2 hours and 40 minutes before the treatment. During this stage the patients rated the time duration with a 6 out of 10 on average, with 0 being the perfect situation and a 10 being the worst possible situation. Also, the pain levels increased over time, due to anesthesia fading away. On average the pain levels went from close to 0 to up to level 3. [van Vliet-Perez et al., 2022]. This shows the need for optimization of the procedure time of brachytherapy treatment.

B.3 Problem Cluster

As expressed in the first part of this chapter, there are still many challenges to overcome for brachytherapy. It is clearly not optimal, and hence also not used as often in hospitals yet. Which can go at the expense of the clinical outcome of the patient. Since there are many problems different problems to focus on to improve brachytherapy, a main problem will be established according to the managerial systematically problem-solving method

[Heerkens and van Winden, 2021]. Figure 17 shows the problem cluster fitted for the brachytherapy treatment experiences for patients (also described in B.2) and staff. This problem cluster is also based on a list several problems that patients or staff encountered during brachytherapy treatment. This list consists of problems in this list are found in literature or given to me on the work floor.

Problems Problem Cluster:
The problems found before conducting this research can be divided over four main problem factors: personnel, patient, equipment, and society. The problems come from either literature, or they are given to me from personnel of the AMC brachytherapy department. The total list of problems used to construct the problem cluster and the problem cluster itself (Figure 17) can be found below:

Personnel (BLUE in problem cluster)
- Long procedure times brachytherapy cervix cancer patients in hospitals [heard on work floor]
- Brachytherapy is more skill dependent, than similar therapies [Sturdza et al., 2022]
- It takes long to learn how to proceed a brachytherapy treatment [Sturdza et al., 2022]
- Performing brachytherapy is relatively high-risk compared to similar therapies [explained in 1.2]
- Large dose of radiation given per fraction, compared to similar therapies [explained in 1.2]
- Not many staff members want to perform brachytherapy [Sturdza et al., 2022]
- Lack of standardization for brachytherapy treatments [Sturdza et al., 2022]
- Staff members and equipment are needed for a long time per treatment

Patient (PINK in problem cluster)
- Anesthesia fading away [van Vliet-Perez et al., 2022]
- Increased pain patients [van Vliet-Perez et al., 2022]
- Dissatisfaction patients [van Vliet-Perez et al., 2022]

Equipment (PURPLE in problem cluster)
- Lack of optimal hospital infrastructure within the brachy performing hospitals [heard on work floor]
- Few procedures can be done in one day

Society (GREEN in problem cluster)
- Expected increase in the number of cancer patients in the future [European Commission, 2022]
- Increase in the demand of brachytherapy sessions in the future
- Increase in the waiting time for a brachytherapy session the future
- Expected decrease in the labor force in Europe [Smit et al., 2020]
- Expected decrease in the doctors that can perform brachytherapy

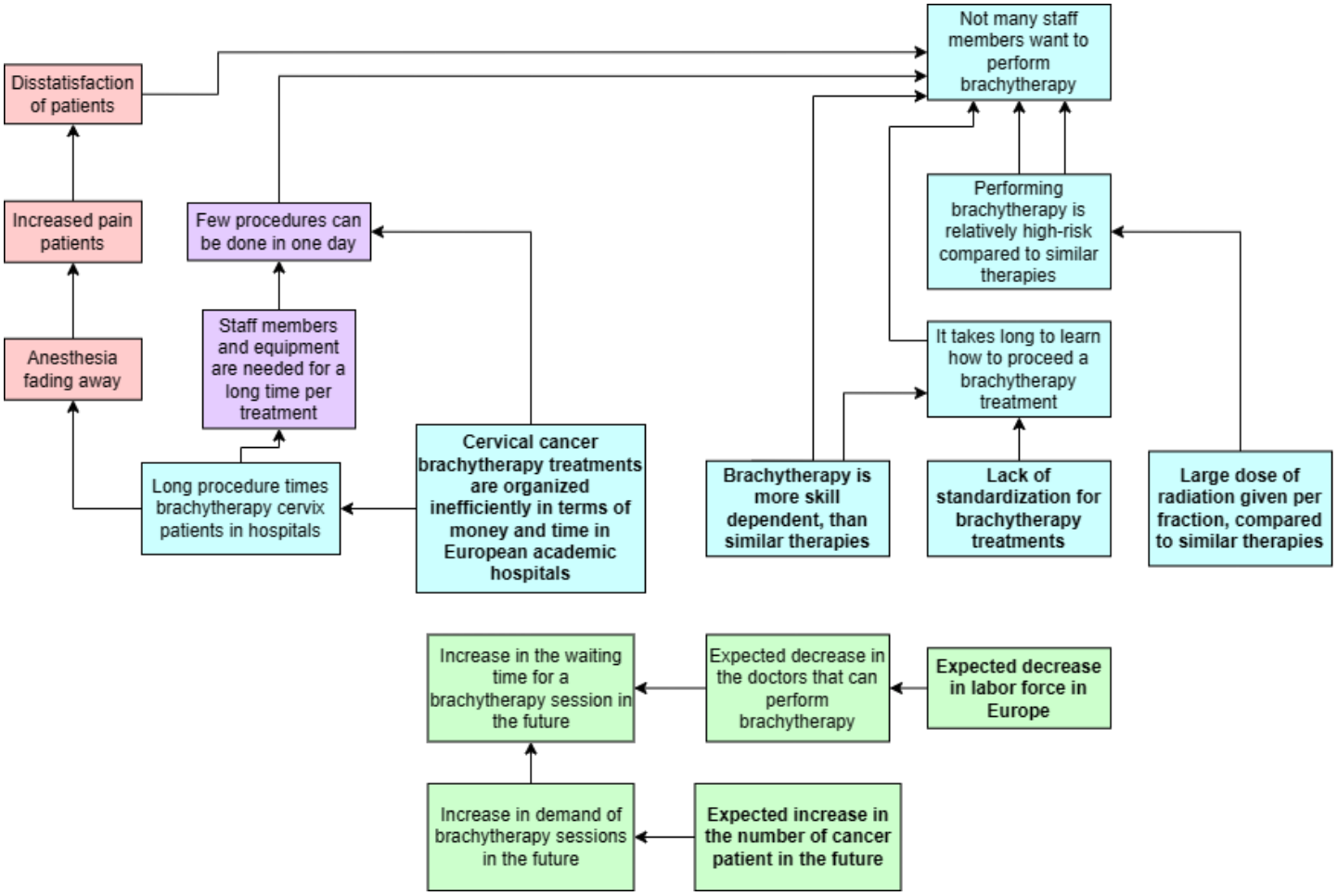

FIGURE 17: Problem Cluster Cervical Cancer Brachytherapy Treatment

The casual relations between all problems on the list are mapped out in Figure 17. For convenience, the figure's explanation is divided over three main parts: Bottom, left side and right side of the figure.

Bottom of Figure 17
Starting at the bottom the expected number of cancer patients in the future will increase [European Commission, 2022]. The European Commission estimated the intercedence to go from 2.86 million in 2020 to 3.24 million cases in 2040. This increase will make the demand for cancer treatment procedures and thus also brachytherapy sessions go up. This will result in an increase in the waiting time for brachytherapy sessions in the future. Besides the labor force in Europe will go down in the future [Smit et al., 2020]. Which will cause a decrease in the number of doctors that can perform brachytherapy. And thus, again cause an increase in the waiting time for brachytherapy sessions in the future.

Left side Figure 17
Next brachytherapy has relatively long procedure times
[van Vliet-Perez et al., 2022]. These long procedure times make the anesthesia fade away, which results in pain for the patient. This all together, makes the patient uncomfortable and dissatisfied. This dissatisfaction of patients results in staff members not wanting to perform brachytherapy.
Besides these long procedure times also result in the staff and equipment for brachytherapy treatments being occupied for longer. This together with the lack of optimal hospital infrastructure, results in only few procedures possible to perform in a day. the main policy tools for budgeting healthcare in Europe is reimbursement per procedure. For cancer healthcare this is also the case [Borras and Lievens, 2020]. Thus, the doctor gets paid only once for a relatively long-lasting procedure. Instead of multiple times for multiple external beam procedures. The costs of one brachytherapy procedure might simply not even outweigh the reimbursement given per session. Therefore, many staff members do not want to perform brachytherapy.

Right side Figure 17
Besides, brachytherapy is relatively skill dependent compared to different radiotherapy forms. A big part of the procedure is done manually (inserting the needles, inserting the applicator etc.). Doctors need to follow a training in order to be able to confidentially perform a brachytherapy procedure [Sturdza et al., 2022]. Beside there is no standardization in performing a brachytherapy treatment. Hence, it does take much time to learn how to perform a brachytherapy procedure, compared to other radiotherapy treatments. Which will result in many doctors not wanting to perform brachytherapy.
Furthermore, the large dose given (explained in 1.2) compared to similar therapies, makes the brachytherapy treatment relatively risk full. Simply, because the high dose makes that the procedure has to be executed very precisely. After all, one centimeter too much to the right, has bigger consequences for toxicity in brachytherapy, than for example external beam. This is again a reason that many staff do not wish to perform brachytherapy treatment.

B.4 Core Problem

In order to identify the core problem to focus on for this research, all potential core problems will be analyzed. The potential core problems are depicted by the problems with the bolt letters in Figure 17. Table 4 gives an overview of them and their matching viability according to the theory of Heerkens and van Winden [Heerkens and van Winden, 2021].

Potential core problem	Viable?	Reason, if not viable	Next problem in line viable?
Expected increase in the number of cancer patients in the future	No	It cannot be influenced	No, it cannot be influenced
Expected decrease in the labor force in Europe	No	It cannot be influenced	No, it cannot be influenced
Cervical cancer brachytherapy treatments are organized inefficiently in terms of money and time in European academic hospitals	Yes	-	-
Lack of optimal hospital infrastructure within the brachy performing hospitals	No	Since this research is about all hospitals in Europe. You cannot influence the optimal infrastructure for all these hospitals.	Yes
Brachytherapy is more skill dependent, than similar therapies	No	This lays outside the scope of this research, because clinical research and development has to be done to improve this.	No, this lies outside the scope of this research, because clinical development has to take place for this.
Large dose of radiation given per fraction, compared to similar therapies	No	Lowering this will result in more procedures needed for the same clinical result, which will result in all other problems increasing.	No, this lies outside the scope of this research, because clinical development has to take place for this.

Table 4: Potential Core Problems

There are is only one viable core problems left:

1. Cervical cancer brachytherapy treatments are organized inefficiently in terms of money and time in European academic hospitals

This problem is chosen as the core problem for this research.

C Survey questions

We would like you to participate in our survey. Your participation is voluntary. You have the right to withdraw at any point during the questionnaire, for any reason, and without any prejudice. If you have any questions regarding the survey, please contact jesse.smits@elekta.com. For more information on the Elekta Privacy Notice please click here.

We are interested in the current utilization of brachytherapy and why hospitals have implemented today's workflows to treat (locally advanced) cervical cancer. We aim to map out the current brachytherapy practices for cervical cancer across different types of clinical settings. Data from this survey may guide future development of products to address our customer's needs.

Please note that this survey will be best displayed on a laptop or desktop computer. Some features may be less compatible for use on a mobile device. It takes approximately 15-20 minutes to complete the survey.

- ○ I consent, begin the survey
- ○ I do not consent, I do not wish to participate

Personal Information

What is your profession? *you can select multiple answers when for example the survey is completed by a multidisciplinary team

- ☐ (Medical) Physicist
- ☐ Radiation Oncologist
- ☐ Radiotherapist
- ☐ Dosimetrist
- ☐ Nurse
- ☐ Anesthesiologist
- ☐ _____ Other

I have personally been involved in ..... brachytherapy procedures in the past year.

- ○ Less than 10
- ○ 10-20
- ○ 20-50
- ○ more than 50

General Information/Reference

Please estimate the number of patients (per indication) that have been treated in your hospital in the **past year with brachytherapy**

Endometrium	
Cervix	
GYN other	
GYN recurrence	
Prostate	
Prostate recurrence	
Breast	
Head & Neck	
Liver	
Skin	
Soft Tissue Sarcoma	
Rectum	
Esophagus	
Lung	
Bladder	

Which dose prescription guidelines do you apply for the treatment of cervical cancer using brachytherapy?

- ◯ GEC-ESTRO (EMBRACE)
- ◯ ESMO-ESGO-ESTRO
- ◯ ASTRO / ASCO
- ◯ ABS
- ◯ Other:

Do you use an adaptive protocol similar to EMBRACE?

- ◯ Yes, please explain:
- ◯ No

Which of the following tumor and target definitions of the EMBRACE protocol are implemented in your workflow?

- ☐ Initial GTV
- ☐ Initial HR CTV-T
- ☐ Initial LR CTV-T
- ☐ ITV-T
- ☐ GTV-N
- ☐ CTV-N
- ☐ CTV-E
- ☐ PTV

Which staging information is available and used during the brachytherapy procedure?

(You can select multiple options)

- ☐ Histology
- ☐ Radiology imaging sets
- ☐ Biomarkers
- ☐ I don't know
- ☐ Other:

Is the target definition, determined by a radiologist during staging, available for the brachytherapy treatment?

- ◯ Yes
- ◯ No

Do you perform any preplanning and/or applicator selection based on staging information preoperatively?

- ◯ Yes
- ◯ No

Do you perform image registration for the brachytherapy procedure?

- ◯ Yes

○ No

Time & Personnel

We are interested in the utilization of resources in your organization for cervical cancer brachytherapy procedures. Please select from the dropdown menu who performs each action and estimate the time it takes to perform each action in your setting. When estimating the times try to keep in mind the time it takes on average.

*If a step is not applicable to your situation please select 'not applicable' in the first column.

Preoperative Preparation

	Performed by:	Time (in minutes)	. Comment(s)
Target definition			
Preoperative planning + applicator selection			

Applicator Insertion

	Performed by:	Time (in minutes)	. Comment(s)
Patient positioning (the time from entering the room until the first proceeding)			
Anesthesia			
Imaging (for image registration)			
Target delineation (before applicator insertion)			
Delination of OAR (before applicator insertion)			
Image registration (before applicator implantation)			
Extract information out of the preoperative image			
Applicator assembly (+labeling)			
Applicator insertion			
Needle insertion (if applicable)			
Applicator fixation			

Applicator Insertion

	Performed by:	Time (in minutes)	. Comment(s)
Patient positioning (the time from entering the room until the first proceeding)			
Anesthesia			
Applicator assembly (+labeling)			
Applicator insertion			
Needle insertion (if applicable)			
Applicator fixation			

Imaging for planning

	Performed by:	Time (in minutes)	. Comment(s)
Imaging for treatment planning			

Treatment Planning

	Performed by:	Time (in minutes)	. Comment(s)
Data import + data selection			
Delineation review fused volume + adjustment if needed			

Treatment Planning

	Performed by:	Time (in minutes)	. Comment(s)
Data import + selection			
Delineation: Target			
Delineation: OARs			

Treatment Planning (reconstruction/review)

	Performed by:	Time (in minutes)	. Comment(s)
Applicator reconstruction			
Needle reconstruction			

Treatment Planning (treatment optimization)

	Performed by:	Time (in minutes)	. Comment(s)
Plan optimization			
Plan evaluation			
Inserting additional needles if needed			
Dose summation (EQD2)			
Plan acceptance			

Treatment delivery

	Performed by:	Time (in minutes)	. Comment(s)
Connect afterloader with applicator			
QA connection afterloader and applicator			
Pre-treatment QA			
Execution (+ monitoring treatment)			

Applicator removal

	Performed by:	Time (in minutes)	. Comment(s)
Applicator removal			

Please estimate on average the **total treatment time** (time from the start of applicator insertion to the end of fraction 1) of the brachytherapy procedure for (locally advanced) cervical cancer:

Treatment Time (in minutes):

Do you think the **total treatment time** is acceptable?

- ◯ Yes
- ◯ [ ] No, please indicate an acceptable total treatment time:

Please estimate on average the time (in minutes) needed for **treatment planning** for (locally advanced) cervical cancer:

Treatment planning Time (in minutes): [ ]

Do you think the time needed for **treatment planning** is acceptable?

- ◯ Yes
- ◯ [ ] No, please indicate an acceptable treatment planning time:

Please estimate the average total waiting time (in minutes) during a brachytherapy procedure for cervical cancer due to:

Anesthesia capacity	0
OR Recovery	0
Operating room unavailability	0
Imaging room unavailability	0
Brachy-trained personnel capacity	0
Patient transport	0
Total	0

Technology & Equipment

How is the infrastructure of your hospital set up for brachytherapy procedures?

- ◯ Dedicated room to perform the complete brachytherapy procedure (including imaging, applicator insertion, and treatment delivery)
- ◯ Operating room + brachybunker including in-room imaging (complete brachytherapy procedure is executed in two rooms)
- ◯ Operating room + brachybunker + imaging room (Complete brachytherapy procedure is executed in three rooms)
- ◯ Other:

[ ]

Imaging

During the brachytherapy procedure, images are typically made in different stages of the procedure. Please select for each stage:

1) Which imaging modality is used in your hospital

2) In which department the images are made

*If a step is not performed in your workflow please select 'not applicable'.

	Image Modality	Department	. Comment(s)
Preoperative imaging for staging	[ ]	[ ]	[ ]
Imaging for image registration	[ ]	[ ]	[ ]
Imaging for therapy planning first fraction	[ ]	[ ]	[ ]

	Image Modality	Department	. Comment(s)
Imaging for therapy planning remaining fractions (day verification)			
Imaging during procedure (guidance)			
Imaging in follow-up period			

Imaging

Please select which technology you use to make (multiparametric) MR images and the slice thickness you use for imaging

(You can select multiple options)

	Technology					Slice Thickness	.
	T1	T2	Dynamic Contrast Enhanced	Diffusion Weighted	Other	(in mm)	Comment(s)
Preoperative imaging for staging	☐	☐	☐	☐	☐		
Imaging for image registration	☐	☐	☐	☐	☐		
Imaging for therapy planning first fraction	☐	☐	☐	☐	☐		
Imaging for therapy planning remaining fractions (day verification)	☐	☐	☐	☐	☐		
Imaging during procedure (guidance)	☐	☐	☐	☐	☐		
Imaging in follow-up period	☐	☐	☐	☐	☐		

Volume delineation

During the brachytherapy treatment, target definitions are determined and volume delineations are performed. Please select which contouring functionality and which software application you use.

*If a step is not performed in your workflow please select 'not applicable'.

	Functionality	Software Application	. Comment(s)
Preoperative target definition (diagnose/staging)			
Target definition before applicator insertion (adaptive protocol)			
Volume delineation after applicator insertion			

Image registration

Please select the functionality and software that are used for image registration.

*If this step is not performed in your workflow please select 'not applicable'.

	Functionality	Software application	. Comment(s)
Image registration (before applicator insertion)			
Image registration (after applicator insertion)			

Do you use 3D printed applicators?

- ◯ Yes
- ◯ No

What is on average the production time for printing a 3D applicator?

Hours

Minutes

Applicator reconstruction

Please select the resources used for the following actions:

*If a step is not performed in your workflow please select 'not applicable'.

	Technology	Software application	. Comment(s)
Which technology is used for applicator reconstruction? And which software is used?			
Which technology is used for needle reconstruction? And which software is used?			

Treatment optimization

	Technology	Software application	. Comment(s)
Which technology is used for plan optimization? And which software is used?			

Treatment evaluation

	Technology							Software application	. Comment(s)
	Dose volume histogram	3D dose distribution in 3D view	3D dose distribution on transversal / sagital / coronal view	Dosimetric endpoint	Other	Not applicable			
Which technology is used for plan evaluation? And which software is used?	☐	☐	☐	☐	☐	☐	☐		

Dose Summation EBRT + brachy

	Yes/No	Software application	. Comment(s)
Do you take dose summation (EQD2) into account for plan evaluation? If yes, which software do you use?			

Treatment delivery

Please select the technology and system that are used for in-vivo dosimetry.

*If this step is not performed in your workflow please select 'not applicable'.

	Technology	. Comment(s)
Which technology is used for dose monitoring?		

Which afterloader is used in your hospital for brachytherapy treatments?

(you can select multiple options)

- [ ] Flexitron
- [ ] microSelectron
- [ ] VariSource
- [ ] GammaMedplus
- [ ] Bravos
- [ ] Saginova
- [ ] MultiSource
- [ ] Best HDR
- [ ] Other:

Please describe how the visualization of needles is performed (e.g. markers, image processing tools, etc)

Please describe how the visualization of applicators is performed (e.g. markers, image processing tools, etc)

Which method do you use for guiding needles?

- ○ I don't use needles
- ○ Insertion without guidance
- ○ Insertion with ultrasound guidance
- ○ Insertion with CT image guidance
- ○ Insertion with MRI guidance
- ○ Free length measurement
- ○ Other:

Please select the type of anesthesia used for the brachytherapy procedure of cervical cancer

- ○ Full
- ○ Epidural
- ○ Caudal block
- ○ No anesthesia
- ○ I don't know

Please select the type of after care that is applicable in your hospital

	Discharge	Department
After care		

AddComment

In which country is your hospital located?

Please select the type of hospital you work in

- [ ] Teaching hospital / University hospital
- [ ] Privat hospital
- [ ] Specialized hospital
- [ ] District general hospital
- [ ] Other

Final question:

Do you have any additional comments or remarks you would like to share with us about the brachytherapy practices in your hospital?

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D Spreadsheet simulation - user manual

An overview of the spreadsheet simulation can be found in Figure 21. The spreadsheet simulation is made to make it easier to compare investments in terms of money and time. More information on the methods used to calculate these costs and times can be found in 2.3 Below the explanation per part can be found.

D.1 Input [Blue]

Firstly, data has to be filled in to make the spreadsheet simulation work. You can do this by clicking the buttons within the blue square. If you click on the Initial Process button, the screen from Figure 18 will pop up. In this screen you can fill in the times needed per step in the initial situation. Furthermore, you can add the performer(s) for each step. You can go through each bigger sub-step by clicking on the different tabs at the top of the window. Once you are finished you can save the data to the spreadsheet simulation by pressing the save button. For the proposed process a similar screen will pop up.

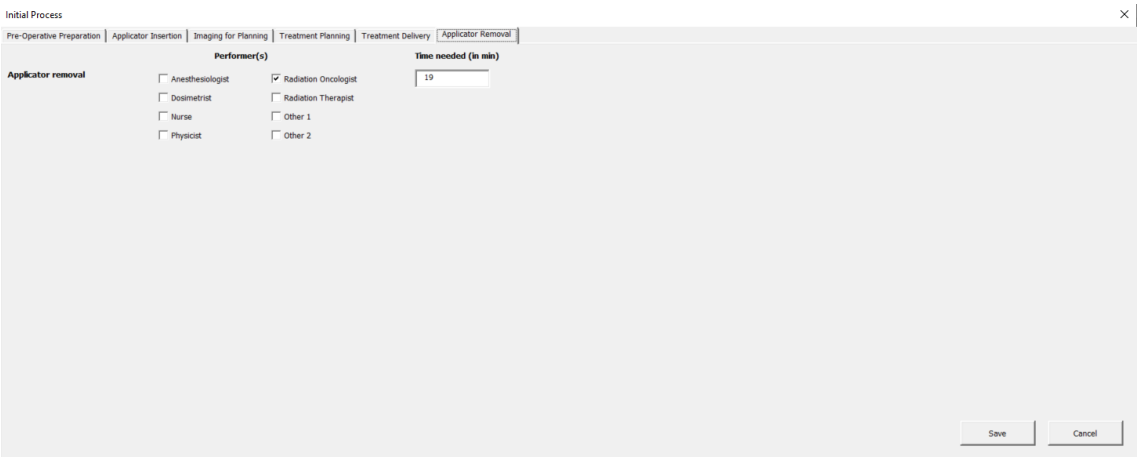
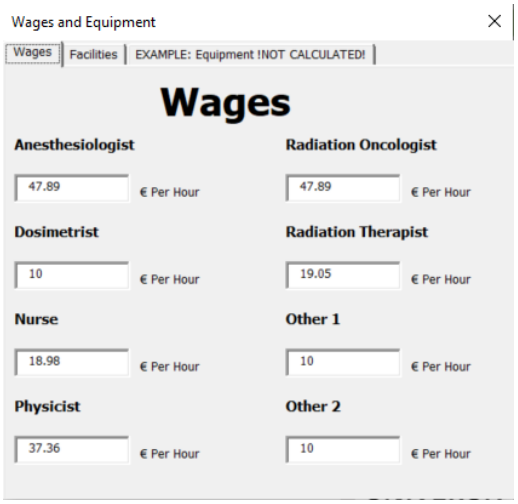
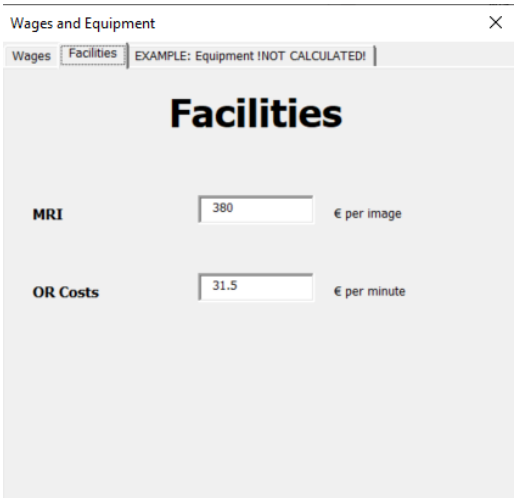


FIGURE 18: Userform Initial Process

Next, the Wages and Equipment button should be clicked on. This opens the window in Figure 19a. Here the wages for each profession should be filled in per hour. In the next tab facilities [Figure 19b] the facility costs should be filled in. In this spreadsheet simulation, only the facilities MRI and OR costs are used for the cost calculation. Lastly, the last tab Equipment [Figure 20] should be filled in. Unfortunately, due to time shortage, we could not take the equipment values into account for the facility calculations. We did however make a sample pages for potential future development. After all these values are filled in, you should click the save button, to start the calculations.



(A) Userform Wages



(B) Userform Facilities

FIGURE 19: Userforms Wages and Facilities

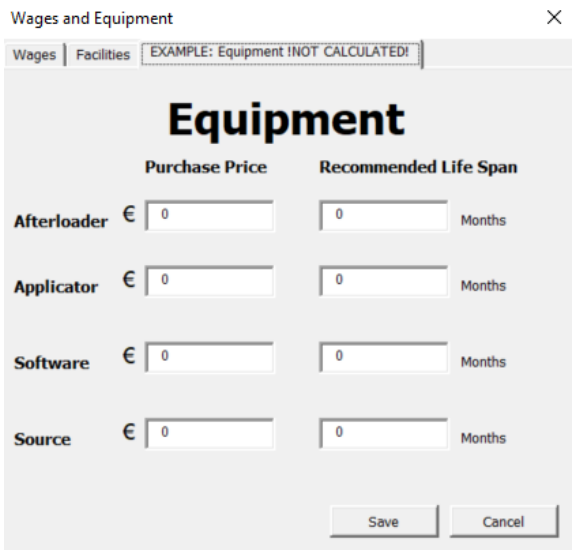


FIGURE 20: Userform Initial Process

D.2 Personnel Costs [Red]

Once you filled in the input, the outcome of the personnel costs can be found in the red square [Figure 21]. As can be seen the table on the left displays the times spent on each step and the accompanying costs. The last column tells you the time and/or money saved in each step. More information on how these costs are calculated can be found in 2.3. Next, the top pie chart displays the personnel costs per big step in the proposed process. The two bottom pie charts tell you the cost distributions over the different professions in the initial and proposed process. We added these, so that effect when different professions perform a step can also be seen easier. Besides the charts on the right display the costs and time per step. The steps that are shown within this chart can be changed on the bottom of the charts. When you click on big step, you can select the substep (e.g. Treatment

Planning). And when you click on the small step, you can select the individual steps (e.g. Needle reconstruction).

D.3 Facility Costs [Yellow]

The outcome of the facility costs can be found in the yellow square [Figure 21]. This table displays the OR time, OR costs, and MRI costs. How these costs are calculated can be found in 2.3.

D.4 Improvements [Green]

The improvement is displayed in the green square [Figure 21]. In this part both the personnel costs and facility costs are added for the initial and proposed process. An improvement compared to the original process is given in terms of money and time, both absolute and relative. The arrow displays the relative improvement on the initial process.

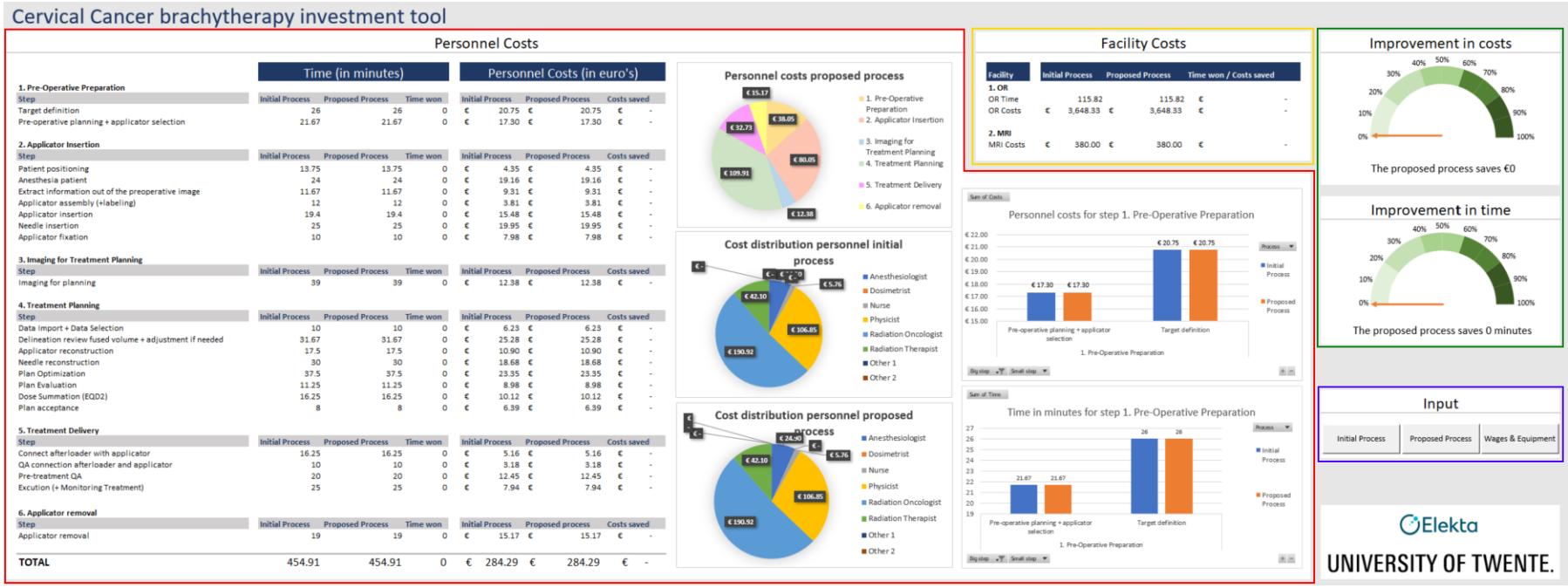


FIGURE 21: spreadsheet simulation overview

E Tables Survey Results

Step	Average Time (in minutes)
1. Target definition	26
1. Preoperative planning & applicator selection	21.67
2. Patient positioning	13.75
2. Anaesthesia patient	24
2. Extract information out of the preoperative image	11.67
2. Applicator assembly (& labeling)	12
2. Applicator insertion	19.4
2. Needle insertion	25
2. Applicator fixation	10
3. Imaging for treatment planning	39
4. Data Import & Data Selection	10
4. Delineation review fused volume & adjustment if needed	31.67
4. Applicator reconstruction	17.5
4. Needle reconstruction	30
4. Plan Optimization	37.5
4. Plan Evaluation	11.25
4. Dose Summation (EQD2)	16.25
4. Plan acceptance	8
5. Connect afterloader with applicator	16.25
5. QA connection afterloader and applicator	10
5. Pre-treatment QA	20
5. Execution (& Monitoring Treatment)	25
6. Applicator removal	19

Table 5: Average times per step

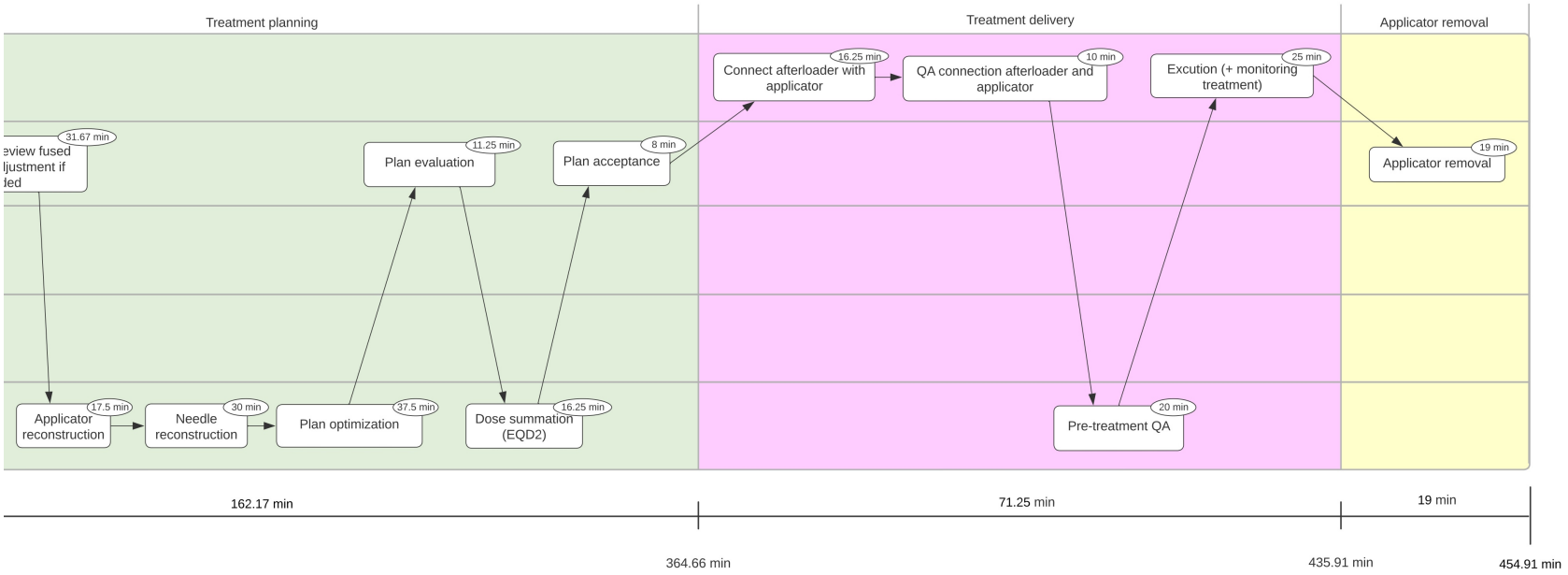
Step	Median Time in Minutes	Left- or right skewed?
1. Target definition	15	Right-skewed
1. Preoperative planning & applicator selection	15	Right-skewed
2. Patient positioning	15	Left-skewed
2. Anaesthesia patient	20	Right-skewed
2. Extract information out of the pre-operative image	10	Right-skewed
2. Applicator assembly (& labeling)	15	Left-skewed
2. Applicator insertion	22	Left-skewed
2. Needle insertion	20	Normal distribution
2. Applicator fixation	10	Left-skewed
3. Imaging for treatment planning	45	Left-skewed
4. Data Import & Data Selection	10	Normal distribution
4. Delineation review fused volume & adjustment if needed	30	Right-skewed
4. Applicator reconstruction	15	Right skewed
4. Needle reconstruction	30	Normal distribution
4. Plan Optimization	37.5	Normal distribution
4. Plan Evaluation	12.5	Left-skewed
4. Dose Summation (EQD2)	12.5	Right-skewed
4. Plan acceptance	7.5	Right-skewed
5. Connect afterloader with applicator	15	Right-skewed
5. QA connection afterloader and applicator	10	Normal distribution
5. Pre-treatment QA	10	Right-skewed
5. Execution (& Monitoring Treatment)	25	Normal distribution
6. Applicator removal	15	Right-skewed

TABLE 6: Median and skewness per step

Step	Profession performing the sub-step	Percentage of respondents that filled in the average profession
1. Target definition	Radiation Oncologist	100%
1. Preoperative planning & applicator selection	Radiation Oncologist	100%
2. Patient positioning	Nurse	33.3%
2. Anaesthesia patient	Anaesthesiologist	100%
2. Extract information out of the preoperative image	Radiation Oncologist	66.7%
2. Applicator assembly (& labeling)	Radiation Therapist	50%
2. Applicator insertion	Radiation Oncologist	50%
2. Needle insertion	Radiation Oncologist	50%
2. Applicator fixation	Radiation Oncologist	33.3%
3. Imaging for treatment planning	Radiation Therapist	83.8%
4. Data Import & Data Selection	Physicist	50%
4. Delineation review fused volume & adjustment if needed	Radiation Oncologist	66.7%
4. Applicator reconstruction	Physicist	50%
4. Needle reconstruction	Physicist	50%
4. Plan Optimization	Physicist	50%
4. Plan Evaluation	Radiation Oncologist	50%
4. Dose Summation (EQD2)	Physicist	50%
4. Plan acceptance	Radiation Oncologist	83.3%
5. Connect afterloader with applicator	Radiation Therapist	83.3%
5. QA connection afterloader and applicator	Radiation Therapist	83.3%
5. Pre-treatment QA	Physicist	66.7%
5. Execution (& Monitoring Treatment)	Radiation Therapist	83.3%
6. Applicator removal	Radiation Oncologist	66.7%

TABLE 7: Average profession performing each sub-step

F Average Workflow Survey Results


Treatment planning
Treatment delivery
Applicator removal
eview fused
ljustment if
ded
31.67 min
Applicator reconstruction
17.5 min
Needle reconstruction
30 min
Plan optimization
37.5 min
Dose summation (EQD2)
16.25 min
Plan evaluation
11.25 min
Plan acceptance
8 min
Connect afterloader with applicator
16.25 min
QA connection afterloader and applicator
10 min
Excution (+ monitoring treatment)
25 min
Pre-treatment QA
20 min
Applicator removal
19 min
162.17 min
71.25 min
19 min
364.66 min
435.91 min
454.91 min

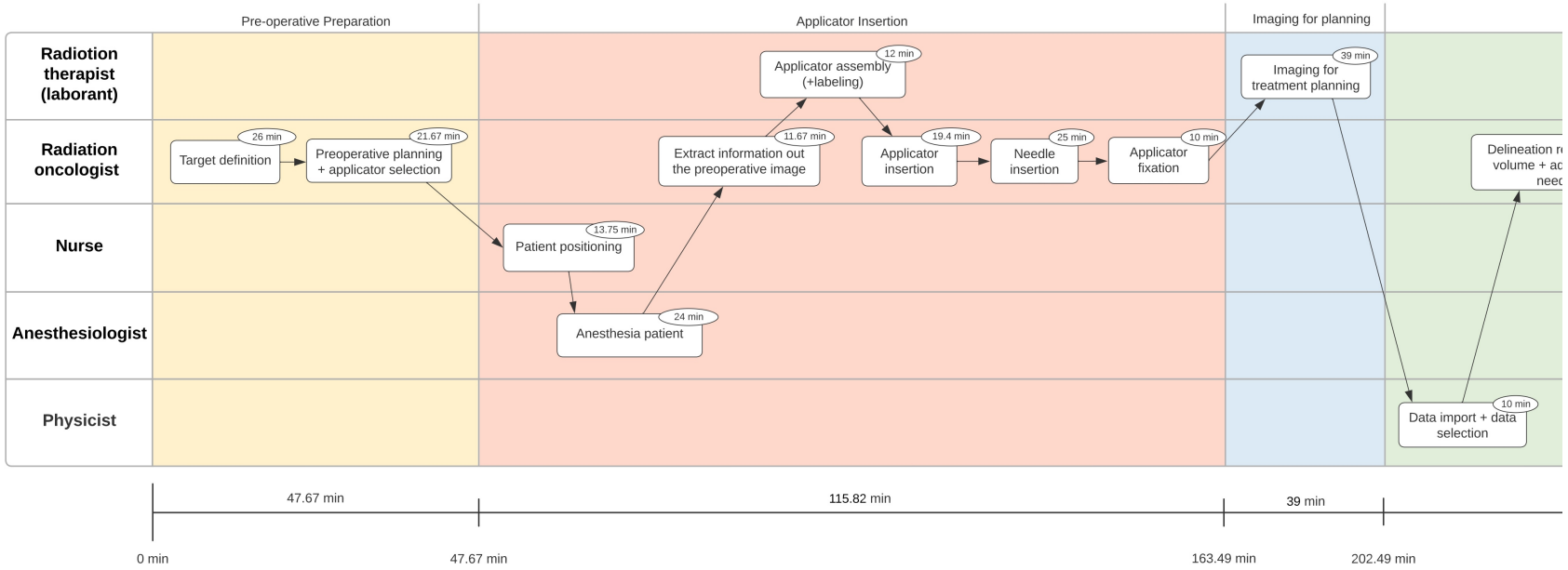


FIGURE 22: Average Workflow survey results