EVALUATE THE DOSES TO THE ORGANS AT RISK (OAR) CALCULATED BY USING ONCENTRA TREATMENT PLANNING SYSTEM FOR CERVICAL CANCER

by

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CERTIFICATE

This is to certify that the dissertation entitled

TO EVALUATE THE DOSES TO THE ORGANS AT RISK (OAR) CALCULATED BY USING ONCENTRA TREATMENT PLANNING SYSTEM FOR CERVICAL CANCER

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In the name of Allah, the Most Gracious, and the Most Merciful.

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Abbreviations

OAR	Organ at risk
ICRU	International Commission on Radiation Unit and Measurement

ABSTRACT

Objective: The aim of this work was to determine doses to rectum and bladder for dose behaviors in the treatment of cervical cancer by high dose rate (HDR) intracavitary brachytherapy (ICRT) using Ocentra treatment planning system.

Materials and methods: A retrospective study was carried out on 10 patients with a total of 20 fractions (1st and 2st fractions for each patient) of cervical cancer treated with HDR intracavitary brachytherapy in addition to external radiotherapy (EBRT). Brachytherapy treatment planning was performed using Ocentra Treatment Planning System (Nucletron). Before this, the treatment was done using Plato treatment planning. Fletcher-suit applicators (Nucletron) with different size of ovoid which are mini (1.5 mm), small (2.0mm) and medium (2.5mm) are used for ICBT. The prescibed doses 900 cGy (9 Gy) for each fraction is normalised at applicator point. Normal distributions were tested for the rectum and bladder doses for any statistical conclusions.

Results: It was observed that rICUR and bICRU were found to show normal distribution for fraction one with mean dose of 38% and 46% and standard deviation of 16% and 17%, respectively. Then rICUR and bICRU for fraction two with mean dose of 35% and 41% and standard deviation of 13% and 10 % respectively.

Conclusions: The normality behavior of the rectal and bladder point dose show that less than 60% and 80 % of the prescribed dose at point A which means is in the limit of International Commission on Radiation Units (ICRU).

ABSTRAK

Objektif: Tujuan kajian ini adalah untuk menentukan dos dengan rektum dan pundi kencing untuk tingkah laku dos dalam rawatan kanser pangkal rahim dengan kadar dos tinggi (HDR) brakiterapi intracavitary (ICRT) menggunakan Ocentra sistem perancangan rawatan.

Bahan dan kaedah: Satu kajian retrospektif telah dijalankan ke atas 10 pesakit yang mempunyai sejumlah 20 pecahan (pecahan 1 dan 2st untuk setiap pesakit) kanser serviks dirawat dengan HDR brakiterapi intracavitary di samping radioterapi luaran (EBRT). Perancangan rawatan brakiterapi dilakukan dengan menggunakan Ocentra Rawatan Sistem Perancangan (Nucletron). Sebelum ini, rawatan yang telah dilakukan dengan menggunakan Plato perancangan rawatan. Aplikator Fletcher (Nucletron) dengan saiz yang berbeza daripada yang mini (1.5 mm), kecil (2.0 mm) dan sederhana (2.5 mm) digunakan untuk ICBT. Anggaran dos adalah 900 CGY (9 Gy) bagi setiap pecahan adalah normal pada ketika pemakai. Taburan normal telah diuji untuk rektum dan pundi kencing dos bagi apa-apa kesimpulan statistik.

Keputusan: Diperhatikan bahawa rICUR dan bICRU didapati menunjukkan taburan normal untuk pecahan satu dengan dos min 38% dan 46% dan sisihan piawai 16% dan 17% masing-masing. Kemudian rICUR dan bICRU untuk pecahan dua dengan dos min 35% dan 41% dan sisihan piawai masing-masing sebanyak 13% dan 10%.

Kesimpulan: Kelakuan normal persembahan titik dos rektum dan pundi kencing yang kurang daripada 60% dan 80% daripada dos yang ditetapkan itu pada titik A yang bermaksud adalah dalam had Suruhanjaya Antarabangsa bagi Unit Sinaran (ICRU).

CHAPTER 1

1.0 INTRODUCTION

'*Brachy*' means '*short-range'* in Greek. The term brachytherapy means near treatment. By theory the brachytherapy is the delivery of radiation therapy using sealed sources that replaced as close as possible to the site to be treated. This treatment can be used for the treatment of tumours where radiation source can be placed within body cavity example the uterus, vagina, oesophagus or bronchus, or where the tumour can be enter by needle or catheter sources being placed within it for example the breast, head and neck. In fact, brachytherapy can be applied to most tumour sites. It can be used as primary treatment or in combination with external beam radiotherapy (Coyle, 2005)

The principal advantages of brachytherapy lie in the physics of the dose distribution around radiation source. This results in a high concentration of dose immediately round the source and rapid fall-off of dose away from the source with distance according to the inverse square law. Besides, this technique gives accurate localization of the gross tumour volume and immobilization of the area to be treated. It is different with the external beam treatment when organ movement and set-up errors are introduced (Hoskin, 2005)

Cervical cancer or cancer of cervix is cancer of the entrance to the uterus (womb). Cervical cancer is a disease in which malignant (cancer) cells form in the tissues of the cervix. The cervix is the lower aspect of the uterus. It is roughly cylindrical in shape, projects through the superior-anterior vaginal wall, and communicates with the vagina through the endocervical canal, which terminates in the external os located at the top of the vagina. Cancer of the cervix may originate from the mucosa of the surface of the cervix or from within the canal. Carcinoma of the uterine cervix grows locally and may extend in continuity to the uterus and paracervical tissues, and pelvic organs. Cervical cancer may spread to regional lymph nodes, and only later metastasize hematogenously to distant structures.

The cervix is drained into the following first echelon nodal stations: parametrial, internal iliac (obturator–hypogastric), external iliac, and presacral, followed by drainage to the common iliac nodes. From the common iliac nodes, lymph drainage goes to the paraaortic nodes. The most common sites of distant spread include the para-aortic, mediastinal and supraclavicular nodes, the lungs, liver, and skeleton (Ericka, 2012). Figure 1.0.1 shows the anatomy of the female reproductive system. The organs in the female reproductive system include the uterus, ovaries, fallopian tubes, cervix, and vagina. The uterus has a muscular outer layer called the myometrium and an inner lining called the endometrium (National Cancer Institute, 2015)

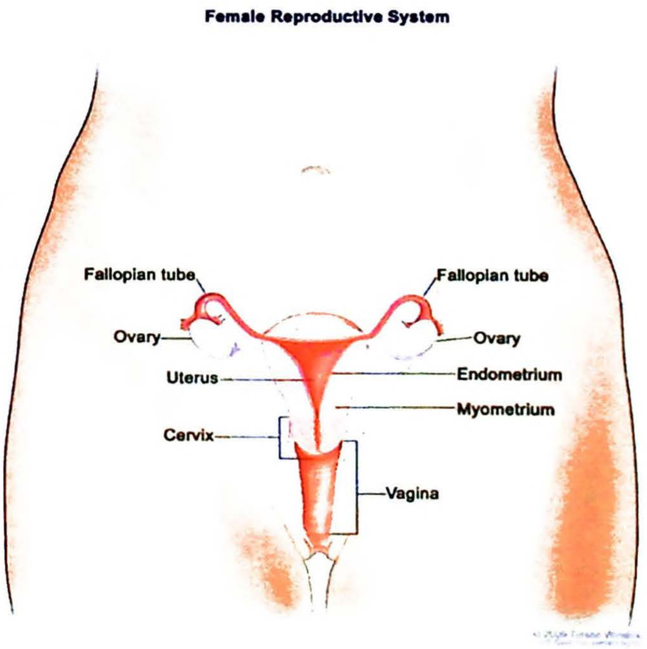

Figure 1.0.1: Anatomy of Female Reproductive System

In radiotherapy, brachytherapy is essential to deliver high dose to the tumour while sparing surrounding normal tissues. Brachytherapy is only a practical option to access the tumour using the radioactive sources. The radioactive sources are placed in a variety of ways which are intracavitary, interstitial, intravascular insertion, intraluminal and surface moulds (Bownes, 2012). Brachytherapy plays a very important role in curing cervical cancer. For the cervical cancer the way of intracavitary is used where the sources are placed in body cavities close to the tumour volume. Intracavitary treatments are always temporary which means that temporary dose is delivered over a short period of time and the sources are removed after the prescribed dose has been reached (Tolli, 2012).

HDR afterloading units came into use in the late 1960s. The advantage of HDR treatments is the shorter treatment times, just a few minutes although the treatments have to be fractionated so the overall treatment time is not needed shorten. Particularly for cervix treatments, the short treatment times allow the use of rigid rectal retractors that is more effective to reduce the rectal dose. HDR afterloading machines need to be housed in substantial shielded treatment rooms with appropriate interlocks, warning signs, patient monitoring equipment, etc. The first type to be installed in UK was the Cathetron in 19678 then new version has been introduced , HDR Selectron (Nucletron) in the mid – 1980s. The late 1980s, new generation of afterloading machines based on using a single high activity iridium-92 source is introduced (Bownes, 2012).

Cervical cancer is the fourth most common cancer affecting women worldwide, after breast, colorectal, and lung cancers. It is also the fourth most common cause of cancer death (266 000 deaths in 2012) in women worldwide. Cervical cancer, an avoidable cause of death among women in sub-Saharan Africa with 528 000 new cases every year, it is most notable in the lower resource countries of sub-Saharan Africa.

Almost 70% of the global burden falls in areas with lower levels of development, and more than one fifth of all new cases are diagnosed in India. Cervical cancer can have devastating effects with a very high human, social, and economic cost, affecting women in their prime (Geneva, 2013).

Cervical cancer is the third most common cancer after breast and colorectal cancer and the fourth leading cause of death among women in Malaysia. It remains to be one of the major cancers that burden worldwide particularly in under-developed and developing countries. In Malaysia, the incidence rate of 12.2 per 100,000 in 2006 was higher compared to other developed countries such as Australia and USA. Cervical cancer incidence rate increased with age after 30 years and has its peak at ages 65-69 years. According to ethnicity in Malaysia, women of Indian ethnic group have the highest incidence for cervical cancer followed by Chinese and Malay (Nurliyana, 2013).

There are different types of treatment for the cervical cancer such as surgery, radiation therapy and chemotherapy. Surgery is the removal of the tumor and surrounding tissue during an operation. Then, radiation therapy is the use of high-energy x-rays or other particles to destroy cancer cells. Radiation therapy may be given alone, before surgery, or instead of surgery to shrink the tumour. Many women may be treated with a combination of radiation therapy and chemotherapy. The most common type of radiation treatment is called external-beam radiation therapy, which is radiation given from a machine outside the body. When radiation treatment is given using implants, it is called internal radiation therapy or brachytherapy. A radiation therapy regimen (schedule) usually consists of a specific number of treatments given over a set period of time. Chemotherapy is the use of drugs to destroy cancer cells, usually by stopping the cancer cells' ability to grow and divide. Cervical cancer is often treated along with radiation therapy. The goal of chemotherapy when given with radiation therapy is to increase the effectiveness of the radiation treatment (2014).

Brachytherapy is an important component of the treatment of cervical cancer with or without external beam radiotherapy (EBRT). For cervical cancer, the tandem or ovoid can be used in treatment. Organ at risk that should be take note for the cervical cancer are rectum and bladder. The bladder point dose should be to < 80% and rectum point dose <60% follow the International Commission on Radiation Units (ICRU) (Wolfson, 2008).

1.1 AIM

To evaluate the doses to the organs at risk (OAR) calculated by using Oncentra treatment planning system for cervical cancer.

1.2 OBJECTIVES

The objectives of this study are:-

1: to determine the doses to organ at risk of 2D intracavitary brachytherapy (ICBT) for cervical cancer.

2: to identify the total doses obtained from both the pre-brachytherapy (external beam) and post-brachytherapy (external beam and ICBT).

3: to determine the effects of different sizes of ovoid applicator to doses at OAR used in cervical treatment.

CHAPTER 2

2.0 LITERATURE REVIEW

Brachytherapy is normally used either alone or, more commonly, as a part of multi-modality approach with EBRT, surgery, and/or chemotherapy. In a typical radiotherapy department, about 10-20% of all radiotherapy patients are treated with brachytherapy (Brahmacharimayum, 2005).

Brachytherapy plays a significant role in the treatment of many cancers. High dose rate (HDR) brachytherapy with remote after loading system using Ir-192 radioisotope became the major treatment modality for gynaecological cancers. In some advanced cases where surgery is not possible, brachytherapy is very useful. Cervix cancer is one of the leading causes of cancer morbidity among women worldwide and it is the second most common cancer among women in developing countries (Ramachandran, 2005).

For cervical cancer either with or without chemotherapy are strongly recommends to include brachytherapy as a component of treatment (Nag *et al.,* 2005). Cancer cervix is usually treated with radiotherapy which consists of external beam radiotherapy followed by intracavitary brachytherapy. In cervical intracavitary brachytherapy, it is mandatory to evaluate if the doses to bladder and rectum are within tolerance limits.

Bladder and rectum are the main organs at risk (OAR) in the treatment of cervical intracavitary brachytherapy whose doses are ensured not to exceed the limits of tolerance. The organs at risk (OAR) of bladder and rectum is based on International Commission on Radiation Units and Measurements (ICRU). ICRU bladder (bICRU) and rectum (rICRU) points must be < 80% and < 60% respectively (Yuu Inn, 2010).

There were different ways of reducing the dose to these organs at risk, bladder and rectum explained by Jain and Haie-Meder et al (2010):

1. The Geometry Of The Intracavitary Applicators,
2. Age Of Patient,
3. Disease Stage,
4. Length And Angulation Of The Tandem,
5. Size Of The Ovoid And Tandem,
6. Volume Of Bladder And Rectum,
7. Dwell Position Of Source,
8. Proximity Of The Applicator To The Bladder And Rectum Do Affect The Dose To Organs At Risk,
9. Proper Vaginal Packing,
10. Patient Anatomy,
11. Adjust The Dwell Positions And Relative Dwell Times Of Source Positions.

The success of radiation therapy of cervical cancer requires the delivery of high radiation dose directly to the tumour while sparing, to some degree, the surrounding healthy tissues. Brachytherapy treatment planning systems have increased in complexity so planning quality control should be designed to ensure the quality of treatment plans, minimize the possibility of systematic errors and be designed to complement checks on individual treatment plans.

CHAPTER 3

3.0 MATERIALS AND METHODS

A) Patients selection

10 patients of histopathologically confirmed cervical cancer were selected for this retrospective study. Both, first and second fractions of each patient were used in this study. The selected patients were treated with EBRT and high dose rate ICRT from 2012 to 2015 in Radiotherapy Department, Hospital USM.

B) ICBT Applicator Insertion

Fletcher-suit applicators (Nucletron) with different sizes of ovoids which are mini (1.5 mm), small (2.0mm) and medium (2.5mm) as shown in Figure 3.01 were used. In this study, no tandem is used. Packing was done to avoid any shifting or changes in the geometry of the applicators placement and prevent the relocation of rectum and bladder. All the procedures were done under conscious sedation without general or spinal anesthesia, after which patients were shifted to simulator room for taking orthogonal films for brachytherapy treatment planning.

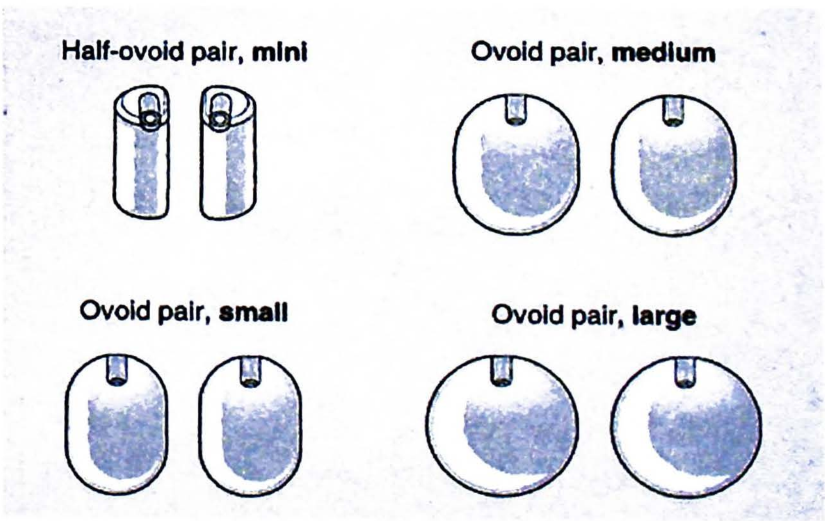

Figure 3.0.1: Types of Ovoid

C) Brachytherapy Treatment Planning

Brachytherapy treatment planning was performed by using Oncentra Treatment Planning System (Nucletron). Ocentra Masterplan basically involved the physics and algorithms to produce the dose calculation. Based on AAPM task group no.43 protocol for brachytherapy dose calculation. Figure 3.0.3 showed the opening window of the Ocentra software.

Prescribed dose is 900 cGy (9 Gy) for each fraction were normalized at applicator point without optimization. In the planning process, bladder and rectum doses were planned to keep below 80% and 60% respectively of prescribed dose for each planned fraction. Since two fractions were given for each patient, so the total dose received for each patient was 1800 cGy (18 Gy). For this rectrospective study the image is reconstructed again using the 2D Ocentra treatment planning to get the calculated dose. The steps of treatment planning are shown in Figure 3.0.2. The details of these steps are shown in Figure 3.0.4 to Figure 3.0.8.

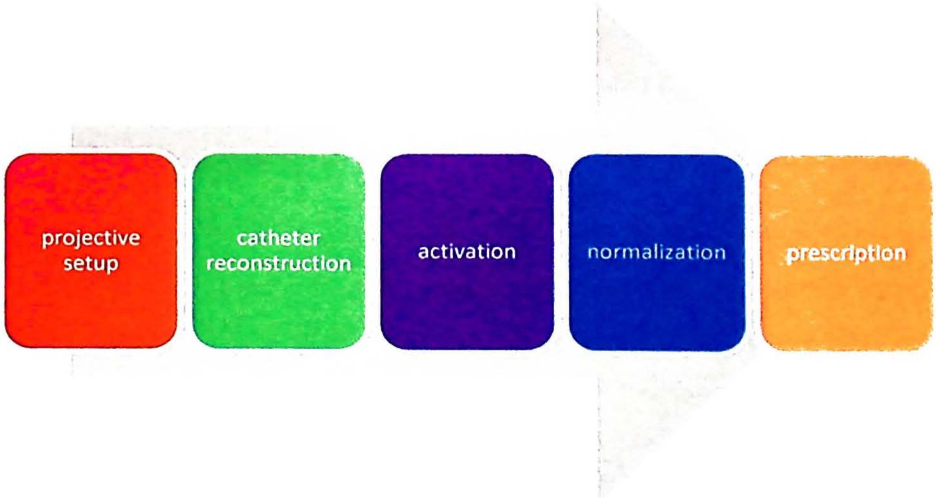

Figure 3.0.2: Steps of treatment planning

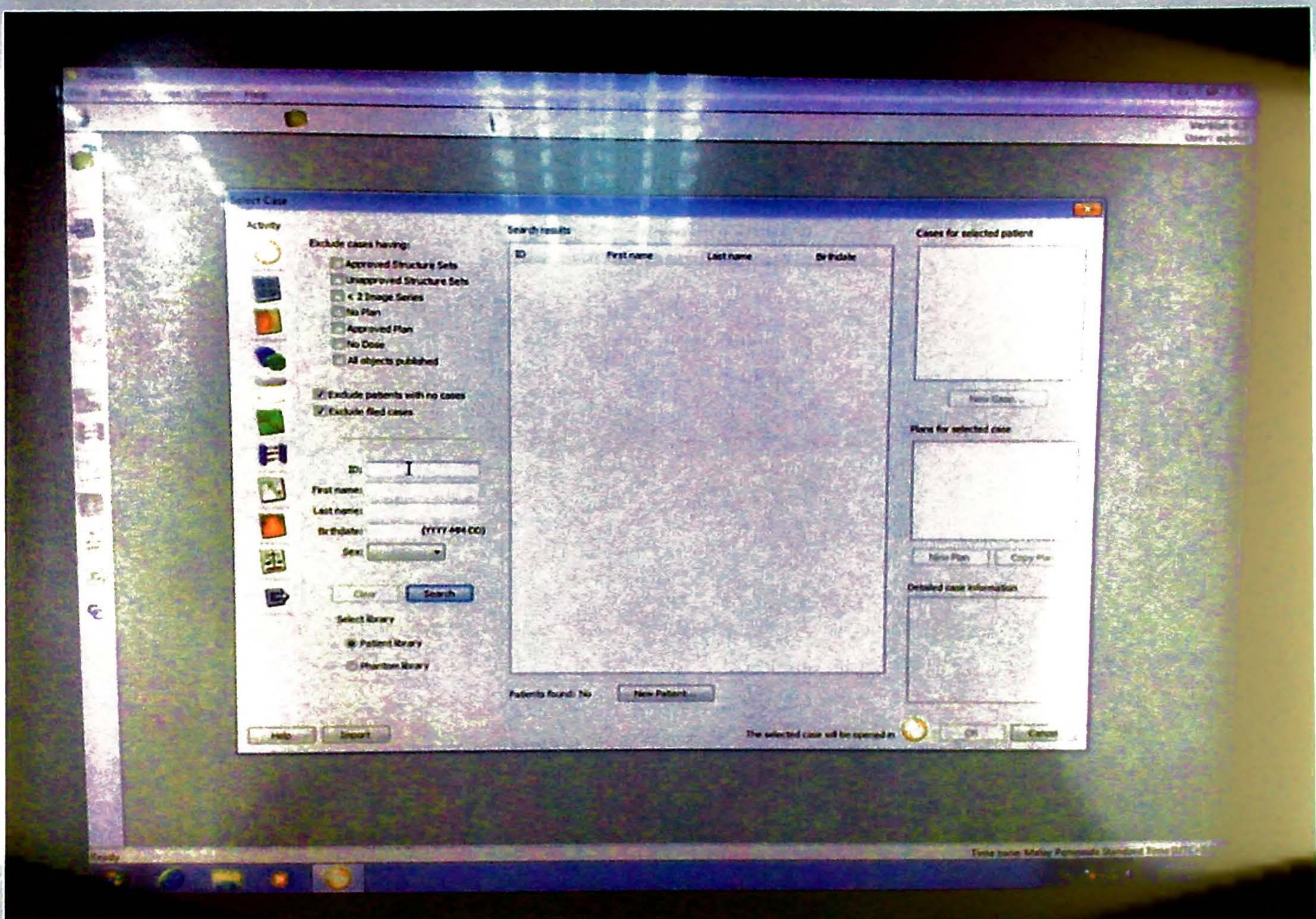

Figure 3.0.3: Ocentra Masterplan treatment planning system

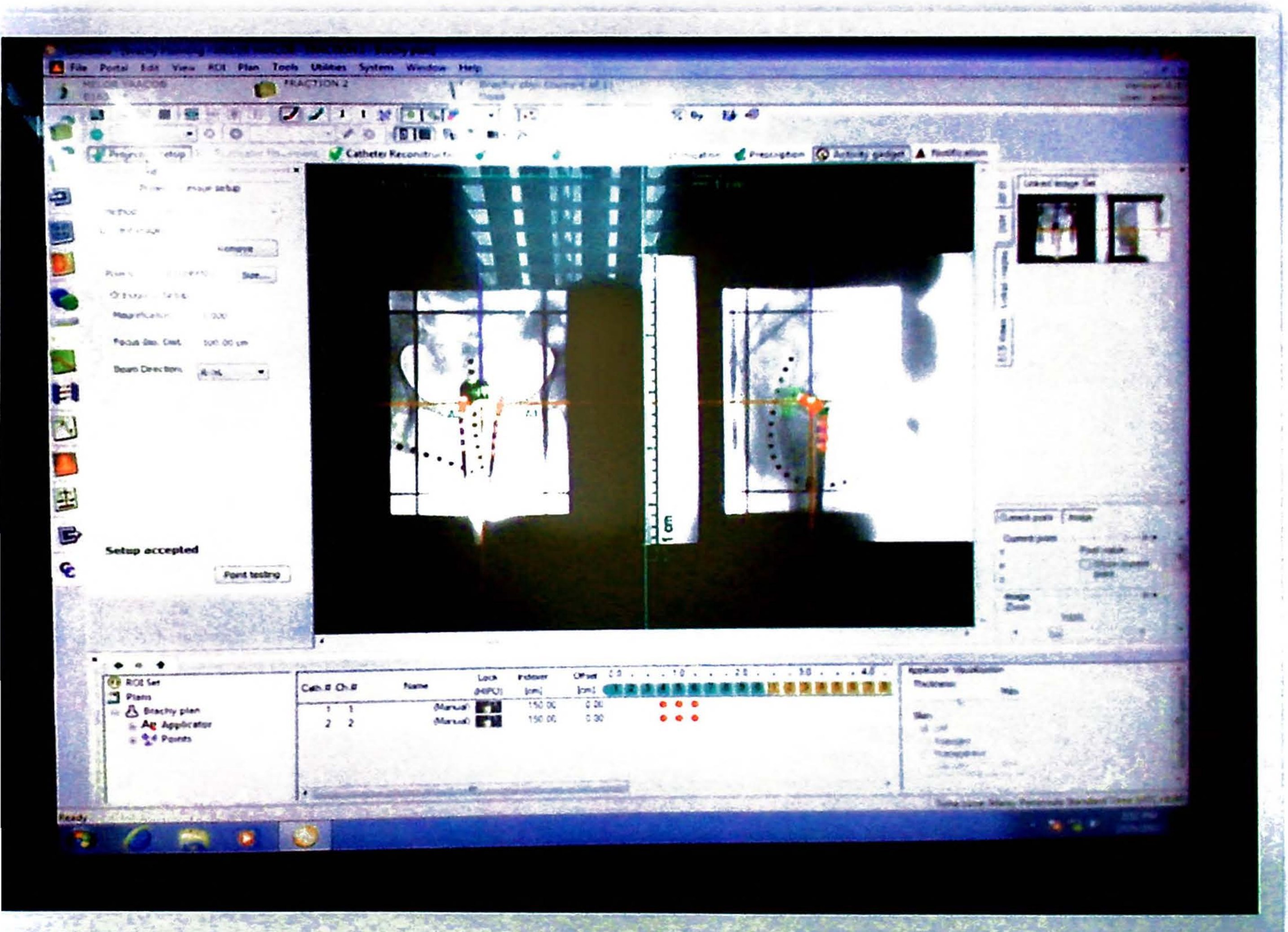

Figure 3.0.4: Projective setup of treatment planning

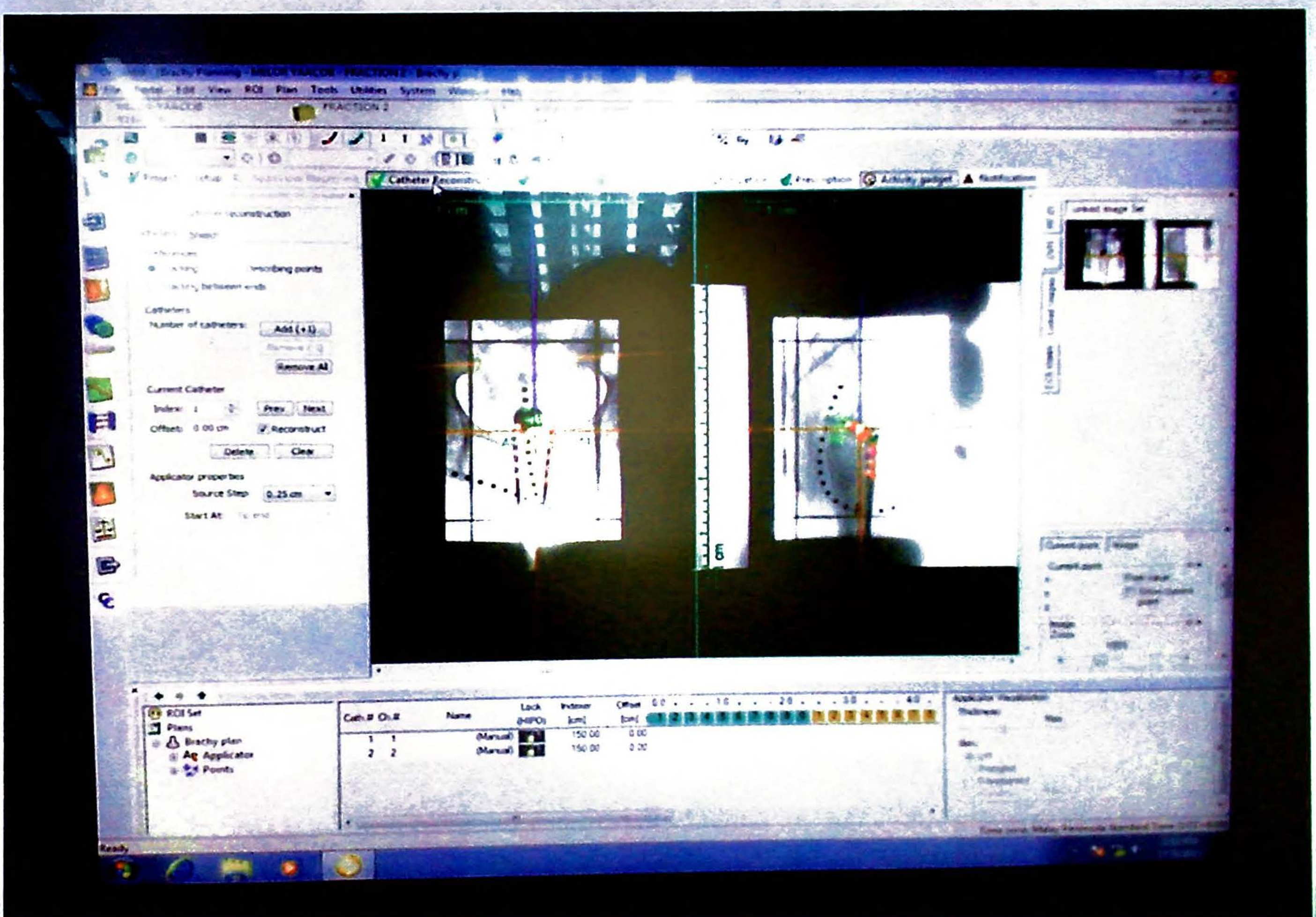

Figure 3.0.5: Catheter reconstruction

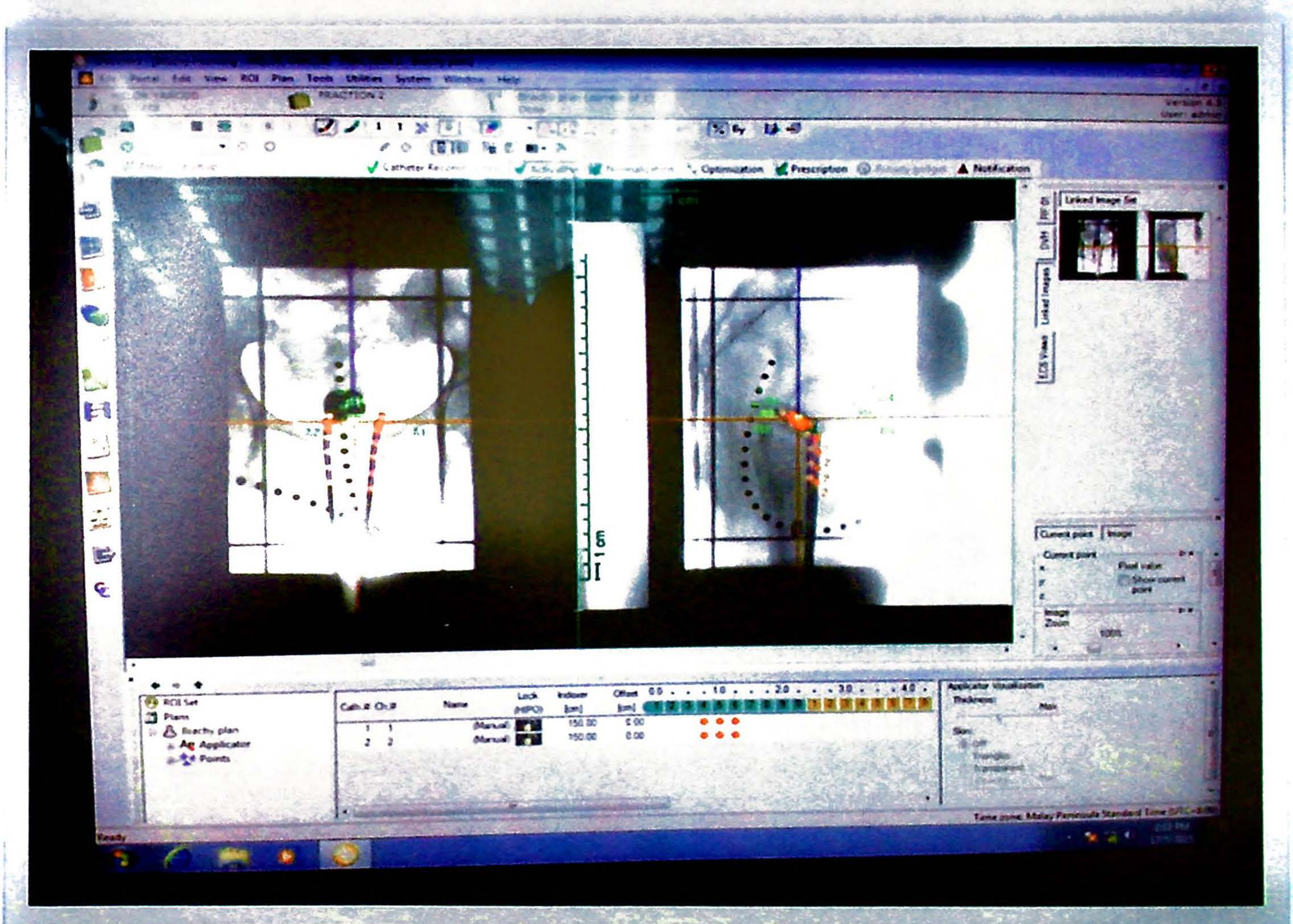

Figure 3.06: Activation of treatment planning

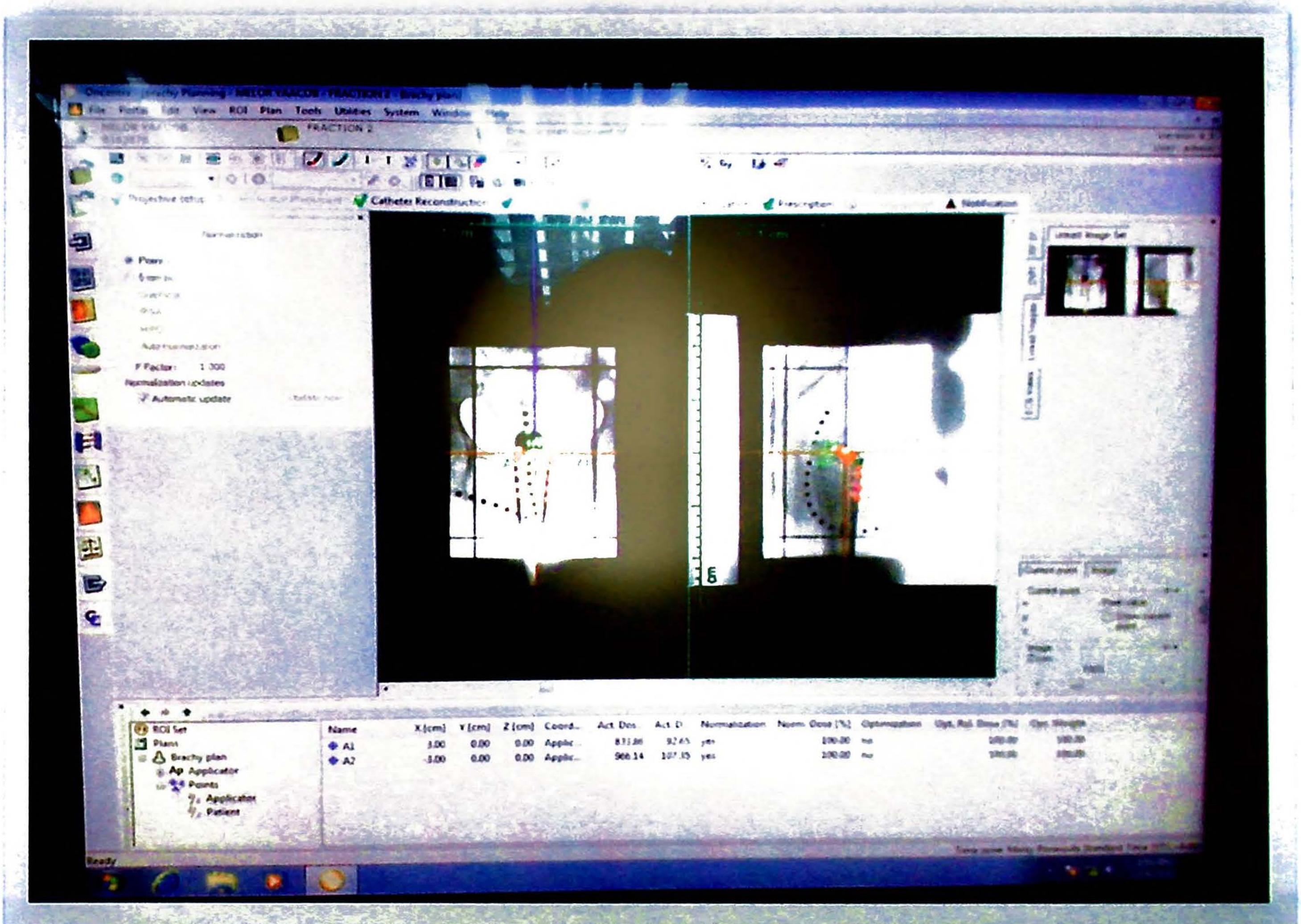

Figure 3.0.7: Normalization of treatment planning

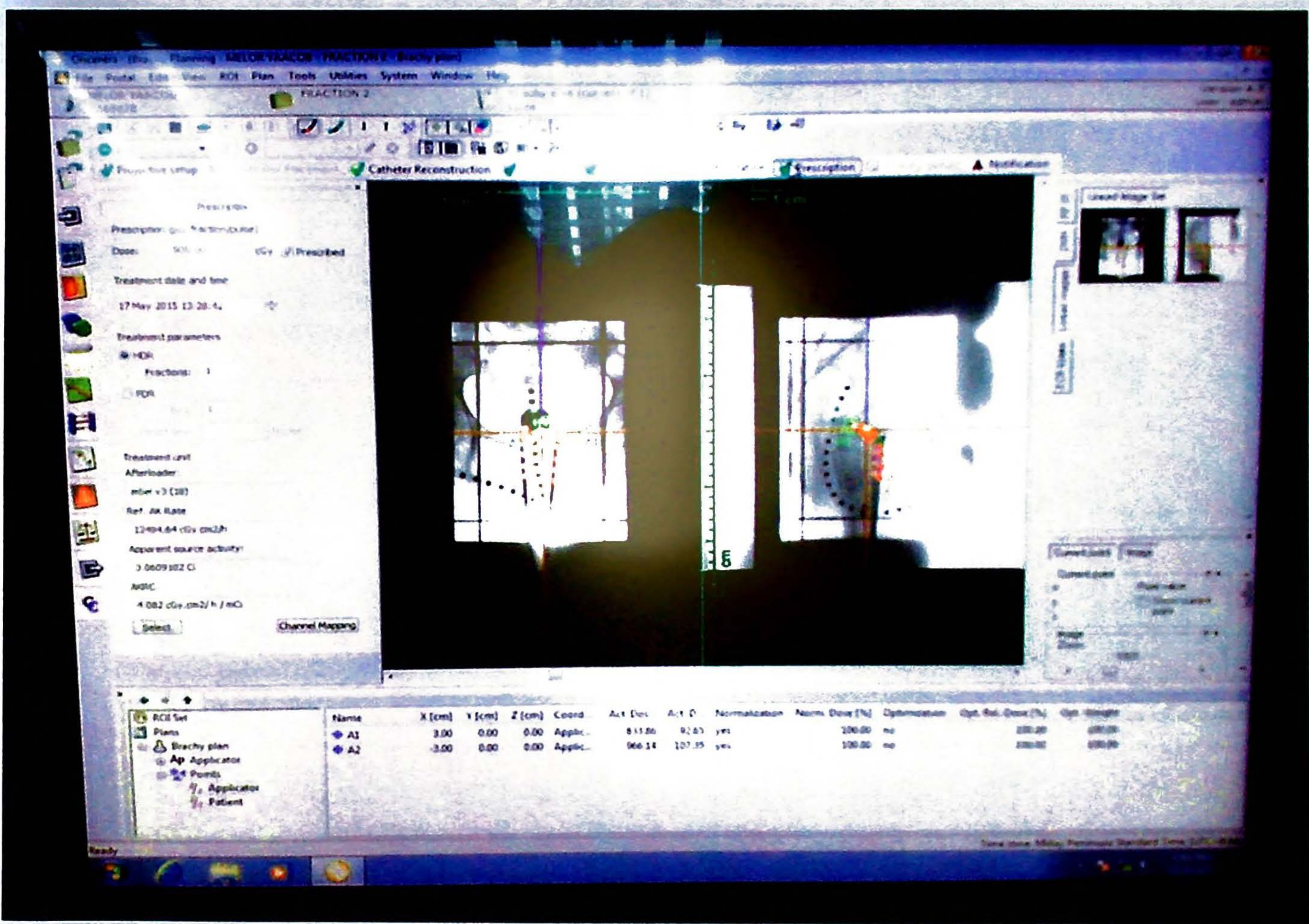

Figure 3.0.8: Prescription for treatment

CHAPTER 4

RESULTS

Dose to organs at risk of 2D intracavitary brachytherapy for cervical cancer. Table 4.1.1 (a) and (b): The calculated dose to organ at risk of 2D intracavitary brachytherapy (ICBT) for cervical cancer obtained from the Ocentra treatment planning.

a) Fraction one

No. of Patient	Dose (cGy) (Fraction 1)	
	Rectum (%)	Bladder (%)
1	254.94	465.27
2	214.25	398.80
3	382.14	544.35
4	246.81	647.36
5	291.36	342.25
6	288.01	329.87
7	283.13	395.46
8	399.49	326.56
9	307.56	584.64
10	790.69	107.66

Figure 4.1.1 (a) and (b) represented the doses of rectum and bladder percentage for fraction one of each patient.

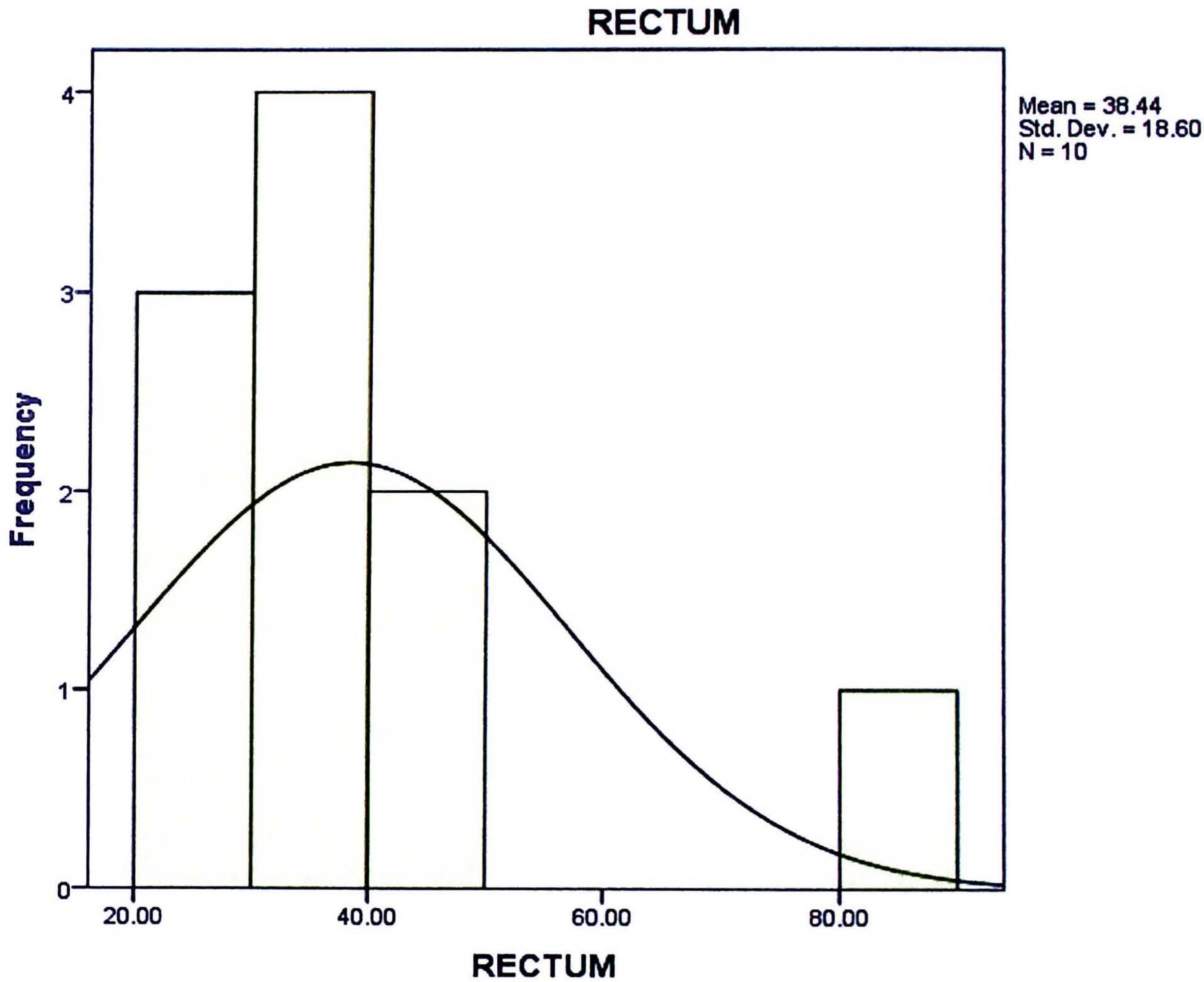

Figure 4.1.1: a) Histogram of rectal doses in percentage (number of patient versus. class interval of dose rectum in % for fraction 1)

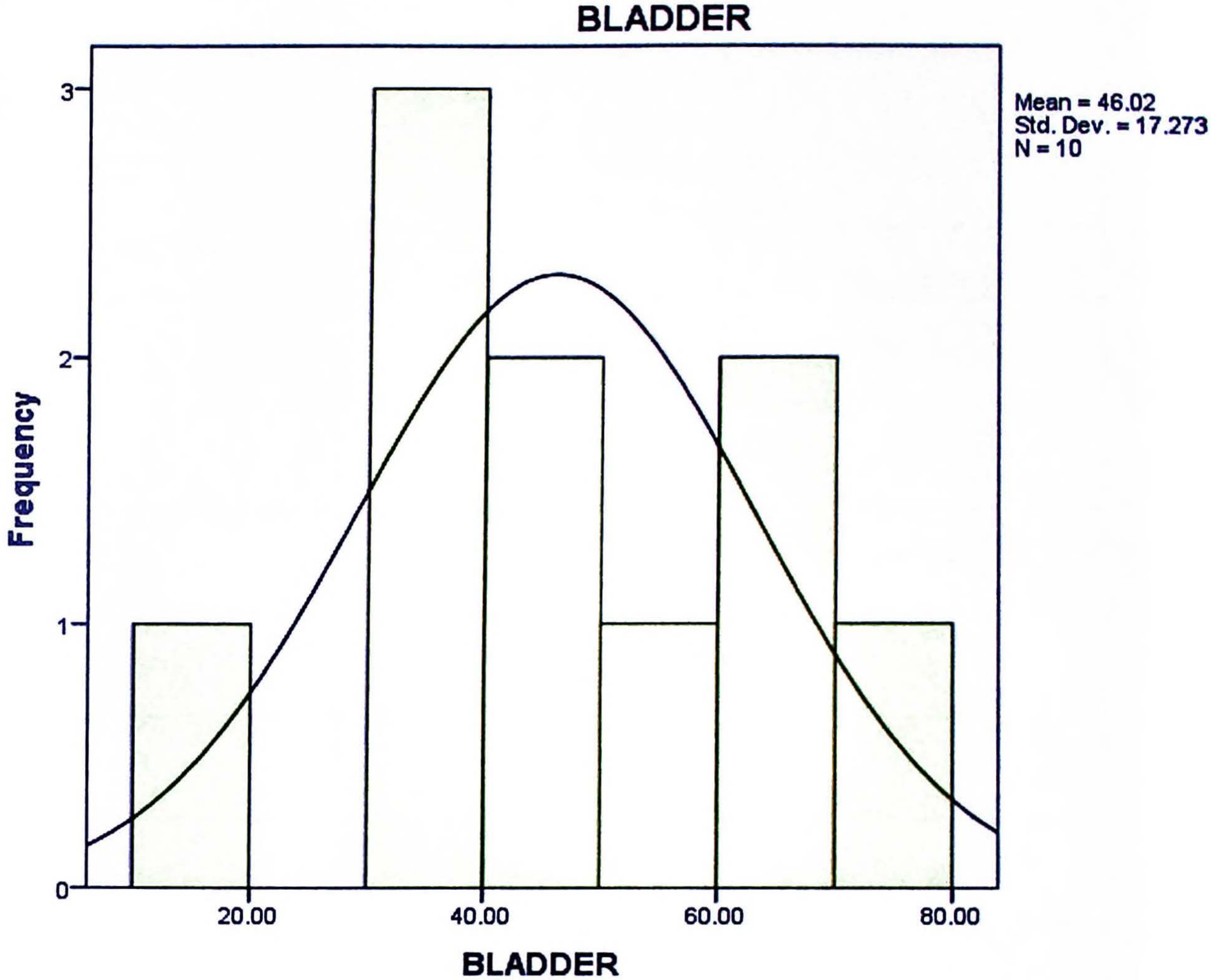

Figure 4.1.1: b) Histogram of bladder doses in percentage (number of patient versus. class interval of dose rectum in % for fraction 1)

b) Fraction two

No. of Patient	Dose (cGy) (Fraction 2)	
	Rectum (%)	Bladder (%)
1	255.26	381.16
2	248.87	389.40
3	392.01	481.69
4	359.08	225.34
5	280.74	253.89
6	302.72	342.56
7	177.11	329.63
8	405.30	445.68
9	213.23	410.78
10	599.54	507.82

The detailed result of Table 4.1.1 (a) and (b) is placed at Appendix A as reference.

Figure 4.1.2 (a) and (b) represented the doses of rectum and bladder percentage for fraction two of each patient.

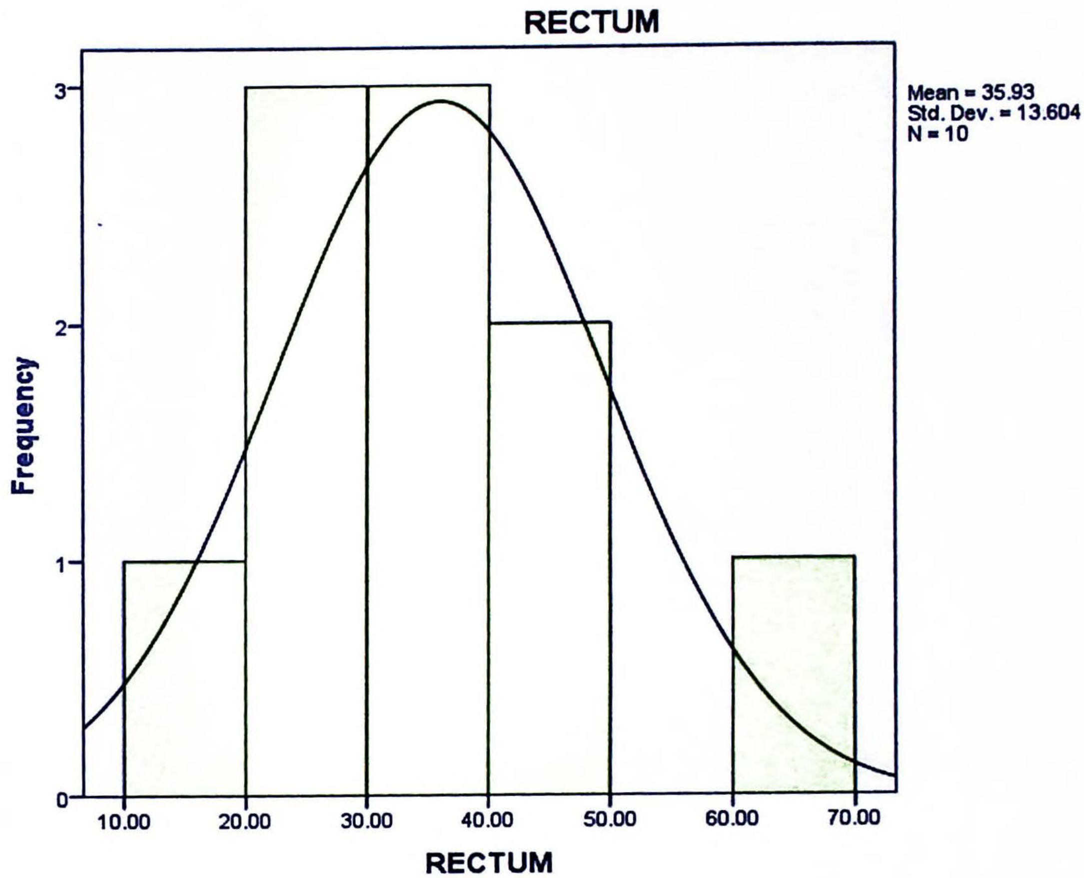

Figure 4.1.2 (a) represented the doses of rectum and bladder percentage for fraction one of each patient.

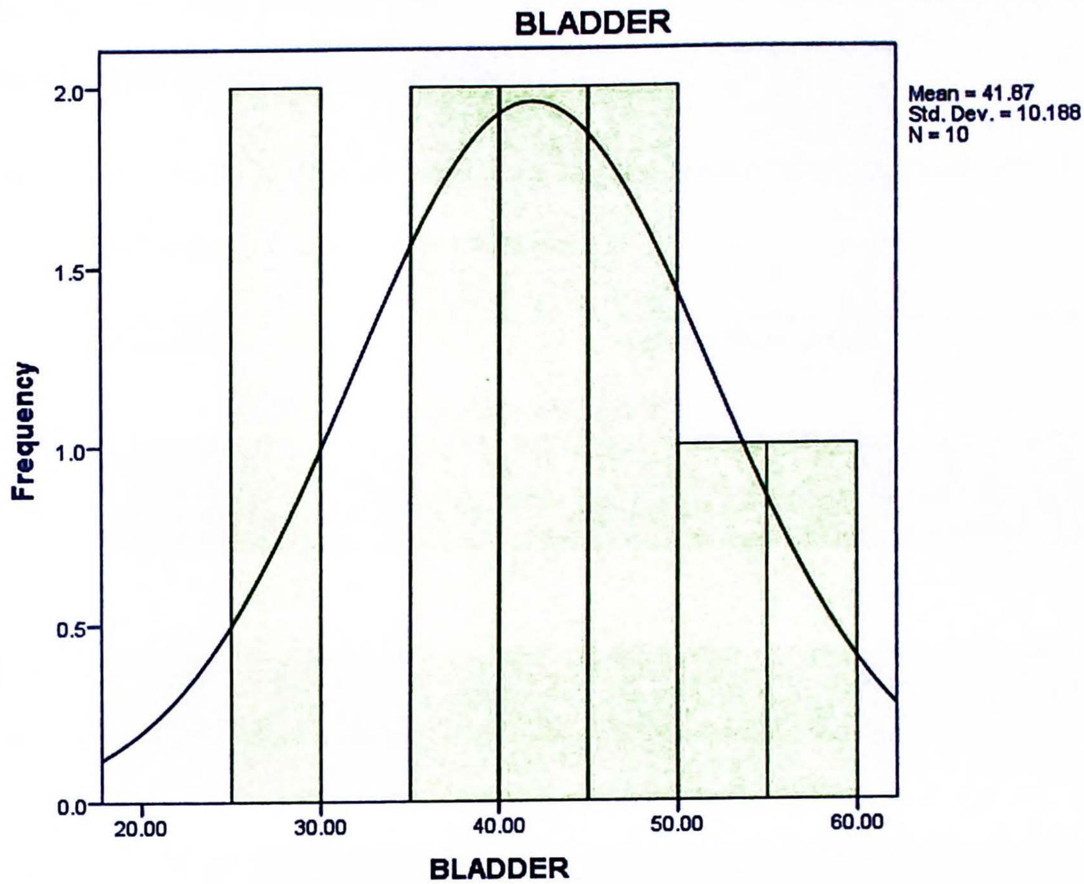

Figure 4.1.2: b) Histogram of bladder doses in percentage (number of patient versus. class interval of dose bladder in %)

Histogram of rectal and bladder dose distribution of 10 patients who underwent HDR intracavitary brachytherapy is shown in Figure 4.1.1(a) (b) and Figure 4.1.2 (a) (b) and along with normal distribution curves. The mean ± standard deviation of the distribution of rectal and bladder doses for fraction one are 38± 16% and 46 ± 17 % respectively. Then the mean ± standard deviation of the distribution of rectal and bladder doses for fraction two are 35± 13% and 41 ± 10 % respectively.

4.2 The total dose obtained from the pre-brachytherapy (external beam) and post-brachytherapy (external beam + ICBT).

Table 4.2.1: The total dose obtained from the pre-brachytherapy (external beam) and post-brachytherapy (external beam + ICBT).

No. Of patient	**Total Dose (cGy)**	
	Pre-brachytherapy (EBRT)	Post-brachytherapy (EBRT + ICBT)
1.	4500	5856.63
2.	4500	5751.32
3.	4500	6300.19
4.	4500	5978.59
5.	4500	5668.14
6.	4500	5763.16
7.	4500	5685.33
8.	4500	6077.03
9.	4500	6505.71
10.	4500	6016.21

Figure 4.1.2 below shown the graph that represent the total dose of post-brachytherapy (EBRT + ICBT) for each patient. During the external beam radiotherapy teatment, the doses given to each patient is 4500 cGy (45 Gy).

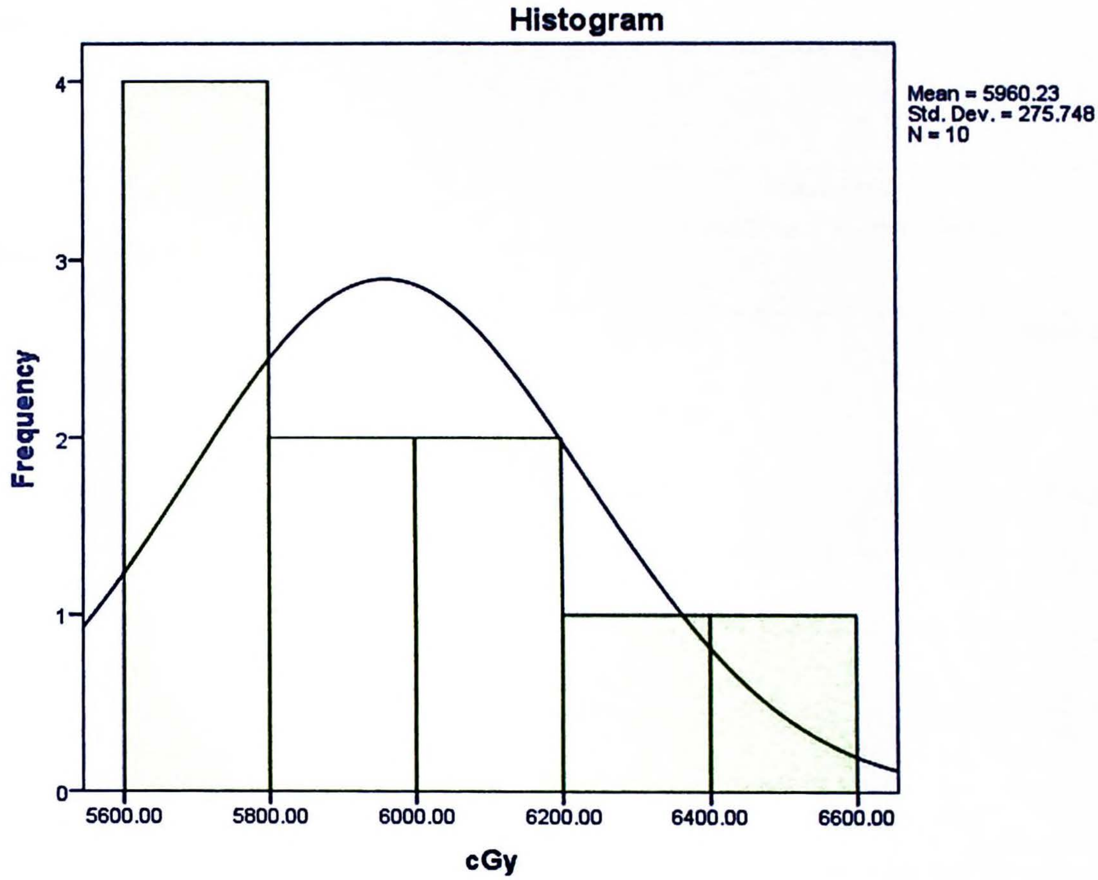

Figure 4.2.1: The total dose obtained from the pre-brachytherapy (external beam) and post-brachytherapy (external beam + ICBT).