

**INVESTIGATION ON THE RADIATION DOSE
DISTRIBUTION IN HIGH DOSE RATE (HDR)
GYNAECOLOGICAL BRACHYTHERAPY
TREATMENT USING MONTE CARLO
CALCULATION**

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UNIVERSITI SAINS MALAYSIA

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by

AHMAD NAQUIDDIN BIN AZAHARI

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LIST OF SYMBOLS

LINAC	Linear Accelerator
MC	MC Monte Carlo
IVD	In-vivo dosimetry
OAR	Organ at risk
ROI	Region of interest
SSD	Source to skin /surface distance
TLD	Thermoluminescence dosimeter
TPS	Treatment Planning System
ECC	Element Correction Coefficient

LIST OF ABBREVIATIONS

AAPM	American Association of Physicists in Medicine
cGy	Centi gray
cm	centimetre
dmax	depth of maximum dose
g cm ⁻³	Gram per centimeter cubic
Gy	Gray
HDR	High Dose Rate
HU	Hounsfield Unit
kV	kilovoltage
MC	Monte Carlo
MU	Monitor unit
MV	Megavoltage
OAR	Organs at Risk
OSL	Optically Stimulated Luminescence
OSLD	Optically Stimulated Luminescence Dosimeter
PHITS	Particle and Heavy Ion Transport Code System
s	Second
TG-43	Task Group 43 (AAPM Dosimetry Protocol)
TLD	Thermoluminescent Dosimeter

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- Appendix B Energy Correction Factor
- Appendix C Input file PHITS Code

**KAJIAN TERHADAP TABURAN DOS SINARAN DALAM RAWATAN
BRAKITERAPI GINEKOLOGI KADAR DOS TINGGI (HDR)
MENGUNAKAN PENGIRAAN MONTE CARLO**

ABSTRAK

Pengiraan dos yang tepat dalam brakiterapi kadar dos tinggi (HDR) untuk kanser ginekologi adalah penting bagi memastikan kawalan tumor yang berkesan serta meminimumkan pendedahan radiasi kepada tisu sihat sekeliling. Walau bagaimanapun, sistem perancangan rawatan (TPS) konvensional yang berasaskan formalisme TG-43 lazimnya mengabaikan tisu heterogeniti dan kesan geometri aplikator, yang boleh menyebabkan ketidaktepatan pengiraan dos terutamanya di kawasan kecerunan dos yang tinggi dan antara muka tisu. Kajian ini dijalankan untuk menangani jurang penyelidikan berkaitan dengan pengaruh heterogeniti tisu dan faktor geometri terhadap pengagihan dos serta meneroka kaedah alternatif bagi pengesahan dos yang lebih tepat. Tujuan kajian ini adalah untuk menilai ketepatan dosimetrik dalam brakiterapi Dos Tinggi endometrium melalui pendekatan eksperimental dan simulasi. Objektif khusus kajian ini merangkumi: (1) menilai kesesuaian bahan untuk pembangunan fantom mewakili organ berisiko (OAR), (2) menganalisis pengagihan dos menggunakan fantom yang dibangunkan, (3) mengesahkan model Monte Carlo (MC) melalui perbandingan dengan ukuran eksperimental, dan (4) menganggarkan faktor pembetulan heterogeniti tisu sebagai penambahbaikan kepada formalism TG-43. Fantom pelvis dibina menggunakan bahan setara tisu dan tulang yang telah disahkan melalui analisis Unit Hounsfield (HU) berasaskan imbasan CT. Dosimetri eksperimental dilaksanakan menggunakan dosimeter Pendar Kilau Terma (TLD-100) dan dosimeter pendarcahaya rangsangan optik (OSLD) (OSL nanoDot) yang

diletakkan pada permukaan pundi kencing, rektum, dan tulang pelvis. Simulasi Monte Carlo dijalankan menggunakan perisian PHITS, dengan model geometri sumber Ir-192 MicroSelectron Kadar Dos Tinggi, konfigurasi aplikator, kedudukan masa klinikal, dan aktiviti sumber sebenar. Pengiraan dos mutlak diperoleh dengan menskalakan output Monte Carlo berdasarkan masa penyinaran klinikal, bagi membolehkan perbandingan langsung dengan data TPS dan ukuran eksperimen. Dapatan kajian menunjukkan bahawa simulasi PHITS memberikan kesepakatan yang baik dengan ukuran eksperimen dan pengiraan TPS di kawasan belakang dinding pelvis dan pundi kencing, di mana struktur anatomi yang lebih seragam menghasilkan sisihan dos dalam julat klinikal yang boleh diterima. Walau bagaimanapun, perbezaan ketara diperhatikan di kawasan pelvis anterior dan zon kecerunan dos tinggi di rektum, disebabkan oleh kerumitan kecerunan dos serta heterogeniti tisu-udara yang tidak diambil kira sepenuhnya dalam model simulasi. Ketidaktepatan ini menegaskan sensitiviti pengagihan dos terhadap kerumitan anatomi walaupun dalam model simulasi lanjutan. Kajian ini memberikan sumbangan penting dalam bidang dosimetri brakiterapi dengan menunjukkan bahawa gabungan simulasi Monte Carlo dan dosimetri eksperimen berasaskan fantom mampu menawarkan pendekatan verifikasi dos yang lebih tepat dan komprehensif. Penemuan kajian menyokong keperluan penambahbaikan protokol pengiraan dos klinikal melalui pembetulan heterogeniti tisu bagi meningkatkan keselamatan rawatan, ketepatan dos dan hasil klinikal pesakit.

**INVESTIGATION ON THE RADIATION DOSE DISTRIBUTION IN
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TREATMENT USING MONTE CARLO CALCULATION**

ABSTRACT

Accurate dose calculation is crucial in high-dose-rate (HDR) brachytherapy for gynecological cancers to ensure effective tumor control while minimizing radiation exposure to surrounding healthy tissues. However, conventional treatment planning systems (TPS), primarily based on the TG-43 formalism, often neglect tissue heterogeneity and applicator effects, leading to potential inaccuracies especially near steep dose gradients and tissue interfaces. This study addresses the research gap by evaluating the influence of tissue heterogeneity and geometric factors on dose distribution, while exploring alternative methods for more accurate dose verification. The purpose of this study was to evaluate dosimetric accuracy in endometrial HDR brachytherapy through experimental and simulation approaches. Specifically, the study aimed to: (1) assess suitable materials for phantom development representing organs at risk (OARs), (2) investigate dose distribution using the constructed phantom, (3) validate Monte Carlo (MC) modelling against experimental measurements, and (4) estimate tissue inhomogeneity correction factors to complement the TG-43 formalism. A patient-equivalent brachytherapy phantom was constructed using tissue-equivalent and bone-equivalent materials, validated through CT-based Hounsfield Unit (HU) analysis. Experimental dosimetry was performed using thermoluminescent dosimeters (TLD-100) and optically stimulated luminescent dosimeters (OSL nanoDot) placed at the surfaces of the bladder, rectum, and pelvic bones. Monte Carlo simulations were performed using PHITS, with detailed modeling of the MicroSelectron HDR Ir-192

source geometry, applicator configuration, clinical dwell positions, and source activity. Absolute dose calculations were obtained by scaling Monte Carlo outputs according to clinical dwell times, allowing direct comparison with TPS and experimental data. The findings demonstrated that PHITS simulations produced strong agreement with experimental measurements and TPS calculations at posterior pelvic walls and bladder regions, where anatomical uniformity resulted in dose deviations within clinically acceptable limits. However, larger discrepancies were observed at anterior pelvic regions and high-gradient rectal sites, primarily due to complex dose gradients and unaccounted tissue-air heterogeneities. These deviations highlight the sensitivity of dose distribution to anatomical complexity, even in advanced simulation models. This study contributes to the field by demonstrating that combined Monte Carlo simulation and phantom-based experimental dosimetry offer a more precise and comprehensive approach to dose verification in HDR brachytherapy. The findings provide essential insights into the clinical relevance of tissue heterogeneity corrections, supporting future refinement of dose calculation protocols and contributing to improved treatment safety, accuracy, and patient outcomes.

CHAPTER 1

INTRODUCTION

1.1 Overview

Radiation therapy, known as radiotherapy in medical parlance, is a therapeutic modality employed in cancer management. This treatment approach harnesses the power of high-energy X-ray or other particles to eradicate cancer cells and effectively reduce tumors' size. Radiation therapy, when administered at high doses, induces cell death or retards the proliferation of cancer cells through the infliction of DNA damage. Cancer cells that have incurred irreparable damage to their DNA undergo either cell cycle arrest or apoptosis (Jackson and Bartek, 2009). Upon the demise of the impaired cells, the body proceeds to disintegrate and eliminate them. Radiation is employed at lower levels in medical imaging techniques such as X-rays to facilitate internal visualization of bodily structures, including dental and skeletal examinations. A typical radiation therapy protocol typically comprises a predetermined number of treatment sessions administered within a designated timeframe. Radiation therapy can effectively manage a wide range of cancerous conditions (Barnett *et al.*, 2009).

Furthermore, it can be used with other therapeutic modalities for cancer management, including chemotherapy and surgical interventions. Radiation therapy may be administered internally or externally to the patient's body. Two primary categories of radiation therapy exist external beam and internal radiation therapy. The predominant form of radiation therapy is external beam radiation therapy. External beam radiation therapy is classified as a localized therapeutic intervention, wherein it is designed to target and treat a specific anatomical region within the body. The therapeutic intervention employs a sizable apparatus known as a linear accelerator. The machine directs high-energy beams toward a specific location on the individual's body.

External radiation therapy utilizes radiation beams emitted by three distinct types of particles: photons, protons, and electrons (Wu *et al.*, 2008; Baskar *et al.*, 2012).

The majority of radiation therapy machines employ photon beams. Photons are also utilized in X-ray imaging, albeit at lower levels of radiation exposure. Photon beams possess the capability to effectively penetrate and selectively target tumors situated at considerable depths within the anatomical structure of the human body. Photons passing through the human body scatter minute quantities of radiation particles along their path. The beams continue to penetrate beyond the tumor and into the surrounding normal tissue. Electrons are subatomic particles characterized by their negative electric charge. The propagation distance of electron beams within body tissues is limited. Hence, their application is restricted to neoplasms on the dermis or close to the body's surface (Verheij, 2008; Eriksson and Stigbrand, 2010). Protons are subatomic particles that possess a fundamental positive electric charge. Like photon beams, proton beams can penetrate deep into the body and target tumors.

Nevertheless, it should be noted that proton beams exhibit minimal radiation scattering as they traverse the human body, ultimately ceasing their propagation upon reaching the targeted tumor. Medical professionals hypothesize that using proton beams may potentially mitigate the extent of radiation exposure to healthy tissue. Ongoing clinical trials are being conducted to evaluate and compare the efficacy of radiation therapy utilizing proton beams versus photon beams. The utilization of proton beams in radiation therapy is observed in specific cancer centers; however, the restricted adoption of this technique is primarily attributed to the considerable expenses and large dimensions associated with the proton beam machines (Schulz-Ertner and Tsujii, 2007).

Internal radiotherapy, also known as brachytherapy, involves the administration of radiation from a source positioned within the body. Internal radiotherapy, also known as brachytherapy, administers a concentrated dose of radiation to the targeted area, reducing adverse effects compared to external radiotherapy. The rationale behind utilizing internal radiotherapy lies in its ability to administer radiation from within the body, close to the cancerous cells, thereby minimizing the impact on healthy cells (Sadeghi *et al.*, 2010). There are usually two primary forms of internal radiation. The first type of treatment is termed radioisotope or radionuclide therapy. In this type of treatment, the patient drinks or injects radioactive material into their circulation. This approach works well for tumours that extend to many places, such as thyroid cancer or bone metastases, since the radioactive material naturally builds up in the organs or tissues that are being treated. Brachytherapy, or radioactive implant treatment, is the second form. With brachytherapy, small sealed radioactive sources are put just inside or close to the tumour. This lets doctors give a large dose exactly where it's required, which protects healthy tissue around. Both methods are useful for treating cancer, but the best one depends on where and what form of cancer it is.

Brachytherapy, alternatively referred to as internal radiation, is a medical procedure. A radioactive implant is inserted within the anatomical structure, either directly within the tumor or close to it. The utilization of a radiation source is typically facilitated through containment within a compact enclosure referred to as an implant. Various forms of implants can be referred to as pellets, seeds, ribbons, wires, needles, capsules, balloons, or tubes. Brachytherapy is a therapeutic approach employed for treating various types of cancers affecting different body parts, such as the eye, lung, breast, head and neck, larynx, prostate, skin, gallbladder, cervix, uterus, and rectum (Vicens *et al.*, 2015; Hoffman *et al.*, 2016). Most brachytherapy procedures involve the

insertion of a catheter for placement. Occasionally, the administration of brachytherapy involves the utilization of a larger instrument known as an applicator. The method of brachytherapy placement is contingent upon the specific type of cancer being treated.

Brachytherapy can be classified into two categories: temporary and permanent. Temporary brachytherapy is a medical procedure wherein radioactive pellets are inserted into the patient's body. The pellets emit radiation in order to eradicate adjacent cancer cells and persist until the conclusion of the therapeutic intervention. Temporary brachytherapy, also known as high dose rate (HDR) brachytherapy, is a medical procedure utilized in the treatment of various conditions. In the context of permanent brachytherapy, the procedure involves the insertion of pre-filled needles containing radioactive seeds directly into the tumor. Over several months, the seeds gradually emit minimal radiation within the vicinity of the cancerous region. The term "permanent seed brachytherapy" is synonymous with "permanent brachytherapy" or "low dose rate (LDR) brachytherapy" (Fischer-Valuck *et al.*, 2019).

Cervical cancer is a prominent global public health issue and ranks as the fourth most common cause of cancer-related deaths among women (Bray *et al.*, 2018). According to the Malaysian National Cancer Registry report, cervical cancer is the most prevalent type of cancer among women. The report indicates that a total of 3,981 patients were diagnosed with cervical cancer between 2012 and 2016 (Zaridah, 2014; MNCRR, 2019). Cervical cancer treatment is stage-dependent, depending on tumour size, vaginal or parametrial involvement, and distant metastases. It is sometimes combined with surgical resection, chemotherapy, radiotherapy, or a combination of these treatments (Colombo *et al.*, 2012; Koh *et al.*, 2015; Small *et al.*, 2017). Thus, due to the advanced quality of medical facilities in Malaysia, hospitals have implemented

brachytherapy as a method for treating and preventing cervical cancer (Wan Zamaniah *et al.*, 2014; Azahari *et al.*, 2022). As a result, brachytherapy is critical in the treatment of cervical cancer because it allows for the administration of concentrated radiation doses to the cervical tumour while protecting nearby organs such as the bladder, rectum, and sigmoid colon (Weiner and Schwarz, 2015).

Radiation therapy is a sophisticated procedure that consists of several stages, where the precision of each stage can have an impact on the control of tumours or the occurrence of complications in normal tissues. The human body consists of various tissues and cavities that have unique physical and radiological properties. Tissues and cavities that display radiological dissimilarities to water, including lungs, oral cavities, teeth, nasal passages, sinuses, and bones, are of particular importance in radiation dosimetry ((AAPM), 2004).

Currently, the dose calculations for patient treatment in brachytherapy are based on the formalism of Task Group 43 (TG-43) of the American Association of Physicists in Medicine (AAPM). The method has been widely adopted in various brachytherapy treatment planning systems (TPSs) and is also utilized for dose calculation in brachytherapy at our institution. The TG-43 protocol offers a computational approach for determining the dose to the patient based on the point source approximation, dosimetry in a homogeneous medium, and the assumption of negligible interseed effect. As mentioned earlier, the assumption can result in significant inaccuracies when determining the dosage administered to patients during their medical treatments. This is primarily due to variations in tissue composition compared to water and the absence of an infinitely scattering medium caused by the finite size of patients. The approach of

performing a basic summation of dose contributions from individual sources also fails to account for the impact of interseed attenuation (Oliveira *et al.*, 2014).

Currently, researchers are exploring model-based dose calculation algorithms (MBDCAs) as alternative methods to enhance the accuracy of brachytherapy dose calculations. These Algorithms, such as the collapsed-cone superposition/convolution algorithm, grid-based Boltzmann equation solver, and the Monte Carlo (MC) method, have been developed and demonstrate the ability to accurately model the dose distribution, as compared to the TG-43 method (Beaulieu *et al.*, 2012; Tedgren, 2021).

The application of Monte Carlo simulation in brachytherapy for radiation transport is widely acknowledged as a highly efficient method because it has ability to accurately models the random nature of radiation interaction at the microscopic level. (Williamson, 2006). The application of the Monte Carlo method is essential in the context of radiation transport across various media such as biological tissue, air cavity and shielding materials. When a particle, such as a neutron, photon, electron, or proton, moves across a boundary, it quickly incorporates a new set of interaction cross-sections. This allows the simulation to continue as if the new medium were infinite until it reaches the next boundary. By utilising the method of stochastic sampling from a designated distribution, it is feasible to deduce a model that accurately portrays a specific behaviour (Andreo, 2018). The utilisation of Monte-Carlo simulation as a comparison tool to verify the accuracy of the absorbed dose distribution within the patient can be of great significance in various phases of brachytherapy treatment planning. The Monte Carlo simulation is an appropriate method for determining the distribution of radiation dosage in a patient undergoing radiotherapy, particularly in cases involving heterogeneous

anatomical structures. This approach is also applicable to brachytherapy due to accurate dose distribution and model individual particles interactions (Park *et al.*, 2021).

1.2 Motivations and goals

High Dose Rate (HDR) brachytherapy is widely used in the management of gynecological cancers due to its ability to deliver high radiation doses directly to the tumor with minimal exposure to surrounding healthy tissues. Treatment planning for HDR brachytherapy typically relies on the American Association of Physicists in Medicine Task Group No. 43 (AAPM TG-43) formalism, which assumes a uniform water-equivalent medium (Asnaashari *et al.*, 2013). While this approach simplifies calculations, it fails to account for the heterogeneities in tissue composition and the presence of non-water-equivalent materials such as applicators and bone, potentially leading to inaccurate dose delivery (Bayati *et al.*, 2022).

Although Monte Carlo (MC) simulations offer a powerful method to accurately model dose distribution by incorporating these heterogeneities, the clinical adoption of such techniques remains limited due to the complexity of implementation, lack of standardized phantom designs for validation, and limited experimental verification using actual dosimetric measurements. Furthermore, previous studies either focus on prostate or breast brachytherapy, or use simplified phantom geometries that do not reflect the anatomical complexities of female pelvic structures (Hueso-González *et al.*, 2017).

To address this gap, this study aims to develop a dedicated gynecological brachytherapy phantom that accurately mimics human anatomy, integrates realistic organ-at-risk (OAR) representations, and allows for dosimetric validation using thermoluminescent dosimeters (TLDs) and optically stimulated luminescence

dosimeters (OSLs). The integration of such a phantom with MC simulations is expected to improve dose accuracy, particularly for inhomogeneous regions, and to establish correction factors for TG-43 dose estimates.

This research contributes to the field by bridging the gap between theoretical dose modelling and experimental validation, ultimately enhancing the precision of brachytherapy dosimetry for clinical applications in gynaecological cancer treatment.

1.3 Problem Statement

High Dose Rate (HDR) brachytherapy plays a critical role in the treatment of gynaecological cancers by delivering highly localized radiation to tumor sites. However, the current dosimetric formalism used in most treatment planning systems assumes a homogeneous water-equivalent medium, disregarding tissue heterogeneities and the physical properties of applicators and surrounding organs. This simplification can lead to inaccurate dose estimations, particularly in anatomically complex regions such as the pelvis, where organs at risk (OARs) such as the bladder and rectum are in close proximity to the treatment site (Hermani *et al.*, 2019).

Although several studies have applied Monte Carlo (MC) simulation to improve dose accuracy by accounting for tissue heterogeneity, these investigations often rely on computational models without experimental verification, or they utilize generic phantom designs not tailored for endometrial or vaginal brachytherapy. Moreover, there is limited evidence validating such simulations with in-vivo-like measurements or dosimeters placed in anatomically relevant positions (Assam *et al.*, 2022).

Therefore, there is a pressing need to develop and validate a brachytherapy phantom that mimics anatomical heterogeneities, to integrate experimental measurements with MC simulations, and to estimate correction factors for dose deviation due to inhomogeneity. Addressing this gap will contribute to more accurate, patient-specific dosimetry in gynecological HDR brachytherapy.

1.4 Research Objective

The aim of this study is to enhance the accuracy of dose estimation in high dose rate (HDR) gynecological brachytherapy, particularly for endometrial cancer treatment. This is achieved by addressing known limitations in the widely adopted TG-43 formalism, which assumes a homogeneous water medium and does not account for patient-specific tissue heterogeneity. To bridge this gap, the research integrates experimental dosimetry with Monte Carlo simulation using a custom-developed brachytherapy phantom. The specific objectives of this study are as follows:

1. To evaluate the suitability of various materials for the development of a brachytherapy phantom and for representing organs at risk (OARs). This objective involves the selection and assessment of materials that closely resemble human tissues in terms of their radiological properties. CT-based Hounsfield Unit (HU) analysis was used to compare these materials against reference values, ensuring that the phantom components realistically represent anatomical structures such as the bladder, rectum, and pelvic bone.
2. To assess the dose distribution in endometrial brachytherapy treatment using the developed brachytherapy phantom. This objective focuses on verifying the clinical dose delivery by conducting point dose measurements on the phantom using thermoluminescent dosimeters (TLDs) and optically

stimulated luminescent dosimeters (OSLDs). These measurements aim to evaluate the accuracy of the treatment planning system (TPS) in delivering prescribed doses to the target and surrounding OARs under realistic anatomical conditions

3. To simulate and validate the Monte Carlo (MC) model through comparison with measured data in gynecological brachytherapy dose calculations. This objective ensures the accuracy and reliability of the MC simulation using the PHITS code. The simulation results are compared against both TPS-calculated doses and experimental measurements, serving as a critical validation step before applying the model to further analysis.
4. To estimate organ-specific correction factors for tissue inhomogeneity in the TG-43 formalism based on Monte Carlo dose calculations. This objective addresses the dosimetric inaccuracies introduced by the TG-43 assumption of a uniform water medium. Using the validated Monte Carlo model, organ-specific correction factors were derived by comparing dose distributions in heterogeneous anatomical regions with those assumed in a homogeneous water phantom. These correction factors are intended to improve dose accuracy for critical structures such as the bladder, rectum, and pelvic bone in HDR brachytherapy, particularly in clinical scenarios where tissue heterogeneity plays a significant role. Experimental measurements were excluded from this analysis due to inconsistency in comparison.

1.5 Scope of Research

This research focuses on the development, simulation, and experimental validation of a customized brachytherapy phantom for endometrial HDR treatment, with the overall aim of enhancing dose calculation accuracy in clinical applications. The scope includes evaluating the suitability of various materials for the development of a brachytherapy phantom that accurately represents organs at risk (OARs), ensuring anatomical and radiological relevance. It further involves assessing the dose distribution in endometrial HDR brachytherapy using the developed phantom under clinically realistic conditions. The study also encompasses the simulation and validation of the Monte Carlo (MC) model through comparison with measured dosimetric data, thereby establishing the model's reliability in representing gynecological brachytherapy scenarios. Lastly, the research aims to estimate tissue inhomogeneity correction factors within the TG-43 formalism, based on detailed Monte Carlo calculations and experimental dose measurements, to support improved accuracy in current treatment planning protocols.

1.6 Study limitations

The scope of this study was restricted to the collection and examination of data exclusively from a fabricated brachytherapy phantom. The Monte Carlo simulation was performed exclusively on Particle and Heavy Ion Transport Code System (PHITS) software to calculate the Ir-192 brachytherapy treatment planning system (TPS) dose and compare it with the results obtained from the Treatment Planning System (TPS). The point dose within the phantom was measured exclusively by utilizing thermoluminescent dosimeters (TLD) and optically stimulated luminescent dosimeters (OSLD).

1.7 Outline of the thesis

This thesis is structured into five chapters. Chapter 2 provides a comprehensive review of High Dose Rate (HDR) brachytherapy, including its clinical application in gynecological cancer and the limitations of the AAPM TG-43 formalism. It also explores the advantages of Monte Carlo simulation techniques in improving dose calculation accuracy in brachytherapy.

Chapter 3 outlines the research methodology, detailing the development of the brachytherapy phantom, the selection of tissue-equivalent materials, and the integration of thermoluminescent dosimeters (TLDs) and optically stimulated luminescence dosimeters (OSLs) for dose measurement. The chapter also explains the Monte Carlo simulation setup using the PHITS code, including source activation, scoring geometry, and normalization techniques. It concludes with the procedures used to validate simulation results against experimental data.

Chapter 4 presents the results obtained from both simulations and physical measurements. The analysis focuses on dose distribution in the presence of inhomogeneous media and evaluates the impact of tissue heterogeneity on TG-43-based dose calculations. Correction factors are derived and discussed based on the comparison between Monte Carlo results and measured doses.

Finally, Chapter 5 discusses the significance of the study's findings in the context of existing literature. It highlights the contributions and limitations of the research, proposes areas for future investigation, and concludes with a summary of the main outcomes of the study.

CHAPTER 2

LITERATURE REVIEW

2.1 High Dose Rate (HDR) Brachytherapy

High-dose-rate (HDR) brachytherapy is an advanced internal radiation therapy technique that uses transiently positioned radioactive sources to deliver highly conformal doses directly to tumour sites. Iridium-192 (Ir-192) and cobalt-60 (Co-60) are frequently used isotopes that can administer doses greater than 12 Gy/hour, allowing for quick treatment administration in a matter of minutes (Patankar *et al.*, 2015). A remote afterloader system manipulates these sources by moving them into applicators at predetermined dwell positions and times, in accordance with a treatment plan developed through dosimetric optimisation and 3D imaging (Wen *et al.*, 2022).

HDR brachytherapy is frequently used to treat breast, prostate, and gynaecological cancers. It is generally divided into two methods: interstitial brachytherapy, which is frequently used for breast and prostate cancers, and intracavitary brachytherapy, which is frequently used for cervical cancer (Lim and Kim, 2021). The steep dose gradient that HDR sources produce is a significant benefit because it allows for precise dose localisation with little exposure to nearby organs at risk (OARs), including the rectum, bladder, and sigmoid colon (Shi *et al.*, 2025).

HDR has major clinical and logistical advantages over conventional low dose rate (LDR) brachytherapy. While LDR usually necessitates radiation delivery over 24 to 72 hours, HDR treatments are finished in a matter of minutes. This time efficiency lowers the chance of applicator displacement during treatment, increases patient comfort, and eliminates the need for prolonged hospital stays. Additionally, unlike LDR treatments, which leave patients radioactive for extended periods of time, HDR's remote afterloading technique shields the radioactive source until momentary

deployment, improving safety for clinical staff (Abdel-Wahab *et al.*, 2017; Serarslan *et al.*, 2019).

HDR brachytherapy's exceptional capacity for dose modulation is another asset. Clinicians can precisely mould isodose distributions around intricate tumour geometries thanks to the stepping source mechanism and programmable dwell times. In LDR brachytherapy, where fixed seeds or tubes provide little post-implant adjustment, this degree of dosimetric control is not possible (Lim and Kim, 2021).

In terms of local control, overall survival, and late toxicity in cervical cancer, HDR brachytherapy is oncologically equivalent to LDR, according to multiple randomised controlled trials and meta-analyses (Viani *et al.*, 2009). Additionally, HDR's favourable safety profile, flexibility in treatment planning, and ease of implementation have made it the most popular technique in clinical practice (Abdel-Wahab *et al.*, 2017). About 75% of cervical cancer brachytherapy cases in the US by 2011 involved HDR (Patankar *et al.*, 2015).

In addition to LDR, HDR brachytherapy offers strong benefits over external beam radiation therapy (EBRT). HDR brachytherapy achieves unparalleled dose conformity by placing the source inside or adjacent to the tumour, whereas EBRT necessitates high-energy radiation to enter the body from outside sources. Particularly helpful in pelvic cancers where protecting the bladder, rectum, and small bowel is crucial, the sharp dose fall-off from the source reduces radiation exposure to healthy tissues (Fischer-Valuck *et al.*, 2019).

HDR brachytherapy outperforms sophisticated EBRT techniques in prostate cancer by achieving higher conformity indices, which allows for safe dose escalation and enhanced biochemical relapse-free survival, especially in high-risk cases (Oshikane *et al.*, 2021). Without causing an increase in toxicity, HDR in hypofractionated schemes

can deliver a higher biologically effective dose (BED) than EBRT alone (Fischer-Valuck *et al.*, 2019).

HDR brachytherapy allows for outpatient treatments, improves scheduling efficiency, and lessens the radiological burden on healthcare systems from a radiobiological and logistical perspective. Crucially, treatment accuracy and reproducibility across fractions are further enhanced by contemporary image-guided HDR planning. International clinical guidelines, including those issued by the American Society for Radiation Oncology (ASTRO), recommend it as the standard of care for cervical and other cancers because of these factors (Chino *et al.*, 2020).

HDR brachytherapy still has drawbacks in spite of these advantages. The use of the TG-43 dosimetry formalism, which disregards tissue heterogeneity and applicator effects and assumes homogeneous water-equivalent media, is one major problem. Actual clinical dose delivery may become inaccurate as a result of this simplification. The current study fills this gap by creating a customised water-equivalent phantom and using Monte Carlo simulations to look into dose distributions and increase the precision of HDR brachytherapy planning.

2.2 Gynecological brachytherapy

Gynecological brachytherapy, particularly for cervical and endometrial cancers, involves the precise placement of radioactive sources directly into or near the tumor site using specialized applicators. The success of high-dose-rate (HDR) brachytherapy in gynecologic oncology is contingent on the individualized selection and accurate placement of these applicators. Typically, the applicators include tandem-and-ovoid (T&O), tandem and ring (T&R), and cylinder-based systems for intracavitary brachytherapy, or interstitial needles guided by templates for more extensive disease

involvement (Serban *et al.*, 2020; Wang *et al.*, 2024). The selection is tailored to tumor size, location, and infiltration extent, allowing optimal target coverage while sparing organs at risk (OARs).

Recent advances in imaging have significantly improved the accuracy of applicator placement and treatment planning. Computed tomography (CT) and magnetic resonance imaging (MRI) are commonly utilized to ensure optimal positioning of the applicator and to delineate the high-risk clinical target volume (HR-CTV) and OARs, such as the bladder, rectum, sigmoid colon, and urethra. MRI, in particular, provides superior soft tissue contrast, enabling more accurate definition of tumor margins and reducing interobserver variability (Tharmalingam *et al.*, 2018; Mahantshetty *et al.*, 2021).

In modern HDR treatment planning, dose optimisation plays a pivotal role in ensuring therapeutic efficacy while minimizing toxicity. The treatment planning system (TPS) allows the user to define HR-CTV and OARs and apply different dose constraints and optimization strategies. Manual dwell time adjustments, geometric optimization (GO), and dose-point optimization (DPO) have traditionally been employed (Azahari *et al.*, 2022). However, advanced inverse planning algorithms such as inverse planning simulated annealing (IPSA) and hybrid inverse planning and optimization (HIPO) are increasingly used due to their ability to produce highly conformal dose distributions (Yang *et al.*, 2022).

Inverse planning techniques optimize dwell positions and times by balancing prescribed doses to target volumes while minimizing exposure to OARs. These algorithms utilize dose-volume constraints and priority settings to refine dose delivery, making them particularly effective for complex interstitial or hybrid intracavitary-interstitial implants. Studies have demonstrated that IPSA and Manual optimization

(MO) outperform conventional techniques in achieving better OAR sparing, leading to improved clinical outcomes (GÜL *et al.*, 2024). Overall, advanced optimization methods have become integral to HDR brachytherapy, ensuring each treatment is highly conformed to the patient's anatomy and clinical goals.

2.3 Treatment Planning System

A Treatment Planning System (TPS) is a core component of modern radiation therapy, responsible for simulating, optimizing, and verifying dose distribution before treatment delivery. In brachytherapy, the TPS enables clinicians to define source dwell positions and times based on anatomical images, most commonly acquired via computed tomography (CT) or magnetic resonance imaging (MRI). For HDR brachytherapy, these systems provide real-time dose calculations, allowing for iterative plan optimization to achieve therapeutic goals while minimizing radiation to organs at risk (OARs) (Jayakody *et al.*, 2022).

Most TPSs in clinical use for HDR brachytherapy relies on the AAPM Task Group 43 (TG-43) dosimetry formalism. This model simplifies the complex radiological environment by assuming a water-equivalent medium surrounding a symmetric source geometry, without accounting for patient-specific tissue heterogeneities or applicator materials (Thomson *et al.*, 2020). While TG-43-based algorithms are computationally efficient and widely validated for general clinical practice, several studies have demonstrated their limitations, particularly in scenarios where dose gradients are steep or material inhomogeneities are significant—such as in gynaecologic brachytherapy involving air cavities, bony structures, or non-water-equivalent applicators (Ahnesjö *et al.*, 2017; Enger *et al.*, 2020; Yousif *et al.*, 2021).

To address these shortcomings, model-based dose calculation algorithms (MBDCAs) such as Advanced Collapsed Cone Engine (ACE) and Monte Carlo-based engines have been introduced in some commercial TPS platforms. These algorithms enable patient-specific dose by incorporating CT-derived electron density maps and detailed source. Studies have shown that MBDCAs can result in dose differences exceeding 10% when compared to TG-43 in heterogeneous anatomical regions, particularly for vaginal cylinder and tandem-and-ovoids applicator setups (Abe *et al.*, 2018; Puriparthi *et al.*, 2023). However, the adoption of MBDCAs remains limited due to regulatory constraints, computational demand, lack of clinical validation, and the need for phantom-based benchmarking.

Moreover, most commercial TPSs do not support Monte Carlo simulation as an internal module, requiring researchers and clinicians to perform independent MC calculations outside the clinical workflow. This disconnect presents challenges in integrating MC-based corrections into routine patient planning and in validating TPS performance against experimental dose measurements (Chetty *et al.*, 2007; Downes *et al.*, 2010; Ma *et al.*, 2014).

Recent efforts have highlighted the importance of phantom-guided TPS validation, particularly in non-uniform media. Dosimetric benchmarking using anthropomorphic phantoms equipped with high-resolution dosimeters provides a valuable framework to test TPS accuracy and identify areas for algorithmic improvement (Hadad *et al.*, 2015; Moon *et al.*, 2018; Mohyedin *et al.*, 2024)

Despite advancements in TPS algorithms, there remains a critical lack of validated, anatomically realistic phantom data to support the clinical implementation of MC-based corrections. This study addresses this gap by experimentally benchmarking a gynecological brachytherapy phantom using in-vivo dosimetry and MC simulations,

to assess the dosimetric accuracy of TG-43-based TPS calculations under realistic conditions

2.4 AAPM TASK GROUP 43

The dosimetry protocol for calculating doses and the dataset containing values for dosimetry parameters in interstitial brachytherapy were published and endorsed by The American Association of Physicists in Medicine's Task-Group 43 (TG-43) in 1995. The objective of this protocol is to establish a uniform method for performing brachytherapy dosimetry using Ir-192, Pd-103, and I-125 sources. The protocol included various essential parameters, such as the anisotropy function, dose rate constant, geometry factor, radial dose function, and air kerma strength (Wu *et al.*, 2021). However, the protocol was revised to TG-43U1 in order to describe and adapt to new brachytherapy sources and dosimetric functions (Rivard *et al.*, 2004). Figure 2.1 illustrates the spatial parameters and coordinate system used in TG-43 dose calculations, highlighting the geometric framework for evaluating dose distribution around a linear source. The general formalism for the two-dimensional case gives the dose rate D at point in water with coordinates (r, θ) from the centre of the source as in equation 2.1:

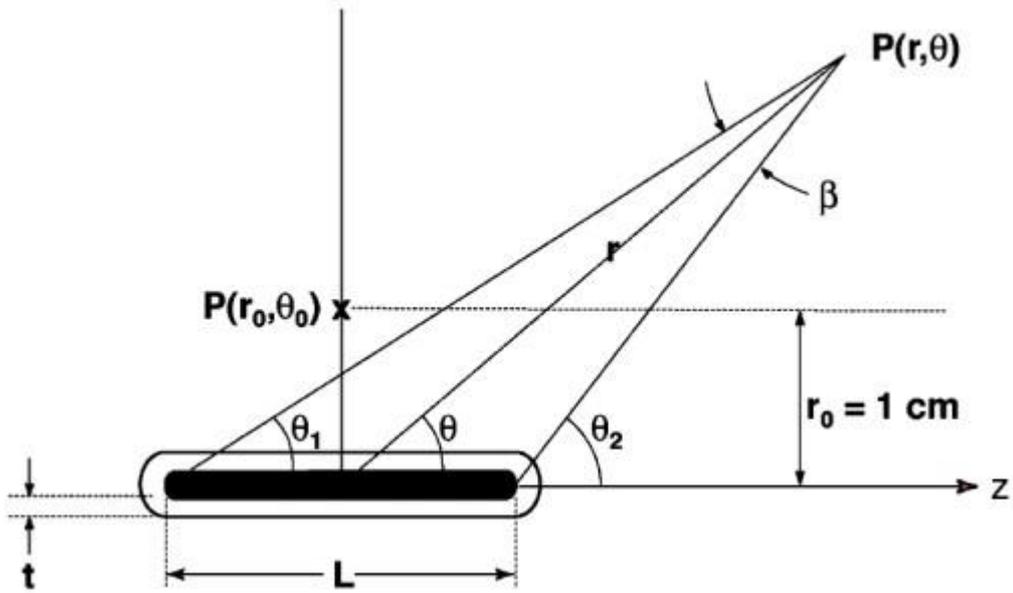


Figure 2.1 Schematic representation of the TG-43 coordinate system showing the line source geometry and reference dose calculation point at $P(r, \theta)$.

$$D(r, \theta) = S_k \cdot \Lambda \cdot \frac{G_L(r, \theta)}{G_L(r_0, \theta_0)} \cdot g_L(r) \cdot F(r, \theta) \quad \text{Eq 2.1}$$

Where:

- r = Distance from the center of the seed to the point of interest P.
- θ = polar angle between the radius vector point of interest $P(r, \theta)$ and longitudinal axis of the seed.
- Λ = Dose rate constant with units in $\text{cGy h}^{-1} \text{U}^{-1}$
- S_k = Air kerma strength which is specified air kerma rate along the transverse axis of the source in free space. The units denoted as $\mu\text{Gy m}^2 \text{h}^{-1}$
- $G(r, \theta)$ = The geometry function incorporates an inverse square correction to accurately calculate the dose rate. The geometry function does not account for attenuation and scatter, but instead applies an inverse square correction based on an approximate model of the activity distribution in the source.

- G_L = The radial dose function considers the influence of scatter and absorption in the medium along the transverse axis of the source. The exclusion of any correction based on the inverse square relationship is due to its incorporation within the geometry function.
- $F(r, \theta)$ = The anisotropy function accounts for the anisotropic dose distribution around the source. This function provides the angular variation of the rate at which the dose is delivered around the source at different distances. This dependence is caused by the combination of self-absorption, oblique filtration of photons through the seed capsule, and the scattering and absorption of photons in the surrounding medium.

While TG-43 has played a pivotal role in the clinical standardization of brachytherapy dosimetry, its key limitation lies in the neglect of tissue heterogeneity and applicator effects. By assuming a uniform water medium, TG-43 does not account for patient-specific anatomical variations, air gaps, bone, or the non-water-equivalent materials used in applicators. Multiple studies have reported deviations of up to 10–20% in dose distribution when comparing TG-43 calculations with Monte Carlo (MC)-based models that incorporate real anatomical and material heterogeneities (Haidari *et al.*, 2019; Mishra *et al.*, 2022; Rossi *et al.*, 2024).

Given the inherent simplifications in the TG-43 formalism, there is a pressing need to validate its accuracy in clinically realistic scenarios. This study responds to this need by comparing TG-43-based dose predictions with Monte Carlo simulations and experimental measurements using a custom-developed gynecological brachytherapy phantom that includes heterogeneities. Such validation efforts are crucial for identifying when correction factors are necessary and for improving treatment precision in HDR brachytherapy.

2.5 In-Vivo Dosimetry (IVD)

In-vivo dosimetry (IVD) refers to the direct measurement of radiation dose received by a patient during actual treatment delivery. In HDR brachytherapy, where dose gradients are extremely steep and treatment volumes are confined to small anatomical spaces, IVD serves as a vital quality assurance (QA) tool to verify that the planned dose corresponds to the delivered dose at critical anatomical locations. The technique is especially important in gynecological brachytherapy, where applicator misplacement, patient movement, or anatomical changes between fractions can significantly alter dose distribution (Adliene *et al.*, 2015; Jaselskè *et al.*, 2017)

Commonly used IVD tools in brachytherapy include thermoluminescent dosimeters (TLDs), optically stimulated luminescence dosimeters (OSLDs), metal-oxide semiconductor field-effect transistors (MOSFETs), and diode detectors. Each has specific advantages in terms of sensitivity, spatial resolution, real-time capability, and clinical usability. Among these, TLDs and OSLDs are the most frequently employed in phantom-based HDR studies due to their small size, energy dependence in the kilovoltage–megavoltage range, and suitability for measuring cumulative dose in inhomogeneous setups (Babaloui *et al.*, 2020; Bassi *et al.*, 2020; Choi *et al.*, 2022)

The integration of IVD in brachytherapy serves multiple purposes: (1) validating the accuracy of dose distributions calculated by the treatment planning system, particularly in anatomically challenging regions; (2) detecting deviations between planned and delivered doses due to human or mechanical errors; and (3) benchmarking computational algorithms such as TG-43 and Monte Carlo simulations (Lohrabian *et al.*, 2021; Marvi *et al.*, 2021; Doudoo *et al.*, 2023). IVD data is also useful in retrospective analyses of treatment outcomes and in generating clinical dose-response correlations.

However, the use of IVD in clinical brachytherapy remains limited, especially for routine patient treatment. Challenges include the need for precise and reproducible dosimeter placement, complex calibration protocols, and time constraints during clinical workflows. Additionally, dose perturbation caused by the dosimeter itself, especially near the source or in small cavities, must be carefully considered during analysis (Muhammad *et al.*, 2018; Moradi *et al.*, 2022).

From a research standpoint, IVD has proven essential in validating experimental phantom models designed to mimic patient anatomy. In studies involving anthropomorphic or water-equivalent phantoms, dosimeters are embedded at locations corresponding to organs at risk (OARs) such as the bladder, rectum, and vaginal wall to compare measured dose with TPS predictions and Monte Carlo results. Such phantom-based IVD measurements offer valuable insight into the reliability of TPS algorithms and can support the development of TG-43 correction (Sun *et al.*, 2021; Merrell *et al.*, 2023).

Despite its proven value, IVD remains underutilized in the clinical validation of gynecological HDR brachytherapy dose planning. This study integrates TLDs and OSLDs into a customized phantom setup to experimentally validate Monte Carlo simulations and TG-43-based calculations, enhancing the dosimetric accuracy and clinical relevance of brachytherapy in heterogeneous pelvic environments.

2.5.1 Thermoluminescent Dosimetry in brachytherapy

Thermoluminescent dosimeters (TLDs) are widely used devices for measuring absorbed radiation doses in clinical and experimental settings. They operate based on the principle that certain crystalline materials emit light when heated after exposure to ionizing radiation. The intensity of this emitted light is proportional to the accumulated radiation dose (Almeida *et al.*, 2018).

TLDs are typically composed of inorganic scintillating crystals, such as lithium fluoride (LiF), which contain intentionally introduced impurities to create trapping and luminescence centers. Upon exposure to radiation, electrons are excited from the valence to the conduction band and become trapped at defect sites within the crystal lattice. During the readout process, the dosimeter is gradually heated under a controlled nitrogen atmosphere. As the temperature increases, the trapped electrons gain sufficient thermal energy to escape and recombine at luminescent centers, releasing photons. These light signals are collected by a photomultiplier tube and converted into an electrical signal proportional to the dose (Fartode *et al.*, 2024). Figure 2.2 illustrates a typical TLD glow curve, which plots luminescence intensity against temperature, indicating different trap depths and energy release points.

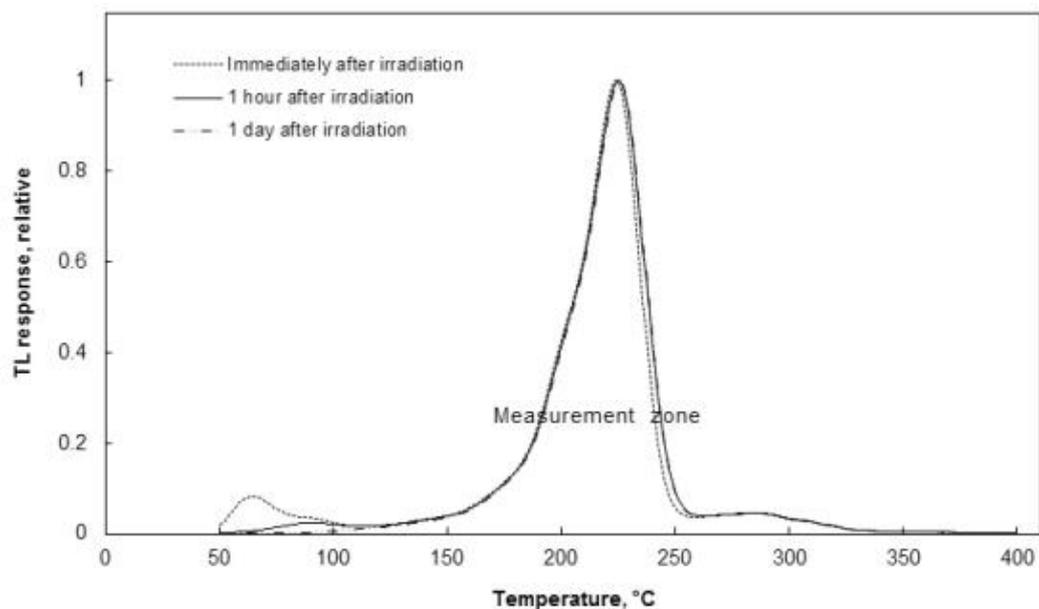


Figure 2.2 Example of TLD 100 glow curve (Mayles, 2011)

LiF:Mg,Ti commercially known as TLD-100 is the most widely used material due to its near-tissue equivalence, high sensitivity, signal stability and compact (Rivera, 2012; Budzanowski *et al.*, 2013; Almeida *et al.*, 2024). According to the AAPM TG-43U1 report, LiF-based dosimeters are recommended for experimental dosimetry in