PRE-ARCHITECT: Workflow, time-action, and patient experience of the current clinical practice of brachytherapy in patients with cervical cancer.

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PRE-ARCHITECT: WORKFLOW, TIME-ACTION ANALYSIS, AND PATIENT EXPERIENCE OF THE CURRENT CLINICAL PRACTICE OF BRACHYTHERAPY IN PATIENTS WITH CERVICAL CANCER

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Abstract

Introduction: The Erasmus MC and TU Delft started the ARCHITECT project to develop a personalised applicator design approach for performing brachytherapy in patients with cervical cancer. Workflow for executing brachytherapy differs a lot between institutions. An overview of the workflow was created and time analysis of the steps was performed to identify bottlenecks and points of improvement in the current clinical practice of brachytherapy in cervical cancer. This overview could also be used as a reference for future research.

Methods: An overview of the workflow was created, the time needed for the different steps was registered and patients were asked to fill out questionnaires on patient experience. The current clinical practice was observed to create the workflow overview and define the steps of which time should be registered. As some steps occurred in parallel the radiotherapy technicians, radiation oncologists and nurses were asked to assist in reporting of times. Matlab was used to calculate the duration of the steps and SPSS was used to determine the descriptive statistics.

The research protocol written for the patient experience study was approved but the medical ethics committee. Patients were informed on the study so they could provide informed consent. The EQ-5D questionnaire was used to asses initial pain, anxiety and quality of life. A questionnaire on pain, anxiety and duration of each step during treatment day that was used for evaluating patient experience.

Result: A workflow overview per location was created. Data of forty implantations in fifteen patients were included for time analysis. The general steps and mean time needed for these steps were: operating room (55 minutes), waiting before arrival at imaging (80 minutes), applicator reconstruction (57 minutes), contouring (50 minutes), treatment planning (50 minutes), clinical physicist check (22 minutes) and treatment room (41 minutes). The mean total procedure time from patient entering the operating room until leaving the treatment room was 391 minutes.

The time needed for implantation of subsequent treatment fractions compared to the first treatment fraction decreased in sixteen out of the twenty fractions. The time needed at the operating room in patients receiving spinal anesthesia did not differ from patients receiving general anesthesia.

Four patients provided informed consent and filled out the questionnaires on patient experience. Patient experience differed a lot in these four patients. Overall, highest anxiety scores were found during the first brachytherapy day and highest pain scores were found during the waiting time at the short stay unit.

Discussion: The steps observed in the Erasmus MC did not agree on all steps that were found in literature. Time needed for these steps also differed when comparing to literature. The total waiting time could be decreased when enabling a more smooth transition between the recovery room and imaging step.

Adaptions to the time registration sheet should include the time needed for assembling the applicator at the operating room. The contouring step should be separated in contouring of the OAR and target volume. Time needed for imaging is not that important as the imaging protocol is the same in all patients. The decrease in waiting time for imaging when using the hyperthermia MRI should be evaluated. The influence of the amount of patients treated during one day would also be interesting to evaluate when more data has been collected. Another interesting factor would be differences in duration of the steps and pain experienced in patients treated with the Venezia applicator compared to the Utrecht applicator. More patients need to be included in the questionnaire study to draw conclusions on patient experience.

2

General introduction

2.0.1. Cervical cancer

In women, cervical cancer is the fourth most common form of cancer worldwide with an estimated 604.127 women diagnosed in 2020 [1]. Brachytherapy using an intracavitary cervix applicator and interstitial needles is one of the main components of the curative treatment of cervical cancer. Most of the patients are treated with a combination of chemotherapy, external beam radiotherapy and (interstitial) brachytherapy. In some centers, such as the Erasmus Medical Center (MC), hyperthermia is also a major component in the curative treatment of cervical cancer [2].

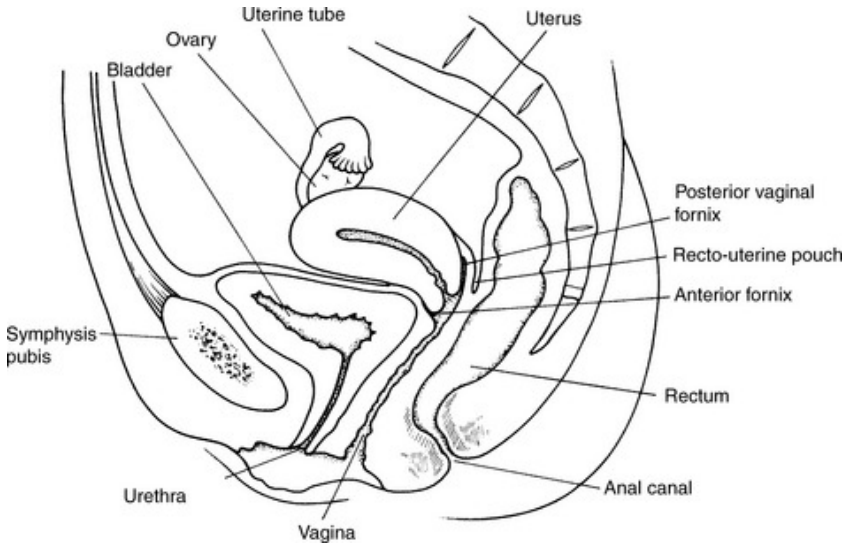

Figure 2.1: Anatomy of the female reproductive system [3].

2.0.2. Treatment of cervical cancer

The treatment options for treating cervical cancer are surgery, chemotherapy, external beam radiation therapy, brachytherapy and hyperthermia [4, 5]. Most patients receive a combination of these treatments based on the stage of the tumor. The FIGO staging is most commonly used and is explained in table 2.1.

The lower stage patients are suitable for surgical treatment with or without adjuvant chemoradiation. Patients with more advanced cervical cancer will be treated with a combination of treatments. All patients with locally advanced cervical cancer, FIGO stage IB2-IVA, should be considered to have brachytherapy as part of their treatment [4].

In patients with a low stage and low volume tumor (stage IB1 or IIA $\leq$ 4cm), external beam radiation therapy without additional brachytherapy might be sufficient and needs to be considered.

Hyperthermia is used as a radiosensitizer in patients receiving radiation therapy for cervical cancer based on a Dutch multicenter study which showed the significantly improved local control and survival when compared to only radiation therapy [5, 7, 8]. The added value of hyperthermia is mostly shown in larger tumors,

Table 2.1: Figo staging for cervical cancer [6].

Stage	Description
I	The carcinoma is strictly confined to the cervix(extension to the uterine corpus should be disregarded)
IA	Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5 mm
IA1	Measured stromal invasion <3 mm in depth
IA2	Measured stromal invasion ≥ 3 mm and <5 mm in depth
IB	Invasive carcinoma with measured deepest invasion ≥5 mm (greater than Stage IA), lesion limited to the cervix uteri
IB1	Invasive carcinoma ≥5 mm depth of stromal invasion, and < 2 cm in greatest dimension
IB2	Invasive carcinoma ≥ 2cm and < 4 cm in greatest dimension
IB3	Invasive carcinoma ≥ 4cm in greatest dimension
II	The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall
IIA	Involvement limited to the upper two-thirds of the vagina without parametrial involvement
IIA1	Invasive carcinoma < 4cm in greatest dimension
IIA2	Invasive carcinoma ≥ 4cm in greatest dimension
IIB	With parametrial involvement but not to the pelvic wall
III	The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortic lymph nodes
IIIA	The carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
IIIC	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with notations from radiology and pathology)
IIIC1	Pelvic lymph node metastasis only
IIIC2	Para-aortic lymph node metastasis
IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. (A bullous edemea, as such, does not permit a case to be allotted to Stage IV)
IVA	Spread to adjacent pelvic organs
IVB	Spread to distant organs

while the added value of chemotherapy with cisplatin is mostly present in smaller tumors [9, 10]. Therefore, hyperthermia is mostly used in combination with radiation therapy in patients with stage IIB, III and IV ≥ 4 cm.

In FIGO stages below IIB, hyperthermia is only used when there is a contra-indication for chemotherapy with cisplatin combined with radiation therapy. In the Erasmus MC, the combination of hyperthermia with radiation therapy is more likely to be chosen in patients with larger tumors, because the combination with cisplatin risks worsening of acute toxicity.

Patients with FIGO stage II, III, IV tumors larger than six centimeter receive induction chemotherapy followed with the combination of hyperthermia with radiation therapy. They are treated with concomitant hyperthermia instead of chemotherapy out of fear for the risk of toxicity in patients that also received chemotherapy on forehand [11].

The difficulty in treating cervical cancer lies in the anatomy of the female pelvis, see figure 2.1. The bladder and rectum are at risk of obtaining a lot of radiation dose when irradiating a cervical tumor using only external beam radiation therapy. By irradiating using an intracavitary tandem applicator and interstitial needles, a high dose in the tumor can be obtained while minimizing the dose to the organs at risk (OAR). This high tumor dose cannot be obtained with only external beam radiation therapy due to the high dose to the OAR that can cause toxicity [4, 12].

(a) The Utrecht applicator with the parallel catheters

(b) The Venezia applicator with parallel catheters and catheters through the grid

Figure 2.2: The two applicators currently used for brachytherapy in cervical cancer patients in the Erasmus MC

2.0.3. Changes in the practice of brachytherapy over the years

The practice of brachytherapy has changed over the years, this is due to the developments of imaging techniques and treatment planning techniques [13]. The dose used to be prescribed to point A, which was defined as a point lying 2 cm lateral to the center of the uterine canal and 2 cm superior to the mucosa of the lateral fornix in the paracervical triangle [14]. For these dose calculations, regular xray imaging was used. The treatment using the 2D xray imaging still resulted in poor organs of risk sparing and side effects. Dose prescription changed when 3D imaging became available for treatment planning and dose was no longer prescribed to point A. 3D dose optimization became possible since the introduction of computed tomography (CT) and magnetic reconance imaging (MRI). MRI had superior soft tissue contrast to CT and other imaging techniques which made it able to detect subtle abnormalities and changes in tumor volume that may not have been found using other imaging techniques [14].

2.0.4. ARCHITECT project

The current applicators used consist of a tandem and either two ovoids or a ring through which interstitial catheters can be positioned near the tumor. Figure 2.2a and 2.2b show the current applicators used in the Erasmus MC. The Fletcher (Utrecht) applicator consists of a intrauterine tandem with two ovoids on which interstitial catheters can be positioned. There are three different sizes of ovoids available. The length of the intrauterine tandem inserted in the uterus could be adapted. The Venezia applicator consists of a intrauterine tandem with a ring consisting of two parts in which the interstitial catheters can be positioned. The Venezia applicator has two different ring sizes and offers to place oblique catheters. The intrauterine tandem of the Venezia could not be adapted, the correct length and angle must be selected out of the provided set. The Venezia applicator has the option to place caps to treat the cervical wall.

An optimal treatment plan has high conformity, resulting in optimal target coverage and low dose to the surrounding healthy tissue. The positioning of the applicator and needles is of importance in reaching the high conformity. The applicators currently used are 'one-size-fits-all' applicators, which do not always optimally align with patient anatomy and have fixed needle positions and angles limiting the treatment plan conformity. The Venezia applicator offers oblique paths for positioning the catheters which allow to bring the radioactive source closer to wider tumors. However in larger tumours, the target coverage and local tumour control remain low [15, 16]. Personalised applicators with optimally planned channels for catheters could be the solution for this problem.

The Erasmus MC and TU Delft started the ARCHITECT (Adaptive Brachytherapy using Customized Needle Applicators) program, which aims to develop a systematic personalized brachytherapy applicator design approach by constructing fundamental design rules, needle channel path planners and product development tools. The hypothesis is that customized brachytherapy applicators result in enhanced conformity between the target and the prescribed dose. Ultimately, the improved conformity will lead to increase in local tumour control, less side effects, lower dose to the OAR and a better quality of life. The aim of the ARCHITECT project is to improve dose conformity with little influence on the workflow and time needed for the procedure.

2.0.5. Master thesis

The aim of this master thesis is to create a baseline of the current clinical practice of brachytherapy in patients with cervical cancer. The aspects of interest were the workflow, the time needed for the steps in the workflow and the patient experience. The ARCHITECT applicator approach should not prolong the duration of the steps executed during the day or worsen patient experience.

Of which steps is the current workflow in brachytherapy for cervical cancer composed and what is the variability of these steps? How long does each step of the workflow take? Which steps should be improved to increase patient satisfaction and shorten the treatment time. Which steps need to be adapted to allow personalised 3D printed applicators to be used? How do patients experience the treatment of cervical cancer with brachytherapy in the current clinical setting?

The current workflow will be mapped and the duration of the different steps of the brachytherapy treatment day will be evaluated. The current patient experience is also included in the baseline study. The information collected will be used to identify current bottlenecks during the treatment day and as a reference for later research. The baseline created will function as a reference for future research on implementing the ARCHITECT design approach in the clinical practice.

The baseline created consisted of different parts:

- Chapter 3: Workflow analysis.
- Chapter 4: Time analysis.
- Chapter 5 Patient experience.
- Chapter 6: General discussion.

3

Workflow analysis

3.1. Introduction

The literature review performed in the context of this master thesis showed that there is a variety of approaches to perform the brachytherapy procedure in cervical cancer. There is a difference in imaging modalities, sequence of steps and locations utilized for the procedure. Also, not all articles reported the steps in the same way. Zhang et al. started their workflow overview on the moment of diagnosis while others started their workflow overview at the time the patient entered the operating room [17–21].

The Groupe Européen de Curiethérapie - European Society for Radiotherapy and Oncology (GEC-ESTRO) published guidelines for the treatment of cervical cancer with high-dose-rate (HDR) brachytherapy in 2005 which resulted in a shift in brachytherapy practice [22]. The availability of imaging modalities differs between radiation therapy centers. The workflow of the entire treatment could differ even when the same recommendations, the GEC-ESTRO recommendations, were used. These recommendations were mainly based on MRI for each fraction of brachytherapy. MRI is an expensive and time consuming imaging method and due to costs and/or logistic reasons, an MRI-guided brachytherapy workflow might not be feasible for all institutions practicing brachytherapy [23, 24]. There are a lot of articles available focusing on the use of different imaging modalities to obtain the best results compared to MRI-guided brachytherapy. Most institutions currently use either MRI [20, 25–27] or a combination of CT and MRI [21, 23, 24, 28–35] for treatment planning. The tumor and OAR are best visible on MRI while the applicator and catheters are visualized best on CT images. Both are used for treatment planning. When the MRI is not readily available after implantation of the applicator for the second fraction, a CT scan might be used for treatment planning and the MRI from the first fraction could be registered to the CT scan for the most optimal delineation. Other centers perform the implantation at the radiation therapy department instead of the operating room. The personnel needed and used for the whole treatment process might also be different.

The patient workflow starts at the diagnosis and not at the moment the brachytherapy treatment starts. Brachytherapy is an important component of the entire treatment [4, 12]. The treatment consists of different components depending on the staging at diagnosis as described in chapter 2. The entire workflow of the current clinical practice of brachytherapy in cervical cancer was mapped with the aim to identify all steps and substeps performed during the brachytherapy procedure.

Of which steps and substeps is the workflow of brachytherapy in cervical cancer composed in the Erasmus MC and who is involved in the different steps?

3.2. Methods

The workflow in the Erasmus MC was observed for a total of 10 weeks. During the start of the observations, a general overview of the steps of the workflow as resulted from the literature study was used as a starting point. This basic workflow consisted of a pre-implantation phase, applicator insertion, post-anesthesia recovery, imaging, contouring, treatment planning, quality control, treatment delivery and applicator removal and is shown in figure 3.1 and table 3.1. The literature study showed that these steps consisted of multiple substeps that are also shown in table 3.1.

Table 3.1: General overview of the steps during brachytherapy in cervical cancer as found in literature.

	Step	Substeps
1.	Pre-implantation fase	Diagnosis, consultation, pre-implantation MRI
2.	Applicator insertion	Inserting the bladder catheter, intrauterine tube and ovoids/ring and the catheters
3.	Postanesthesia recovery	
4.	Imaging	MRI or CT-scan
5.	Contouring of the target and the organs at risk	Gross tumor volume, intermediate and high risk tumor volume, bladder, rectum, sigmoid, bowel
6.	Treatment planning	
7.	Quality control of the treatment plan	
8.	Treatment delivery	
9.	Applicator removal	Removal of the catheters, intrauterine tube and ovoids and the bladder catheter

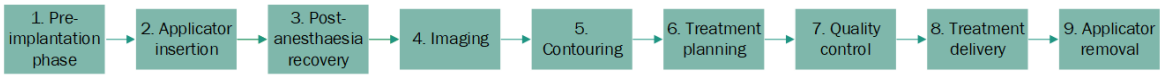

Figure 3.1: Flowchart overview of the general workflow that was used as a start to map the workflow in the Erasmus MC. The steps are ordered chronologically. The numbers correspond to the numbers in table 3.1.

This basic workflow was adapted and expanded after each day of observing the whole treatment procedure. The workflow overview that resulted from observing was checked for errors by radiation oncologists, radiotherapy technicians and clinical physicists. If needed, the workflow overview was adapted and after approval of all involved professionals, the workflow overview was declared definitive.

3.3. Results

3.3.1. Brachytherapy activities by location

The workflow as observed in the Erasmus MC is shown in figure 7.1 in the Appendix and consisted of multiple (complex) steps executed at different locations by different personnel during the same treatment day. The simplified version of the entire workflow during the treatment day is shown in figure 3.2. The whole treatment day process takes place at six different locations within the hospital.

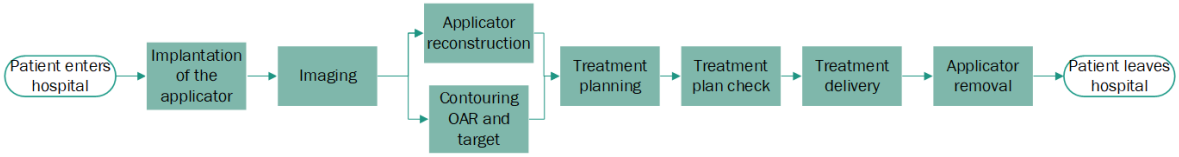

Figure 3.2: Overview of the general sequential and parallel steps executed during the treatment day. Patient enters the hospital, the applicator is implanted at the operating room, imaging is performed, target and organs at risk are contoured and the applicator is reconstructed, the treatment plan is created and checked, treatment is delivered, the applicator is removed and the patient leaves the hospital.

The procedure starts when the patient enters the operating room. After the implantation phase at the operating room, the patient is transferred to the recovery room. From the recovery room, the patient is transported to the radiology department for MRI or to the short stay unit to wait for the imaging appointment at the radiology department. The patient waits at the short stay unit until the treatment plan is completed. When the treatment plan is completed and approved, the patient is transferred to the treatment room. The treatment plan is created in the backoffice which, in this case, consist of two different rooms. Namely, the brachytherapy planning room of the radiotherapy technicians and the office of the radiation oncologist. The (sub)steps performed during each treatment day are described in the subsections below.

3.3.2. Pre-implantation phase

The pre-implantation phase was not included in figure 3.2, only the steps executed during the treatment day were shown. Steps executed before the treatment day were: diagnosis, consulation, pre-treatment planning and the intake at the short stay unit. The pre-implantation phase also consists of the (combination of) other treatment modalities used.

3.3.3. Operating room

The anesthetics are administered and the applicator and catheters are implanted at the operating room. The radiotherapy technicians are also present at the operating room to make sure the catheters are inserted at the correct depth at the pre-planned position on the ovoid/ring. See table 3.2 and figure 3.3 for an overview of the (sub)steps executed at the operating room. The operating room assistants assemble the applicator and label the numbers of the catheters while the anesthesiologist and the anaesthetic technician focus on administering sedation to the patient.

Table 3.2: Overview of the steps and the personnel involved at the operating room.

	Step	**Who is involved?**
1.	Patient enters the operating room	Anesthetics team
2.	Patient transfer from the patient bed to the operating table	Anesthetics team
3.	Time out procedure	Anesthetics team, radiation oncologist, OR assistent, radiotherapy technician
4.	Anesthesia	Anesthesiologist and anesthetics team
5.	Applicator is assembled and the catheters are connected to the correct positions on the ovoid/ring	OR assistant and radiotherapy technician
6.	Patient positioning in the lithotomy position	Radiation oncologist and OR assistant
7.	Bladder catheter is inserted	OR assistant
8.	Speculum insertion	Radiation oncologist and OR assistant
9.	Inspection of the cervix	Radiation oncologist and OR assistant
10.	Uterine sounding and measuring the length of the uterus	Radiation oncologist and OR assistant
11.	Dilatation of the cervical ostium using hegars	Radiation oncologist and OR assistant
12.	Implantation of the intrauterine applicator (using ultrasound if necessary)	Radiation oncologist and OR assistant
13.	Implantation of the ovoids/ring and the catheters	Radiation oncologist and OR assistant
14.	Internal fixation of the applicator using gauzes	Radiation oncologist and OR assistant
15.	Inserting the catheters to the correct depth	Radiation oncologist and OR assistant
16.	Measuring the exterior part of the catheters	Radiation oncologist, OR assistant and radiotherapy technician
17.	Labelling the exterior part of the catheters using a marker	Radiotherapy technician
18.	Fixation of the exterior part of the catheters	Radiation oncologist
19.	Transfer the patient back to the patient bed	Radiation oncologist, anesthetics team, OR assistants, radiotherapy technologists
20.	Patient leaves the operating room	anesthetics team

Present personnel at the operating room are the anesthesiologist, anesthetics technician, radiation oncologist, radiotherapy technician and operating room assistants. The procedure starts when the patient enters the operating room. First, the time out procedure (TOP) is performed to identify if all personnel and the patient is present, to verify the procedure performed and check if all equipment is ready. After that, the anesthesiologist focuses on the sedation of the patient while the operating room assistants start to set up the sterile equipment and assembling the applicator with the catheters in the pre-defined positions. After the anesthetics begin to work, the patient is positioned in the lithotomy position and the sterile workfield is applied. The urinary catheter is inserted in bladder. The bladder might be filled with Uro-Trainer NaCl (Braun)

if necessary. Reason for bladder filling is the location of the uterus. The uterus rests on top of the bladder and if the bladder is empty, it might be difficult to implant the applicator due to the angle of the cervical canal, see figure 2.1. Another reason to fill the bladder at the operating room during implantation is to visualize the bladder on the ultrasound (US). Transabdominal and/or transrectal US is used in difficult cases to implant the intrauterine applicator.

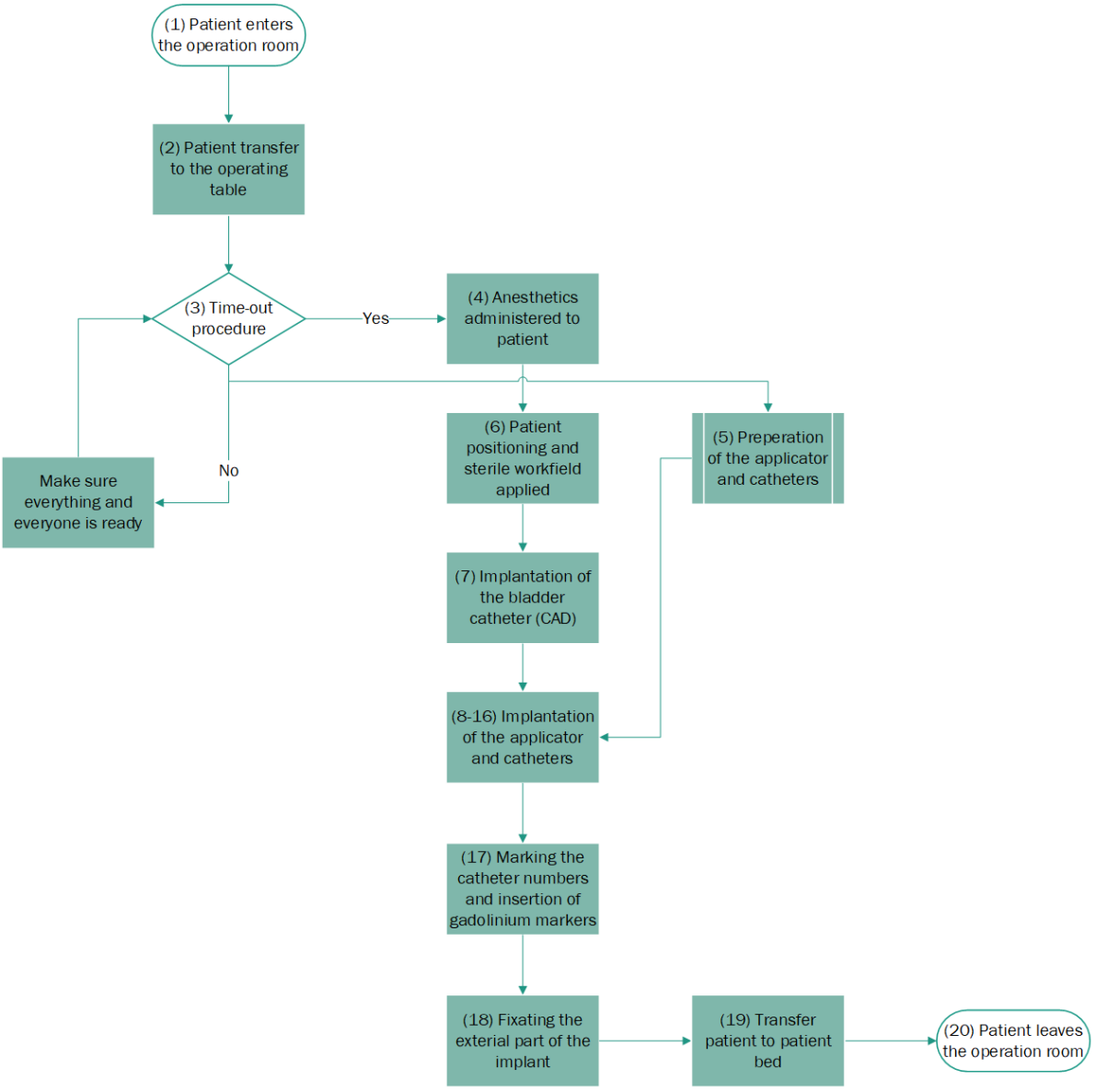

Figure 3.3: Overview of the (sub)steps of the procedure at the operating room. A more extensive description of the corresponding numbers is shown in table 3.2.

The speculum is inserted, uterine sounding is performed and cervical hegars are used to induce cervical dilation to allow implantation of the applicator. The intrauterine applicator is inserted first, following by both the ovoids or parts of the ring. Internal fixation using sterile gauzes is performed and after that, the catheters are inserted until the pre-defined distance. The part of the catheters remaining outside of the patient is measured and the exterior part of the applicator is secured using gauzes. The radiotherapy technician inserts three gadolinium markers for MRI contrast into the intrauterine tandem and ovoids/ring channels and labels the catheters to ensure the visibility of the labels when connecting the catheters to the afterloader. The patient is transferred from the operating table back to the patient bed and transported to the recovery room.

3.3.4. Recovery room

The patient enters the recovery room after the implantation phase at the operating room is finished. Ideally, the patient stays at the recovery room until the MRI appointment at the radiology department. However, the patient needs to be discharged by anesthesiology before leaving the recovery room. For most patients, the appointments for the MRI are not immediately after discharge from the recovery room. When the patient could not be transferred directly from the recovery room to the radiology department, they were first transported to the short stay unit.

3.3.5. Radiology department

The patient is transferred from either the recovery room or the short stay unit to the radiology department for MRI. See table 3.3 for all steps. The patient is always brought to the radiology department by the radiotherapy technician, they need to ensure that the bladder is filled with the correct amount of Uro-Trainer as during treatment delivery. Step two and three are interchangeable. The bladder is filled before or after the patient is moved from the patient bed to the MRI table. After imaging, the patient is transferred back to the patient bed and transported back to the short stay unit. The images need to be uploaded to the picture archiving and communication system of the radiotherapy department (PACS-RT) which can take some time.

Table 3.3: Overview of the different (sub)steps at the radiology department.

	Step	**Who is involved?**
1.	Arrival at the radiology department	Radiotherapy technicians
2.	Bladder filling	Radiotherapy technicians
3.	Transfer from the patient bed to the imaging table	Radiotherapy technicians and Radiology technicians
4.	Imaging	Radiology technicians
5.	Transfer back to the patient bed	Radiology technicians and nurses
6.	Leave the radiology department	Nurses

In some exceptional cases, the MRI was not available and therefore the patient only underwent a CT-scan for a treatment fraction. CT imaging is performed at the radiotherapy department, which ensures more smooth transitions between the steps. However, using CT is not desirable because of the lower soft tissue contrast compared to MRI. Contouring on an MRI is more accurate than on CT. CT-only treatment planning occurred in eight treatment fractions observed out of a total of 40 treatment fractions. Four of these patients received two treatment fractions during one day of which the second treatment fraction was planned using MRI. These patients already had their first treatment fraction using MRI following the EMBRACE-II guidelines [36].

3.3.6. Short stay unit

The patient starts the treatment day when entering the short stay unit. The waiting time can be divided into four different periods shown in table 3.4. See figure 3.4 for a flowchart representing the patient stay at the short stay unit. The patient stays at the short stay unit until leaving for the operating room. After implantation is performed, some of the patients wait for the MRI appointment at the short stay unit. The patient returns from imaging and waits at the short stay unit until the treatment plan is finished and approved. After the treatment plan is delivered and the applicator is removed, the nurses at the short stay unit take care of the patient until discharge.

Table 3.4: Overview of the different waiting times at the short stay unit.

	Step	Who is involved?
1.	Waiting time before leaving the short stay unit to the operating room	Nurse
2.	Waiting time between discharge by anesthesiology at the recovery room and MRI at the radiology department	Nurse
3.	Waiting time between imaging and treatment delivery	Nurse
4.	Waiting time between treatment delivery and patient discharge from the hospital	Nurse

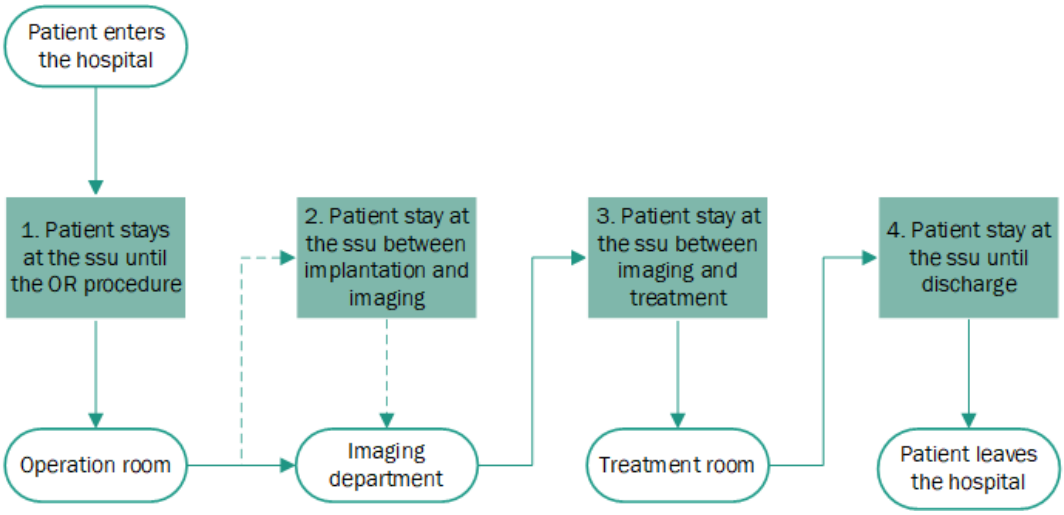

Figure 3.4: The waiting time spent at the short stay unit. The dotted line is applicable in patients that wait at the short stay unit before the MRI. Other patients skip this step when they are directly transferred to the MRI from the recovery room. SSU = short stay unit.

3.3.7. Backoffice

While the patient waits at the short stay unit, a lot of steps are executed in the backoffice. An overview of these steps and substeps is shown in figure 3.5 and table 3.5. The images are downloaded to MIM (MIM Software Inc., United States) for contouring by the radiation oncologist and to OnCentra-Brachy (Elekta, Sweden) for applicator reconstruction and treatment planning by the radiotherapy technician. The radiation oncologist delineates the target and OAR (tumor (GTV, CTV-HR and CTV-IR) bowel, rectum, bladder, sigmoid) while at the same time, the radiotherapy technician reconstructs the implanted applicator and catheters. A second radiation oncologist checks the delineated contours. The applicator reconstruction is checked by another radiotherapy technician before the delineated structures are imported into the treatment planning software (Oncentra, Elekta, Sweden) and treatment planning by the radiotherapy technician starts. When the treatment plan is complete, the radiation oncologist checks and adjusts the plan if necessary. The clinical physicist performs the last check of both the applicator reconstruction and the treatment plan following a checklist. After approval of the clinical physicists, the treatment plan can be uploaded to the Flexitron (Elekta, Sweden) afterloader as ready for treatment delivery.

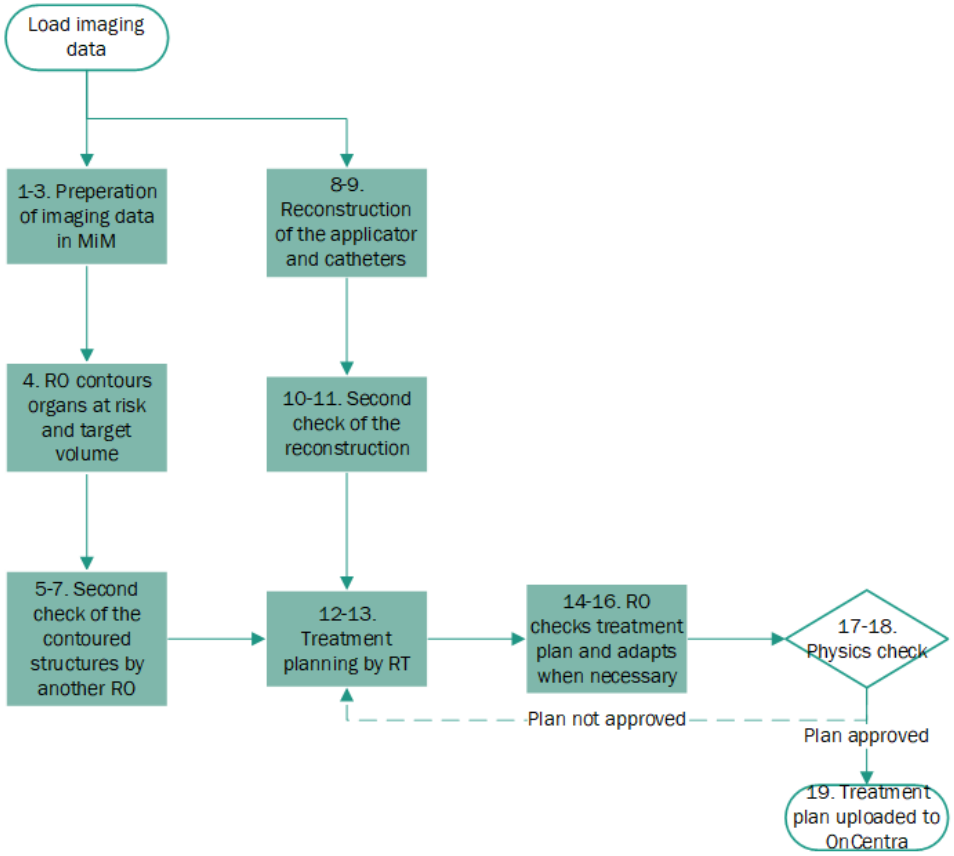

Figure 3.5: Steps of the reconstruction and treatment planning phase executed at the backoffice. RO = radiation oncologist. RT = radiotherapy technician. The numbers correspond to the numbers in table 3.5.

3.3.8. Treatment room

The patient is transferred from the short stay unit to the treatment room. In the mean time, the treatment plan is loaded on the computer in the treatment room that controls the flexitron afterloader. The implanted applicator and catheters are connected to the afterloader. The patient stays in bed during treatment delivery. Before the treatment is delivered, a dummy run is performed to ensure correct coupling of the afterloader to the implant and bladder is filled to the correct amount using Urotrainer. After the dummy run is performed successfully, the shielded door is closed and the treatment delivery is started. After treatment is delivered, the applicator is disconnected from the afterloader and the radiation oncologist will remove applicator starting with the interstitial catheters, followed by the ring/ovoids and the intrauterine tandem. See table 3.6 for an overview of the steps and personnel involved. The patient is transferred back to the short stay unit to recover from the procedure until being discharged.

3.3.9. Second fraction at the same day

In five out of the fifteen patients observed, a second treatment fraction during one of the treatment days occurred. In four of these patients, a fourth treatment fraction was needed to obtain optimal tumor dose coverage and a lowest dose possible to the OAR. The most common reason for needing a fourth fraction is too much dose in the OAR when they lie too close to the tumour. To better spare these OAR, the total brachytherapy dose is divided between four fractions instead of three. The fourth fraction is delivered on the same day as the third fraction at least six hours apart. One patient received the second and third treatment fraction during one day and did not need a fourth fraction.

The workflow for this treatment day differs from the normal workflow. See figure 3.6 for an overview of the treatment in patients receiving two fractions during one day. The patient enters the operating room and implantation is performed as described above. After the patient returns from the operating room, imaging that will be used for planning the first treatment fraction is performed. Treatment planning, evaluation, and

Table 3.5: Overview of the steps and the personnel involved during applicator reconstruction and treatment planning. [a] RT = radiotherapy technician. [b] RO = radiation oncologist.

	Step	Who is involved?
1.	Set up imaging data in MIM for the radiation oncologist	Radiotherapy technician
2.	Call radiation oncologist that everything is ready to start contouring	Radiotherapy technician
3.	Load imaging data in MIM	Radiation oncologist
4.	Delineate the organs at risk and the target volume	Radiation oncologist
5.	Call other radiation oncologist for verification of the contours	Radiation oncologist
6.	Verification of the contoured structures	Radiation oncologist
7.	Uploading the contoured structures	Radiation oncologist
8.	Load imaging data into OnCentra-Brachy	Radiotherapy technician
9.	Applicator and catheter reconstruction	Radiotherapy technician
10.	Ask another RT[a] to check the reconstruction	Radiotherapy technician
11.	Second check of the reconstruction by another RT	Radiotherapy technician
12.	Receive call from the radiation oncologist that the contours are ready for treatment planning	Radiotherapy technician, radiation oncologist
13.	Treatment planning	Radiotherapy technician
14.	Call radiation oncologist that the treatment plan is ready for verification	Radiotherapy technician, radiation oncologist
15.	Radiation oncologist checks the treatment plan and adapts if necessary	Radiotherapy technician, radiation oncologist
16.	Call clinical physics for the last check	Radiotherapy technician
17.	Clinical physicist checks the treatment plan and reconstruction of the applicator and catheters following a checklist	Radiotherapy technician, clinical physicist
18.	Approval of the treatment plan	Radiotherapy technician, clinical physicist, radiation oncologist
19.	Change the name of the treatment plan and upload it to the Flexitron afterloader	Radiotherapy technician, clinical physicist, radiation oncologist

delivery are then executed in the same way as for patients that receive only one treatment fraction during the day. However, the applicator, catheters and bladder catheter are not removed after the delivery of the first treatment fraction. The applicator and catheters stay in place after treatment delivery and the patient is brought back to the short stay unit. Imaging is performed again for treatment planning of the second treatment fraction of that day. The patient stays at the short stay unit until the second fraction can be administered at least six hours after the first fraction. The general workflow of the treatment day when administering two fractions at the same day is shown in table 3.7.

Ideally, the first treatment fraction of the day is planned using an MRI imaging. The contoured structures on MRI can be adjusted on the CT images made later that day and because both images are of the same implantation, the accuracy of the registered contours is much higher than when the contoured structures of the week before are projected onto the CT images.

CT is considered for planning of the first treatment fraction when MRI is not directly available. CT imaging is used to make sure the first treatment fraction of the day is administered before 12:00 pm. The second treatment fraction of the day could then be administered six hours later, around 18:00 pm. The radiotherapy department has their own CT scanners and are therefore not dependent on the radiology department for imaging with CT. The patient is transported from the recovery room to the CT scanner immediately when discharged by the anesthesiology. Another reason for CT imaging for the first treatment fraction is the time needed for imaging itself. The MRI protocol used in patients with cervical cancer takes approximately 25 minutes of imaging time while a CT scan takes less time.

Table 3.6: Overview of the steps and the personnel involved during treatment delivery.

	Step	Who is involved?
1.	Patient enters the treatment room	Radiotherapy technician
2.	Connect the afterloader to the applicator and catheters	Radiotherapy technician
3.	Dummy run	Radiotherapy technician
4.	Bladder filling	Radiotherapy technician
5.	Treatment delivery	Radiotherapy technician
6.	Disconnect the afterloader from the applicator and catheters	Radiotherapy technician
7.	Remove the applicator, catheters and bladder catheter	Radiation oncologist, radiotherapy technician
8.	Patient leaves the treatment room	Radiation oncologist, radiotherapy technician

Table 3.7: Overview of the general steps followed when administering two fractions at one treatment delivery.

	Step	Who is involved?
1.	Implantation at the operation room	Radiotherapy technician
2.	Patient stay at the recovery room	Radiotherapy technician
3.	First imaging of the day	Radiotherapy technician, radiology technician
4.	Contouring of the target and OAR	Radiotherapy technician
5.	Applicator reconstruction and treatment planning	Radiotherapy technician, radiation oncologist
6.	Treatment delivery	Radiotherapy technician
7.	Second imaging of the day	Radiotherapy technician, radiology technician
8.	Contouring of the target and OAR	Radiation oncologist, radiotherapy technician
9.	Applicator reconstruction and treatment planning	Radiotherapy technician, radiation oncologist
10.	Treatment delivery	Radiotherapy technician
11.	Applicator and catheter removal	Radiation oncologist, radiotherapy technician
12.	Patient discharge	Radiation oncologist, nurse

3.4. Discussion

3.4.1. Explanation of results

The workflow overview as shown in figure 3.2 is the simplified version of the workflow shown in figure 7.1 in section 7: Appendix. Figure 7.1 shows the workflow per location in the hospital. As can be seen, there are a lot of different locations during the treatment day.

Five patients received two treatment fractions during one treatment day. Four out of the five patients underwent CT imaging for the first treatment fraction and MRI imaging for the second treatment fraction. In one case observed, this was the other way around, the patient first underwent an MRI and had a CT scan for the second treatment fraction.

Ideally, the patient is transferred directly from the recovery room to the imaging department for MR imaging. The appointments at the radiology department influence the logistics of the rest of the treatment day. Every Thursday is the treatment day for brachytherapy in cervical cancer patients. There are four appointments for MRI available during this day. However, while observing the workflow, more than four patients had to be treated during one week. Two patients were treated on Tuesday and four on Thursday. Three out of the four patients that received one treatment fraction with CT only were treated on a Tuesday. The appointments for the MRI on Tuesday had to be planned last-minute.

3.4.2. Comparison to literature

The general workflow found in literature, see figure 3.1, overlaps with the workflow observed. The differences are in the detailed (sub)steps per location. The workflow as observed in the Erasmus MC included all steps from patient entering the hospital during the treatment day until the patient leaving the hospital at the end of

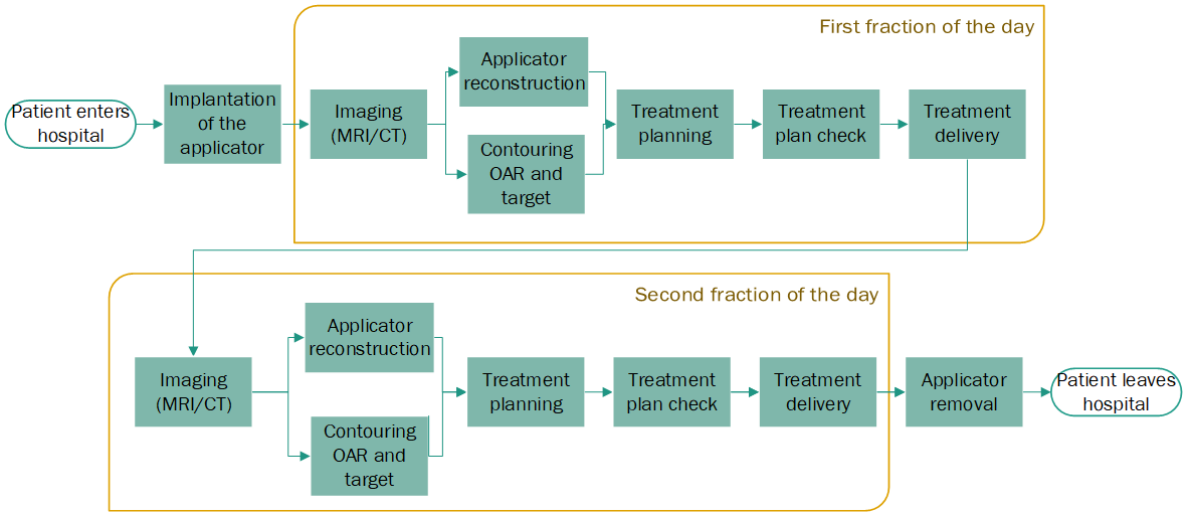

Figure 3.6: Overview of the workflow in patients receiving two fractions during one treatment day. The overview is shown using general sequential and parallel steps.

the treatment day. The patient journey from diagnosis until the start of the brachytherapy was not included in the observations because medical ethics committee approval was necessary. Also, it would take a lot of time to follow patients from diagnosis until treatment was finished. The priority was currently given to identifying the steps and substeps in the brachytherapy workflow.

The general overview of the workflow as found in literature did not include the step of the applicator reconstruction. Applicator reconstruction is defined as a separate step from treatment planning. The applicator is reconstructed by a radiotherapy technician, a second radiotherapy technician checks the reconstruction before the start of treatment planning and the clinical physicist checks the reconstruction again before approval of the treatment plan.

Harkenrider et al. described a workflow in which two treatment fractions were administered using one implantation. The first treatment fraction was delivered on the same day as implantation. The patient stays overnight and the second treatment fraction is delivered the next day [32]. This treatment approach used to be performed in the Erasmus MC in patients that needed a fourth treatment fraction. However, overnight stay requires the patient to stay in bed much longer and more anesthesia needs to be administered as the patient stays longer with the implant inserted. The change in logistics in patients receiving two treatment fractions during one day with only six hours apart was made during the COVID-19 pandemic. Patient beds were scarce and needed for COVID-19 patients. The current approach of two treatment fractions during one day with six hours apart is more patient friendly due to the less time spent with the applicator in situ. However, there is little information on toxicity that might be increased due to less time between treatment fractions.

In Aarhus, Denmark, the applicator is inserted under anesthesia to obtain imaging with the implant in situ in order to make a pre-treatment plan. The applicator is removed after imaging is completed and the patient returns home[37]. This results in a more accurate pre-treatment plan. However, there are risks to implantation of the applicator under anesthesia without actually treating the patient.

3.4.3. Limitations

All steps were observed by one researcher and verified by talking to the radiotherapy technicians and radiation oncologists. It could be possible that the researcher missed some important (sub)steps in the workflow. However, another researcher put together a workflow overview from a different approach. This overview was compared to the one described here and both researchers agreed on all steps.

3.4.4. Recommendations

Logistics during the treatment day will change due to the usage of the hyperthermia MRI at the department of radiotherapy for brachytherapy patients. This MRI will be operated by the radiotherapy technicians and allows to scan the patient immediately after they leave the recovery room. This will result in less waiting time for the MRI for all patients during the day. This seems ideal, but this means that the images are available for

contouring earlier in the day. Currently, two radiation oncologists are responsible for the treatment of four patients during the day. They both treat two patients, assist each other at the operating room if necessary and perform the second check each on each others contours. It is possible that in the future the imaging of the first patient will be available for contouring while both radiation oncologists are still at the operating room.

4

Time-action analysis

4.1. Introduction

The duration of the steps differed a lot when looking at the literature. During the literature study, three articles reported the time needed for the steps during brachytherapy treatment. One article only reported the time needed for treatment planning. When looking at the total procedure times reported by the authors, a large difference was found, see table 4.1. Kim et al. reported a remarkably low total procedure time compared to Chan et al. and Mayadev et al. The duration of the steps depended on the setup of their workflow and the amount of personnel involved. Kim et al. always had backup personnel available to maintain smooth transition between tasks, which was one of the main reasons for their low total procedure time [18]. They also showed that implantation of the applicator and catheters in their own suite at the radiotherapy department took less total procedure time compared to implantation of the applicator at the operating room, 149.3 versus 209.5 minutes respectively. The imaging modality used was also mentioned as an influence on the time needed, as MRI takes longer than CT imaging.

Table 4.1: Comparison of the total procedure time reported by studies found during the literature study. [a] Applicator insertion at the operation room.

Comparison items	**Chan et al. [20]**	**Kim et al. [18]**	**Mayadev et al. [19]**	**Michaud et al. [28]**
Imaging used for planning	MRI	MRI	CT	CT
Mean total procedure time [min]	492	149.3 (209.5[a])	401.1	–
Mean planning time [min]	96	44.3	137.5	96.2
Pre-implantation time [min]	–	38.7	94	–

The purpose of the time analysis performed was to obtain insights in the duration of different steps that might be elongated when using personalised applicators and to identify bottlenecks in the current workflow that could be improved. On forehand, it was expected that the waiting time for the MRI appointment would be one of the main factors for delay in the whole treatment process. Also, it was expected that the type of anesthesia would influence the time needed at the operating room. The radiation oncologists suggested that anesthesia takes longer when spinal anesthesia is used compared to general anesthesia. Another expectation was that the time needed in subsequent treatment fractions in each patient would decline. Implantation time will decrease due to prior knowledge on patient anatomy and the contoured structures could be propagated. There could also be a difference in time needed when four patients are treated compared to less patients treated during one day.

4.2. Methods

To be able to collect timestamps for the evaluation of the time needed for the different steps, multiple time sheets were created. As some steps occurred in parallel the radiotherapy technicians, radiation oncologists and nurses were asked to assist in reporting of times. The duration of the steps and evaluation of the current work procedures could be performed without the approval of the medical ethics committee. Data was collected between the 15th of April and the 17th of May 2021.

4.2.1. Data collection and validation

The specific steps that were timed were chosen using the workflow overview created in section 3. The selection of the steps was made to provide a sheet which was realisable to fill out for the personnel yet still provide necessary data to draw conclusions about the efficiency and actions performed. See table 7.1, 7.2 and 7.3 in the Appendix for the sheets that were used for the time registration. Also, using these time stamps, the duration of other steps could be extracted. With the start and end time of the MRI, not only the duration of the MRI could be calculated but the begin time of the MRI could also be used for extracting the waiting time between the stay at the recovery room and the MRI scan. Table 7.4 in the Appendix shows the steps performed by the researcher to ensure the time registration went as planned. The times were collected per implantation in an excelsheet and later stored in a database. All data was digitised by one researcher and later checked by a second researcher.

4.2.2. Time calculations

Duration of the (sub)steps were calculated. The duration of the steps of interest per location in the hospital are shown in table 7.5 in the Appendix. The difference in duration for subsequent treatment fractions in each patient was determined to find trends in implantation time, time needed for contouring and total procedure time. The duration of each step was calculated using Matlab (Mathworks). Descriptive statistics, such as the mean and standard deviation of the time needed for the steps were determined using SPSS.
The duration of the general steps of interest were:

1. Total time spent at the operating room
2. Time between the implantation phase at the operating room and imaging
3. Total time needed for contouring
4. Total time needed for reconstruction of the applicator and catheters
5. Total time needed for treatment planning
6. Time needed for the check of the treatment plan and applicator reconstruction by the clinical physicist
7. Total time spent in the treatment room
8. Total procedure time, which was defined as the time between patient entering the operating room and leaving the treatment room
9. Total in-house time, which was defined as the time from patient entering until being discharged from the short stay unit

4.3. Results

4.3.1. Data inclusion

Data was collected of 40 implantations in fifteen different patients. Two treatment fractions during one day were administered in five different patients. Each patient was assigned a number (R01-R15) for registering the duration of the steps. Patient R11 - R15 were included in the patient experience study, described in section 5. The duration of the steps in all patients are listed in table 7.6 - 7.12 in the Appendix. Table 7.13, in the Appendix, shows the difference in time needed for the second and third treatment fraction compared to the first treatment fraction.

Calculation of the mean duration of each step was based on the number of data points (N) per step as not all time registrations were completed. Two data points were excluded as they were considered implausible, e.g. reporting 1 minute for the implantation step that took on average 21 minutes.

4.3.2. Time analysis

The mean time needed of the general steps during the treatment day are shown in table 7.15. The mean procedure time ± SD was 391 ± 42 minutes (range, 282 - 502 minutes). Figure 4.1 shows the duration of the general steps at the different locations. The mean time ± SD needed for contouring was 50 minutes ±27 minutes (range, 28 - 131 minutes). The mean time ± SD needed for applicator reconstruction was 57 ± 23 minutes (range, 20 - 120). The mean time ± SD needed for treatment planning was 50 ± 20 minutes (range, 15 - 98) and the mean time ± SD spent in the treatment room was 41 ± 9 minutes (range, 27 - 65 minutes).

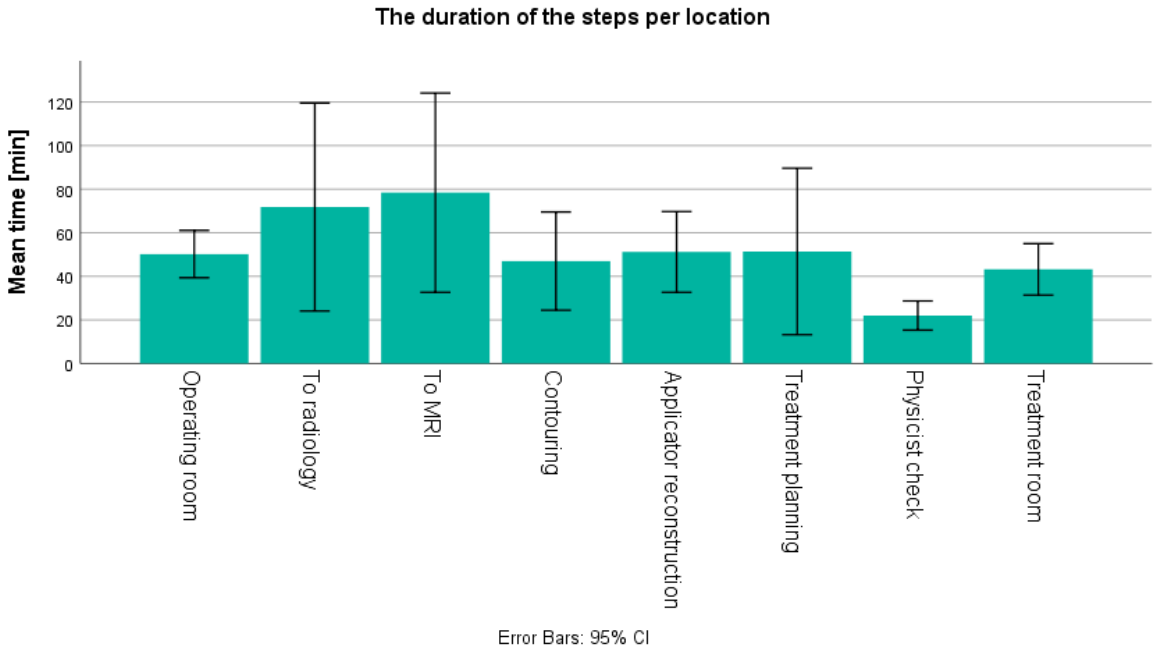

Figure 4.1: Time needed for the general subsequent and parallel steps during the treatment day. Operating room is the total time the patient spent at the operating room. To radiology is the time between leaving the operating room and entering the radiology department. To MRI is the time between leaving the operating room and the start of the MRI. Contouring and reconstruction are the total time needed for the step including the second check by a colleague. Physicist check is the time needed for the check by clinical physics and treatment room is the total time spent at the treatment room. Table 7.15 in the Appendix shows the descriptive statistics on the data used for this figure.

The mean time and duration of the steps per location in the hospital are shown in table 7.16 - 7.20. See figure 4.2 for the mean duration of the steps at the operating room. The mean time ± SD spent at the operating room was 55 ± 11 minutes (range, 35 - 82 minutes). The mean time ± SD between the patient leaving the OR and arrival at the radiology department for MR imaging was 80 ± 39 minutes (range, 19 - 163 minutes). In patients receiving CT imaging, the mean time between patient leaving the OR and arrival at the CT scanner was 30 minutes (range, 7 - 76 minutes). The mean time needed to arrive at the CT/MRI in the five patients that received two treatment fractions during one day was 35 minutes (range, 19 - 45 minutes).

The difference in duration of the steps in subsequent fractions per patient are shown in table 7.13 in the Appendix. In most patients, the time needed for the steps in subsequent treatment fractions decreased. The total procedure time decreased in nine out of the eleven fractions. Time needed for implantation decreased in sixteen out of the twenty fractions with a mean of 13 minutes (range, 2 - 28 minutes).

Descriptive statistics of the duration of the steps at the operating room of patients treated with spinal anesthesia and patients treated with general anesthesia are shown in table 7.21. The mean time ± SD needed at the operating room in patients receiving spinal anesthesia was 55 ± 10 minutes (range, 40 - 82 minutes) compared to time ± SD was 55 ± 12 minutes (range, 35 - 72 minutes) in patients that were treated with general anesthesia. The mean total in-house time ± SD was 531 ± 61 minutes (range, 425 - 650). The waiting times at the short stay unit the between the different steps during the day are shown in figure 4.3. The waiting time between imaging and treatment delivery was the largest period of waiting during the day.

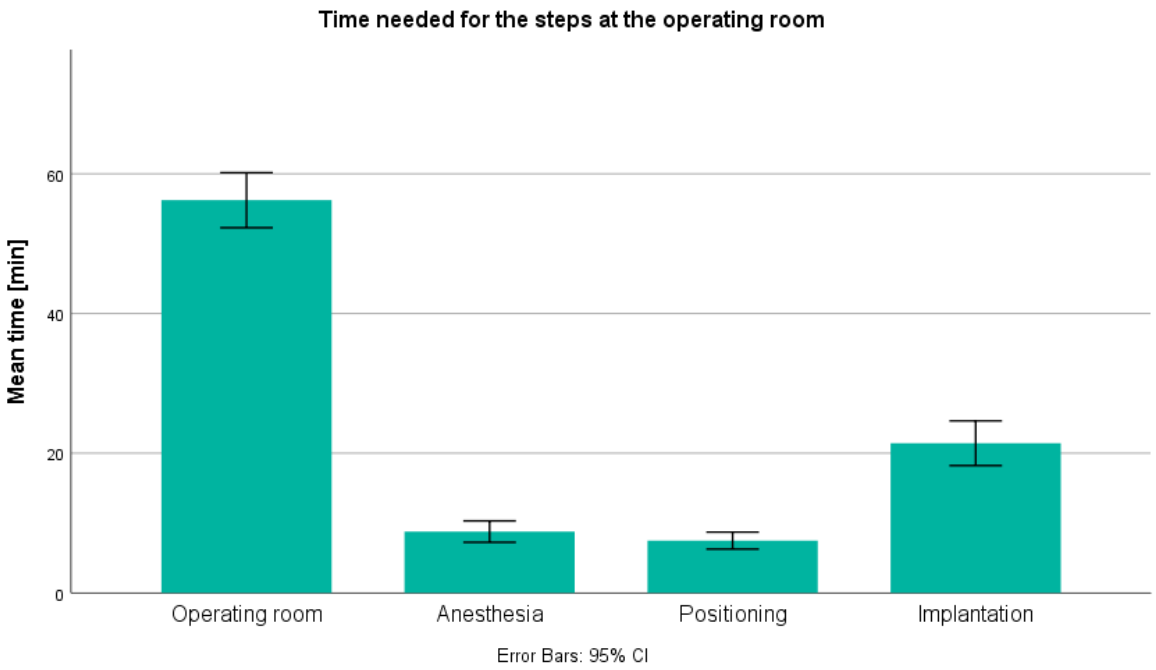

Figure 4.2: Duration of the steps at the operating room. The first bar, Operating room, represents the total time the patient spent at the operating. Implantation was defined as the entire sterile procedure. Table 7.16 in the Appendix shows the descriptive statistics on the data used for this figure.

Figure 4.3: Duration of waiting periods at the short stay unit. Before OR is the time spent at the short stay unit between entering the hospital and leaving to the operating room. Between OR and imaging is the time between return from the recovery room and imaging. Between imaging and treatment delivery and the last bar in the graph is the time between return at the short stay unit after treatment delivery until the patient is discharged.

The time registrations were performed during fourteen different treatment days. During eight of these treatment days, four patients were treated per day. During two treatment days, three patients were treated.

During two treatment days two patients per day were treated and during two treatment days only one patient was treated.

4.4. Discussion

4.4.1. Interpretation of results

The total procedure time in the current setting had a mean of 391 minutes (6.5 hours). This is less compared to the total treatment time of 492 minutes (8.2 hours) reported by Chan et al., see table 4.1. The total procedure time reported by Mayadev et al. corresponded more to the time measured in the Erasmus MC. However, it remains difficult to compare time needed to the time reported by other institutions due to differences in workflow and personnel. The total procedure time reported by Kim et al. was much lower than the time we found during this study (149.3 versus 391 minutes). They performed implantation in a special brachytherapy suite located next to the imaging department and not at the operating room. When implanting the applicator at the operating room this took 209.5 minutes [18]. The mean time needed for treatment planning found was 50 minutes, which is close to the 44.3 minutes reported by Kim et al., however, mean planning time is also difficult to compare. This because of some authors probably included the reconstruction step in the planning phase, which explains the longer planning time needed by Chan et al., Mayadev et al. and Michaud et al.

The time needed for subsequent treatment fractions declined when compared to the time needed for the first treatment fraction (see table 7.13). However, this was not the case in all steps. There were a lot of differences in increase and decrease in time needed for anesthesia. This can be explained by different personnel that executed the steps in the subsequent week compared to the first treatment fraction. Patients that receive their first treatment fraction are the first or second patient of the day in most cases. In these patients, the time spent at the operating room might be longer due to difficulties in implantation and the assembly of the applicator which is done after internal investigation. This could result in more waiting time before leaving to the operating room in the other patients.

The duration the patient spent at the operating room did not differ when using spinal or general anesthesia. On forehand, it was expected that time needed for anesthesia was longer when the patient was sedated using spinal anesthesia. This was not found as time needed for anesthesia was 9 minutes for both techniques. The range was larger in patients receiving general anesthesia due to one outlier. This patients was intubated using a laryngeal mask and she started aspirating at the moment the implantation procedure was about to start. The anesthetic team needed to stabilize the patient and intubate her again. Time between leaving the operating room and arrival at the radiology department seemed to differ a bit in these patients. This could be due to a longer stay at the recovery room for patients that had spinal anesthesia but this is unlikely. Most patients were first transported to the short stay unit to wait for the MRI appointment.

Patients treated with CT had a mean time between operating room and imaging of 30 minutes. Patients receiving two treatment fractions during the day the mean time between operating room and imaging was 35 minutes. While the mean time between leaving the OR and imaging in patients treated with MRI was 80 minutes. The availability of imaging directly after discharge at the recovery room saves approximately 50 minutes of waiting time.

Three out of the four patients treated with CT instead of MRI, that received only one treatment fraction during the day, were treated on a Tuesday instead of on a Thursday. Each Thursday, there are four MRI appointments reserved for brachytherapy patients, while this is not easily arranged on all Tuesdays. These three patients were treated using CT when there was no appointment made for an MRI due to no reserved time for brachytherapy patients and the late switch to Tuesday.

The patient spends the most waiting time at the short stay unit. Waiting during the treatment day is unavoidable for some steps, especially when multiple patients are treated during the same treatment day. The treatment room needs to be available before treatment delivery can take place and waiting before the operating room procedure is dependent on the availability of the OR. This was not always the case.

Time needed for applicator reconstruction in the second fraction for patient R10 was remarkably high, even though the reconstruction was performed on a CT scan, in which the applicator and catheters are better visible than on an MRI. This applicator reconstruction was performed by a radiotherapy technician in training. The same can be seen in the time needed for contouring the first fraction for R07. This was much higher than the time needed for contouring in the subsequent fractions, because contouring was performed by the radiation oncologist in training.

The influence of the amount of patients treated during one day on the duration of the steps could not be determined using the current data. Most patients were treated during busy treatment days. On forehand, it

could be expected that the total procedural time would be lower in these patients because all personnel is focused on treating the one patient and there is no waiting time for the treatment room to be available.

4.4.2. Limitations

The main limitation is the interpretation of the steps that were reported by different personnel. There were four different radiation oncologist that perform brachytherapy treatments and at least ten different radiotherapy technicians working during the different treatment days. The treatment days sometimes get chaotic which causes the personnel to forget to write down the time. The time reported could differ when not immediately written down. Also, the accuracy of the time measurements may have declined during the treatment day, especially when four patients were treated at the same day. The amount of checks of the time registration during the treatment day should increase when the researcher notices that time registration was not performed accurate enough.

Another check that needs to be performed more often is checking if the radiation oncologist write the times down accurately. The treatment room, planning room and short stay unit are all next to eachother, while the offices of the radiation oncologists are located more remote. When the start of end time was missing, the duration could not be calculated and the measurement was excluded for analysis.

At the beginning of 2021, the Venezia applicator was introduced into practice in the Erasmus MC. Not all radiation oncologist and radiotherapy technician were completely used to the Venezia applicator when time measurements started. Data in the first few patients treated using the Venezia applicator could have been biased by the learning process of the radiation oncologists.

The time the patient spent at the recovery room might be biased when the patient had an appointment at the radiology department a short time after the implantation phase ended. In this case, the patient could already be discharged by anesthesiology but waits some more time at the recovery room so that the radiotherapy technician could move the patient directly to the radiology department. If the time between the appointment at the radiology department and the implantation phase is longer, the patient is first transported to the short stay unit. The time spent at the recovery room will then be shorter than when the patient is moved directly from the recovery room to the radiology department. In the current study on time analysis, the time at the recovery room was not reported very often. The time of arrival at the recovery room needed to be registered by the radiotherapy technician, who was not always the person that delivered the patient to the short stay unit. The time sheets were left with the patient and either the nurses or another radiation technician. The personnel involved in time registration for the same patient changed during the day which caused some missing data. Logistics of time registration need to be adapted when continued to ensure correct data on recovery room time.

Another limitation is missing data. In some cases, only the start time of a step was written down. This happened the most during the applicator reconstruction and treatment planning phase. In that case, the time of the start of the next step could be used as endtime. This might lead to an overestimation of the time needed for these steps.

The Erasmus MC is a teaching hospital in which radiotherapy technicians, radiation oncologists and clinical physicists who are in training work under supervision. The radiation oncologist in training also takes part in the implantation and contouring steps.

4.4.3. Recommendation

The main component in the unnecessary waiting time was due to waiting for the MRI appointment. The mean time of 80 minutes between leaving the operating room and arrival at the radiology department could be improved. The radiotherapy technicians are currently in training in using the MRI that is used for the hyperthermia treatments, which is managed by the radiation therapy department and allows smooth transition between the patient leaving the operating room and imaging. The images will directly be imported into the picture archiving and communication system (PACS) of the radiation therapy department. This saves time in sending over the images from the radiology department and radiation therapy department. However, this might lead to other problems during the day as more imaging will be performed early in the day when some personnel is still at the operating room. More personnel might be needed to prevent delay in start of contouring and applicator reconstruction.

The check of the applicator reconstruction and treatment plan by the clinical physicist could be separated. The applicator reconstruction check could be performed parallel to treatment planning and save time.

Using the current sheets for time registration, the time needed for imaging was supposed to be registered. However, all patients had an MRI scan following the exact same scanning protocol and therefore the time

needed for imaging in all patients is approximately the same. This imaging data were not registered in much patients because of the different personnel involved in the step. The radiotherapy technician delivers the patient to the radiology department, the radiology technician then performs imaging and the nurses bring the patient back to the short stay unit. The time between leaving the OR and arrival at the MRI is a lot more interesting as it say something about efficiency during the treatment day.

For the time measurements that will be executed in the future, the researcher may be more strict with the personnel performing time registration. One of the radiation oncologists suggested to alter the sheet and split the time needed for contouring the OAR and the tumor volume. This to be able to determine if the time needed for contouring is mainly dominated by the (sometimes difficult to visualize) tumor volume or the OAR. The OAR might take a lot of time to contour, especially because the position of the sigmoid and the bowel changes a lot between the treatment fractions. Time needed for contouring could be due to difficult anatomy of the OAR or different tumor topology, in the current setting this could not be distinguished.

The alternation of the sheet for registration of the time should also include adding the duration of assembling the current applicators by the operating room assistants. This happens parallel to administering the anesthetics and positioning the patient at the operating room. The time needed for anesthesia was expected to influence the total time at the operating room and this is why the assembling step was not included in the current evaluation. This step could influence the total time spent at the operating room especially in patients receiving their first treatment fraction. In these patients, the applicator is assembled after internal examination and determining the length of the uterus.

The influence of the amount of patients treated during one day on the duration of the steps should be evaluated when more data are available.

5

Patient experiences during brachytherapy

5.1. Introduction

This part of the master thesis focusing on patient's experience in the Erasmus MC maps the current experience of patients undergoing brachytherapy for cervical cancer. The aim was to obtain insights in patient's experiences and to identify the most painful and anxious moments during treatment. The information on patient experience obtained will be used to improve the current clinical practice. It will also function as a reference for patient experience when changing parts of the workflow in the future.

Patients receiving brachytherapy for cervical cancer need to stay with the implanted applicator and interstitial catheters in situ for quite a long time [20]. The pressure on the vaginal wall by the implant and gauzes used for fixation can cause pain during the day and therefore sufficient pain management is necessary [38]. Not only the implant causes pain, the patient also has to remain in bed for the entire procedure and is only allowed to lift the head of the bed for maximum fifteen degrees. The experience of patients undergoing treatment for cancer is difficult to comprehend due to fear and other psychological problems caused by dealing with the uncertainty of having cancer [39].

5.2. Methods

5.2.1. Questionnaires

Two different questionnaires were used to evaluate the patient experience during the treatment day. The first questionnaire, the EQ-5D, was used to obtain insight in the quality of life of the patient before the treatment started and the second questionnaire focused on the experience during the treatment day. The EQ-5D is a verified questionnaire to assess quality of life on five different aspects: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. A perfect score with no limitations is represented as a 1 and the worst score on the EQ-5D is represented by a 5. The total score on the five aspects can be expressed by five numbers. A score of 11111 represents the best health while a score of 11131 represents the best health in four out of the five aspects. In this case, the patient scored moderate on pain or discomfort. The Dutch version of the EQ-5D was used. The patients filled out the EQ-5D before each treatment day, so that the EQ-5D results represent the health of the patient in the week before the brachytherapy treatment. This way it was also possible to identify changes in general quality of life between the treatment days.

The second questionnaire focused on the experience of the patient during the different steps of the treatment day. The level of pain, anxiety and experience of duration of the steps were asked using a eleven step numeric rating scale (NRS) ranging from zero to ten. Zero represented the most optimal situation and ten the worst situation possible. The numeric rating scale is a numeric version of the visual analogue scale (VAS) which resulted in fewer errors than the VAS [40].

Section 4 showed that the waiting time for the MRI was one of the main bottlenecks in the total procedure. Therefore, one extra question on the duration of the waiting time for imaging was added to the patient experience questionnaire.

Patients that underwent two treatment fractions during one treatment day received an extended version of the questionnaire in which the pain, anxiety and duration of the waiting time between two treatment fractions and the second treatment fraction were added to the questionnaire, see table 3.7.

Table 5.1: Comparison on locations in the questionnaire in patients receiving one and two treatment fractions during the day.

Step	Normal	Two treatment fractions during one day
1.	Operating room	Operating room
2.	Recovery room	Recovery room
3.	Radiology department	Radiology department
4.	Stay at the short stay unit	Stay at the short stay unit
5.	Treatment delivery	First fraction treatment delivery
6.	Removal of the applicator	Waiting between the first and second treatment fraction
7.		Second fraction treatment delivery
8.		Removal of the applicator

Patients were asked to fill out the EQ-5D questionnaire at arrival at the hospital in the (early) morning before leaving to the operating room for the implantation of the applicator. The questionnaire on patient experience was given to the patient during the treatment day while they were waiting at the short stay unit.

5.2.2. Medical Ethics Committee Application (METC)

To obtain patient information and to include patients to participate in the questionnaire study, a METC application was written. A research protocol and patient information letter (PIL) were written to submit to the METC to obtain approval. The research protocol shows what data we wanted to use and for which reasons and the PIL was written to inform the patient on the study and the potential risks they would take so that informed consent could be provided. The questionnaires that were used were also submitted to the METC committee. The documents that were handed in to obtain approval can be found a seperate Appendix. Approval was obtained at 13 march 2021, the PRE-ARCHITECT study was registered by the medical ethics committee as trial EMC21-0336.
Patients could be included in the PRE-ARCHITECT study if they underwent brachytherapy for cervical cancer in the Erasmus MC and if they were adequate enough to understand, read and write in Dutch. Patients who speak and understand English will be included in a later part of the study but to ensure that the patients understood the questionnaire and no translation mistakes were made, only Dutch patients were included for now. Currently, language was the only exclusion criteria used.

5.2.3. Data storage

The included patients were assigned a pseudonyms. All collected data of these patients was stored in a database that was created for the PRE-ARCHITECT study using Castor EDC, which is a validated data management system. This included clinical information on the patient and the duration of the steps during the treatment day.

5.3. Results

5.3.1. Patient inclusion

A total of five patients provided informed consent between the 13th of May and the 17th of June 2021. Four out of these five patients filled out all questionnaires. One patient filled out the informed consent but only completed the EQ-5D at the second treatment day. This patient was excluded from data analysis. This patient was an exceptional case as she broke her wrist and pelvis the day before the first brachytherapy fraction was planned. The first fraction was postponed with a week and the second and third treatment fraction were delivered at the same day to be able to deliver all fractions before the total treatment time, i.e. EBRT and BT, exceeded the limit and to reduce the number of implantations in the fragile pelvis.

5.3.2. Patient description

Table 5.2 shows the clinical description of the five patients that provided informed consent. The age of the patients differed from 36 to 76 years old. One patient had a small cell neuroendocrine carcinoma for whom the initial treatment plan was induction chemotherapy followed by surgery. However, the tumor did not respond to chemotherapy as desired and, therefore, surgery was not an option anymore. To give the patient the best chance of survival, a combination of external beam radiotherapy, brachytherapy and hyperthermia was given after the induction chemotherapy was finished. Two other patients also received induction

Table 5.2: Clinical patient information of the five included patients. Patients were assigned a pseudonym which is show in the table.

Patient	**R11**	**R12**	**R13**	**R14**	**R15**
Age	48	48	36	47	76
Tumor	Squamous cell carcinoma	small cell neuroendocrine carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Squamous cell carcinoma
Staging	IIIC1	IVa	IIIB (N+)	IIIC1	IIIC1
Treatment composition	Chemo radiotherapy	Induction chemotherapy, EBRT, BT and hyperthermia	Induction chemotherapy, EBRT, BT and hyperthermia	Induction chemotherapy, EBRT, BT and hyperthermia	EBRT, BT
N fractions BT	4	3	3	4	3

chemotherapy followed by EBRT, BT and HT. Another patient was treated with chemoradiation, which consisted of EBRT and BT with a weekly dose of chemotherapy during the treatment. The last patient could not receive chemotherapy due to bad kidney function caused by hydronephrosis. The tumor blocked the lower part of the right ureter so no urine could flow from the kidney to the bladder which caused the hydronefrosis. This patient only received only EBRT and BT, as hyperthermia was also not an option due to hip implants on both sides.

Three out of the five patients were diagnosed and treated for FIGO stage IIIC1 cervical cancer. The patient with the neuroendocrine carcinoma was diagnosed with stage IVa and the last patient with FIGO stage IIIB squamous cell carcinoma. See table 5.2 for details.

5.3.3. EQ-5D questionnaire

The results of the EQ-5D questionnaire for the first four included patients are shown in table 5.5. The score in all patients changed over the three treatment weeks. As can be seen in table 5.4, the EQ-5D scores in all patients worsened during the weeks between the brachytherapy treatments.

Table 5.3: Results of the EQ5D questionnaire per patient. 1 = no problems, 2 = slight problems , 3 = moderate problems, 4 = severe problems, 5 = unable to or extremely anxious/depressed

Patient	**R11**			**R12**			**R13**			**R14**		
Week	1	2	3	1	2	3	1	2	3	1	2	3
Mobility	1	1	1	1	1	2	1	1	1	1	1	1
Self-care	1	1	1	1	1	1	1	1	1	1	1	1
Usual activities	1	1	1	2	3	3	1	1	2	1	1	2
Pain / discomfort	1	1	1	3	3	3	2	3	1	1	2	2
Anxiety / depression	1	1	2	3	3	3	2	1	1	1	1	1

The first patient reported to have no problems in the first two weeks but this changed in the last week when she reported to be slightly anxious or depressed. The second patient started with a score of 11233, which meant she had slight problems doing usual activities, was in moderate pain or discomfort and moderately anxious or depressed. This changed to moderate problems doing usual activities in week 2 (11333) and slight problems with walking about in week 3 (21333). The third patient reported a slight problems pain or discomfort and to be slightly anxious or depressed in the first week (11122) which changed to moderate pain or discomfort and not feeling anxious or depressed in the second week (11131). In the last week, the EQ-5D score changed to have slight problems doing usual activities and improving to healthy on the other scores. The fourth patient started with a perfectly healthy score (11111) which worsened to slight pain or discomfort in the second week (11121) and slight problems doing usual activities in the third week (11221).

5.3.4. Patient experience questionnaire

Experience on the treatment day differed a lot between patient, as can be seen in table 5.4. Overall, patients scored the highest pain scores during the waiting time at the short stay unit and during applicator removal. Anxiety was worst during the first treatment day and declined slightly in the subsequent weeks. Highest

anxiety scores were given during applicator removal. The score on duration differed a lot. Patient R12 and R13 scored the waiting time at the short stay unit as way too long while patient R11 and R14 scored the waiting time as acceptable and medium, respectively. Table 5.5 shows the results of the score given to the waiting time on imaging.

5.4. Discussion

5.4.1. Clinical data

As can be seen in table 5.5, none of the patients experienced the duration of waiting time on the imaging as much too long. The highest score given was a 4 on a scale from 0 to 10, with zero being acceptable and 10 being much too long. This indicates that the patients do not experience the waiting time for imaging as too long. However, section 4 suggested that the waiting time for the MRI is the longest and needs to be shortened to improve the treatment day as patients develop pain later during the day at the short stay unit.

With only four patients included, it is too early to draw any conclusions. However, it seems that the highest pain scores over all patients were given during the waiting time at the short stay unit which suggest that proper pain management by the nurses is essential.

The four patients that were included thus far scored differently on both questionnaires suggesting that patient experience is very personal. Patient R11 had no problems with all steps during the treatment day and was very positive during treatment. Her pain scores were the highest during the last treatment day, when she received two fractions during one day. The only time she scored a moderate score on the duration was in the last week when she waited at the short stay unit between the two treatment fractions.

The second patient, R12, had more pain during the treatment day. The pain was the worst during the first treatment day compared to the other two treatment days, but overall she was in quite some pain during all treatment days. She was also a lot more anxious than the other patients. The anxiety was worst during the first brachytherapy treatment and slightly decreased during the second and third week. The patient was very anxious during removal of the applicator.

Patient R13 reported the most pain during the first treatment day because of pain in the back caused by laying down for a long time. The pain was most severe at the short stay unit in the first week and at the recovery room in the second week, but overall she was in a lot of pain during the treatment day. Anxiety was worst during applicator removal during the first treatment day. After that, the anxiety dropped to zero in the second week and moderate anxiety in the third week. She did experience the waiting time at the short stay unit as too long.

The fourth patient, R14, started without pain during the first treatment day. However, she suddenly was in immense pain moments before she was moved from the short stay unit to the treatment room. She was in a lot of pain during treatment delivery and removal of the applicator. The removal of the applicator was more difficult in this patient due to cramping of the pelvic muscles caused by the pain of the patient. The second week went much better with more adequate pain management. But she was still in pain during the waiting time and the removal of the applicator. Anxiety in this patient was highest during applicator removal during all treatment fractions.

5.4.2. Pain, anxiety and duration

Pain management in patients receiving brachytherapy is an important aspect of the treatment day and a main focus for the nurses at the short stay unit. When patients receive spinal anesthesia, the anesthetic works out during the treatment day and not directly after implantation. This is why patients that receive general anesthesia often show a lot more pain at the recovery room than patients that received spinal anesthesia. Adequate pain management for the second and third treatment day is based on patient desires and experience from the week before. If the patient is in a lot of pain the first week, it is likely that the anesthesiologist prescribes a patient controlled anesthetics pump (PCA-pump) for the following treatment day. The PCA-pump will be used for self management of pain medication by the patient. One major disadvantage of the PCA-pump is the nausea the patients develop as a side effect of the medication. This nausea caused patient R14 to not press the PCA-pump anymore. She was in a lot of pain but did not want to throw up and therefore did not press the pump for more medication anymore. Nausea is a common side effect of morphine and needs to be managed during the day as well.

Another aspect that is of influence is the anxiety of the patients. The patients are most anxious at the first brachytherapy treatment.

The first patient, R11, scores very low on the EQ-5D which corresponds to her scores on the patient expe-

Table 5.4: Results of the questionnaires for the four included patients. The patients were asked to score the pain, anxiety and duration of the steps on a scale of 0 - 10. For pain 0 = no pain and 10 = worst pain imaginable, for anxiety 0 = comfortable and 10 = extremely anxious and for duration 0 = acceptable and 10 = much too long. [a] The patient did not report a score on duration of applicator removal during the first week.

Patient R11	**Pain**	[0 - 10]		**Anxiety**	[0 - 10]		**Duration**	[0 - 10]	
Location	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3
Operating room	0	0	0	0	0	0	0	0	0
Recovery room	0	0	0	0	0	0	0	0	0
Imaging	1	0	7	0	0	0	0	0	0
short stay unit	8	1	7	0	0	0	0	0	0
Treatment delivery	0	1	0	0	0	0	0	0	0
Waiting time between first and second fraction			7			0			5
Second treatment delivery			0			0			0
Applicator removal	0	0	0	0	0	0	0	0	0
Patient R12	**Pain**	[0 - 10]		**Anxiety**	[0 - 10]		**Duration**	[0 - 10]	
Location	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3
Operating room	0	0	0	9	4	2	1	0	0
Recovery room	8	0	0	7	4	4	8	1	0
Imaging	7	1	1	2	4	4	6	6	7
short stay unit	8	7	7	5	7	4	6	8	7
Treatment delivery	5	8	6	9	6	5	5	5	4
Applicator removal	8	8	7	10	9	8	-[a]	1	3
Patient R13	**Pain**	[0 - 10]		**Anxiety**	[0 - 10]		**Duration**	[0 - 10]	
Location	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3
Operating room	0	0	0	0	0	0	0	0	0
Recovery room	7	9	8	2	0	0	3	0	0
Imaging	7	7	7	2	0	0	3	0	0
short stay unit	9	7.5	6	1	0	0	9	9.5	7.5
Treatment delivery	1	3	4	1	0	0	1	0	0
Applicator removal	7.5	6.5	9	8	0	4.5	2	0	1
Patient R14	**Pain**	[0 - 10]		**Anxiety**	[0 - 10]		**Duration**	[0 - 10]	
Location	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3
Operating room	0	0	0	0	0	0	0	0	0
Recovery room	0	0	2	0	0	0	0	0	2
Imaging	0	0	4	0	0	0	5	5	3
short stay unit	5	6	7	2	3	1	5	6	4
Treatment delivery	10	6	6	1	5	1	8	2	2
Waiting time between first and second fraction			7			1			2
Second treatment delivery			7			1			1
Applicator removal	10	7	9	9	7	9	4	2	9

rience questionnaires. The two patients that scored a 2 or higher on pain or anxiety on the EQ-5D also scored reported higher scores of pain and anxiety during the treatment day, which was as expected. It would have been a bad sign when the patients scored perfect health on the EQ-5D and extremely high scores on anxiety

Table 5.5: Score on waiting time for imaging for the four included patients per week. The patients were asked to score the duration of the waiting time before imaging on a scale of 0 - 10. 0 = acceptable and 10 = much too long.

Patient	R11 [0 - 10]	R12 [0 - 10]	R13 [0 - 10]	R14 [0 - 10]
Week 1	0	3	4	0
Week 2	2	2	0	0
Week 3	0	2	0	1

and pain in the patient experience questionnaire. This would indicate that a lot of adjustments in medication need to be made.

There are more clinical and personal aspects that could influence the amount of pain and anxiety patients experience. The amount of interstitial catheters placed might be related to the amount of pain a patient experience and could also be related to the stage of the tumor. As higher stage tumors are more likely to be positioned more lateral and difficult to reach.

Although we expected to find a relation between pain and parity, this was not evident from the patients included. If the women never gave birth, the cervical canal is still narrow which could make implanting an intrauterine tube more painful [41]. In the four patients that filled out the questionnaires, three out of the four never had children. Only patient R12 had children, however she did experience a lot of pain and anxiety which contradicts this hypotheses.

The waiting time for the MRI is expected to decrease from August on wards because of the use of the hyperthermia MRI. This MRI will be managed by the radiotherapy technician themselves which means that they will be able to immediately transport the patient from the recovery room to the MRI and scan the patient themselves. It is expected that the waiting time will decrease and also that the time the images will be available for contouring and reconstruction will decrease. This because the images will be directly uploaded into the picture archiving and communication system (PACS) of the radiation therapy department instead of the PACS from the radiology department. This is beneficial to the patients as the total waiting time at the short stay unit will decrease.

5.4.3. Patient inclusion

The METC approved the research protocol at 13 may 2021. Patients were included between the 13th of May and the 17th of June. Six patients were treated with brachytherapy for cervical cancer during the inclusion period. Five of these patients were asked to participate in the study, the sixth patient was not included due to limited comprehension of the Dutch language.

After the 17th of June, two weeks went by without brachytherapy treatment for cervical cancer patients. The next two patients that started both did not speak Dutch or English and had their consultations with the radiation oncologist and nurses via a translator on the phone. The first dutch speaking patient after the 17th of June started her brachytherapy treatment on the 29th of July. The patient inclusion will be continued by the PhD student that is working on the ARCHITECT project.

There were only four patients included in the questionnaire study until now. However, the METC approved inclusion of 28 patients for the patient experience study. The questionnaires and the workflow around the patient experience study has been set up and more patients will be included to complete the baseline on patient experience and to identify the major pain, anxiety and duration problems during the treatment day that need to be improved.

5.4.4. Literature review

Humphrey et al. performed a systematic literature review on the experiences of women receiving brachytherapy for cervical cancer. They concluded that brachytherapy in women leads to varying levels of distress, pain and anxiety. They also stated that the distress in patients decreased with each procedure. To be able to improve the treatment for patient, it was suggested that pain management, patient interventions and the development of non-pharmacological interventions need to improve [41].

Long et al. concluded that the patients needed better information on the disease and treatment verbally as well as written in the patient's first language [42]. This is difficult in some of the patients in treated in the Erasmus MC, due to the multicultural population in the city of Rotterdam and large amount of migrant workers in the region.

Leon-Pizzaro et al. investigated the influence of non-pharmacological interventions on the psycholog-

ical and quality-of-life indices for breast and gynaecological brachytherapy and showed that patients that received training in relaxation reported lower anxiety and depression during the brachytherapy [43].

The four included patients scored the most pain during applicator removal. This was also shown by Kwekkeboom et al., they found that women described the removal of the applicator, when the sedatives had worn off, as the most physically uncomfortable aspect of treatment [44].

5.4.5. Limitations

Patients should fill in the EQ-5D before the treatment day started and the questionnaire on patient experience should be filled in per location a short time after the patient underwent that step. However, most patients filled in the questionnaire on patient experiences in total at the end of the treatment day after the removal of the applicator. The EQ-5D was almost always filled in before the patient left the short stay unit for the OR.

Currently, there was no distinction made in the different waiting times at the short stay unit in the patient experience questionnaire. The patient scored relatively high pain scores while waiting at the short stay unit, which is most likely in the period between imaging and treatment delivery. It is unlikely that they scored pain when entering the hospital as the EQ5D results did not show high pain scores or after treatment delivery as most patients were relieved of their pain after removal of the applicator.

5.4.6. Recommendation

In the future, it would be interesting to determine the difference in patient questionnaires between the different treatment fractions and between different patients. Comparison between the difference in pain score in patients treated with the Venezia applicator and the Utrecht applicator might also be useful for determining the design approach of the ARCHITECT applicator.

Adding non-pharmaceutical interventions to the waiting time at the short stay unit might be useful for reducing pain and anxiety.

6

General discussion

6.1. Tips and tricks

6.1.1. Workflow evaluation

Observation of the workflow in the beginning of the master thesis helped a lot in understanding the different steps executed during the treatment day. The steps found in literature did not always correspond to the steps observed. Multiple observations were necessary to obtain a full overview and to fully understand all steps.

6.1.2. Time measurements

The time measurements started while waiting for approval of the research protocol by the METC. The time measurements were expanded each treatment day so the researcher could oversee all measurements and the personnel could slowly get used to registering the time. The METC approval was not necessary for this part because it focused on the procedure evaluation. Every treatment day, a new step was added to the time registration. The first treatment day, only the times at the operating room were registered by the researcher. The next treatment day, the radiotherapy technicians were instructed to register the time at the operating room, during applicator reconstruction, treatment planning and at the treatment room. The researcher was present during the day to give instructions and remind the personnel that the time needed to be registered. The time needed for contouring by the radiation oncologists was added to the time registrations after that. The last location that was added to the time registrations was the short stay unit.

The extension of the time registrations each week made it possible for the researcher to ensure accurate registration by all personnel involved.

6.1.3. METC approval

The research protocol and patient information letter were written in a short time span with the help of a lot of people. The protocol was written in collaboration with a clinical physicist, a biomedical engineering PhD student, a post-doc and a radiation oncologists. Feedback was given in very early in the process, which worked positive on the writing process.

6.1.4. Questionnaires on patient experience

After all time registrations went smoothly, the patient questionnaires were added. The four patients were included and filled out the questionnaires. In order to include the patients, close cooperation with the nurses at the short stay unit was necessary. All patients have an intake with the nurse at the short stay unit to talk about the brachytherapy procedure. For future inclusion of patients, the nurse will call the researcher who then informed the patient on the PRE-ARCHITECT study so that informed consent could be provided.

6.2. Adaptions to the current workflow

Currently, the radiotherapy technicians are following training to be allowed to operate the hyperthermia MRI. Using the hyperthermia MRI will allow more smooth transfer of patients from the recovery room to imaging without waiting at the short stay unit. Section 4 showed a mean difference of almost fifty minutes in patients

that were directly transported to the CT scan that is also operated by the radiotherapy technicians. It is possible that new problems during the treatment process will occur due to imaging being performed sooner after leaving the operating room in all patients. For example, there might be more personnel needed to be able to benefit from the shorter time between the operating room and imaging. Currently, two radiation oncologists perform the implantation in four patients treated that day. It could be possible that waiting time before the start of contouring increases, because both radiation oncologists are still needed at the operating room.

Secondly, the clinical physicist currently checks both the applicator and catheters reconstruction and the treatment plan at the end of the treatment planning process. The mean time needed for this step was 22 minutes. The check of the reconstruction could also be performed earlier in the treatment planning process. The main limitation here is the number of Oncentra-Brachy licences. When there are a lot of patients treated during the same day, there is no extra Oncentra-Brachy station available for the clinical physicist to perform the check. Also, the clinical physicist is not available all day and has other clinical obligations. The radiation oncologists also have other obligations during the treatment day.

Both these adaptions together could shorten the mean waiting time of the patient at the short stay unit with an hour. This would be beneficial to the patient, as they reported the highest pain scores during the waiting time at the short stay unit.

6.3. ARCHITECT project

The current plan is to create a 3D model of the vaginal vault using gel during an MRI, as been shown by Laan et al. [45]. It could be expected that customised applicators stabilise applicator positions, improve lesion access, optimise catheter distributions and enhance access to tumors in less frequent positions. This would lead to improvements in brachytherapy treatment conformity with increased local control in large extensive tumors that are currently difficult to treat. Higher conformity could then lead to longer survival and might also impact the quality of life [45]. With pre-planned interstitial catheter paths, the amount of catheters used will be minimized, causing less pain of the implant in the patient. The shape of the implant that matches the anatomy could lead to less pain, but this could also work contradictory, as pressure on the vaginal wall causes pain during the treatment day [38]. Personalized applicators are also of great promise for treating patients with a retroverted uterus. In these patients it is extremely difficult to insert the intracavitary tandem without causing perforation of the uterus [46].

In the current clinical practice, most treatment dose is given through the intrauterine component, as it is inserted into the cervix and very close to the tumor. In the personalised, additive manufactured applicator, an intrauterine component needs to be added to ensure tumor coverage. Implantation of a conically shaped applicator with an intrauterine component will be impossible to perform if the applicator consists of one component. Insertion through the small vaginal opening could be difficult when using the 3D printed component if consisting of one piece [47]. Wiebes et al. created a personalised applicator for vaginal vault brachytherapy that consisted of two dove-tailing parts. This to enable implantation of a conical applicator shape through the more narrow and round vaginal opening [47]. First, during the pre-implantation phase, extra steps need to be added. A pre-implantation MRI must be made with gel inserted to be able to obtain information on the vaginal vault. Catheter path planning is needed and there is time needed for the 3D model to be made and manufactured. Time needed for planning and printing of the 3D model is estimated to be about a week. However, the tumour and the OAR change in topology during external beam radiation therapy. Most changes occur in the initial 2 - 3 weeks of EBRT. Therefore, it is of importance that the pre-implantation MRI is made as late as planning of the personalised applicator allows [48].

It could be expected that the time needed for implantation at the OR will increase due to the complex composition of the personalised applicator. The delay will be caused by longer implantation time because the personalised applicator used and has a more complex shape. Ideally, the assembly will consist of the same steps as in the Venezia applicator in which the only assembly step is the positioning of the catheters on the ring. The time needed for assembling the applicator might increase as the locations in which the catheters are positioned will be different in all patients. The labelling of the catheters need to be performed and checked multiple times. The location of the catheter is not directly linked to a position on the applicator as in the current situation. The labelling of the catheters will also change in the personalized approach as the catheters will be more widely spread with less structure as on the ovoids/ring. The second check in which catheter is labeled should be performed extra carefully. This will probably also increase the workload on the radiotherapy technician and clinical physicist as they perform and check the applicator reconstruction, respectively.

The contouring step will not change when using a new applicator, however, the radiation oncologists need to get used to the shape of the tumor surrounded by the personalized applicator. Applicator reconstruction could be performed using the 3D model created for 3D printing in the same way as the current applicator library is used. This should not take extra time. Treatment planning will not have to change. However, the check of the treatment plan and reconstructed applicator by the clinical physicist will probably take more time, because the shape of the applicator is different in each patient and. As discussed before, it might be of help to split the check of the applicator reconstruction and treatment planning process and perform the check of the reconstruction earlier during the day in parallel to treatment planning. This way, the delay in time needed will be of limited influence on the total waiting time of the patient.

The baseline study performed for the purpose of this master thesis could be expanded and used as a reference for the clinical feasibility study of the ARCHITECT applicator design approach. The variations in the workflow that were found during the observations of the workflow and time registrations are expected to still be present in the future, as the Erasmus MC is a teaching hospital and patients fluctuations will always occur.

6.4. General conclusion

The steps observed in the Erasmus MC did not agree on all steps that were found in literature. Time needed for these steps also differed when comparing to literature. Brachytherapy procedures were observed in fifteen different patients. The mean total procedural time was 391 minutes of which the mean waiting time for imaging was 80 minutes. The total waiting time could be decreased when enabling a more smooth transition between the recovery room and imaging step. This will happen in the near future when the hyperthermia MRI becomes available for the brachytherapy procedures. The time needed for implantation decreased in subsequent treatment fractions, compared to the first treatment fraction, in sixteen out of the twenty treatment fractions. The time needed at the operating room in patients receiving spinal anesthesia did not differ from patients receiving general anesthesia.

Adaptions to the sheet currently used for time registration should include the time needed for assembling the applicator at the operating room, contouring separated for OAR and target volume. Time needed for imaging is not that important as the imaging protocol is the same in all patients. The decrease in waiting time for imaging when using the hyperthermia MRI should be evaluated. The influence of the amount of patients treated during one day would be interesting to evaluate when more data has been collected. Another interesting factor would be differences in duration of the steps and pain experienced in patients treated with the Venezia applicator compared to the Utrecht applicator.

Patient experience score was different in all patients. Overall, highest anxiety scores were found during the first brachytherapy day and highest pain scores were found during the waiting time at the short stay unit. More patients need to be included in the questionnaire study to draw conclusions, but adequate pain management remains important.

7

Appendix

7.1. Appendix: Workflow

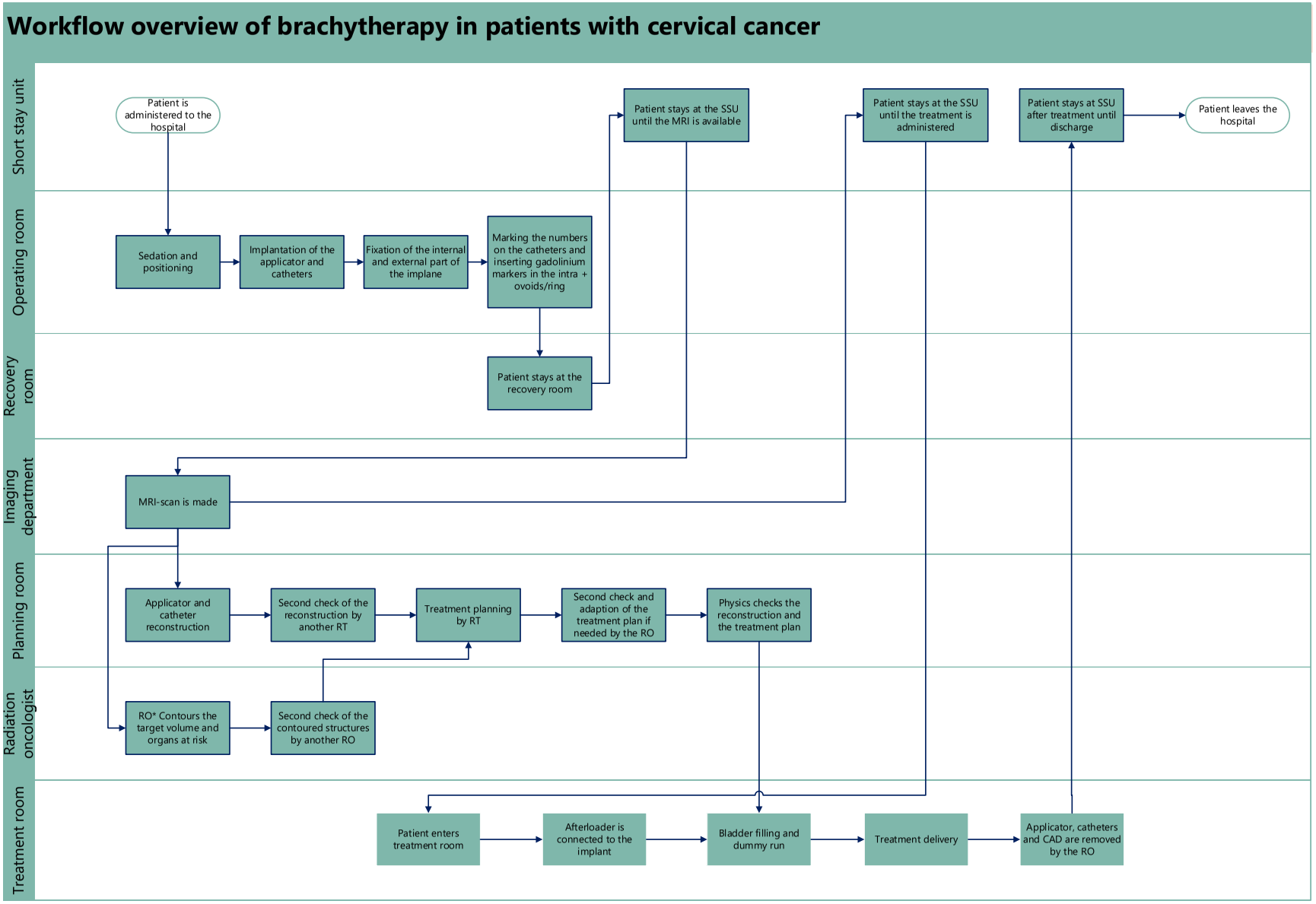

Figure 7.1: Workflow overview of the brachytherapy process in the Erasmus MC by location. The patient starts and ends the treatment day at the short stay unit. Implantation occurs at the operating room. Imaging is performed. OAR and the target volume are contoured. Applicator reconstruction, treatment planning and the quality check are performed, followed by treatment delivery and applicator removal. RT = radiotherapy technician, RO = radiation oncologist, SSU = short stay unit. CAD = Cathéter à demeure = urinary catheter.

7.2. Appendix: Time measurements

Table 7.1: Sheet used by the radiotherapy technicians for time registration at different locations. The step only had a start time if the end time is marked black.

Location	Step	Start time	End time	Remarks
Operation room	Arrival at the operating room			
	Time out procedure			
	Anesthetics: O spinal anesthesia O general anesthesia			
	Start positioning of the patient until finishing application of the sterile workfield			
	Implantation of the applicator (entire sterile procedure)			
	Patient leaves the operation room			
Recovery room	Patient stays at the recovery room			
Radiology department	Patient arrives at the radiology department			
	Imaging: O MRI O CT			
	Patient leaves the radiology department			
Planning room	Load images			
	Reconstruction of the applicator and catheters			
	Second check of the reconstruction			
	Load the contoured structures			
	Treatment planning			
	Call radiation oncologist			
	Second check of the treatment plan and adaptions when necessary by the radiation oncologist			
	Call physicist			
	Physicist checks the treatment plan and reconstruction using a checklist			
	Upload approved treatment plan to OnCentra			
Treatment room	Patient enters the treatment room			
	Connecting the afterloader to the implant			
	Treatment delivery			
	Arrival of the radiation oncologist at the treatment room			
	Removal of the implanted applicator, catheters and CAD O In bed O In lithotomy position on table			
	Patient leaves the treatment room			

Table 7.2: Sheet used by the radiation oncologists for time registration during contouring of the target volume and organs at risk.

Location	Step	Start time	End time	Remarks
Doctors office	Contouring the target volume (GTV, CTV, ITV, PTV) and organs at risk			
	Second check of the contoured structures by another radiation oncologist			

Table 7.3: Sheet used by the nurses at the short stay unit for time registration.

Location	Step	Start time	End time	Remarks
Short stay unit	Stay at the short stay unit until move to the OR			
	Stay at the short stay unit between the stay at the recovery room and imaging			
	Stay at the short stay unit between imaging and treatment delivery			
	Stay at the short stay unit between treatment delivery and patient discharge			

Table 7.4: Steps executed by the researcher to be sure that time registration was performed and patient questionnaires were filled out.

Day	Step	Location
1 day before treatment	Check how many patients are up for treatment the next day	
	Print sheets for radiotherapy technologist to fill in	Leave the sheets on the whiteboard in the treatment room
	Print sheet for the nurses to fill in	Leave the sheet at the short stay unit
	Print sheets for the radiation oncologists to fill in	Leave these at the office of the radiation oncologist or keep them with you and hand them to the radiation oncologist at the operating room the next day
	Check the time of the appointment of the patients at the radiology department	
	Print the EQ-5D questionnaire and the questionnaire on patient experience	The EQ-5D questionnaire is given to the patient at arrival on the treatment day and needs to be delivered to the short stay unit. Leave the questionnaire on patient experience at the treatment room.
Treatment day	Check (around 07:45 am) if the nurses at the short stay unit and the radiotherapy technologist have the correct sheet present	Short stay unit, treatment room before the radiotherapy technologists leave for the operating room or at the operating room
	Clinical activities at the operating room such as inserting the bladder catheter (CAD) or helping positioning the patient	Operating room
	Hand the sheet for contouring to the radiation oncologist and remind them to fill in the time	Operating room
	Collect the EQ-5D questionnaires the patients filled out at arrival and give the questionnaire on patient experience to the patients	Short stay unit
	Check regularly if the time measurements during treatment planning and contouring are written down	Planning room, radiation oncologist office
	Stay at the treatment room to make sure times are written down during treatment delivery and applicator removal	Treatment room
	Remind the patient to fill out the questionnaire on patient experience after they left the treatment room Collect the questionnaire on patient experience of each patient Collect filled out sheets from radiotherapy technologist and radiation oncologist	Short stay unit Short stay unit Treatment room, planning room, radiation oncologist office
1 day after treatment	Collect filled out sheet from the nurses at the short stay unit	Short stay unit
	Digitize all data	Office of researcher

Table 7.5: Times of interest at each location. The duration of these steps were determined using the registered times. [a] From patient entering the operating room until leaving the treatment room after treatment delivery. [b] From patient entering the short stay unit until discharge at the end of the day.

Location	**Step**
Operating room	Total operating room time
	Time needed for anesthetics
	Time needed for positioning
	Time needed for implantation
Recovery room and short stay unit	Waiting time between leaving the operating room until imaging
Radiology department	Imaging
Backoffice radiation oncologist	Total time needed for contouring
	Contouring target volume and organs at risk
	Second check of the contoured volumes by another radiation oncologist
Backoffice radiotherapy technologist	Total time needed for reconstruction
	Reconstruction of applicator and catheters
	Second check of the reconstruction by second RT
	Total treatment planning time
	Treatment planning by radiotherapy technician
	Handoff to radiation oncologist
	Check and adaption of the treatment plan by radiation oncologist
	Handoff to the clinical physicist
	Check of the treatment plan and reconstruction by clinical physicist
Treatment room	Total time in the treatment room
	Waiting time for start of treatment delivery
	Treatment delivery time
	Waiting time for radiation oncologist
	Removal of the applicator, catheters and CAD
	Total procedure time [a]
Short stay unit	Total time spent at the short stay unit
	Waiting until leaving for the OR
	Waiting after return from the OR until imaging
	Waiting after imaging until treatment delivery
	Waiting from treatment delivery and applicator removal until discharge
	Total in-house time [b]

Table 7.6: The duration of the steps in different patients. [a] To radiology is the time between leaving the operating room until arrival at the radiology department. [b] To MRI is the time between leaving the operating room until the start of the MRI. [c]The total time spent at the operating room in patients receiving two treatment fractions during the day was included. [d] When the end time of the check and adaptions by the radiation oncologist was not written down, the time of calling the clinical physicist might be used as endtime. [e] The duration of the steps in patients receiving two treatment fractions during the day were added to the rest of the operating room data as the procedure at the operating room did not deviate from the regular procedure at the operating room. [f] Performed by personnel in training.

Patient	Fraction	Operating room [min]	To radiology[a] [min]	To MRI[b] [min]	Contouring [min]	Reconstruction [min]	Treatment planning [min]	Treatment planning 2[d] [min]	Total in-house time	Treatment room [min]	Total procedure [min]
R01	2	40									
	3	57	16	26		45		7		27	365
R02	2	40				51	14	18		48	386
	3	72	54	64		76	9	9		36	412
R03	1	40									
	2					55	18	18			386
	3	55	77	80		65	22	23		48	418
R04	1	72	48	53		61	35	36		48	388
	2	67	87	95							
	3	59	40	70	35					43	383
R05	2 & 3[e]	42									
R06	1	67		55		80		35			
	2 & 3[e]	50									
	4	67	7			25	20	20	480	50	282
R07	1	65	85		131[f]	53				38	450
	2	51	47	52	28	30	10	10	425	47	314
	3		155			29		20			
R08	1	63				90	50	50		45	422
	2	53	130	136	31	64	18	20	590	53	502
	3					20		2			
R09	1	47	113	123			6	10	470	40	385
	2	43	123	128	46	50				31	437
	3	49	76	81		55	19	20	530	35	366
R10	1	56	68	72	68	61	22	26		41	395
	2	62	22	31	43	120[f]	14	14	465	39	348
	3	60	163	178	33			16		35	440
R11	1	60	85	90		83	26	26	485	35	380
	2	48		72		80	24	25	560	28	370
	3 & 4[e]	47									
R12	1	56	84	89	45	60	15	5		47	387
	2		78	80					495	40	
	3	56	31		50			5	535	58	369
R13	1	46	99	103		70	36	36	570	40	395
	2	43	52	62				20		28	358
	3	35	30	43	63	41	25	26	580	28	391
R14	1	82		83	37	44	12	12	650	65	418
	2	66	19		44	50	4	4	590	33	388
	3 & 4[e]	63									
R15	1	55	95	100		29	13	13	540	38	420
	2 & 3[e]	57									

Table 7.7: Time needed per implantation at the operating room. [a] OR = operating room. [b] The duration of the steps in patients receiving two treatment fractions during the day were added to the rest of the operating room data as the procedure at the operating room did not deviate from the regular procedure at the operating room.

Patient	Fraction	Total OR[a] [min]	Anesthesia [min]	Positioning [min]	Implantation [min]
R01	2	40	7	8	10
	3	57	8	4	14
R02	2	40			11
	3	72	24	18	19
R03	1	40	5	5	17
	2		10	8	18
	3	55		10	19
R04	1	72	14	5	25
	2	67	6	12	30
	3	59	4	6	36
R05	2 & 3[b]	42		7	15
R06	1	67	14	8	27
	2 & 3[b]	50	7	4	18
	4	67	4	2	8
R07	1	65		6	33
	2	51	9	11	23
	3		7	20	
R08	1	63	6	8	33
	2	53	5	8	21
	3		10	17	
R09	1	47	7	7	22
	2	43	7	6	11
	3	49	7	8	20
R10	1	56	6	7	30
	2	62	12	8	22
	3	60	7	10	28
R11	1	60	10	5	25
	2	48	13	6	15
	3 & 4[b]	47	9	8	14
R12	1	56	5	11	27
	2		10		
	3	56	14	6	20
R13	1	46		5	30
	2	43	10	4	11
	3	35	4	6	10
R14	1	82	9	2	47
	2	66	10	9	26
	3 & 4[b]	63	11	10	19
R15	1	55	6	7	25
	2 & 3[b]	57	12	13	11

Table 7.8: Time needed for imaging at the radiology department. [a] OR to radiology is defined as the time between patient leaving the OR until arrival at the radiology department. [b] OR to start MRI is the time between leaving the OR and the start of MR imaging. [c] CT was used as imaging modality instead of MRI for this treatment fraction.

Patient	Fraction	OR to radiology [min] [a]	OR to start MRI [min] [b]	Imaging [min]
R01	3[c]	16	26	
R02	2			
	3	54	64	35
R03	2			24
	3	77	80	43
R04	1	48	53	25
	2	87	95	
	3	40	70	
R06	1		55	
	4[c]	7		
R07	1	85		
	2	47	52	
	3	155		
R08	2	130	136	44
R09	1	113	123	
	2	123	128	40
	3[c]	76	81	5
R10	1	68	72	32
	2[c]	22	31	1
	3	163	178	31
R11	1	85	90	30
	2		72	
R12	1	84	89	30
	2	78	80	
	3	31		
R13	1	99	103	30
	2	52	62	
	3	30	43	32
R14	1		83	
	2	19		
R15	1	95	100	25

Table 7.9: Time needed for contouring the target volume and organs at risk and the second check of the contours by the other radiation oncologist. [a] Radiation oncologist in training contoured the target and OAR. [b] CT was used as imaging modality instead of MRI for this treatment fraction.

Patient	Fraction	Total contouring [min]	Contouring [min]	Contour check [min]
R04	2			3
	3	35	27	5
R07	1	131[a]	95	16
	2	28	23	5
	3		5	
R08	1		32	
	2	31	28	2
	3		5	
R09	2	46	30	4
	3[b]		35	
R10	1	68	50	13
	2[b]	43	33	7
	3	33	25	8
R11	1		45	
	2		14	
R12	1	45	54	5
	2		26	
	3	50	17	
R13	1		32	
	2		19	
	3	63	38	8
R14	1	37	19	4
	2	44	32	3
R15	1		33	

Table 7.10: Duration of the steps at the backoffice of the radiotherapy technicians. [a] When the end time of treatment planning was not written down, the time of calling the radiation oncologist might be used as endtime. [b] RO = radiation oncologist. [c] When the end time of the check and adaptions by the radiation oncologist was not written down, the time of calling the clinical physicist might be used as endtime. [d] CT was used as imaging modality instead of MRI for this treatment fraction. [e] Applicator reconstruction was performed by a radiotherapy technician in training.

Patient	Fraction	Total reconstruction [min]	Applicator reconstruction [min]	Check applicator reconstruction [min]	Treatment planning [min]	Treatment planning 2[a] [min]	Handoff to RO[b] [min]	RO[b] checks and adapts plan [min]	RO checks and adapts plan 2[c] [min]	Total treatment planning [min]	Handoff to clinical physicist [min]	Check by clinical physicist [min]
R01	3[d]	45	35	10		7	0		22			
R02	2	51	34	17	14	18	14	26	32	58	0	38
	3	76	48	23	9	9	55	6	6	70	0	29
R03	2	55	41	12	18	18	5	25	42	48		
	3	65	20	24	22	23	1	19	29	43	1	30
R04	1	61	33	15	35	36	1	10	11	47	1	
	3							10	10			
R06	1	80	65	15		35	30	5	10	70	1	19
	4[d]	25	12	11	20	20	35	5	5	60	5	
R07	1	53	35	15						48	4	16
	2	30	20	10	10	10	15	10	10	35	5	23
	3	29	16	2		20	11		9		0	
R08	1	90	65	25	50	50	5	10	10	65	5	20
	2	64	54	10	18	20	0	36	43	56	4	29
	3	20	13	5		2	10		5		25	
R09	1		15		6	10	2	5	8	17	1	16
	2	50	30	10								
	3[d]	55	31	24	19	20	20	20	20	60	15	27
R10	1	61	46	14	22	26	3	24	26	53	1	21
	2[d]	120[e]	94	25	14	14	0	13	12	27	4	14
	3		28			16	6	33	32	55	7	14
R11	1	83	73	10	26	26	0	14	14	40	5	23
	2	80	70	10	24	25	1	13	13	39	1	20
R12	1	60	30	20	15	5	0	10	12	15	0	14
	3					5	5		25			
R13	1	70	55	10	36	36	10	20	22	66	2	18
	2					20	5					16
	3	41	28	12	25	26	57	15	16	98	1	23
R14	1	44	34	10	12	12	15	55	55	82	5	
	2	50	20	30	4	4	0	20	21	24		
R15	1	29	20	8	13	13	10	10	14	33	4	22

Table 7.11: Duration of the steps at the treatment room. [a] The waiting time for the start of treatment delivery is defined as the difference in time between patient entering the treatment room and start of treatment delivery. [b] RO = radiation oncologist. [c] Waiting for the radiation oncologist is the time between the the end of treatment delivery and arrival of the radiation oncologist.

Patient	**Fraction**	**Total time treatment room [min]**	**Waiting for start treatment delivery[a] [min]**	**Treatment delivery [min]**	**Waiting for RO[b,c] [min]**	**Applicator removal [min]**
R01	3	27	6	13	-9	4
R02	2	48	9	16		12
	3	36	7	14	-11	11
R03	3	48	3	12	3	
R04	1	48	13	10	2	
	3	43	16	15	3	4
R06	4	50	14	13	5	14
R07	1	38	7	13	3	
	2	47	6	13	14	12
	3		26			
R08	1	45	9	15		15
	2	53	13			
	3		24			
R09	1	40	10	9	4	10
	2	31	7	15		4
	3	35	5	14	2	13
R10	1	41	16	13	1	6
	2	39	10	18	0	7
	3	35	11	11	6	5
R11	1	35	11	14	2	6
	2	28	3	18		3
R12	1	47	9	19		7
	2	40	10	16	2	8
	3	58	22	13	-2	4
R13	1	40	13	11	5	3
	2	28	7	12	0	3
	3	28	12	7	2	4
R14	1	65	15	17	2	16
	2	33	6	10	3	6
R15	1	38	7	18	1	5

Table 7.12: The different periods of waiting time spent by the patient at the short stay unit. [a] Some patients do not spent this time at the short stay unit but are directly transported to the radiology department from the recovery room.

Patient	Fraction	Waiting between:					
		Before OR	OR and imaging[a] [min]	Imaging and treatment delivery [min]	Treatment delivery and discharge [min]	Total waiting time at the SSU [min]	Total in-house time [min]
R06	4	80	0	135			480
R07	2	20		120	45		425
	3	95					
R08	2	25	35	220	45	325	590
	3	50	170	55			
R09	1	15	35		40		470
	2	80		189			
	3	40		210	70		530
R10	1	90		175			
	2	50					465
	3	35	115	125			
R11	1	25	42	135	50	252	485
	2	80		175	60		560
R12	1	105	30	140			
	2	15			70		495
	3	30		185	80		535
R13	1	55	30	152	85	322	570
	2			125			
	3	35		235	95		580
R14	1	65		156	130		650
	2	80		220	80		590
R15	1	50	40	175	50	315	540

Table 7.13: The difference in duration of steps for subsequent treatment fractions. A positive value means a increase in time needed and a negative value means the time needed decreased. [a] The duration of the steps at the operating room pf the patients receiving two treatment fractions during one day were included in this analysis. [b] Contouring for the first treatment fraction was performed by the radiation oncologist in training.

Patient	Δ Fraction	Total OR	Anesthetics	Implantation time	Contouring	Total treatment planning	Total procedure	Total in-house time
R03	Fr1 - Fr2		5	1				
	Fr1 - Fr3	15		2				
R04	Fr1 - Fr2	-5	-8	5				
	Fr1 - Fr3	-13	-10	11			-5	
R06	Fr1 - Fr2/3[a]	-17	-7	-9				
	Fr1 - Fr4	0	-10	-19		-10		
R07	Fr1 - Fr2	-14		-10	-103[b]	-13	-136	
R08	Fr1 - Fr2	-10	-1	-12	-4	-9	-80	
	Fr1 - Fr3		4		-27			
R09	Fr1 - Fr2	-4	0	-11			52	
	Fr1 - Fr3	2	0	-2		43	-19	60
R10	Fr1 - Fr2	6	6	-8	-17	-26	-47	
	Fr1 - Fr3	4	1	-2	-25	2	45	
R11	Fr1 - Fr2	-12	3	-10	-31	-1	-10	75
	Fr1 - Fr3/4[a]	-13	-1	-11				
R12	Fr1 - Fr2		5		-28			
	Fr1 - Fr3	0	9	-7	-37		-18	
R13	Fr1 - Fr2	-3		-19	-13		-37	
	Fr1 - Fr3	-11		-20	6	32		10
R14	Fr1 - Fr2	-16	1	-21	13	-58	-30	-60
	Fr1 - Fr3/4[a]	-19	2	-28				
R15	Fr1 - Fr2/3[a]	2	6	-14				

Table 7.14: Duration of all steps per location for the five patients receiving two treatment fractions during one day. RO = radiation oncologist, RT = radiotherapy technician, CP = clinical physicist. [a] One MRI and one CT scan are made during the treatment day. [b] Fr1 = first treatment fraction of the day. [c]Fr1 to radiology is the time between delivering the first treatment fraction and the arrival of the patient for the CT/MRI used for treatment planning of the second treatment fraction. [d] Fr2 = second treatment fraction of the day. [e] When the end time of treatment planning was not written down, the time of calling the radiation oncologist might be used as endtime. [f] When the end time of the check and adaptions by the radiation oncologist was not written down, the time of calling the clinical physicist might be used as endtime. [g] The waiting time for the start of treatment delivery is defined as the difference in time between patient entering the treatment room and start of treatment delivery.

fr3 and 4		R05 fr2 and 3	R06 fr2 and 3	R11 fr3 and 4	R14 fr3 and 4	R15 fr2 and 3
Operating room	Total operating room [min]	42	50	47	63	57
	Anesthesia [min]		7	9	11	12
	Positioning [min]	7	4	8	10	13
	Implantation [min]	15	18	14	19	11
Radiology department	OR to radiology [min]	19	43	45	42	28
	OR to MRI [min]		49			
	Imaging Fr1[a]					
	Fr1 to radiology[b] [min]	89	72		191	14
	Fr1 to MRI [min]				210	19
	Imaging Fr2[a] [min]				3	
Backoffice RO	Total contouring Fr'1 [min]				29	69
	Contour Fr1 [min]			31	29	54
	Contour check Fr1 [min]				3	3
	Total contouring Fr2 [min]				15	88
	Contour Fr2 [min]				14	75
	Contour check Fr2 [min]				1	13
Backoffice RT	Total reconstruction Fr1 [min]	26	123			
	Applicator reconstruction Fr1 [min]	18	38		30	
	Check reconstruction Fr1 [min]	7	19			
	Treatment planning Fr1 [min]		32	12		
	Treatment planning 2 Fr1[e] [min]		32	12	11	14
	Handoff to RO'Fr1 [min]	5	1	0	5	2
	RO plan check Fr1 [min]	5	21	9	7	
	RO plan check 2 Fr1[f] [min]	8	24	9	5	0
	Total treatment planning [min]		54	21	23	
	Handoff to CP[g] [min]		2		4	0
	CP check Fr1 [min]		19		27	19
	Total reconstruction Fr2 [min]	60		80		70
	Applicator reconstruction Fr2 [min]	25	60		50	70
	Check reconstruction Fr2 [min]	15		10		70
	Treatment planning Fr2 [min]			17	10	
	Treatment planning 2[e] FR2 [min]			18	30	10
	Handoff to RO Fr2 [min]			5	0	5
	RO plan check Fr2 [min]			4	5	
	RO plan check 2[f] Fr2 [min]			5	5	33
	Total treatment planning Fr2 [min]			27	35	
	Handoff to CP Fr2 [min]					-7
	CP check Fr2 [min]					20
Short stay unit	Before OR [min]			10	17	32
	Between OR and imaging [min][h]					
	Between imaging and treatment Fr1 [min]			115	45	100
	Between treatment Fr1 and imaging Fr2 [min]			100	200	40
	Between imaging Fr2 and treatment Fr2 [min]			190	107	235
	Between treatment Fr2 and discharge [min]			67	75	23
	Total waiting time at the SSU [min]	482			444	
	Total in-house time [min]			725	765	728
Treatment room	Total treatment room Fr1 [min]	36	33		40	37
	Wait for start treatment Fr1 [min]	17	17	13	24	21
	Treatment delivery Fr1 [min]	15	12	1	12	
	Total procedure Fr1 [min]	202	278		278	256
	Total treatment room Fr2 [min]		34	26	40	58
	Wait for start treatment Fr2 [min]		12	7	13	18
	Treatment delivery Fr2 [min]		13	10	15	21
	Wait for RO[g] [min]			-7	-4	8
	Applicator removal [min]			3	6	5
	Total procedure Fr2 [min]		662	606	642	643

Table 7.15: The duration of the general steps as defined in figure 3.2 in section 7. N = number of data points used. [a] To radiology is the time between leaving the operating room until arrival at the radiology department. [b] To MRI is the time between leaving the operating room until the start of the MRI.

Step	Operating room [min]	To radiology[a] [min]	To MRI[b] [min]	Contouring [min]	Reconstruc [min]	Treatment planning [min]	Physicist check [min]	Treatment room [min]	Total procedure [min]
N	36	26	24	13	26	24	20	28	28
Minimum	35	7	26	28	20	15	14	27	282
Maximum	82	163	178	131	120	98	38	65	502
Mean	55	72	82	50	57	50	22	41	391
Standard deviation	11	42	35	27	23	20	6	9	42

Table 7.16: The mean duration of the steps executed at the operating room and at the radiology department. N = number of data points used. [a] To radiology is the time between leaving the operating room until arrival at the radiology department. [b] To MRI is the time between leaving the operating room until the start of the MRI. [c] Only data on imaging using MRI was used in this descriptive.

Step	Total time [min]	Anesthetics [min]	Positioning [min]	Implantation [min]	To radiology[a] [min]	To MRI[b] [min]	Imaging[c] [min]
N	36	35	38	37	22	21	13
Minimum	35	4	2	8	19	43	24
Maximum	82	24	20	47	163	178	44
Mean	55	9	8	21	80	87	32
Standard deviation	11	4	4	9	39	33	7

Table 7.17: Time needed for the steps executed prior treatment planning. Contouring is performed by the radiation oncologists and the reconstruction of the applicator and catheters by the radiotherapy technologists. N = number of data points used.

Step	Time total contouring [min]	Time contour [min]	Time contourcheck [min]	Total reconstruction [min]	App reconstruction [min]	Check reconstruction [min]
N	13	23	13	26	28	26
Minimum	28	5	2	20	12	2
Maximum	131	95	16	120	94	30
Mean	50	31	6	57	38	15
Standard deviation	27	19	4	23	21	7

Table 7.18: Time needed for the steps during treatment planning at the backoffice of the radiotherapy technologists. N = number of data points used. [a] The time of calling the radiation oncologists was used as endtime of treatment planning. [b] Handoff is the period between calling the radiation oncologist and the start of checking and adapting the treatment plan by the RO. [c] The time of calling the clinical physicist was used as endtime instead of the endtime of the check by the radiation oncologist. [d] Total treatment planning time was defined from the start of treatment planning by the radiotherapy technologist until the end of the check by the radiation oncologist. [e] CP = clinical physicist.

Step	Treatment planning [min]	Treatment planning 2[a] [min]	Handoff to RO[b] [min]	RO check [min]	RO check 2[c] [min]	Total planning[d] [min]	Handoff to CP[e] [min]	CP check [min]
N[f]	21	28	28	24	28	24	24	20
Minimum	4	2	0	5	5	15	0	14
Maximum	50	50	57	55	55	98	25	38
Mean	20	19	11	17	19	50	4	22
Standard deviation	11	11	15	12	13	20	6	6

Table 7.19: Time needed for the steps in the treatment room. N = number of data points used. a The waiting time after treatment delivery is finished before the radiation oncologist arrives to remove the applicator and catheters.

Step	Total treatment room [min]	Wait for start treatment delivery [min]	Treatment delivery [min]	Wait for RO [a] [min]	Applicator removal [min]	Total procedure [min]
N	28	30	27	22	24	28
Minimum	27	3	7	-11	3	282
Maximum	65	26	19	14	16	502
Mean	41	11	14	2	8	391
Standard deviation	9	56	3	5	4	42

Table 7.20: Duration of the waiting time at the short stay unit between the steps. N = number of data points used. [a] Some patients do not spent this time at the short stay unit but are directly transported to the radiology department from the recovery room.

Waiting time between:	Before OR [min]	OR and imaging[a] [min]	Imaging and treatment delivery [min]	Treatment delivery and discharge [min]	Time waiting total [min]	Time total in-house [min]
N	21	9	18	13	4	15
Minimum	15	0	55	40	252	425
Maximum	105	170	235	130	325	650
Mean	53	55	163	69	304	531
Standard deviation	28	53	45	25	35	61

Table 7.21: The duration of the steps at the operating room for patients treated with spinal anesthesia and general anesthesia. N = number of data points used.

Spinal anesthesia	Time OR [min]	Time anesthetics [min]	Time position [min]	Time implant [min]	Time OR to radiology [min]	Time OR to MR [min]
N	19	19	20	19	18	13
Minimum	40	5	2	10	16	26
Maximum	82	14	20	47	163	178
Mean	55	9	8	22	71	85
Standard deviation	10	2	4	9	45	41
General anesthesia	**Time OR [min]**	**Time anesthetics [min]**	**Time position [min]**	**Time implant [min]**	**Time OR to radiology [min]**	**Time OR to MR [min]**
N	17	16	18	18	13	12
Minimum	35	4	2	8	7	43
Maximum	72	24	18	36	130	136
Mean	55	9	8	21	61	76
Standard deviation	12	5	4	8	34	28

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