# A COMPREHENSIVE 3D DOSIMETRIC ANALYSIS OF THE VIENNA RING APPLICATOR IN HIGH-DOSE-RATE (HDR) BRACHYTHERAPY FOR CERVICAL CANCER TREATMENT: TLD MEASUREMENT

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**by**

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## TABLE OF CONTENTS

## LIST OF TABLES

## LIST OF FIGURES

## LIST OF SYMBOLS

| | |
|---|---|
| $D_{2\%}$ | Dose to 2% of volume |
| $D_{50\%}$ | Dose to 50% of volume |
| $D_{90}$ | Dose received by 90% of volume |
| $D_{98\%}$ | Dose to 98% of volume |
| $GTV_{95\%PD}$ | 95% of prescribed dose to volume of GTV |
| $R_{avg}$ | Average response of all TLD |
| $R_i$ | Individual response of TLD |
| $V_{GTV}$ | Volume of GTV |
| $>$ | more than |
| ℃ | degree Celsius |
| cGy | centiGray |
| cGy/$\mu$C | centiGray per microcoulomb |
| CI | Conformity index |
| cm | centimeter |
| $D_{0.1cc}$ | Dose to 0.1cm$^3$ volume |
| $D_{1.0cc}$ | Dose to 1cm$^3$ volume |
| $D_{2cc}$ | Dose to 2cm$^3$ volume |
| g/cm$^3$ | gram per centimeter cube |
| Gy | Gray |
| Gy/hour | Gray per hour |
| HI | Homogeneity index |
| HR-CTV | High-risk clinical target volume |
| kVp | Peak kilo Volt |
| mAs | Milliampere per second |
| mm | millimeter |
| $\mu$C | microcoulomb |

## LIST OF ABBREVIATIONS

| | |
|---|---|
| 2D | Two-dimensional |
| 3D | Three-dimensional |
| AAPM | American Association of Physicists in Medicine |
| AMDI | Advanced Medical and Dental Institute |
| BT | Brachytherapy |
| CF | Calibration factor |
| CRT | Chemotherapy and Radiotherapy |
| CT | Computed Tomography |
| CTV | Clinical target volume |
| CV | Coefficient of variation |
| DICOM | Digital Imaging and Communications in Medicine |
| DVH | Dose-volume-histogram |
| EBRT | External Beam Radiation Therapy |
| ECC | Element correction coefficient |
| GTV | Gross tumour volume |
| HDR | High-dose-rate |
| IC | Intracavitary |
| IC/IS | Intracavitary-Interstitial |
| ICRU | International Commission on Radiation Units and Measurements |
| ID | Identification |
| Ir-192 | Iridium-92 |
| IS | Interstitial |
| IVD | In-vivo dosimetry |
| LDR | Low-dose-rate |
| MDR | Medium-dose-rate |
| MRI | Magnetic resonance imaging |
| OAR | Organ at risk |
| PD | Prescribed dose |
| P-ISBT | Perineal-based interstitial brachytherapy |
| PMMA | Polymethyl methacrylate |
| PSQA | Patient-specific quality assurance |

| | |
|---|---|
| QA | Quality Assurance |
| ROI | Region of interest |
| SD | Standard deviation |
| SPSS | Statistical Packages for the Social Sciences |
| TG-43 | Dosimetry of Interstitial Brachytherapy Sources |
| TLD | Thermoluminescence dosimeter |
| TLE | Thermoluminescence efficiency |
| TPS | Treatment Planning System |

## LIST OF APPENDICES

**ANALISIS DOSIMETRIK 3D APLIKATOR VIENNA RING DALAM KADAR DOS TINGGI (HDR) UNTUK RAWATAN KANSER SERVIKS: PENGUKURAN TLD**


## ABSTRAK

**Pengenalan:** Brakiterapi intrakavitari merupakan pendeketan yang paling biasa digunakan untuk kanser ginekologi yang kebetulan menjadi kanser yang paling kerap berlaku di kalangan wanita. Brakiterapi intrakavitari-interstisial (IC/IS) adalah pendekatan yang sedang dibangunkan, dan pelbagai aplikasi digunakan dalam kaedah rawatan ini seperti aplikator Vienna Ring. Walaubagaimanapun, pemahaman yang komprehensif mengenai sifat dosimetrik aplikator Vienna Ring amat diperlukan untuk penggunaan yang berkesan dalam brakiterapi untuk kanser serviks. **Tujuan:** Kajian ini bertujuan untuk menganalisis ciri-ciri dosimetrik aplikator Vienna Ring dalam aspek liputan atas sasaran (tumor), penyelamatan organ berisiko (OAR) dan keupayaan untuk menyampaikan dos yang direncanakan semasa rawatan. **Kaedah dan Bahan:** Aplikator Vienna Ring dipasang dalam fantom pelvis dengan cip dosimeter Termoluminesen (TLD-100) sebagai penanda yang dilampirkan kepada OAR (pundi kencing dan rektum). Imej Tomografi Komputer (CT) diperolehi untuk perancangan rawatan. 7Gy telah dipreskripsikan untuk iradiasi dan rawatan telah dirancang untuk penilaian dos yang diterima oleh sasaran (tumor), OAR dan TLD pada 8 posisi. Dos yang diterima oleh cip TLD-100 semasa iradiasi sebenar dan dos yang dikira oleh Sistem Perancangan Rawatan (TPS) pada titik TLD diperbandingkan. **Keputusan:** Dos yang diterima oleh sasaran, pundi kencing dan rektum ialah 7.1Gy, 2.4Gy dan 7.4Gy. Daripada 8 TLD, 7 TLD mempunyai perbezaan dos kurang daripada 20% manakala 1 TLD (F7) mempunyai perbezaan dos sebanyak 31.03% antara dose yang

diukur dan dos yang dikira. **Kesimpulan:** Aplikator Vienna Ring memberi distribusi dos yang tidak seimbang tetapi mempunyai kepatuhan yang tinggi. Toleransi dos untuk pundi kencing telah dicapai tetapi dos untuk rektum telah melebihi. Walaubagaimanapun, 90% perbezan dos antara TLD dan TPS adalah kurang daripada 20%. Aplikator Vienna Ring dapat menyampaikan dos yang direncanakan semasa rawatan sebenar.

**Kata kunci:** ***brakiterapi, kanser serviks, aplikator Vienna Ring, TLD, TPS***

# A COMPREHENSIVE 3D DOSIMETRIC ANALYSIS OF THE VIENNA RING APPLICATOR IN HIGH-DOSE-RATE (HDR) BRACHYTHERAPY FOR CERVICAL CANCER TREATMENT: TLD MEASUREMENT


## ABSTRACT

**Introduction:** Intracavitary brachytherapy is the most common approach used for gynecological cancers which happens to be the cancer with highest occurrence among women. Intracavitary-interstitial (IC/IS) brachytherapy is an approach that is developed, and various applicators are utilised in this treatment method such as the Vienna Ring applicator. However, a comprehensive understanding on the dosimetric behavior of Vienna Ring applicator is required for efficient use in brachytherapy for cervical cancer. **Purpose:** This study aims to experimentally analyse the dosimetric performance of Vienna Ring applicator in aspects of target coverage, organ at risk (OAR) sparing and ability to deliver the planned dose during treatment. **Methods and Materials:** A Vienna Ring applicator was assembled in a pelvic phantom with Thermoluminescence Dosimeters (TLD-100) chips were attached to the OARs (bladder and rectum) to act as markers. Computed Tomography (CT) images were obtained for treatment planning. 7Gy was prescribed for irradiation and the treatment was planned for the assessment of dose received by target, OAR and the TLDs at 8 points. The dose measured by the TLD-100 chips during the irradiation and dose calculated by treatment planning system (TPS) on the TLD points were compared. **Results:** The dose received by target, bladder and rectum are 7.1 Gy, 2.4 Gy and 7.4 Gy respectively as obtained from TPS. Out of 8 TLDs, 7 TLDs have dose deviation less than 20% while 1 TLD (F7) have dose deviation of 31.03% between measured and calculated dose. **Conclusion:** The dose distribution of Vienna ring applicator to

GTV is not homogenous but has high degree of conformity. The Vienna ring applicator was able to spare the bladder and deliver optimum dose to tumour. The Vienna ring applicator can deliver planned dose during treatment delivery due to 90% of the dose deviation was below 20%. Therefore, the applicator can be categorised as a reliable applicator in brachytherapy for cervical cancer.

**Keywords:** ***brachytherapy, cervical cancer, Vienna Ring applicator, TLD, TPS***

# CHAPTER 1

# INTRODUCTION

## 1.1 Background of Study

Gynecological cancers can be treated using various treatment modalities and the most common treatments are surgery, chemotherapy, radiation therapy and targeted therapy (Rijkmans et al., 2014). Cervical cancer is researched as one of the most highly found cancer in women worldwide in which the annual incidence is 530 000 cases and 250 000 deaths. Surgery will be the treatment option for early stages of cervical carcinoma. However, most of the patients present with bulky or locally advanced diseases, hence these patients are treated using concurrent chemotherapy with radiotherapy (Khan et al., 2022). Radiotherapy is usually given with a combination of external beam radiotherapy (EBRT) and brachytherapy while brachytherapy is known as a standard therapy for cervical cancer in which it delivers high dose radiation dose to tumour while sparing surrounding healthy tissue (Morton et al., 2010).

Brachytherapy is a form of radiation therapy where a sealed radioactive source is placed directly into or near the tumor (Chargari et al., 2019) and brachytherapy alone is known to be effective in treating cancers in various sites of the body (Jreij et al., 2023). D'avino et al. (2020) stated that brachytherapy can be used to treat cancer in cervix, prostate, skin, breast, and gynaecological malignancies. Moreover, low-dose rate (LDR) brachytherapy was used for cervical cancer treatment, but high-dose rate (HDR) brachytherapy has been increasingly preferred due to the advantages such as reduced hospitalization and reduction in radiation hazards.

There are various techniques in which brachytherapy can be performed for cervical cancer, either using intracavitary (IC), interstitial (IS) or a combined intracavitary-interstitial (IC/IS) approach. The choice among the three treatment delivery techniques

depends on disease extent and anatomy (Kamrava & Banerjee, 2014). The type of applicators varies with the technique chosen to deliver the treatment. The Vienna Ring applicator is a hybrid IC/IS applicator that can be used for HDR or pulsed-dose-rate (PDR) brachytherapy. It is a modified version of a tandem and ring applicator in which the ring has holes where titanium or plastic needles can be inserted (Martin, D. A. et al., 2021).

Vienna Ring applicator has been studied by previous researchers. However, the dosimetric performance of this applicator should be analysed to ensure treatment precision and efficacy. Hence, the purpose of this study is to conduct a 3D dosimetric analysis of the Vienna Ring applicator within HDR brachytherapy for cervical cancer treatment.

### 1.2 Problem Statement

The treatment for women with cervical cancer involves EBRT and brachytherapy. There are various designs of applicators available for cervical cancer brachytherapy with tandem and ovoid and it is reported to be the most frequently used applicator for cervix cancer with 75% of cases followed by tandem and ring with a reported number of 24% of cervix cases (Viswanathan et al., 2012). The applicator choice depends on the fit of the applicator to the normal or pathologic anatomy, the ease of applicator insertion, availability of the applicator and the physician's preference.

The advancement in brachytherapy has led to the development of modern intracavitary-interstitial brachytherapy applicators where the classic tandem and ovoid or tandem and ring applicator is modified by placing needles. Intracavitary-interstitial applicators such as Vienna Ring applicator was developed due to conventional intracavitary applicators alone deemed to be not suitable to deliver dose to large tumour at the parametrium and lower vagina region (Aggarwal et al., 2021).

Currently, the experimental verification of the applicator has not been done. Few methods that had been used to verify the performance of the applicator is by using mechanical techniques such as position accuracy and timing accuracy.

However, the dosimetric behaviour using critical measurements such as analysing dose distribution to target and sparing of healthy tissue in utilizing this applicator for cervical cancer brachytherapy is essential to be studied for accurate treatment delivery. There is a requirement to experimentally verify the dosimetric performance of the Vienna Ring applicator and to confirm that the intended dose is delivered when the applicator is used for treatment.

## 1.3 Research Objective

### 1.3.1 General Objective:

To study the 3D dosimetric analysis of Vienna ring applicator in HDR brachytherapy for cervical cancer treatment for the enhancement of treatment precision and efficacy.

### 1.3.2 Specific Objectives:

1. To calibrate Thermoluminescence Dosimeter (TLD) using Ir-192 source.
2. To assess dose distribution to target and healthy tissue sparing achieved by Vienna ring applicator in the treatment plan.
3. To compare the measurements between Thermoluminescence Dosimeters (TLD) and dose calculated by Treatment Planning System (TPS) and acquire percentage deviation of the planned and measured dose to the organ at risk (OAR).

## 1.4 Significance of Study

Intracavitary brachytherapy has been the mostly used form of brachytherapy for cervical cancer. Thus, the utilisation and understanding about intracavitary

brachytherapy and the applicators is more significant than the combined approach of intracavitary and interstitial approach for cervical cancer treatment. In this study, we analysed the dosimetric performance of an intracavitary-interstitial (IC/IS) applicator, the Vienna Ring applicator from the aspects of dose distribution, target coverage and dose to OAR. The efficacy of the Vienna Ring applicator is also explored by analysing the dose deviation between the measured dose and calculated dose by utilising Thermoluminescence Dosimeter (TLD) and Treatment Planning System (TPS) to investigate the ability of the applicator to deliver the intended dose during treatment. The findings of the study provide better understanding of IC/IS approach and applicators to implement the advantages of these different techniques to improve usage of brachytherapy in the treatment of cervical cancer. Medical physicists, radiation oncologists, radiotherapists, researchers and students will have a broader knowledge on brachytherapy and the need to explore different applicator for a more efficient use in treatment of cervical cancer. The study on this applicator can lead to an improved and advanced research in both brachytherapy and cervical cancer.

# CHAPTER 2

# LITERATURE REVIEW

## 2.1 Treatment for Cervical cancer

Cervical cancer is diagnosed in about 500,000 women worldwide each year, and over 300,000 women die from the disease. Infection with high-risk variants of the human papillomavirus is the primary risk factor for the development of cervical cancer (Otter et al., 2019). The treatment given is based on the severity of the disease and locally available resources (Cohen et al., 2019). Surgery is a treatment technique that includes the physical removal of malignant tissue and is the frequently utilised and effective procedure of numerous early-stage malignancies (Burmeister et al., 2022).

Li et al conducted a study to investigate the effects of primary site surgery on individuals with stage 4B (IVB) cervical cancer by employing population-based database. The retrospective analysis included individuals with stage IVB cervical cancer who were undergoing chemotherapy and radiation therapy (CRT). The overall 5-year survival rate was 25.7% and compared to CRT alone, surgery of the primary sites appeared to extend the survival rate. Nevertheless, it merits extensive prospective clinical trials to confirm. For locally advanced cervical cancer, external beam radiotherapy (EBRT) combined with concurrent chemotherapy and brachytherapy boost is the standard protocol (Williamson et al., 2021). Brachytherapy and external beam radiotherapy are major treatment procedures for cervical cancer (Chargari et al., 2022). However, brachytherapy provides dosimetric advantages with extremely steep radiation dose gradients compared to EBRT (Chargari et al., 2019). Brachytherapy is performed either in conjunction with EBRT or following the completion of EBRT. Smaller brachytherapy treatment volumes are possible if the treatment is delivered

later in the treatment cycle due to maximum tumour shrinkage (Kamrava and Banerjee, 2014).

### 2.2 High-dose-rate (HDR) Brachytherapy

The International Commission on Radiation Units and Measurements report 38 (ICRU-38) states that there are 3 types of brachytherapy based on the activity of radioactive source. Brachytherapy can be categorised based on dose rate in which can be divided into low, medium, high, and pulsed dose rate. Low-dose rate (LDR) implants can be utilised with manual or remote afterloading procedures and they deliver dose at the rate of 0.4-2 Gy/hour. The range of medium-dose rate (MDR) brachytherapy is 2-12 Gy/hour. Although remote afterloading is significantly more common, manual afterloading is also an option for MDR delivery. High-dose rate (HDR) brachytherapy delivers dose rate of 12 Gy/hour or more due to the high source activity, therefore only remote afterloading is possible for this type of treatment. High dose rate (HDR) brachytherapy has been explored and utilised more in recent years for cervical cancer treatment. The main benefit of HDR brachytherapy is the short treatment time (Yavaş, 2019). Patankar et al. (2015) performed an analysis and concluded the outcome of HDR brachytherapy for women with cervical cancer. HDR brachytherapy has the advantage in optimising dose to normal tissue, eases the administration and proves to have an upper hand in patient convenience compared to LDR brachytherapy. Although they concluded that the survival rate for cervical cancer using HDR and LDR brachytherapy is similar, HDR is picked as the primarily used technique due to the presence of clinical advantages.

Furthermore, HDR brachytherapy has the superiority over LDR due to the availability of after-loading which leads to the reduced radiation dose to the personnel, shorter treatment time and prevention of complications caused by prolonged immobilization

during LDR treatment (Song, J. et al., 2021). Song, J. et al. conducted a review on the transition from LDR brachytherapy to HDR brachytherapy in treating locally advanced cervical cancer with combined EBRT and concurrent chemotherapy by investigating the effect of this change on patient outcome. They found that five-year progression-free survival and overall survival were 63.7% and 69.3% respectively where the disease control for cervical cancer remained better when EBRT is combined with HDR intracavitary brachytherapy (ICBT) and concurrent chemotherapy instead of LDR brachytherapy.

### 2.3 Advantages of Intracavitary-interstitial (IC/IS) Brachytherapy (BT)

Brachytherapy can be delivered using IC, IS or a combined approach which is known as intracavitary-interstitial brachytherapy. Intracavitary brachytherapy (ICBT) is the common practice of brachytherapy for cervical cancer and the two most usually used applicators are tandem and ovoid or tandem and ring applicators. By implementing ICBT, the uterus, cervix and upper vagina are all treated by inserting the radioactive source through the vaginal cavity using an applicator (Kamrava & Banerjee, 2014). With decades of experience, ICBT is the most suitable technique for superficial and small volume lesions. However, disadvantages such as inadequate dose, poor target volume coverage, or excessive radiation to organ at risk (OAR) might occur when the tumour is large, eccentrically placed, or irregularly shaped (Qu et al., 2021). As for interstitial brachytherapy (ISBT), it is applied when intracavitary approach is found to be not suitable and this approach uses a transperineal template where hollow tubes are inserted into tissues and catheters are inserted directly into and surrounding the residual disease. The transperineal templates used in interstitial brachytherapy are Martinez Universal Perineal Interstitial template (MUPIT) and Syed-Neblett template

with tandem and vaginal cylinder included in the template (Kamrava & Banerjee, 2014).

The applicators used for IC/IS approach is different in which MUPIT and Syed-Neblett template were used as IC/IS applicators in early days (Aggarwal et al., 2021). IC/IS applicators provide advantages such as covering additional region of the tumour compared to IC applicators (Rogowski et al., 2022). According to Aggarwal et al. (2021), modern IC/IS has been developed for the purpose of being computed tomography (CT) or magnetic resonance (MR) compatible. Example of applicators are Vienna Ring applicator, Utrecht applicator, Venezia applicator, Geneva applicator etc. as in Figure 2.1.

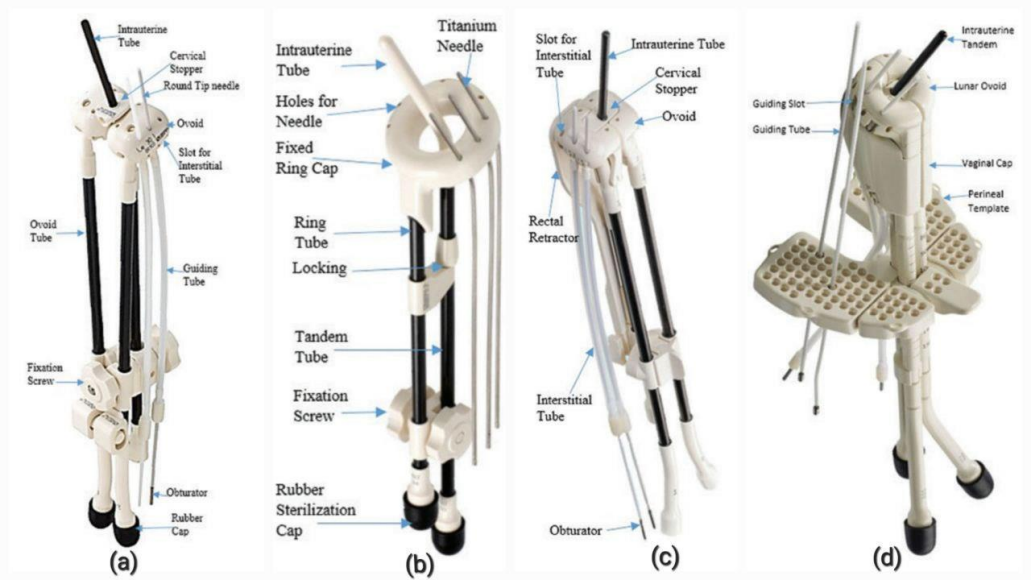


Figure 2. 1. Examples of Intracavitary-Interstitial (IC/IS) applicators (a) Utrecht applicator, (b) Vienna Ring applicator, (c) Geneva applicator, (d) Venezia applicator (Aggarwal, Mourya and Choudhary, 2021)

The literatures found for this study suggest that IC/IS BT has advantages compared to ICBT. Fokdal et al. (2016) conducted a study to evaluate the impact of combined IC/IS BT on local control and late morbidity. The study was conducted by dividing 310

patients in an IC group and 300 of them in IC/IS group and were followed up for morbidity, disease status and dose reporting according to specific timelines. It was found that $D_{90}$ of clinical target volume (CTV) increased from 83 $\pm$ 14Gy to 92 $\pm$ 13Gy which shows better target coverage for IC/IS BT although there was no significant difference found in dose to organ at risk (OAR) and late morbidity between IC and IC/IS group. Hence, they concluded that IC/IS BT can result in higher local control in large tumours without causing additional treatment related late morbidity.

Mendez et al. (2017) performed a systematic review on relevant studies to evaluate toxicities and local control of perineal-based interstitial brachytherapy (P-ISBT) in cervical cancer treated with three-dimensional (3D) image-based planning. The result suggested that P-ISBT with 3D image-based planning provides better local control rates in patients with cervical cancer where a local control rate of 79% was found although 60% of the studied population has stage IIIB disease. It was concluded that cervical cancer treated with P-ISBT serves as an effective and safe treatment for large cervical tumours. Although the study was performed for perineal template, the study also suggested that IS approach by using interstitial needles increases conformality of the delivered dose. Mendez et al. concluded that IS approach allows a safe dose escalation and better therapeutic ratio.

Fokdal et al. (2013) conducted a study to investigate the feasibility of a combined IC/IS BT in locally advanced cervical cancer by utilising magnetic resonance imaging (MRI) with a tandem and ring applicator. They inserted interstitial needles in an intracavitary ring applicator through a custom-made needle cap made using 3D printing. The results concluded that the combined IC/IS applicator is clinically feasible in terms of acute toxicity and 30-days morbidity. From the study, they concluded that the pre-planned

needle positions were reproducible to a large degree which led to improved dose-volume-histogram (DVH) parameters and safe implant of the applicator.

Kamrava and Banerjee (2014) have presented in their literature on the applicator selection for cervical cancer brachytherapy. The red tumour in Figure 2.2 is small at the time of diagnosis and led to the perfect fitting of the green tandem and ovoid. The orange dose distribution can be observed to appropriately cover the disease. However, the red tumour in Figure 2.3 is presented to be large, thus an interstitial approach using multiple tubes (green) is applied to cover the extent of the residual disease. It is stated that the coverage for the full extent of this tumour would not be possible by using intracavitary approach.

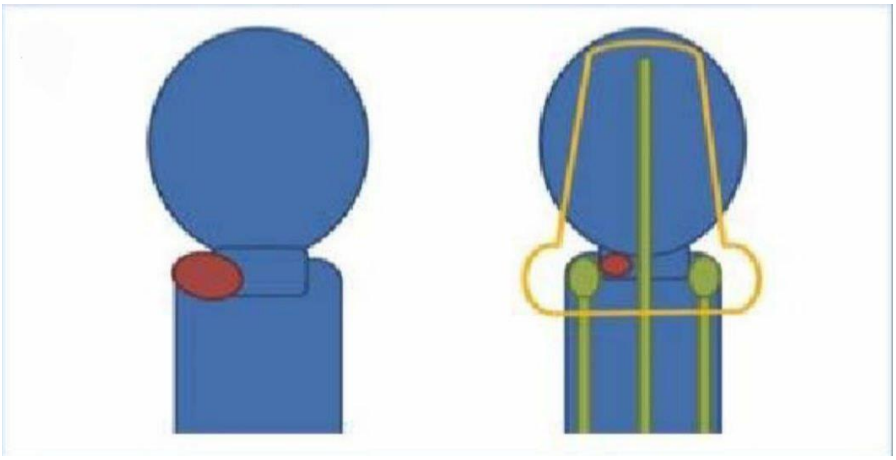

Figure 2. 2. Intracavitary approach (Kamrava and Banerjee, 2014)

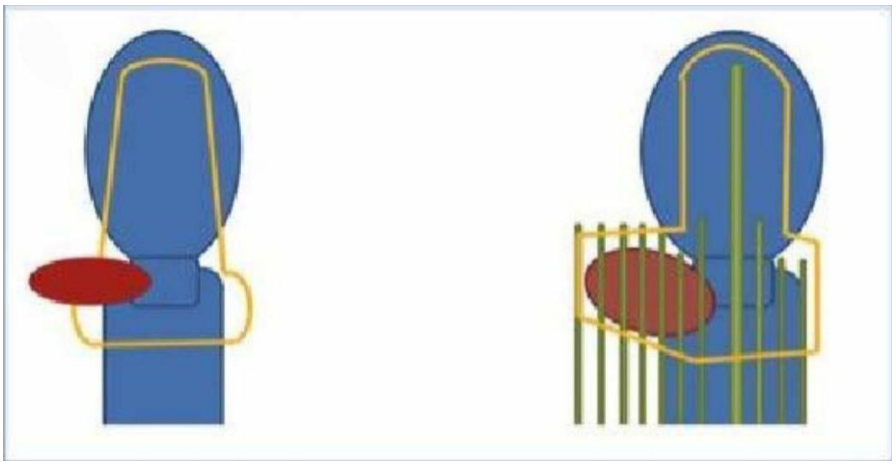

Figure 2. 3. Intracavitary-interstitial approach (Kamrava and Banerjee, 2014)

### 2.4 Thermoluminescence Dosimeter (TLD)

TLD is a radiation detecting device where a process called thermoluminescence (TL) occurs when the dosimeter is exposed to ionising radiation (França, Oliveira and Baffa, 2019). TLDs are widely utilised in radiation dosimetry because of numerous advantages including high sensitivity, small size, and capability to measure low doses. The thermoluminescence properties of TLD is largely dependent on the crystal structure of TLD materials, particularly LiF and $CaF_2$. LiF, for instance, has a face-centred cubic structure that produces low fading rates and high sensitivity to ionising radiation. TLD properties include sensitivity and reproducibility. The term 'sensitivity' refers to the capacity of the TLD materials to detect and respond to low doses of ionising radiation while reproducibility is the ability of TLD to produce same TL signal when irradiated multiple times (Efenji et al., 2024).

When exposed to ionising radiation, the detector material ionises and promotes electrons to the conduction band, leaving holes in the valence band. Until the electrons recombine or are caught by defects, forming an electron trap, these electrons and holes can move freely within respective energy bands. Heat-induced stimulation releases the

trapped charges during the readout process and the trapped electrons recombine with the trapped hole to form a defect in the excited state. Light is emitted and the intensity of the light is proportional to the radiation dose detected. The resultant luminescence is converted into current by a photomultiplier tube (Kry et al., 2019). The working process is shown in Figure 2.4.

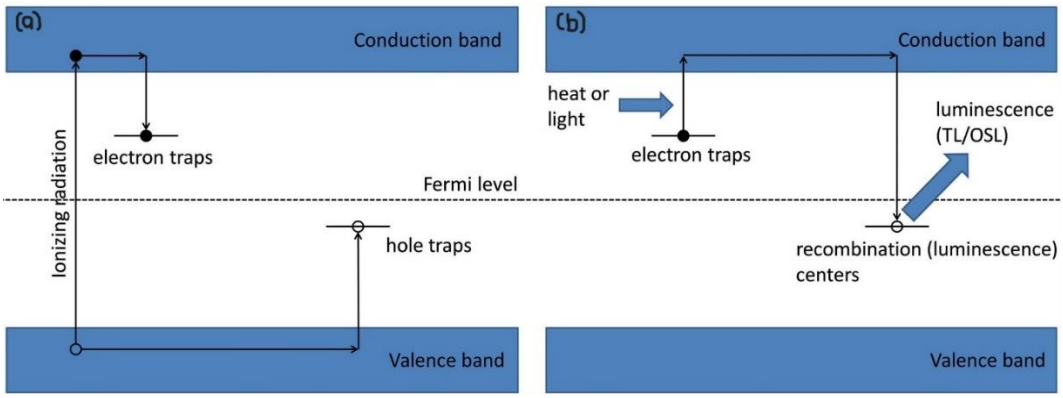


Figure 2. 4. Energy level diagram presenting delocalised bands and electronic transition in TLD during (a) Irradiation process (b) Readout process (Kry et al., 2019)

TLD is used to measure dose in this study by reviewing the literatures that provided evidence on the reliable performance of this dosimeter.

D'avino et al. (2020) investigated the performance of TLD type 100 (TLD-100) in dose verification of HDR treatment with iridium-192 (Ir-192) source where the TLDs were fixed on specific points in a head and neck phantom. The dose measured by TLD-100 was comparable with the expected dose calculated in treatment planning system (TPS), which allowed the researchers to conclude that TLD-100 has good performance and reliability in radiation field investigated.

Jaberi et al. (2022) utilised micro silica bead TLDs in evaluating the feasibility of defining an in vivo dosimetry (IVD) protocol as a patient-specific quality assurance (PSQA) for point. The experimentally obtained absorbed dose by the bead TLDs were compared with the predicted dose by TPS. The result concluded that a 3D IVD protocol implementing bead TLDs to measure absorbed dose delivered to the OAR during gynaecological HDR-BT is a reliable method.

### 2.5 Treatment Planning System (TPS)

This study includes brachytherapy treatment planning for Vienna Ring applicator. TPS is a very crucial component in brachytherapy to deliver an optimum radiation dose to the tumour and lowest dose to surrounding healthy tissue. TPS is essential for the effective use of radiotherapy as it has a direct impact on the treatment planning quality and the precision in dose calculation (Fitriyani et al., 2020). In TPS, contouring, catheter reconstruction, activation, normalisation of dose, optimisation and dose prescription can be performed for brachytherapy. The aim of catheter reconstruction includes matching the anatomical geometries, determining the source path and most distal dwell position. Catheter reconstruction can be done manually. However, there is an alternative reconstruction method that has been in practice which is by using applicator library with precise 3D models. By using reference points located in both the image and model, the corresponding applicator can be chosen, moved and rotated until it aligns with the image. Even so, this method excludes the interstitial part and is only applicable for rigid applicators. Hence, the only method available to reconstruct the needle is by reconstructing manually (Otal et al., 2022).

### 2.6 Comparison between TLD and Treatment Planning System (TPS)

The dose measured by TLDs, and the dose estimated by TPS are compared to obtain the percentage deviation and ensure an effective treatment in using the Vienna Ring applicator in this study.

Elywa et al. (2019) performed research to estimate surface skin dose for patients who undergo breast radiotherapy. They utilised TLDs to measure the dose at 6 different point and investigated if the measurement has significant difference with dose estimated by TPS. The deviation between the results from TLD measurements and TPS calculations are obtained using an equation and presented in percentage. There were positive difference and negative difference found between the values with the highest percentage difference being 25% while the lowest is -4%.

Bahreyni Toossi et al. (2017) wanted to quantify the dose calculation accuracy of a TiGRT TPS for head and neck region by comparing the dose measured by TLD (TLD-100) in RANDO phantom and the dose calculated by TPS. It was proved that TLD can be used for verification of dose calculated by TPS. The highest percentage difference was 26.97% and the lowest percentage difference obtained was 4.97%. The study referred to TECDOC 1540 and TRS 430 protocols and concluded that the percentage difference for most points were within tolerance limit which is 4% and 50% for in-field regions and outside field regions respectively.

### 2.7 Dose to Tumour (GTV) and OAR

The objective of the treatment is to expose and treat the tumour. However, not only the cervix but also the healthy organs adjacent to it, such as the bladder and rectum are exposed to radiation. These organs are known as OAR and they become very

susceptible to radiation when exposed to doses higher than their tolerance (Wibowo et al., 2017).

When the OARs receive dose exceeding tolerance, it will result in toxicities. Toxicity results in reduced quality of life after EBRT and HDR brachytherapy. The rectum and bladder are two organs that are particularly vulnerable (Chanda et al., 2019) as it is most adjacent to cervix.

Estimation of radiation toxicity in HDR brachytherapy requires the evaluation of dose received by OAR (Singh et al., 2019). According to American Brachytherapy Society (ABS), the $D_{2cc}$ which is the minimum dose to the most exposed to $2cm^3$ of tissue (Zhao et al., 2023) should be $\leq$ 90 Gy for bladder and $\leq$ 75 Gy for rectum. When tolerance doses are exceeded for the OARs, there is high possibility for adverse side effect such as incontinence, cystitis, dysuria, fistulas and hematuria (Chanda et al., 2019).

Romano et al. (2018) retrospectively investigated the incidence and risk variables causing genitourinary (GU) and gastrointestinal (GI) toxicity after ICBT for locally advanced cervical cancer. At the end of the study, GU adverse complications occurred in 23.3% of patients and severe adverse event (grade of 3 or above) occurred in 4 patient (7.1%). Among the 4 patients, 1(25%) had bladder $D_{2cc} \leq$ 80Gy, 1(25%) had $D_{2cc}$ of 80-90 Gy and 2 (50%) had bladder $D_{2cc} >$ 90Gy. As for rectal toxicity, 15 individuals (26.8%) suffered a severe GI complication. Severe GI adverse issues occurred in 8 patients (14.3%) where 3 (37.5%) had $D_{2cc}$ of 65-75 Gy, 3 (37.5%) had $D_{2cc} >$ 75 Gy and 2 (25%) had rectal $D_{2cc}$ of $\leq$ 65 Gy. Hence, it was proven that when dose exceeding the tolerance limit is delivered to the OAR, the toxicity is increased to that specific organ.

ICBT and ISBT technique has difference in target coverage and dose delivered to OAR. Zhang et al. (2021) compared the dose to target and OAR and treatment-related complications to investigate difference between Fletcher applicator and needle insertion approach in patients with cervical squamous cell carcinoma. When compared with the needle insertion group, the mean value of $D_{90}$ per fraction for high-risk clinical target volume (HR-CTV) and intermediate-risk clinical target volume (IR-CTV) in the Fletcher applicator group were 101cGy and 60cGy lower, respectively. There was no statistically significant difference in the mean $D_{2cc}$ and $D_{1.0cc}$ per fraction between the two groups for the bladder. However, the $D_{0.1cc}$ per fraction in the Fletcher group was 32cGy lower than that in the needle insertion group. Furthermore, the mean $D_{2cc}$ and $D_{1.0cc}$ per fraction did not differs significantly between the two groups for rectum, but the $D_{0.1cc}$ per fraction in the Fletcher applicator group was 48cGy higher than that in the needle insertion group. Zhang et al. concluded that when brachytherapy with needle insertion technique is used, instead of standard applicators, larger tumour volume with high target dose can be treated. In addition, the OAR from this study received lower dose for needle insertion approach, which suggests that it is a secure and reliable method that should be applied widely. This shows that the type of applicator or brachytherapy technique influences the target coverage and dose to OAR.

The dose received by target and OAR can be evaluated by dose volume histogram (DVH). The result in TPS is presented in the form of DVH which displays correlation between volume of tumour and OAR with the dose on the target and OAR. This histogram is often shown with the dose on the abscissa (y-axis) while the ordinate (x-axis) as a percentage by volume of the total volume (Wibowo et al., 2017).

The dose prescription by radiation oncologist is determined using the DVH curve. The DVH causes the accuracy of TPS calculation on the tissue volume to have significant impact on radiotherapy's success. DVH has become a common tool for assessing radiotherapy treatment planning (Fitriyani et al., 2020).

Wibowo et al. (2017), conducted a study to assess the radiation dose to rectum and bladder using two-dimensional (2D) and three-dimensional (3D) calculation. The International Commission on Radiation Units and Measurements (ICRU) points, $D_{ICRU}$, served as the basis for 2D calculation of radiation doses whereas DVH on a volume of 2cc ($D_{2cc}$) serves as the basis for 3D calculation. With ratios of 1.10227 for the bladder and 1.28127 for rectum, the radiation dose to the bladder and rectum using 3D method was greater than that in 2D method. However, the radiation dose to both bladder and rectum remained below the tolerance. Hence, they concluded that 3D calculation for the dose of bladder and rectum was more accurate than 2D calculation method as 3D method considered the whole volume of the organ

# CHAPTER 3

# MATERIALS AND METHODS

## 3.1 Dosimeters and Annealing

The TLDs used for this work are the LiF:Mg,Ti (TLD-100) chips with dimensions 0.3 cm x 0.3 cm x 0.1 cm. The TLD chips were transferred to an annealing plate with dimensions 8.3 cm x 10.3 cm x 0.4 cm to be placed in the PTW TLD annealing oven. The TLDs were annealed according to the heating profile which is separated into 5 segments prior to each irradiation. All the TLDs were annealed at 400℃ for 1 hour followed by 5 minutes at the same temperature, 100℃ for 20 minutes followed by 2 hours at the same temperature and finally the TLDs were annealed at 50℃ for 5 minutes. The heating profile of TLD-100 chips is presented in Appendix A. The TLD-100 chip, annealing plate and oven are shown in Figure 3.1.

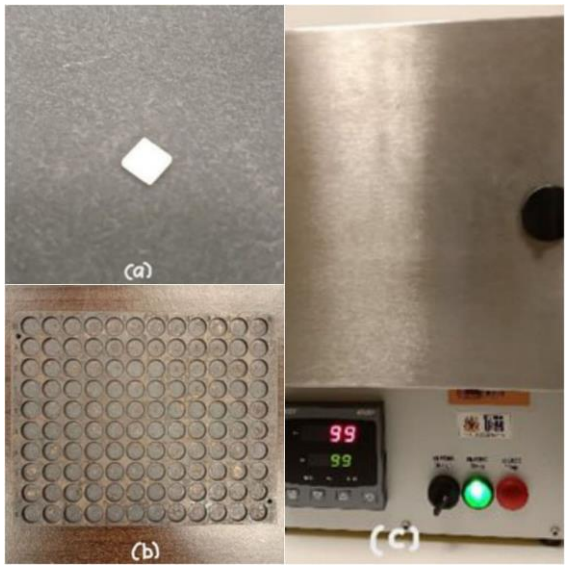


Figure 3. 1. (a) TLD-100 chip, (b) Annealing plate, (c) PTW TLD Annealing Oven

### 3.2 Calibration and Readout of TLD-100

The TLDs were calibrated using the Microselectron HDR digital afterloading system with Iridium-192 source (Ir-192). The afterloading system consists of a treatment unit that contains Ir-192 radioactive source, source safe, channel selector, source drive and control electronic. The system also includes a treatment control station which is a computer with dedicated software that functions to guide the user on the treatment workflow and delivery. A treatment control panel is included in the afterloading system in facilitating the starting and interruption of the treatment sessions.

A polymethyl methacrylate (PMMA) irradiating plate with 1.18 g/cm$^3$ (Figure 3.2) with dimensions 30.0 cm x 30.0 cm x 1.1 cm, 13 solid water phantoms, 1.0 cm and 0.5 cm bolus and a catheter was used to construct the setup and perform the TLD calibration. 10 TLD-100 chips with identification number (ID) ranging from F1 to F10 were arranged in an irradiating plate at the center position, which is the (e) column using forceps. According to the calibration plan, 1.0 Gy was planned to be delivered 4.5 cm distance from the source which is at the central position. A 24 cm catheter was secured to the 1.0 cm bolus with dimensions 30 cm x 30 cm x 1.0 cm using micropore and was positioned between 4 solid water phantoms together with 0.5 cm bolus placed on the 1.0 cm bolus attached with catheter. The irradiating plate that consists of TLD chips was placed 4.0 cm below the bolus and both the bolus were adjusted accordingly so that the catheter is at the same position of the arranged TLD chips.

The TLDs placed were at the center region of the irradiating plate. Thus, both the 1.0 cm bolus with the catheter and 0.5 cm bolus were pushed 3.5 cm anteriorly to ensure that all the 10 TLDs are exposed to 1.0 Gy as planned. The illustration of calibration setup is shown in Figure 3.3.

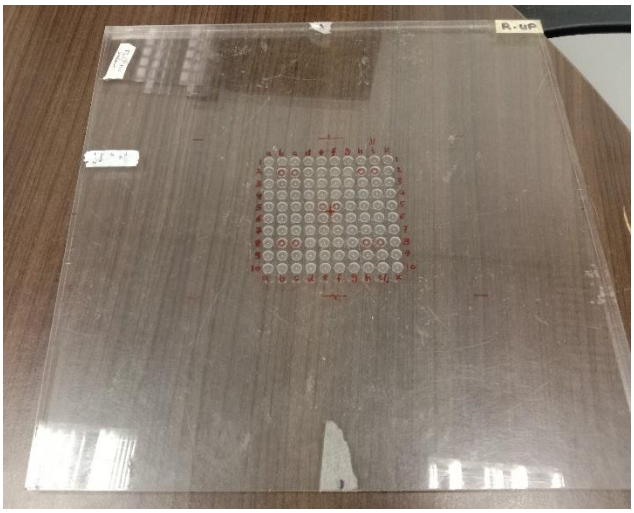

Figure 3. 2. PMMA irradiating plate

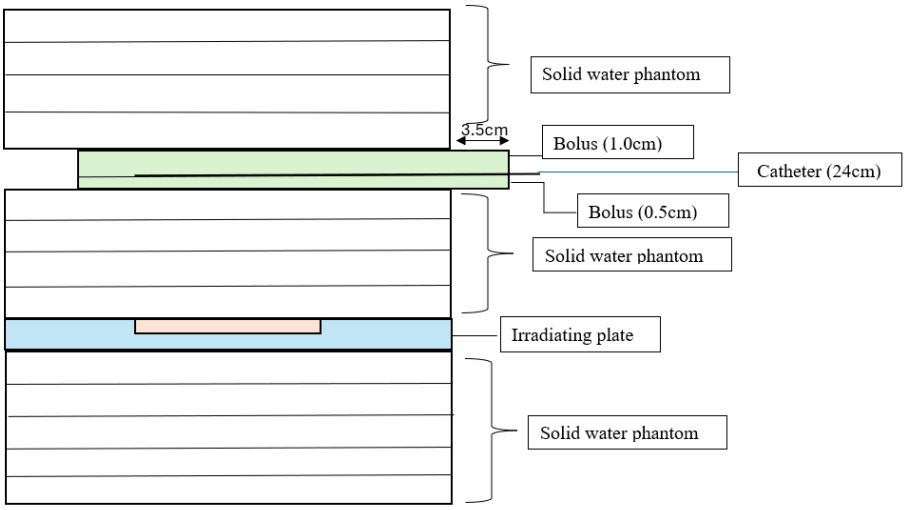


Figure 3. 3. Illustration of TLD Calibration Setup

Calibration plan was done based on a pre-existing CT image. The setup was then modified during calibration to ensure that 1.0 Gy is delivered to the TLDs positioned at the center region of the irradiating plate. The activation of the plan was applied to 10.0 cm of the catheter.

After each irradiation, the readout of the TLDs was performed using a Harshaw model 3500 manual TLD reader (Figure 3.4) installed in Department of Oncology and Radiotherapy of Advanced Medical and Dental Institute (AMDI) with a time gap of 24 hours.


Figure 3. 4. Harshaw model 3500 manual TLD reader (AMDI)

The TLDs was read at 300℃ and the readings were recorded to obtain the reproducibility and sensitivity of the TLDs. The sensitivity factor for each TLD is calculated using Equation (1):

$$\text{Sensitivity} = \frac{R_i}{R_{avg}} \quad (1)$$

Where $R_i$ is the individual response of TLD and $R_{avg}$ is the average response of all 10 TLD-100 chips. The reproducibility test for the TLD-100 chips was performed by repeating the measurement 2 times. Reproducibility of the TLDs is obtained by using Equation (2):

$$\text{CV} = \frac{\text{SD}}{\text{R}_{\text{avg}}} \text{ x } 100 \quad (2)$$

Where CV is the coefficient of variation, $R_{avg}$ is the average reading of all TLD. Furthermore, individual Element Correction Coefficient (ECC) is required as the TLD

is not present with the same TL efficiency (TLE). TLE is the emitted TL light intensity per unit of absorbed dose. Thus, the ECC is calculated using Equation (3):

$$\mathrm{ECC} = \frac{\mathrm{TLE}}{\mathrm{TLE_i}} \quad (3)$$

Where TLE is the average reading of total TLDs and $TLE_i$ is the individual reading. The group calibration factor (CF) is obtained by dividing the irradiated dose (100 cGy) by the average response of the TLD-100 chips (4.069 $\mu$C). The CF for this group of TLD was 24.58 cGy/$\mu$C.

Quality assurance (QA) was performed prior to the irradiation of TLD-100 chips. A source position check ruler (Figure 3.5) is used for the source position verification to measure whether the source goes to the programmed distal position. The reproducibility of the measurement should be within 0.5 mm. The calibration procedure proceeded as the source position verification was a pass.


Figure 3. 5. Source position check ruler

### 3.3 Assembly of applicator

A standard ring applicator composed of CT/MR Ring 60gr-26 mm, fixing nuts and 60 mm, 60° intrauterine tube was assembled carefully according to the manual. The

Vienna ring applicator was assembled by fixing all the components with an addition of 2 proguide needle, 6F circle 249 mm, by inserting them side by side through the holes in the ring. The assembled Vienna Ring applicator is shown in Figure 3.6.

Gauze was used to mimic tumour (Figure 3.7) and the gauze was wrapped around the intrauterine tube and extra pieces of gauze were added to one side of the tumor to represent a thick part of the tumor. The proguide needles were then inserted into the thick region of the tumor. The tumor and the needles were secured to the applicator using micropore to avoid the displacement of the tumor and the needles and for stabilisation. The Vienna Ring applicator with the designed tumour is shown in Figure 3.8.

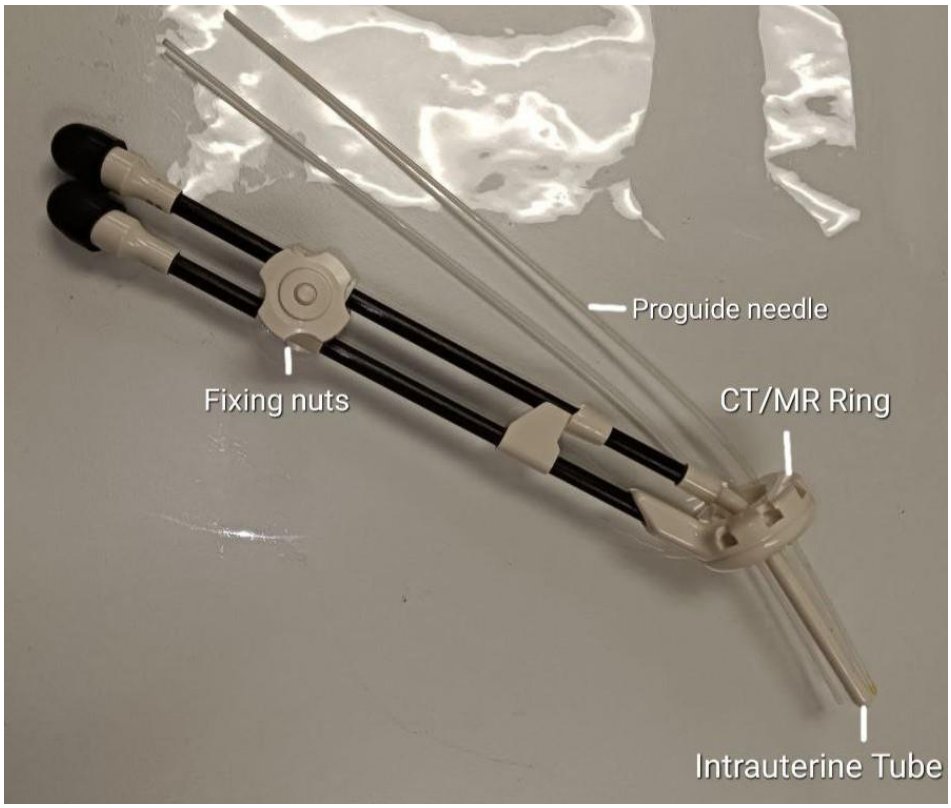


Figure 3. 6. Components of Vienna Ring applicator

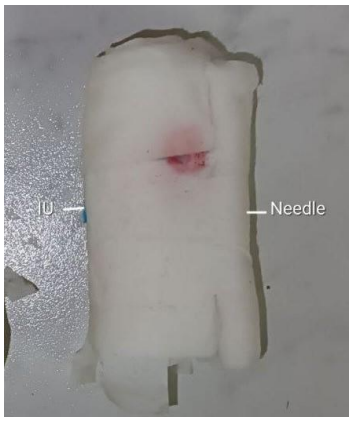


Figure 3. 7. Tumour (gauze) with the thicker part for insertion of needles

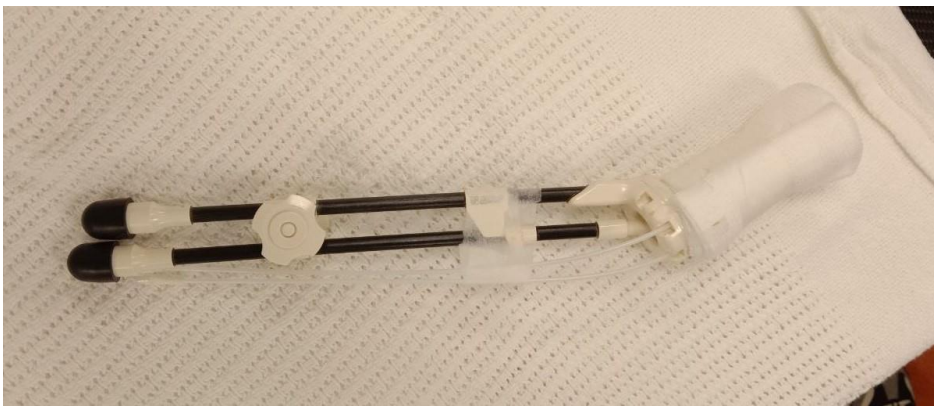

Figure 3. 8. Assembled Vienna Ring applicator with the tumour

A pelvic phantom with length 35.0 cm, width 38.0 cm and height 29.0 cm was used (Figure 3.9). Three organs at risk (OAR) were assembled into the phantom. A sphere with 9.5 cm diameter was used to represent bladder, a cylindrical shaped OAR with length 25.0cm and diameter 3.0cm used to represent rectum and 2 cylinders with length 15.0 cm and 5.0 cm diameter were used to represent left and right femur respectively (Figure 3.10). All the OAR were arranged and assembled in the correct positions and placed into the phantom (Figure 3.11).