DESIGN AND CONSTRUCTION OF A SOURCE HOLDER FOR THE
DETERMINATION OF SOURCE STRENGTH OF IODINE-125 LOW DOSE
RATE BRACHYTHERAPY SOURCES

BY

SARATHIEL TUYIZERE
(10640192)

THIS THESIS IS SUBMITTED TO THE MEDICAL PHYSICS DEPARTMENT,
UNIVERSITY OF GHANA, LEGON

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF
THE
MASTER OF PHILOSOPHY

MEDICAL PHYSICS

JULY, 2019
DECLARATION

Except for references to the other studies which have been duly cited, this thesis is the result of research study undertaken by Sarathiel Tuyizere in the Medical Physics Department, University of Ghana, under the supervision of Professor A. W. K. Kyere, Dr. S. N. A. Tagoe and Dr. E. K. Sosu.

Sarathiel Tuyizere
(Student)

Prof. A. W. K. Kyere
(Principal Supervisor)

Dr. S. N. A. Tagoe
(Co-Supervisor)

Dr. E. K. Sosu
(Co-Supervisor)
ABSTRACT

Iodine-125 brachytherapy (BT) sources have gained a wide application in the treatment of prostate and intraocular cancers. Determination of the source strength of I-125 seeds is, therefore, mandatory to ensure accurate and optimal dose delivery to a patient undergoing BT treatment. There is the need to verify source strength stated or provided by a manufacturer of any BT source prior to clinical use of the source in fulfillment of American Association of Physicists in Medicine and European Society for Therapeutic Radiology and Oncology (AAPM-ESTRO) recommendations for low energy BT sources. For low energy source, this process is sometimes ignored due to unavailability of appropriate equipment to facilitate the measurement of the source strength under clinical conditions. The present study sought to find ways of measuring source strengths of I-125 BT seed sources (model number STM1251) in use at Korle-Bu Teaching Hospital (KBTH) for permanent low dose rate (LDR) prostate BT with a well-type ionization dosimetry system, which is dedicated to high dose rate (HDR) BT source calibration. The BT seed implants are manufactured by Bard BT Inc., and are loaded in a Mick® cartridge which has maximum loading capacity of 15 seeds. To achieve this, a source holder which could be accommodated within the well-type ionization chamber (WTIC) was designed and constructed from Perspex (PMMA). The constructed source holder was designed to hold a whole cartridge of I-125 BT seeds within the WTIC to facilitate batch source strength measurement. The source holder ensuring reproducibility of I-125 seeds placements during source calibration, also enabled placement of a cartridge such that the point of concentration of activity of I-125 seeds coincided with the most sensitive part of the WTIC. Calibration coefficient was established for the dosimeter system (including source holder) through correlation and regression analysis of source strength measurements performed with the dosimeter system which were compared to source strengths with national institute of standards and technology (NIST) traceability provided by manufacturer of the I-125 seed sources. The obtained calibration coefficient was validated by performing I-125 seed source calibrations with the dosimetry system and comparing the source strengths with their counterparts stated by manufacturer of the I-125 seed sources. The dosimeter system was found to have calibration coefficient of \(3.372 \pm 0.200 \times 10^{11}\) U/A for the I-125 seed
sources. The mean percentage deviation of the source strengths was found to be 2.588% which is in agreement with AAPM-ESTRO recommendations. The constructed low cost source holder is, therefore, recommended to be used for Bard I-125 seed source calibration with a HDR 1000 plus WTIC. This source calibration approach comes in handy for BT departments with limited resources.
DEDICATION

I dedicate this research project to Almighty God, the source of all skills and wisdom.
ACKNOWLEDGEMENTS

Special thanks to my supervisors – Prof. A. W. K. Kyere, Dr. S. N. A. Tagoe and Dr. E. K. Sosu – for their regular guidance during the research project. Without them this research study couldn’t come to its successful completion.

I would like to thank my lecturers who never miss classes during the first year of course works. They opened the door of medical physics program for me and gave me a great inspiration to cure cancer. Medical physics is very interesting program where physics skills which involve ionizing radiations (x-rays, gamma rays) and charged particles (electrons and protons) are used to diagnose and treat cancer, a disease traditionally known as incurable. I am much grateful to them.

I highly appreciate the financial sponsorship received from International Atomic Energy Agency (IAEA).

I thank my country (Rwanda) for nominating me to undertake medical physics program.

I also thank my classmates and friends for cooperation here at Graduate School of Nuclear and Allied Science (GSNAS).

Not least, I thank my wonderful wife Francine and my fabulous children – Winny and Aria – for their support and patience during the long months away from them to continue my studies.

God richly bless everyone and organization that contributed on my studies in one way or the other.
# TABLE OF CONTENTS

DECLARATION............................................................................................................ ii

ABSTRACT .................................................................................................................. iii

DEDICATION ................................................................................................ .............. v

ACKNOWLEDGEMENTS ............................................................................................ vi

TABLE OF CONTENTS............................................................................................... vii

LIST OF TABLES ................................................................................................ .......... x

LIST OF FIGURES ........................................................................................................ xi

LIST OF ABBREVIATIONS ...................................................................................... xiii

CHAPTER ONE................................................................................................ .............. 1

INTRODUCTION ................................................................................................ ........... 1

1.1. Background ................................................................................................ .......1

1.2. Problem statement ........................................................................................... 10

1.3. Relevance and justification .............................................................................. 11

1.4. Objectives ....................................................................................................... 12

1.5. Scope and limitation ....................................................................................... 13

1.6. Thesis organization ......................................................................................... 13

CHAPTER TWO ........................................................................................................... 15

LITERATURE REVIEW .............................................................................................. 15

2.1. Introduction .....................................................................................................15

2.2. Brachytherapy sources .................................................................................. 15

2.2.1. Iodine-125 seed source ............................................................................. 17

2.2.2. Palladium-103 seed source ....................................................................... 18

2.2.3. Dosimetric characteristics of I-125 brachytherapy sources......................20
2.2.4. Physical characteristics of I-125 brachytherapy sources ........................................22
2.2.5. I-125 seeds model STM1251 in the Mick® cartridge ........................................23
2.2.6. Source holder ................................................................................................................24

2.3. Application of LDR brachytherapy sources in treatment of prostate cancer ..........26
2.4. Source strength specification in brachytherapy .........................................................28
2.5. Calibration of radioactive sources in brachytherapy ..................................................30
2.6. Determination of source strength for low dose rate brachytherapy sources ..........33

CHAPTER THREE ...............................................................................................................37

MATERIALS AND METHODS .............................................................................................37

3.1. Materials .........................................................................................................................37
3.1.1. Perpex material ...........................................................................................................37
3.1.2. Well type ionization chamber .....................................................................................38
3.1.3. Electrometer ................................................................................................................42
3.1.4. Barometer ....................................................................................................................44
3.1.5. Thermometer ..............................................................................................................45

3.2. Methods ............................................................................................................................46
3.2.1. Calibration of well type ionization chamber ...............................................................46
3.2.2. Design and construction of source holder .................................................................47
3.2.3. Stability test of well type ionization chamber ...............................................................49
3.2.4. Fabricated source holder for sweet position determination .......................................50
3.2.5. Determination of calibration point (sweet point) ..........................................................51
3.2.6. Determination of source strength for I-125 seeds .......................................................54
3.2.7. Determination of correction factors ............................................................................55
3.2.8. Derivation of calibration coefficient for I-125 brachytherapy sources .................56
3.2.9. Measurements of source strength .................................................................................57
3.2.10. Measurements of single seeds ............................................................... 60

CHAPTER FOUR ......................................................................................................... 62

RESULTS AND DISCUSSIONS .................................................................................. 62
  4.1. Results............................................................................................................. 62
  4.2. Discussions ..................................................................................................... 68

CHAPTER FIVE........................................................................................................... 73

CONCLUSIONS AND RECOMMENDATIONS......................................................... 73
  5.1. Conclusions ..................................................................................................... 73
  5.2. Recommendations ........................................................................................... 74

REFERENCES.............................................................................................................. 75

APPENDIX A: Calibration certificate of I-125 brachytherapy sources and traceability to
NIST ............................................................................................................................. 80
LIST OF TABLES

Table 2.1: Features of some brachytherapy sources mostly used (from [4]). ...................16
Table 2.2: Common types of seeds and their manufacturers ...........................................19
Table 3.1: Single seed measurements for batches of different total air kerma strengths. .61
Table 4.1: Corrected chamber response at different source dwell position. .......................62
Table 4.2: Comparison between manufacturer stated and measured source strength. ......66
LIST OF FIGURES

Figure 1.1: A schematic illustration of I-125 source model STM1251............................. 4
Figure 2.1: Schematic illustration of source model: (a) Oncura 6711, (b) Intersource 1251L, (c) Best 125I 2301 and (d) Isoseed I25.S06................................................................. 23
Figure 2.2: A picture of the Mick® cartridge and its rigid shielding material for I-125 source model STM1251....................................................................................................... 24
Figure 2.3: A picture of Iridium-192 source holder for Leipzig applicator (from [10]). ..25
Figure 2.4: Commercial source holder: (a) for single source measurements of I-125 and Pd-109; (b) for multiple (or batch) source measurements of I-125 and Pd-109; and (c) for measurement of sources presented in the form of needles (from [10]). ......................... 26
Figure 3.1: A standard imaging WTIC with constructed source holder and thermometer inside.......................................................................................................................... 40
Figure 3.4: The experimental set up of standard imaging electrometer connected to the WTIC. .......................................................................................................................... 43
Figure 3.5: A picture of barometer used in measurements .............................................. 44
Figure 3.6: A picture of digital thermometer used in measurements. ............................ 45
Figure 3.2: Schematic diagram of source holder............................................................. 48
Figure 3.3: A picture of clinical constructed source holder............................................. 49
Figure 3.7: Front (left) and back (right) views of constructed source holder. ............... 51
Figure 3.8: An experimental set up in the process of obtaining the calibration point in the well chamber. ................................................................................................. 53
Figure 4.1: Normalized chamber response versus dwell position of the source.............. 63
Figure 4.2: Chamber response for batches of 15 seeds. ............................................... 63
Figure 4.3: Chamber response for a batch of 12 seeds................................................ 64
Figure 4.4: Chamber response for batches of 5 seeds. ................................................ 64
Figure 4.5: Manufacturer stated source strength versus electrometer reading corrected for temperature and pressure. ................................................................. 68
Figure 4.6: Chamber response against the source position (from [43]). ...................... 69
Figure 4.7: Percentage deviation of measurements between stated and measured source strength................................................................. 71
Figure 4.8: Air Kerma strength of Ir-192 seeds measured in WTIC (from [16]). ..........72
# LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAPM</td>
<td>American Association of Physicists in Medicine</td>
</tr>
<tr>
<td>ADCL</td>
<td>Accredited Dosimetry Calibration Laboratory</td>
</tr>
<tr>
<td>BT</td>
<td>Brachytherapy</td>
</tr>
<tr>
<td>COMS</td>
<td>Collaborative Ocular Melanoma Study</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>ESTRO</td>
<td>European Society for Therapeutic Radiology and Oncology</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>HDR</td>
<td>High Dose Rate</td>
</tr>
<tr>
<td>HVL</td>
<td>Half Value Layer</td>
</tr>
<tr>
<td>IAEA</td>
<td>International Atomic Energy Agency</td>
</tr>
<tr>
<td>ICRU</td>
<td>International Commission of Radiation Units and Measurements</td>
</tr>
<tr>
<td>KBTH</td>
<td>Korle-Bu Teaching Hospital</td>
</tr>
<tr>
<td>LDR</td>
<td>Low Dose Rate</td>
</tr>
<tr>
<td>MC</td>
<td>Monte Carlo</td>
</tr>
<tr>
<td>MDR</td>
<td>Medium Dose Rate</td>
</tr>
<tr>
<td>mgRaEq</td>
<td>milligrams radium equivalent</td>
</tr>
<tr>
<td>NBS</td>
<td>National Bureau of Standards</td>
</tr>
<tr>
<td>NIST</td>
<td>National Institute of Standards and Technology</td>
</tr>
<tr>
<td>NPL</td>
<td>National Physical Laboratory</td>
</tr>
<tr>
<td>NSL</td>
<td>National Standard Laboratory</td>
</tr>
<tr>
<td>PDR</td>
<td>Pulsed Dose Rate</td>
</tr>
<tr>
<td>PMMA</td>
<td>Polymethyl methacrylate</td>
</tr>
<tr>
<td>PSDL</td>
<td>Primary Standard Dosimetry Laboratory</td>
</tr>
<tr>
<td>QA</td>
<td>Quality Assurance</td>
</tr>
<tr>
<td>QC</td>
<td>Quality Control</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>------------------------------------</td>
</tr>
<tr>
<td>RAKR</td>
<td>Reference Air Kerma Rate</td>
</tr>
<tr>
<td>SSDL</td>
<td>Secondary Standard Dosimetry Laboratory</td>
</tr>
<tr>
<td>TG</td>
<td>Task Group</td>
</tr>
<tr>
<td>TPS</td>
<td>Treatment Planning System</td>
</tr>
<tr>
<td>WTIC</td>
<td>Well type ionization chamber</td>
</tr>
</tbody>
</table>
CHAPTER ONE

INTRODUCTION

1.1. Background

Brachytherapy (BT) is derived from ancient Greek words for ‘short distance’ (brachios) and ‘treatment’ (therapy), and it is sometimes referred to as internal beam radiotherapy or Curietherapy [1]. In the process of BT treatment, encapsulated radionuclides (sealed sources) having the same or different source strengths are placed into or near the target volume (tumour) to be treated. With BT one is able to escalate doses to the target volume whilst minimising doses to surrounding normal tissues below the tolerance limits. Compared to external beam radiotherapy, better dose conformity is achieved with BT. Brachytherapy is limited to the treatment of small and well localised tumours that are easily accessible from any part of the body for the application of the sources [2]. This limitation is as a result of the level of dose inhomogeneity associated with BT implants [3].

Brachytherapy treatment outcome is greatly influenced by the method or approach to be used in the determination of the strength of sources for the BT implant or treatment. Source strength determination in BT, also known as source calibration has been identified to be one of the major sources of error in BT dose calculations. Source calibration is therefore considered as an essential component of quality assurance (QA) management programme for BT. Other factors that are identified to cause errors in BT dose delivery and thus affect BT treatment outcome are: the specific model utilized for distribution of sources in the
tumour volume, the particular algorithm utilized for dose computation, the prescribed dose and dose rate utilized in the treatment [4].

Brachytherapy sources may be categorized into three groups [4]. These are photon sources, beta sources and neutron sources. Photon sources produce gamma rays through gamma decay and probably characteristic X-rays by internal conversion and electron capture. Examples of photon emitting sources are Cs-137, Co-60, I-125, Ir-192 and Pd-103. Beta sources produce electrons following beta decay. A very common example of beta source is Sr-90/Y-90. Neutron sources produce neutrons resulting from spontaneous nuclear fission. A very common example of neutron source is Cf-252.

Photon sources are found in different forms such as: seeds, tubes, needles, wires, pellets but are more often than not used as sealed sources. However I-125 sources are exclusively supplied as seeds loose or loaded in shielded reusable Mick cartridges [4]. The production mechanism of I-125 sources is via nuclear reactor by irradiating Xe-124 gas with neutron. The reaction produce unstable proton rich I-125 isotope (with half-life of 59.6 days) which decays through electron capture process to stable tellurium-125 (Te-125) with emissions of characteristic X-rays (with energies of 27.4 keV and 31 keV) and gamma rays (with energy of 35.5 keV). Iodine-125 sources are supplied in different models by various manufacturers. Some source model examples are: model STM1251 Intersource and Interstrand are supplied by Bard BT inc.; models I25.S17 Isocord & I25.S06 Isoseed are supplied by Bebig; model 2301 is supplied by Best; model 1251L is supplied by International brachytherapy (IBt); model 130.002 selectSeed is supplied by Isotron and model 6711 Rapid strand is supplied by Oncura.
The design of I-125 source (model STM1251 which is the concern of this study) is shown in Figure 1.1. The sealed capsule of I-125 source is made from titanium. Due to low energy of I-125, the titanium capsule absorbs a significant amount of emitted photons. Much of photon absorption occurs in the radio-opaque portion of the source and in weld ends. Electrons which are emitted as a result of electron capture process are completely absorbed by titanium capsule of the source. The outer dimensions of titanium capsule are 0.8 mm in diameter and 4.55 mm in length. The source inner core consists of gold rod in cylindrical shape with a diameter of 0.361 mm. The source outer core consists of aluminium hollow wire with a diameter of 0.51 mm and length of 3.81 mm. The sides of aluminium wire are all coated by copper layer onto which I-125 activity is adsorbed [5], [6]. The inner core gold rod assists as a marker of X-ray to aid in visualization of the source implant during radiographic, computed tomography (CT) or fluoroscopic imaging procedures [7].
The techniques of source implantation into the tumour volume are classified into six categories. These are intracavitary, interstitial, surface plaque, intraluminal, intraoperative, and intravascular. In case of intracavitary implant, sources are implanted into the tumour through body cavity by means of applicator. An example of intracavitary implant technique application is in the treatment of gynaecological diseases. For interstitial implant, sources are implanted into tumour mass. Interstitial implant technique has got application in the treatment breast cancer, prostate cancer and sometimes in brain and neck cancer. For surface plaque implant, sources are implanted into plaques that are placed in contact with the skin surface of the tumour. Surface plaque BT implant technique has gained wide use in the treatment of eye tumours (intraocular cancers) and less often in the treatment of skin cancer. For intraluminal implant, sources are inserted into a lumen (example: treatment of head and neck cancer). For intraoperative implant, sources are implanted surgically near or
into the tumour mass (example: treatment of stomach cancer). For intravascular implant, sources are implanted intravascularly near or into a lesion (example: treatment of metastasized bone cancer).

Brachytherapy surface plaque loaded with I-125 seeds has gained a broad application in the treatment of eye tumours even though there are still problems of a significant dose reduction caused by materials heterogeneity in the plaque. With eye plaque I-125 BT, there is a possibility that the patient may lose vision. This risk can be minimized by accurate calculation of dose distributions in the plaque material. The interstitial BT technique by using I-125 seeds has been most commonly applied in the treatment of prostate cancer [7]. Some prostate cancer cases were also treated by applying I-125 seeds through intraoperative implant technique following surgery operation. In these cases, intraoperative implantation technique with I-125 seeds presented an optimal dose coverage to the prostate gland with minimal dose delivery to urethra and rectum [9].

With respect to the duration BT sources spend inside the area or volume being treated, two groups of implants are applicable: (i) temporary implant and (ii) permanent implant. For temporary implant, dose from radioactive sources is presented to the tumour volume in a time period which is shorter compared to the half-life of the source. Sources are then transferred back when the desirable prescribed dose is achieved. For permanent implant, dose from radioactive sources is delivered over the tumour volume during the entire lifetime of the sources. In permanent implant, sources decays into the tumour volume completely. Iodine-125 sources which are often used as seeds are applied for permanent
implantations in brain, breast and prostate for temporary implantation in the treatment of eye tumours.

With respect to dose delivered by sources during BT treatment, three categories are commonly applicable. These are low dose rate (LDR), medium dose rate (MDR) and high dose rate (HDR). According to International Commission of Radiation Units and Measurements (ICRU), the value of dose specification at a point is $0.4-2 \text{ Gy h}^{-1}$ for LDR, $2-12 \text{ Gy h}^{-1}$ for MDR and greater than $12 \text{ Gy h}^{-1}$ for HDR. High dose rate treatments are applied with a substantially higher doses than the lower limit of $12 \text{ Gy h}^{-1}$. Medium dose rate delivery technique is not commonly used. In few instances in which it was applied, the treatment results were quite poor compared with LDR or HDR treatment outcome. Besides LDR, MDR, and HDR treatment techniques, another approach of afterloading treatment known as pulse dose rate (PDR) brachytherapy was established. In this treatment technique, a continuous LDR treatment is delivered to the tumour volume in sequences of short duration known as dose pulses. The pulses are delivered in 30 mins time duration separated by 1 to several hours’ intervals without treatment.

Low dose rate brachytherapy demonstrated excellent radiobiological treatment outcome of early staged prostate cancer [10]. In this case, the cancer has not yet spread into nearby critical organs such as the pelvis, bladder, gonadal glands, and rectum. Low dose rate technique is applied in the treatment of prostate cancer treatment: (1) As a sole treatment modality, by using short lived radionuclide such as Pd-103 for fast growing tumour and I-125 for slow growing tumour. (2) In conjunction with external beam radiotherapy to give a boost dose to the tumour bed. Similar treatment can also be delivered with course of
single session or fractionated treatments using HDR afterloader BT machine. Low dose rate prostate BT is considered to be the most effective treatment technique for non-metastatic prostate cancer. For prostate cancer which has already spread to nearby critical structures or distant organs, combination of both external and internal beam radiotherapy for treatment is recommended.

The strength of BT sources are specified in terms of exposure rate in air, air kerma rate in air, reference air kerma rate (RAKR) and air kerma source strength. Because of significant amount of photon emissions which is absorbed by the source capsule, low energy photon emitting sources such as I-125 and Pd-109 are highly recommended to be specified in terms of RAKR and air kerma rate source strength. The source strength of I-125 is recommended to be determined by using a WTIC designed for BT application and having calibration certificate from an accredited dosimetry calibration laboratory (ADCL). The WTIC must have a large detection volume to enable measurement of low ionization signal easily and precisely. Before 1999, Ritz free-air chamber was used for the source strength determination (or source calibration). However due to its small detection volume, single source measurements were impossible or impractical [11]. The dose received by the patient undergoing BT treatment is strongly affected by the strength of radioactive sources being used. It is therefore recommended to every institution planning or providing BT to have an independent method of source strength verification.

A source holder is one of BT dosimetry devices with a central tube designed to hold a particular isotope seed of iodine, palladium, gold etc, at the most sensitive position (commonly known as sweet position) within the WTIC during source calibration
procedure. A perfect phase of source holder is useful in source strength verification for low and/or high dose of different BT sources. A source holder is designed to equip and position a radioactive source or seed in the WTIC for precise, prompt, and reproducible measurements of source strength. Brachytherapy source holders provide a possibility of measuring a batch containing many sources or seeds for up to 500 of I-125 or Pd-103 used in the treatment of prostate cancer [12]. Thus, a source holder is an important device of the dosimetry system in BT source calibration. Without it calibration of sources cannot be achieved.

All sources used in BT must have the source calibration traceable to a standard dosimetry laboratory [13]. An alternative approach to this, is to have a second degree of traceability by comparing calibrated sources (sources with known source strengths) with those of unknown source strengths having the same character and kind to establish the strengths of the unknown. Source calibrations are best performed with WTIC which may be suited for calibration of both high and low strength sources. The dosimeter system (inclusive of the WTIC and its electrometer) must have calibration factor traceable to a standard laboratory [14]. The strength of all sources used in BT departments should be evaluated on their receipt with a calibrated local dosimeter system available. The locally measured source strengths should be compared with stated ones in the source certificate provided by the manufacturer [13]. Any disagreement between the locally measured value and manufacturer stated value exceeding 10% require further investigation. The patient should not be treated until the discrepancy is investigated and justified [13].
The AAPM task group (AAPM TG-40&56) reports recommend an accurate source calibration in terms of a clearly defined physical quantity. The strength of sources should be independently validated by the local medical physicist. At least 10% of sources prior their therapeutic application for every implant should be calibrated locally. The acceptable tolerance limits of 3% minimum mean and 5% maximum mean between manufacturer’s stated value and locally measured value are recommended. It is the responsibility of the local institution to verify manufacturer stated value by using ADCL calibrated equipment. Since there have been cases of dead sources (without any activity) and some sources with twice the strength of the others in the same batch, it is obligatory to measure the strength of sources before use. It is thus unwise approach to just trust what a manufacturer has stated in the accompanying source certificate [15].

An important aspect of any BT treatment is determination of source strength (source calibration) with traceability from standard laboratories. However due to a large number of sources of up to 100 or even more used to treat the patient, it is impossible or impractical to determine the strength of each individual source. It is for this reason that the general guidelines and recommendations of AAPM TG 56 are not practical for low energy BT source calibration. At present, the AAPM-ESTRO recommendations is the recommended guidance to follow during calibration process of low energy sources such as I-125 and Pd-109 [16], [17].

Seeds of I-125 radionuclide are now widely used for permanent LDR prostate BT implants [4]. The recommended dose to the prescription point (usually the boundary of prostate capsule) in case of prostate cancer treatment with I-125 BT seeds ranges from 150 - 160
Gy for full implants. Larry, et al. [18] showed that a particular source holder used with a specific WTIC may influence results of measurement of source strength, and hence caution needs to be exercised in the choice of a source holder to be used for BT source calibration.

This study seeks to design an appropriate source holder made of perspex material with the capacity to accommodate Mick® cartridge containing a maximum number of 15 seeds of I-125 sources (model STM1251) in HDR 1000 plus WTIC during source calibration process. The developed source holder will serve as one of the devices of dosimeter system useful in the verification of I-125 source strength specified by the manufacturer prior to clinical use of sources as strictly recommended by AAPM-ESTRO recommendations for low energy source calibration. An appropriate source holder ensure reproducibility of source placements in the WTIC resulting in precise measurements of source strength. Accurate knowledge of source strength lead to an accurate and optimal dose delivery to patients undergoing BT treatments.

1.2. Problem statement

The major source of error that can affect treatment outcome of any BT technique is determination of the source strength or source calibration of the radioactive sources used for the treatment [4]. It is recommended that prior to any BT application, the strength of any source to be used must be known accurately[16], [17]. Also, there is the need to verify manufacturers' stated source strength prior to the use of any source for BT, as some cases of high discrepancies have been recorded between source manufacturers' stated source strengths and those obtained during source calibration by end users. It is recommended that
If the discrepancy between a source strength obtained by the end user and that stated by the source manufacturer is more than 10%, the source must not be used and there is the need to investigate the source of the error as well as informing the source manufacturers about the abnormality.

For sources with low source strengths such as I-125, source manufacturers’ stated source strengths are often used without verification due to non-availability of appropriate dosimetry equipment to facilitate calibration of such sources. Owing to the design of the I-125 BT source coupled with its low source strength it would require a lot of ingenuity and specialized dosimetry equipment to enable effective calibration of the I-125 source. Well type ionization chambers with specialized commercially available source holders are used for the calibration of the I-125 sources. The Korle-Bu Teaching Hospital lacks a source holder for calibration of I-125 BT sources and this calls for fabrication of one.

1.3. Relevance and justification

As mentioned earlier, calibration of sources has to be traceable to national standard laboratories or an ADCL. An accurate knowledge of BT source strength will reduce the uncertainties in the calculated dose distribution by the BT treatment planning system (TPS). For example appropriate source holder used for determination of source strength will minimize positional uncertainty in the WTIC and thus lead to improved dose accuracy for patients undergoing brachytherapy treatments.
This research seeks to address issues associated with calibration of I-125 BT sources for LDR permanent prostate BT at the oncology department of the KBTH. Constructed local source holder can be used as a redundancy standard at the BT department as well as for routine source calibration.

1.4. Objectives

The aim of this study is to design and construct a source holder for I-125 seeds from locally available materials, which would be compatible with the WTIC in use by Radiation Oncology Department of KBTH.

The objectives of the study are threefold:

1. To use the constructed source holder with the WTIC to measure source strength of I-125 seeds.

2. To compare measured source strength and manufacturer's stated source strength.

3. To establish calibration coefficient for the dosimeter system (including the constructed source holder) based on manufacturer's stated source strength.
1.5. Scope and limitation

The research project covers the design and construction of the source holder, calibration of low dose rate I-125 source using the WTIC and evaluating the quality control of the constructed source holder. Measures were put in place to make sure that the dimensions and components of the locally constructed source holder are precise to fit the mouth and cavity of WTIC using an available model for design and machines at the market. The calibration procedures followed AAPM-ESTRO recommendations for low energy BT sources.

1.6. Thesis organization

This thesis consists of five chapters namely introduction, literature review, methodology, results and discussions, and conclusions and recommendations. The first chapter introduces the research work. It includes adequate background of the study, statement of the problem to address, objectives of the study, relevance and justification of the study, as well as scope and limitation of the study. The second chapter provides a summary description of past literature which are relevant to the research study. The chapter three presents a brief detail of materials and dosimetric equipments used including their manufacturers and serial numbers. The description of methods used are also provided in chapter three. The chapter four presents the results/findings of the study which include tables and graphs. The discussions about significance of the results/findings in relation to other published studies are also provided in chapter four. The last chapter provides the summary/conclusions of
the study. The recommendations to BT departments are also presented in the last chapter of the thesis.
CHAPTER TWO

LITERATURE REVIEW

2.1. Introduction

This chapter presents a brief review of past literature which are related and relevant to the research study. The first section presents a historical review of radioactive sources and their evolution in the field of internal beam radiotherapy. A brief description of most common LDR sources, their dosimetric and physical characteristics and commercially available source holders that are used in BT is also presented in the first section of this chapter. The second and third sections present a literature of how LDR sources are applied in BT to treat prostate cancer and eye tumour. A brief historical review of how BT sources should be specified in terms of quantity of radiation emitted rather than activity contained is provided in the fourth section. The fifth section presents a brief description of source calibration in BT with much emphasis on low energy short half-life sources. AAPM and other recommendations about source strength determination and verification of LDR sources and current related literature are presented in the last section of this chapter.

2.2. Brachytherapy sources

In the earlier years of BT, the naturally occurring radionuclides, such as radium were exclusively used. After almost 50 years, new radionuclides were introduced into the field of BT owing to the advent of production of artificial radionuclides in nuclear reactor [19], [20]. There is an extensive menu of radionuclides emitting gammas, betas, or neutrons with
a broad range of energies and half-lives, used in medicine. For BT applications, they are encapsulated in biocompatible, sealed capsules made of materials such as titanium. Photon-emitting radionuclides used in BT include Ra-226, Cs-137, Ir-192, Au-198, Cs-131, I-125 and Pd-103. Among these I-125 and Pd-103 are used for permanent prostate BT, with I-125 being the most commonly used [21]. Table 2.1 shows physical characteristics of contemporary BT sources that are most used for BT applications, and in Table 2.2 are listed common types of I-125 and Pd-103 seeds and their corresponding manufacturers.

Table 2.1: Features of some brachytherapy sources mostly used (from [4]).

<table>
<thead>
<tr>
<th>Source</th>
<th>Average Photon energy (Mev)</th>
<th>Half-life</th>
<th>HVL (mm)</th>
<th>$\Gamma_{AKR}^{2,4}$ ($\mu$Gy.m$^2$/GBq.h)</th>
<th>$\Lambda^{3,4}$ (Gy h$^{-1}$/Gy m$^2$h$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-60</td>
<td>1.25</td>
<td>5.26 years</td>
<td>11</td>
<td>309</td>
<td>1.11</td>
</tr>
<tr>
<td>Cs-137</td>
<td>0.66</td>
<td>30 years</td>
<td>6.5</td>
<td>77.3</td>
<td>1.11</td>
</tr>
<tr>
<td>Au-198</td>
<td>0.41</td>
<td>2.7 days</td>
<td>2.5</td>
<td>56.2</td>
<td>1.13</td>
</tr>
<tr>
<td>Ir-192</td>
<td>0.38</td>
<td>73.8 days</td>
<td>3</td>
<td>108</td>
<td>1.12</td>
</tr>
<tr>
<td>I-125</td>
<td>0.028</td>
<td>59.6 days</td>
<td>0.02</td>
<td>33.7</td>
<td>_</td>
</tr>
<tr>
<td>Pd-103</td>
<td>0.021</td>
<td>17 days</td>
<td>0.01</td>
<td>_</td>
<td>_</td>
</tr>
</tbody>
</table>

Note:

1 These are only appropriate values which depend on the source presentation and filtration.

2 $\Gamma_{AKR}$ is the air kerma rate constant.

3 $\Lambda$ is the dose rate constant.

4 Using generic values of the air kerma rate constant or dose rate constant for a low energy photon source may lead to significant errors in dose calculations. That is why they are thus not provided here for I-125 and Pd-103.
2.2.1. Iodine-125 seed source

Iodine-125 is produced by thermal neutron bombardment of Xe-124 gas in nuclear reactor with activity concentration of about 3.7 GBq mm$^{-3}$[22]. Iodine-125 with a half-life of 59.6 days decays exclusively by the electron capture process [23]. The principal characteristic X-rays of energies ranging from 27.4 to 31 keV and a low energy gamma rays of approximately 35.5 keV are emitted during the decay process. The average photon energy is approximated to 28 keV. The half value layer (HVL) for the emitted photons by encapsulated sources containing this radionuclide is about 0.025 mm of lead, making it comparatively easy to shield personnel from its emissions. I-125 seeds are employed mainly for permanent implants, but are likewise suited for temporary operations. Several manufacturers supply I-125 seeds for BT, and each uses a somewhat different source design. Most designs are cylindrical and have outer dimensions of about 0.8 mm diameter and 4.5-5.0 mm length. They are frequently supplied to as brachytherapy “seeds”.

I-125 sources are often used in BT to treat prostate cancers [9], and intraocular tumours (retinoblastoma and choroidal melanomas) [24]. I-125 seeds are indicated for the treatment of tumours that have the following characteristics: slow growing rate, localized, and low to moderate ratio sensitivity. The tumours with low to moderate ratio sensitivity contain individual cells referred to as hypoxic cells that are more resistant to ionizing radiation. The treatment of these type of tumours require extra high doses to achieve optimal treatment. Iodine-125 seeds are also indicated for the treatment of residual tumours and recurrent tumours following a practice of external radiation therapy. Required activity of I-125 seed used in ophthalmic application is, on average, 20 mCi (equivalent to 740 MBq).
and in other applications most often 4-5 mCi (equivalent to 148-185 MBq). It is important to note that BT using I-125 sources is very effective in the treatment of prostate cancer [4].

2.2.2. Palladium-103 seed source

Palladium-103 is produced by cyclotron irradiation of rhodium targets with accelerated protons. This process permits the output of carrier free Pd-103 having near theoretical value of specific activity of 75000 Cig\(^{-1}\) which is equivalent to 2.8 \times 10^6 GBqg\(^{-1}\). However, the carrier (metal palladium) is usually added to stabilize its behavior at isolation from radioactive impurities and at seed core production. In such a case the Pd-103 specific activity decreases, but it should be at least 5 Cig\(^{-1}\) which is equivalent to 185 GBqg\(^{-1}\) for successful source production. The disadvantage of cyclotron production of Pd-103 is the relatively high cost of this radioisotope. An alternative approach to Pd-103 production mechanism is nuclear reactor irradiation of Pd-102. The low natural isotopic abundance of Pd-102 which is about 1.02% requires the exercise of moderate to highly enriched Pd-102 target material of no less than 50%.

Under an IAEA co-ordinated research project, methods for the production of Pd-103 and seed cores of palladium were prepared by a Russian Federation participant [23]. A method based on nuclear reactor irradiation of isotopically enriched Pd-102 up to 80% was tested for Pd-103 production [23]. Irradiation in the high-flux reactor provides Pd-103 with specific activity up to approximately 500 Cig\(^{-1}\) which is equivalent to 1.85\times10^4 GBqg\(^{-1}\). Based on this result, it can be seen that moderate flux reactors with a neutron flux density of 1014 cm\(^{-2}\) s\(^{-1}\) can also be used in Pd-103 production with specific activities much more
higher than the required minimum of 5 Cig$^{-1}$ which is equivalent to 185 GBqg$^{-1}$ for BT application.

Pd-103 with a half-life of 17 days, decays via the electron capture process with the emission of characteristic X-rays in the energy range of 20-23 keV, and Auger electrons. The weighted mean photon energy is 20.7 keV. The HVL required to shield the emitted photons from Pd-103 is about 0.004mm of lead.

Table 2.2: Common types of seeds and their manufacturers

<table>
<thead>
<tr>
<th>Common types of seeds</th>
<th>Seed manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodine-125</td>
<td></td>
</tr>
<tr>
<td>OncoSeed</td>
<td>Oncura, Inc.</td>
</tr>
<tr>
<td>EchoSeed</td>
<td>Amersham</td>
</tr>
<tr>
<td>RAPID Strand</td>
<td>Oncura, Inc.</td>
</tr>
<tr>
<td>IoGold</td>
<td>North American Scientific</td>
</tr>
<tr>
<td>BEST Iodine-125</td>
<td>Best Industries</td>
</tr>
<tr>
<td>Symmetra</td>
<td>Bebig</td>
</tr>
<tr>
<td>ProstaSeed</td>
<td>Mills Biopharmaceuticals</td>
</tr>
<tr>
<td>PharmaSeed</td>
<td>Syncor</td>
</tr>
<tr>
<td>ISoStar</td>
<td>International Isotopes</td>
</tr>
<tr>
<td>I-Plant</td>
<td>Implant Sciences</td>
</tr>
<tr>
<td>InterSource-125</td>
<td>International Brachytherapy</td>
</tr>
<tr>
<td>Advantage I-125</td>
<td>IsoAid</td>
</tr>
</tbody>
</table>
STM1251  BARD, Inc.
BrachySeed  DRAXIMAGE, Inc.

Palladium-103
Pd Gold  North American Scientific
Theraseed 200  Theragenics
BEST Palladium-103  Best Industries
InterSource 103  International Brachytherapy

2.2.3. Dosimetric characteristics of I-125 brachytherapy sources

External design of I-125 BT sources appear to be the same but their dosimetric characteristics are different. Dosimetric characteristics of I-125 BT sources are all reported according to the AAPM-TG43 recommendations. However the association recommends various source manufacturers to have at least two independent methods of dosimetric measurements and one Monte Carlo (MC) simulation for confirmation of dosimetric characteristics of new sources before its clinical application. Dosimetric characteristics to be verified are: air kerma source strength, dose rate constant, geometry function, radial dose function and anisotropy function [25], [26]. The air kerma source strength as an important dosimetric quantity which is required to deliver dose to the prescription point, depends on both dosimetric and physical characteristics of the source.

Heintz et al. [7] conducted an extensive comparison study on dosimetric characteristics of I-125 BT sources that are used for permanent interstitial implants. Source models considered in their study are: OncoSeed model 6711& 6702, IoGold, Symmetra, IsoSTAR,
ProstaSeed, PharmaSeed, 125Implant BrachySource, I-Plant, Best Medical Model 2301, BrachySeed, and InterSource125. The measurements of dosimetric characteristics were performed by using ion chambers, thermoluminescent dosimeters, and films whilst the calculations were performed by using MC software programs with different data of photon beam attenuation coefficients. Afterwards, they compared dosimetric parameters of considered sources with that of oncoseed model 6711 as a reference source. In the end, the author came up with a simple equation useful to determine the source strength of a new source design. Their equation to calculate the unknown source strength is:

\[
(S_k)_{unknown} = \frac{\Lambda_{6711} \times (\phi_{an})_{6711}}{\Lambda_{unknown} \times (\phi_{an})_{unknown}} \times (S_k)_{6711}
\]

(2.1)

where \(\Lambda\) is the dose rate constant in CGyh\(^{-1}\)U and \(\phi_{an}\) is the anisotropy factor.

The dose rate constants of each considered source were compared based on one dimensional TG-43 formalism. Even though the dose rate constants were calculated at radial distances ranging from 0.3 to 1.5 cm, the author reported that the best approximation of source strength determination was obtained at 1 cm radial distance.

On the other hand, Solberg et al. [25] studied dosimetric characteristics of three new commercially available I-125 BT sources namely Pharmaseed BT-125-1, BT-125-2 and ADVANTAGE sources. By following AAPM TG-43 standard, the authors obtained dosimetric parameters including radial dose function, dose rate constant and anisotropy function. By using MC approach, point and line source approximations; the authors determined geometry function. By following the 1999 NIST standard, the air kerma source strength was also determined. The author observed that MC methodology resulted in more
accurate dosimetric parameters for low energy BT sources compared to thermoluminescent dosimeter measurements.

2.2.4. Physical characteristics of I-125 brachytherapy sources

Iodine-125 BT sources are physically characterized based on three properties. The first one is the physical construction of the source; the second is the visualization property of the source during imaging; and the third is activity distribution within the inner core of the source [7]. The cross sectional view of some selected source design is illustrated in Figure 2.1. Materials that are often used to design and construct the inner core of the source are resin, ceramic, glass and high Z materials. The distribution of I-125 activity is either by volume distribution where activity is absorbed throughout the inner core or by surface distribution where activity is adsorbed across the surface of the inner core.
Figure 2.1: Schematic illustration of source model: (a) Oncura 6711, (b) Intersource 1251L, (c) Best 125I 2301 and (d) Isoseed I25.S06 (from [8]).

2.2.5. I-125 seeds model STM1251 in the Mick® cartridge

The Mick® cartridge for I-125 source model STM1251 manufactured by Bard BT, Inc. comprises a number of 5-15 seed implants loaded parallel to one another and a plunger revised to transfer one of the seeds at a time from the cartridge into a Mick® TPV applicator. A picture of the Mick® cartridge and its rigid shielding material (i.e container) is shown in Figure 2.2. The Mick® cartridge consists of a small hole when the hollow needle can pass and be used to implant the seeds into patient organ or tissue [27]. Each I-125 seed implant contains a radioactive material including a metallic housing. The metallic housing has first
and second longitudinal ends and a longitudinal length between the first and second longitudinal ends. Additionally, each seed consists of a polymeric material (titanium casing) molded to completely encapsulate the metallic housing of the radioactive seed. A portion of the molded titanium casing extends from one of the first and second longitudinal ends of the metallic housing to decrease a tendency of the seed to rotate and migrate within the patient body after implantation. In addition, the titanium capsule of I-125 source model STM1251 absorbs the emitted electrons from the source.

![Source holder diagram](image)

Figure 2.2: A picture of the Mick® cartridge and its rigid shielding material for I-125 source model STM1251.

2.2.6. Source holder

A source holder is a device usually made from Perspex having central tube designed to hold and accommodate a particular radioactive source at the most sensitive region (sweet position) within the WTIC during calibration of BT sources. Source holders are designed to be specific for a particular BT source and its application. The source holder provides a means to accommodate and position sources in the WTIC to ensure accurate, fast, and
reproducible set up for the measurements of source strength (or activity). Because the response of WTIC on radiation depends on source position and its orientation, its type and its form representation (wire, seed, pellet, tube, etc), it is highly recommended that an appropriate source holder which is capable to reproduce the source geometry in the WTIC in the course of source strength (or activity) measurement should be used. Pictures of commercially available source holders for Ir-192, I-125 and Pd-109 are shown in Figure 2.3 and Figure 2.4.

Figure 2.3: A picture of Iridium-192 source holder for Leipzig applicator (from [12]).

Figure 2.3 shows a picture of Iridium-192 commercial source holder for Leipzig applicator. When the holder is used with Standard Imaging HDR 1000 plus WTIC with an ADCL calibration certificate, forms a complete dosimeter system for measurement of source strength (or activity). There is no additional equipment or device required to verify the source strength (or activity) measurements with published correlation factors.
Figure 2.4: Commercial source holder: (a) for single source measurements of I-125 and Pd-109; (b) for multiple (or batch) source measurements of I-125 and Pd-109; and (c) for measurement of sources presented in the form of needles (from [12]).

2.3. Application of LDR brachytherapy sources in treatment of prostate cancer

Low dose rate brachytherapy sources have gained a wide acceptance in the treatment of early stage prostate cancer. The placement of short lived low photon emitting sources is often used as the primary treatment. Some attempts are also being made to use single or fractionated HDR brachytherapy treatments in conjunction with external beam radiotherapy. In order to use permanent source implants, several factors must be considered. These include the type of radionuclide, the technique used in TPS, the technique of source delivery and total dose prescription.
The use of permanent radioactive seed source in the treatment of early stage prostate cancer has gained renewed interest with the introduction of I-125 and Pd-103 low energy photon emitting sources in BT. Gold-198, a medium energy photon emitting of about 400 keV, were used in the past. However the associated excessive radiation exposure hazard banned the use of Gold-198 radionuclide from acquisition and wide acceptance. Palladium-103, which has almost a third half-life of I-125, provides a higher initial dose rate and hence was found preferable in treating of fast growing high grade prostate cancer [4].

There exists two surgical techniques to perform source implantation in prostate cancer treatment: (1) open (retropubic) and (2) closed (transperineal) with CT or ultrasound. The transperineal technique with guidance of ultrasound has become very popular method because it is fast and permit an outpatient single day procedure.

The transperineal technique lends itself to more accurate placement of sources within the prostate gland which allows dose to critical structures (urethra, rectum) to be minimized. The introduction of high frequency ultrasound probes has shown that the placing of sources and applicators can be monitored in longitudinal and transverse planes. The planning and dosimetry procedure are the same whether using afterloading machine or source implantation. However, permanent source implants of I-125 and Pd-109 seeds distributed within the prostate gland and undergo complete decay in the patient, are more widely used [28], [29].
2.4. Source strength specification in brachytherapy

During the early days of BT, strengths of BT radioactive sources were specified in terms of: apparent activity (mCi/MBq) or radium mass equivalent (mg RaEq). Radium, usually found in the form of tubes and needles, has been initially specified in terms of Ra-226 confined mass. Radium was not used for long as it needed to be prohibited from clinical use owing to its relative long half-life, high linear energy daughter gases it produces through radioactive decay and energy associated with radium source. Source strengths of replacements of radium such as Cs-137 and Ir-192 were specified in terms of Radium mass equivalent, to provide the equivalent dose rate at 10 mm from the source. On the other hand, apparent activity was broadly used. However, these activity definitions can be unclear and lead to numerous errors in measurement of source strength for encapsulated sources used in clinics.

Wambersie and Prignot [30] suggested that the strength of sources should be quantified in terms of the amount of radiation they emitted rather than the activity they contained. This suggestion minimises uncertainties associated with relating strengths of sources to the radiation they emitted. In addition, the approach also reduces errors introduced by filtration and absorption offered by source encapsulation material. It is for this reason that various regulations and international recommendations have suggested that the strength of BT sources should be specified in terms of air kerma to account for the effect of capsules on source activity [31], [32].

The recommended quantity is the reference air kerma rate in air (RAKR). The RAKR is defined as “kerma rate to air determined in air at a reference distance of 1 m, corrected for
air attenuation and scattering [32]”. Meanwhile, Kerma is defined as “a ratio of the summation of all initial kinetic energies of ionizing charged particles produced by uncharged ionizing particles in the volume to the mass of considered material or tissue”. Note that charged particles produced outside the volume of interest do not contribute to kerma and kerma only applies to indirectly ionizing particles (e.g. photons). The unit of kerma is Joules per kilogram (Jkg\(^{-1}\)) or Gray (Gy). In RAKR measurements, the direction from the source center to the reference point will be at right angles to the long axis of the source for needles, tubes, wires and other rigid sources. It is highly recommended that for wire sources, the RAKR is specified for a 1 mm length of wire [33]. The RAKR unit is Gy s\(^{-1}\) at reference distance of 1 m. However, it is recommended to use µGy h\(^{-1}\) at 1 m for LDR sources, and µGy s\(^{-1}\) or mGy h\(^{-1}\) at 1 m reference distance for HDR sources.

The AAPM TG 32 [14] had recommended a different dosimetric quantity air kerma strength, \(S_k\). By definition, “air kerma strength is the product of air kerma rate in air and the square of the distance from the source to the calibration point”. Mathematically, \(S_k\) is given by equation (2.2).

\[
S_k = \dot{K}_R \times d_{ref}^2
\]  

(2.2)

Where \(\dot{K}_R\) is RAKR again defined by “the ICRU as the air kerma rate in air at a reference distance of 1 m, \(d_{ref}\) corrected for scattering and attenuation in air”. It is recommended that during calibration measurement, the distance from the ionization chamber to the source should be large enough so that the source can be considered as a point source and the chamber as a point detector. Ideally, the recommended distance from the chamber to the source should be at least 10 times the source length. The air kerma strength unit recommended by AAPM is µGy m\(^2\) h\(^{-1}\) or cGy cm\(^2\) h\(^{-1}\) which is short noted by the upper
case character U. Practically, the dosimetric quantities RAKR and air kerma strength are arithmetically the same but dimensionally different [13].

The RAKR, $\dot{K}_R$, is related to the source activity expressed in Bq, as follows:

$$\dot{K}_R = \frac{\Gamma A}{d^2}$$

The exposure rate constant, $\Gamma$ and contained activity are problematic to measure accurately. Because of the uncertainties posed by these quantities in the measurement of source strength, they are currently not recommended to be used in clinics [15].

2.5. Calibration of radioactive sources in brachytherapy

The strength of sources for BT applications is usually specified in terms of air kerma rate in air at a point of interest for a reference distance of 1 m from the source. The point is located on the radial plane of symmetry which intersects the active length through the cylindrical axis of the source. For the case of wire source, the strength of sources must be specified in terms of the RAKR per mm for a 10 mm source length.

It is recommended that before using BT sources at the clinic, they should be measured by the user to check their strength (or activity). At present, there exist two methods that are often used for BT source calibration. (i) a calibrated WTIC can be used, and is frequently the recommended method in most cases. (ii) air kerma measurement in air can as well be used with an ionization chamber at a recommended distance from a point source. A correction for the chamber volume has to be done for in-air air kerma calibration method. When the distance from the point source to the detector point is smaller in comparison with the size of the detector, the volume chamber factor can influence the result of
measurements significantly. The recommended measurement equipment for low energy sources is the method of using calibrated WTIC [34]. Calibration of the WTIC should be performed by primary standard dosimetry laboratory (PSDL) or SSDL. The performance of a calibrated dosimeter system should be checked frequently using radioactive source of known source strength which is considered as a reference or standard source. For low energy sources, this calibration can be done by using radioactive sources calibrated at national standard laboratory (NSL). Air kerma rate calibration of Co-60, Cs-137, Ra-226, and Ir-192 sources have been performed at the national physical laboratory (NPL), U.K [35]. The overall approximated uncertainty with 95% confidence level was found to be ±1.4% for Co-60, Cs-137 and Ra-226 and ±1.5% for Ir-192 respectively [35].

WTIC that is used for source calibration must respond linearly with source strength (or energy of radiation from source) for the measuring range. The energy response of WTIC should be known accurately. Attention should be paid to ensure that the chamber sensitivity doesn’t drop during measurements. Before being used, the relationship between the chamber sensitivity and the source position inside the well of the chamber must be obtained experimentally. Normally, the sensitivity of WTIC increases slowly with distance from the chamber base to its maximum value where the response is uniform, and then starts to fall down as one approaches the mouth of WTIC. For some WTICs, where the surface portion of the chamber is also accumulating the ionization, maximum response might be determined there. In order to establish how the chamber reacts to source strengths of different types, characteristic response of WTIC for every source should be obtained.

A source holder made from PMMA (perspex) must be used during source calibration procedure to ensure accurate reproducibility of source position in the WTIC. It is advisable
to position the source in the region of highest sensitivity within WTIC where variation in chamber response with position of the source is very insignificant. It is also recommended that the WTIC must be placed at 30 cm minimum distance from neighboring items that could cause scattering of radiation. The user should be mindful that the chamber’s response also depends on encapsulation of the source and filtration [36].

As aforementioned brachytherapy source calibration measurements might as well be made in air by use of an ionization chamber as a detector. Even though the RAKR is specified at reference distance of 1 m, in practice measurements are not performed at this distance. Reference air kerma rate of measurements performed in air, $\dot{K}_R$, could be obtained using the following equation (2.4):

$$\dot{K}_R = N_K \times (M_u / t) \times k_{air} \times k_{scatt} \times k_n \times \left(\frac{d}{d_{ref}}\right)^2 \quad (2.4)$$

where “$N_K$ denotes ionization chamber air kerma calibration factor; $M_u$ denotes the measured charge in time interval $t$ and corrected for temperature and pressure, saturation and transit effects; $k_{air}$ denotes the correction factor for photon attenuation in air; $k_{scatt}$ denotes the correction factor for scattering of radiation; $k_n$ denotes the non-uniformity correction factor; $d$ denotes measurement distance; and $d_{ref}$ denotes 1 m as the reference distance”.

Methods of obtaining these factors are provided in IAEA technical document (TECDOC) 1274 [34]. The document gives explanations of methods for obtaining room radiation scattering and investigations from Kondo and Randolph [37] and Bielajew [38] about chamber correction factors in photon emitting sources. The distance between the source and the chamber depends on the strength of source and the chamber sensitivity. The
recommended distance ranges from 5 cm to 20 cm for chambers volume of up to 30 cm$^3$. For low energy sources, chambers of large volume from 30 cm$^3$ to 100 cm$^3$ are recommended for improving their sensitivity. Leakage currents greater than 0.1% of the signal require attention and should be corrected. Very big chambers present significant non-uniformity error and consequently they are rarely used in practice.

Air kerma rates must be measured and be compared with the RAKR in the manufacturer certificate. Divergences greater than tolerance limits which are provided by the manufacturer require further investigation. The most suitable method of determining individual source strength depends mainly on source type.

2.6. Determination of source strength for low dose rate brachytherapy sources

In LDR applications of seeds comprising I-125 or Pd-103, there have been productions of new seeds and clinical convenience packing options. To preserve consistency in seed dosimetry, studies have been published [39], [40] to guarantee the values for the air kerma strength dosimetry and calibration, especially the dose rate constants are consistent. On every ADCL calibration report, there is a date to which a certain seed is traceable to NIST so that the correct air kerma strength is related with the correct published dose rate constant as recommended in DeWerd et al [39]. This date is very relevant because the initial baseline dosimetry for usage in the AAPM TG43 formalism [13] is traced to this NIST date, which is also applied by ADCLs for calibration of clinical equipment.

Manufacturers customarily provide the clinical sites with batches of seeds partaking a single designated source strength value, which have a large window of uncertainty,
commonly in the range of ±4% to ±7%. According to the data prior to 1995, as given in prior AAPM summer school publications [41], [42] and a categorical course at the Radiological Society of North America, DeWerd et al. [40] showed that the air kerma strength of some sources were obtained to be 10% greater than the labeled output strength. There are a number of subjective examples of the manufacturer’s stated activity being different by 7% or greater for all source types for both HDR and LDR measurements [40]–[42]. While a ±10% tolerance level as listed by manufacturers is practicable for diagnostic and regulatory purposes, each clinic should appreciate the significance of verifying the average manufacturer stated source strength to within the 5% tolerance level as urged in the TG56 report [15]. Because of large additional uncertainty in the post implant migration of seeds and the implant process itself and, it is obligatory to determine the source strength as accurately as possible in order to minimize the total treatment uncertainty.

The procedure of QA of the AAPM and ESTRO recommendations [16], [17] for low energy source calibrations state that: “(1) For each multi-source implant with a great amount of movable seeds, AAPM recommends that a random sample containing at least 10% of the seeds must be examined. For seeds procured in a sterile configuration, AAPM recommends procuring and examining a number of non-sterile movable seeds equivalent to 5% of the total number of seeds or five seeds, whichever is lesser. (2) AAPM also recommends that (a) if the mean value of user’s individually measured seed strength for the examined batch differs with the manufacturer’s stated value by more than 3%, the user must investigate the origin of the discrepancy; (b) an unexplained discrepancy exceeding
5% must be reported to the manufacturer; (c) the measured strength of each distinct seed should be within 5% of the measured mean for the batch”.

Generally, WTICs are used for BT source calibration dedications. Moreover, the source holder for each well chamber should be able to reproduce accurately the central position or NIST traceability geometry of source calibration. This central position is essential when performing multiple source measurements as discussed in the summer school proceedings [42], [43]. The whole source train should be positioned within axial region of the chamber of uniform response denoted to as the “sweet length”. The influence of the source holder on the measurement is taken into account in the calibration coefficient, and the recommended practice is to use a WTIC calibrated by an ADCL, which is directly traced to NIST as suggested by the AAPM TG40 report [44].

In order to fulfill AAPM-ESTRO recommendations of I-125 seeds quality assurance, Candela, et al. [45] designed a new source holder for the WTIC to evaluate the air kerma source strength of I-125 sources at PTW, Germany. The developed holder is capable of measuring the source strength of 10 seeds in the cartridge at once. In the study, a calibration coefficient of new holder which allows to convert WTIC response readings when 10 seeds are measured to their mean air kerma source strength was determined. The measurements of source strength obtained by using the new holder was compared with those obtained by using PTW source holder which can evaluate individual seed measurements. The results of source strength obtained using new holder were found to be consistent with those obtained using PTW holder.
Otani, et al. [46] designed a novel jig made of transparent acrylic material useful to determine the source strength of I-125 single seed (OncoSeed model 6711) by using a WTIC. The developed jig allows to assay the source strength of each I-125 seeds while they are still within cartridge sealed within a sterilized package and hence helps to detect aberrant (out of calibration) seed in the cartridge. This method permits to minimize the issues concerned with seeds contamination and duration of measurement. The method offers a fast practical application for all BT departments that needs to verify the source strength of seeds contained in a sterile convenient blister package.

This research project aims to design and construct a source holder (or sometimes called an insert in literature) to allow verification and determination of air kerma source strength for I-125 seeds in order to fulfill the AAPM-ESTRO recommendations at KBTH. A WTIC which is from ADCL and traceable to NIST, USA was provided by KBTH to facilitate measurements.
CHAPTER THREE

MATERIALS AND METHODS

3.1. Materials

The materials and BT dosimetry system that were used to conduct this research are: (1) Perspex material for construction of I-125 source holder; (2) WTIC available at Korle-Bu Teaching Hospital for calibration procedure and is traced to ADCL; (3) The designed source holder for I-125 seeds to hold the seed at different position within the WTIC and to accommodate the cartridge of I-125 seeds allowing measurement of source strength of various batches; (4) Electrometer for ionization current and charge measurements; (5) Barometer to measure atmospheric pressure and (6) Digital thermometer to measure temperature inside the WTIC at clinic site to allow correction of environmental variations that influence measurements. In the following subsections, a brief description of each material or device is made.

3.1.1. Perspex material

Perspex material also known as Polymethyl Methacrylate (PMMA) is a transparent thermoplastic often used in sheet form as a lightweight or shatter-resistant alternative to methamphetamine. It is much chosen because of its moderate properties, soft manipulation and processing, and low price. Non-modified PMMA behaves in a brittle manner when under load, particularly under an impact force, and is more prone to scratching than conventional inorganic glass, but modified PMMA is sometimes able to achieve high
scratch and shock resistance. PMMA has density ranging from 1.17 to 1.20 g/cm³. The environmental stability of PMMA is far greater than that of polystyrene and polyethylene plastic materials. Therefore, PMMA has been often the fabric of choice for outdoor applications.

Commercially available source holders for I-125 used in BT are made from perpex materials [18]. Perspex material is a tissue equivalent material which is capable to absorb and scatter radiation in the same manner as water or tissue can do. The malleability property of perspex material facilitates shaping during fabrication procedures. PMMA materials have therefore become a material of choice in construction of BT dosimetry equipment and devices such as source holders, phantoms and ion chambers.

3.1.2. **Well type ionization chamber**

Ionization chambers are used in BT as detectors to measure radiation emitted by radioactive sources. Ionization chambers are available in several forms and sizes, depending on the specific application [22], but they all share the following two basic modes function: (1) An ionization chamber works like a gas filled cavity detector surrounded by a conducting outer wall and having a central collecting electrode. The conducting wall and the collecting electrode are separated by an insulator of high quality to cut down the leakage current when voltage is applied to it. (2) A guard electrode provided in the ionization chamber allows to further minimize the leakage current. It also helps to improve field uniformity in the sensitive volume of the chamber resulting in improved charge collection efficiency. It is
important to note that measurements done by using open ionization chambers to atmosphere require correction of temperature and pressure effects.

Low energy radioactive sources used in BT require chambers of sufficient volume for adequate sensitivity [35]. Well type ionization chambers are recommended for calibration of low energy BT sources [21]. Accredited Dosimetry Calibration Laboratory calibrated WTIC provides the most accurate, precise and suitable way to measure the source strength of particular BT source. Figure 3.1 illustrates a WTIC fitted with constructed source holder and thermometer. The WTIC was supplied by Standard Imaging Company, USA; model: HDR 1000 plus with serial number A083262. Well type ionization chambers and their specific source holders should be designed to fit the size and shape of sources which are in use at certain BT department. Well type ionization chambers are normally calibrated in terms of the RAKR.
Figure 3.1: A standard imaging WTIC with constructed source holder and thermometer inside.
In BT measurements, it is not recommended to use pressurized ionization chambers from the department of nuclear medicine because of the following reasons: (1) The chambers only perform measurement in activity units; (2) The chamber settings are for radionuclides used in nuclear medicine but not for radioactive sources used in BT; (3) Because the gas might leak from the pressurized volume, the chamber response may present significant variation over source position and time; (4) The dense walls needed for the pressurization may absorb an important part of the radiation to be measured; (5) If there is no close control, the general usage of the chamber can get contamination from nuclear medicine processes.

Despite the above mentioned reasons of not using ionization chambers commonly referred to as dose calibrators in nuclear medicine, Metyko et al. [47] recently conducted a study of verifying the source strength of I-125 BT source model IAI-125A by using a dose calibrator. Normally, dose calibrators used by nuclear medicine departments or clinics are designed for activity measurement of unsealed radioactive sources. In addition, these instruments do not have an accessory for positioning a BT source in a consistent geometry. The authors [47] created two different geometry configurations to assess dose calibrator reproducibility which is likely to be exchanged over time. The first geometry consisted of single source holder from the HDR 1000 plus model 70016 and an insert known as dipper which came together with the dose calibrator. The second geometry consisted of the dipper and a 7.5 ml glass vial that were seed containers. The results of their study showed that radionuclide dose calibrator can be used to calibrate I-125 BT source model IAI-125A. They found that the dose calibrator can be calibrated to verify I-125 source strength so that
the source strengths are in agreement to within 5% compared to manufacturers stated source strength. They also showed that their developed two geometry configurations were proven to be sufficiently reproducible for considered source model. Since source design differs from one manufacturer to another, the authors highlighted that the response of dose calibrator would likely to be different from one source to another.

There is possibility where electrometer and the WTIC have different calibration factors. If so, the overall calibration factor of the system is the product of WTIC calibration factor by electrometer calibration factor. Except for the case where the WTIC and its electrometer have been calibrated by an ADCL, the electrometer needs to be calibrated by the SSDL separately. This can be done by comparison method with other calibrated electrometers from an ADCL.

3.1.3. Electrometer

Electrometer manufactured by Standard Imaging Company, USA; model: Max 400 and serial number: F083103 was used in this work measurements. This BT electrometer is a device which is capable of measuring low ionization current in the order of $10^{-9}$ A or less. The electrometer used is a high gain operational amplifier with a standard resistor and capacitor in its negative feedback path to enable measurement of collected charge. The time interval considered during measurements is 60 seconds. Measurements were taken in electrical units of pC for charges and pA or nA for ionization currents. During measurements, the WTIC with source holder was connected to the electrometer to obtain the chamber response to radiation as shown in Figure 3.2.
Figure 3.2: The experimental set up of standard imaging electrometer connected to the WTIC.
3.1.4. Barometer

An anaerobic barometer shown in Figure 3.3 was used to correct for the effect of pressure differences that occurred between standard reference pressure (1013.25 hPa) and pressure recorded at KBTH. This device is manufactured by Prazisions, compensier model and with serial number, SN=98889. It is calibrated to execute measurements in hPa.

Figure 3.3: A picture of barometer used in measurements
3.1.5. Thermometer

A digital thermometer supplied by Extech Company, USA; serial number, SN=39240 was used for measurements in this work. The thermometer was used for correction of temperature difference effect that occurred between standard reference temperature quantified by standard laboratory (22.0°C) and the room temperature recorded at KBTH under different weather conditions. The device measures temperature in °C or °F in the ranges of -40°C to 200°C and -40°F to 392°F respectively. To measure the temperature, the thermometer was placed inside the WTIC for about 5 minutes and then taken out to read and record the temperature. Figure 3.4 represents the picture of the thermometer used in measurements.

Figure 3.4: A picture of digital thermometer used in measurements.
3.2. Methods

3.2.1. Calibration of well type ionization chamber

In order to establish a traceability for source calibrations in BT, from the PSDL via the
SSDL to the users at the level of hospital, joint use of WTICs and reference sources is
recommended. The traceability link from the user to the SSDL is developed via the
calibration of hospital’s WTICs with the help of WTICs maintained by the SSDL and
reference sources. An extension of this method via in-air measurements can be adapted for
Ir-192, Cs-137 and Co-60 HDR sources but I-125 sources are of special consideration.

Because the PSDLs do not offer calibrations for Ir-192 HDR sources straightforward, the
calibration of these sources necessitate the use of in-air measurements approach, with
substantial calibration of WTICs with the calibrated sources. In order to calibrate of I-125
sources, SSDLs must obtain a calibration factor which can in turn be conveyed to the
hospital. Because of the short half-life of I-125 sources, the constancy test of the calibration
factor of the WTIC shall be verified by using an appropriate long lived source such as Cs-
137 or Co-60 sources.

For all source calibrations done by using WTICs, the calibration point of the chamber is
at the depth of maximum and uniform response. The calibration point depends on the
type of source and should be determined before the calibration.
3.2.2. Design and construction of source holder

A source holder constructed from perpex material was used to hold I-125 BT seeds in the cartridge at different depths within the WTIC. The schematic diagram of the holder with dimensions in millimeters (mm) is shown in Figure 3.5. Dashed lines represent internal parts of the holder and solid lines represent external parts of the holder. It is important to highlight that the response of the chamber depends on source geometry and configuration, its encapsulation and filtration. The source orientation and its position in the WTIC affects the chamber response. Thus it is vital to develop an appropriate source holder that will reproduce the position of source. Figure 3.6 illustrates the parts of constructed source holder. The holder is used to assay the source strength of LDR I-125 seeds prior to their clinical use at KBTH.
Figure 3.5: Schematic diagram of source holder
3.2.3. Stability test of well type ionization chamber

Before starting any measurement of BT sources by using WTIC, it is recommended to test its stability with spontaneous changes. In this work, the stability of WTIC was carried out by irradiating the WTIC using external beam Co-60 as a reference source. The WTIC was found to be stable by providing measurements of ± 0.6 %. The distance from the top of the WTIC to the source of external beam Co-60 was set at 100 cm source surface distance.
(SSD). The field size of 15 cm x 15 cm larger than the chamber diameter was used. The WTIC surface was irradiated with a dose of 1Gy. The measurements corrected for pressure and temperature as well as for source decay was found to remain within ± 1 % at constant dose of 1 Gy.

3.2.4. Fabricated source holder for sweet position determination

Figure 3.7 shows the picture views of the constructed source holder. The left panel represents the front view of the holder and the right panel represents the back view of the holder. The front view has a ruler from the top to the bottom which helps to read the depth of source inside the WTIC. At the ends of the two views, there is a hole where the cartridge containing seeds is placed during measurements. At the tops of the two views, there is a cap connected to the central tube. The top cap is designed in such way that it can rotate in clockwise and anticlockwise directions. Clockwise rotation of the cap allows movement of the cartridge inside the WTIC. Anticlockwise rotation of the cap allows movement of the cartridge out of the WTIC. By positioning the cartridge at different depths within the WTIC, charges or ionization current can be read and recorded at such corresponding depths.
3.2.5. Determination of calibration point (sweet point)

The calibration point (sweet point) of a WTIC is well-defined as the point at which the center of the source is placed during the calibration process. This point differs from one source to another depending on the source design and packaging. Some chambers have a static, immovable, spacer and the source is then handily placed on the top of the spacer.
Other chamber models have an apparatus to change and fix the source holder to different depths. The source is then positioned at the base of mobile holder in the course of source calibration. The position of the calibration point should be specified on the chamber’s calibration documentation. Spacers and the external dimensions of the source used to calibrate the WTIC should be specified in the calibration documentation as well. Spacers must be designated such that there is no room for confusion.

For chambers provided by IAEA standard like the one used in this study, the calibration point is at the position of uniform and maximum chamber response. With the source placed at this point, the positioning uncertainty in the determination of source strength is minimized. Measurements of source strength were performed at different positions along the central axis of the WTIC. This was done by inserting the source holder at known depth from the top of WTIC and kept on modifying the depth to find out the sweet position (calibration point).

Figure 3.8 shows the experimental set up of the WTIC equipped with the constructed source holder and then connected to the electrometer. The WTIC placed at a distance greater than 30 cm away from objects and walls that may scatter radiation back to the chamber. The source holder was designed in such way that it is capable to move in and out at different depths within the chamber. The source holder is designed to be geometrically stable within the WTIC for the purpose of keeping the reproducibility of measurements. The WTIC setting was set to be high for the purpose of minimizing the interference signals.
from the background and the bias voltage was set to 300V to prevent ions from recombination.

Figure 3.8: An experimental set up in the process of obtaining the calibration point in the well chamber.

A cartridge of I-125 sources containing 15 seeds, model STM1251 and having manufacturer stated total air kerma source strength of 8.745 U was used to determine the calibration point within the WTIC. The implant date of the sources was October 13, 2018 and clinical measurements were performed on November 05, 2018 resulting in a decay factor of 0.765. The room temperature and pressure were measured to be 29.8°C and 1009
hPa respectively. The cartridge was fixed inside the constructed source holder and placed within the WTIC to get measurements of chamber sensitivity as function of depth. Table 4.1 represents the corrected chamber response for pressure and temperature effects obtained at different depths. The normalized chamber response relative to the sweet point is presented in column 3 of Table 4.1. The calibration point (or sweet point) was found to be between 4.5 cm and 6 cm distant from the mouth surface of WTIC. Further measurements were performed at this calibration point. Figure 4.1 represents the chamber response (or sensitivity) versus the dwell position of source.

### 3.2.6. Determination of source strength for I-125 seeds

Mathematical expression useful to compute clinical air kerma source strength of low photon emitting sources is presented. To determine air kerma source strength, \( S_k \); the following equation (3.1) was used

\[
S_k = R_{dg} \times N_{sk} \times C_e \times C_{tp} \times C_s \times C_{pol}
\]

(3.1)

where “\( R_{dg} \) is electrometer reading in Amperes (A), \( N_{sk} \) is the single seed calibration factor provided by ADCL in U per A, \( C_e \) is the electrometer scale calibration factor, \( C_{tp} \) is air density (or pressure and temperature) correction factor, \( C_s \) is the ion recombination correction factor, and \( C_{pol} \) is the polarity correction factor”. To obtain an average strength per seed, the total train air kerma strength is divided by the number of seeds in the cartridge.
3.2.7. Determination of correction factors

The correction for temperature and pressure, \( C_{tp} \) is obtained using the equation (3.2) which is

\[
C_{tp} = \frac{101.3}{P} \times \left( \frac{273.15 + T}{273.15 + T_0} \right)
\]

where \( T_0 \) is the reference temperature at ADCL calibration (~22°C) and \( T, P \) are temperature and pressure at measurement institution respectively.

The ion recombination correction factor [48], \( C_s \) is determined using the equation (3.3) which is

\[
C_s = \frac{(V_1/V_2)^2 - 1}{(V_1/V_2)^2 - (M_1/M_2)}
\]

As \( V_1=300V \) and \( V_2=150V \) are often used in the case with WTICs, they were two biases voltages used in measurements; where \( M_1 \) represents the measurement recorded at higher voltage and \( M_2 \) at the lower voltage. Since the ratio of voltage is exactly 2 then the recombination correction expression is simply deduced to

\[
\frac{1}{C_s} = \frac{4}{3} \frac{M_1}{3M_2}
\]

It is important to stress that for LDR brachytherapy sources, good quality WTICs normally demonstrate insignificant recombination effect.

The polarity correction factor, \( C_p \) is determined using the equation (3.5) which is
\[ C_p = \frac{|M_-| + |M_+|}{2|M_+|} \]  

where \( M_- \) and \( M_+ \) are electrometer readings recorded when the positive polarity and negative polarity are applied respectively. In case of an air open WTIC measurements, temperature and pressure corrections should be applied.

### 3.2.8. Derivation of calibration coefficient for I-125 brachytherapy sources

The air kerma calibration coefficient, \( N_{sk} \) which appears in equation (3.1), is normally obtained from a SSDL or directly from a PSDL. However, one of the dosimeter system device which is the source holder was not purchased and shipped to the KBTH to aid in the calibration of I-125 seeds. In this work, a new source holder has been designed and constructed to address the issue of I-125 seeds calibration at the hospital. The WTIC, the electrometer and the constructed source holder are three equipments composing the dosimeter system. The new air kerma calibration coefficient for the assembly was determined by calibrating the chamber for a number of photon qualities and then using either an interpolation procedure or by polynomial fitting between the obtained factors similar to the study of Van Dijk et al. [49]. An alternative method is that the standard laboratory calibrates a source of the same type and model and uses this reference calibrated source to calibrate the user’s measurement device.

The procedure to derive calibration coefficient in this work is connected to the relationship between the ionization current corrected for temperature and pressure with the
manufacturer’s stated strength. This relationship is obtained based on the graphical regression analysis and linear polynomial fitting method as shown in Figure 4.5.

3.2.9. Measurements of source strength

The strength of sources used during BT treatment will influence the dose delivered to a patient. At the supply, BT sources are packaged with a certificate declaring the strength of sources as determined by the manufacturer. Referring to quality control (QC) code practice for BT sources, it is strictly recommended not to use the stated value of source strength as input to dose calculation TPS without verification and validation. In LDR and HDR brachytherapy treatments, there were number accidents reported [50] and [51], caused by inaccurate dose delivered to the patient.

A regular verification and validation of the source strength of I-125 seeds was not given the required attention at KBTH. Data on the agreement between manufacturers stated source strength and locally measured values of source strength were not available. A locally constructed source holder and a WTIC supplied by standard imaging company were utilized to perform source strength measurements. The WTIC was calibrated directly traceable to NIST for all seed types in use at KBTH (see appendix A for certificate of calibration). An independent long term stability of the WTIC was also checked before starting measurements. The results of the measured strength of sources were compared with the values of air kerma strength stated on the manufacturer certificate. The column 5 of Table 4.2 presents the ratio between manufacturer stated source strength and the measured source strength. The lowest ratio measured is 0.811 and the highest ratio is 1.077.
The percentage deviation of measured value from stated value is tabulated in the last column of Table 4.2. The percentage deviation was obtained using the equation (3.6).

\[
Dev(\%) = \frac{S_{K\text{measured}} - S_{K\text{manuf}}}{S_{K\text{measured}}} \quad (3.6)
\]

Where \( S_{K\text{measured}} \) is the locally measured source strength and \( S_{K\text{manuf}} \) is the source strength as stated by the manufacturer. The lowest percentage deviation measured source strength is 0.027\% and the highest deviation is 16.348 \%. The mean percentage deviation of all measurements of source strength was found to be 2.588\%. This mean source strength of the measured sources agrees with the manufacturer’s stated strength to within 3\% as recommended by the AAPM report of low energy BT source calibration [16]. Otherwise, it is recommended that action must be taken to resolve the difference.

Every measurement commenced with zeroing regulation of the electrometer. At least 3 charge readings were taken to further determine the averaged charge. Each charge reading was collected during a time interval of 60 seconds. A typical 300V bias voltage was applied on the chamber. The chamber settings was set to be low for measuring charges in pC and then converted into ionization current in pA. For every measurement of different batches, the readings were corrected to reference temperature (22\(^\circ\)C) and pressure (1013.51 hPa), and background signals as well. After deduction of averaged background signal from the mean ionization current, the net current signal of I-125 seeds was computed. Corrections for recombination and polarity effects were also considered by applying equations (3.3) and (3.5) respectively.
Referring to the reference calibration date from NIST (see appendix A for certificate) and the date of clinical measurement, the manufacturer stated air kerma strength was corrected for spontaneous decay of the sources. This was done by applying the decay equation (3.7) which follows:

\[ S_K(t) = S_k(t_0) \times e^{-\frac{0.693 \times t_{1/2}}{t}} \]  

(3.7)

Where \( S_k(t_0) \) is initial source strength measured by the manufacturer at an ADCL, \( t \) (in days) is the time difference between manufacturer measurement date and local clinical measurement date and \( t_{1/2} \) is the half-life of I-125 source (\( t_{1/2}=59.6 \) days).

The results of manufacturer stated source strength corrected for decay are tabulated in column 3 of Table 4.2. Figure 4.5 presents the relationship between corrected ionization current and manufacturers stated source strength. The calibration coefficient deduced from this relationship is found to be \( 3.372 \times 10^{11} \) U/A with a standard deviation of \( \pm 0.2 \). The ratio between the obtained calibration coefficient to the one provided by the ADCL of PTW (which is \( 6.207 \times 10^{11} \) U/A) [45] for the dosimeter system formed by PTW source holder is 1.785. The correction coefficient between manufacturer stated source strength and corrected reading is found to be 0.986. By using the obtained calibration coefficient to the measured batch of seeds, the value of air kerma strength was determined. Column 4 of Table 4.2 presents the measured source strength corrected for temperature and pressure, polarity and recombination effects.
3.2.10. Measurements of single seeds

By using the clinical designed source holder shown in Figure 3.6, single seed measurements of batches containing total number of 15, 12 and 5 I-125 seeds were performed. The cartridge was removed from each batch and then fixed in the source holder. The electrometer was connected to the WTIC. A typical high bias voltage of 300V was applied to the chamber to prevent charges from recombination. The chamber was left to attain equilibrium with environmental conditions before starting measurements. The minimum time of about 30 min was required as the temperature inside the WTIC was adjusting to the room temperature slowly. Recombination corrections was not required because I-125 seeds are low air kerma rate sources and thus recombination effect is negligible for single seed measurements.

At the beginning, the source holder containing the cartridge of 15, 12, and 5 seeds respectively was placed inside the WTIC to record measurements as tabulated in Table 3.1. Subsequently, a single seed was removed from the cartridge by using the needle. Measurements of subsequent seeds were taken until all seeds got finished in the cartridge by removing one seed at a time for each measurement. Column 2, 3 and 4 of Table 3.1 represent chamber responses for batches of 15 seeds in the cartridge. Column 5 of Table 3.1 represents chamber responses for batches of 12 seeds in the cartridge. Column 6 and 7 of Table 3.1 represent chamber responses for batches of 5 seeds in the cartridge. The last row of Table 3.1 indicates chamber response to the background after each batch measurement. The row 15 of Table 3.1 represents the chamber response for a single seed in the cartridge.
Table 3.1: Single seed measurements for batches of different total air kerma strengths.

<table>
<thead>
<tr>
<th>Number of seeds</th>
<th>Chamber Responses (pA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Batch of 9.54U</td>
</tr>
<tr>
<td>15</td>
<td>21.212</td>
</tr>
<tr>
<td>14</td>
<td>17.322</td>
</tr>
<tr>
<td>13</td>
<td>15.964</td>
</tr>
<tr>
<td>12</td>
<td>15.114</td>
</tr>
<tr>
<td>9</td>
<td>11.653</td>
</tr>
<tr>
<td>8</td>
<td>10.399</td>
</tr>
<tr>
<td>7</td>
<td>9.341</td>
</tr>
<tr>
<td>6</td>
<td>8.251</td>
</tr>
<tr>
<td>5</td>
<td>6.989</td>
</tr>
<tr>
<td>4</td>
<td>5.836</td>
</tr>
<tr>
<td>3</td>
<td>4.531</td>
</tr>
<tr>
<td>2</td>
<td>3.279</td>
</tr>
<tr>
<td>1</td>
<td>1.939</td>
</tr>
<tr>
<td>0</td>
<td>0.399</td>
</tr>
</tbody>
</table>
CHAPTER FOUR

RESULTS AND DISCUSSIONS

4.1. Results

Table 4.1: Corrected chamber response at different source dwell position.

<table>
<thead>
<tr>
<th>Dwell position (cm)</th>
<th>Chamber response (nC)</th>
<th>Normalized chamber response</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.500</td>
<td>1.175</td>
<td>0.942</td>
</tr>
<tr>
<td>9.000</td>
<td>1.206</td>
<td>0.967</td>
</tr>
<tr>
<td>8.500</td>
<td>1.206</td>
<td>0.967</td>
</tr>
<tr>
<td>8.000</td>
<td>1.217</td>
<td>0.975</td>
</tr>
<tr>
<td>7.500</td>
<td>1.227</td>
<td>0.983</td>
</tr>
<tr>
<td>7.000</td>
<td>1.237</td>
<td>0.992</td>
</tr>
<tr>
<td>6.500</td>
<td>1.237</td>
<td>0.992</td>
</tr>
<tr>
<td>6.000</td>
<td>1.248</td>
<td>1.000</td>
</tr>
<tr>
<td>5.500</td>
<td>1.248</td>
<td>1.000</td>
</tr>
<tr>
<td>5.000</td>
<td>1.248</td>
<td>1.000</td>
</tr>
<tr>
<td>4.500</td>
<td>1.248</td>
<td>1.000</td>
</tr>
<tr>
<td>4.000</td>
<td>1.237</td>
<td>0.992</td>
</tr>
</tbody>
</table>
Figure 4.1: Normalized chamber response versus dwell position of the source.

Figure 4.2: Chamber response for batches of 15 seeds.
Figure 4.3: Chamber response for a batch of 12 seeds.

Figure 4.4: Chamber response for batches of 5 seeds.
Figure 4.2, Figure 4.3 and Figure 4.4 represent the chamber response versus number of seeds for batches of 15, 12 and 5 seeds respectively. Generally, it can be seen that the relationship between chamber response and number of seeds is linear as it was expected. As the number of seeds increases, the ionization current increases proportionally and vice-versa. Figure 4.2 reveals that for batches of constant decay factor, the batch of greater total air kerma strength exhibits steeper relationship of chamber response with number of seeds. The smaller total air kerma strength of the batch, the lower is the slope and vice-versa. In Figure 4.4 the batch of 3.180U total air kerma strength has lower slope than the batch of 2.915U because the decay factor of 3.180U batch was smaller than that of 2.915U.
Table 4.2: Comparison between manufacturer stated and measured source strength.

<table>
<thead>
<tr>
<th>Number of seeds in the cartridge</th>
<th>Electrometer reading corrected for $C_{tp}$ (pA)</th>
<th>Stated source strength (U) corrected for decay</th>
<th>Measured source strength (U) corrected for $C_{tp}$, $C_{pol}$ and $C_s$</th>
<th>Ratio of Stated to measured source strength</th>
<th>Percentage deviation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>22.730</td>
<td>7.608</td>
<td>7.348</td>
<td>1.035</td>
<td>-3.541</td>
</tr>
<tr>
<td>5</td>
<td>8.207</td>
<td>2.536</td>
<td>2.653</td>
<td>0.956</td>
<td>4.416</td>
</tr>
<tr>
<td>15</td>
<td>24.029</td>
<td>8.300</td>
<td>7.768</td>
<td>1.068</td>
<td>-6.849</td>
</tr>
<tr>
<td>12</td>
<td>16.226</td>
<td>5.199</td>
<td>5.245</td>
<td>0.991</td>
<td>0.880</td>
</tr>
<tr>
<td>5</td>
<td>7.104</td>
<td>2.166</td>
<td>2.297</td>
<td>0.943</td>
<td>5.674</td>
</tr>
<tr>
<td>15</td>
<td>19.125</td>
<td>6.499</td>
<td>6.182</td>
<td>1.051</td>
<td>-5.120</td>
</tr>
<tr>
<td>15</td>
<td>16.960</td>
<td>6.125</td>
<td>5.689</td>
<td>1.077</td>
<td>-7.662</td>
</tr>
<tr>
<td>5</td>
<td>6.791</td>
<td>2.042</td>
<td>2.278</td>
<td>0.896</td>
<td>10.371</td>
</tr>
<tr>
<td>12</td>
<td>14.847</td>
<td>4.900</td>
<td>4.981</td>
<td>0.984</td>
<td>1.617</td>
</tr>
<tr>
<td>15</td>
<td>22.703</td>
<td>7.823</td>
<td>7.616</td>
<td>1.027</td>
<td>-2.714</td>
</tr>
<tr>
<td>15</td>
<td>18.028</td>
<td>6.125</td>
<td>6.048</td>
<td>1.013</td>
<td>-1.282</td>
</tr>
<tr>
<td>15</td>
<td>20.620</td>
<td>7.171</td>
<td>6.917</td>
<td>1.037</td>
<td>-3.665</td>
</tr>
<tr>
<td>5</td>
<td>8.097</td>
<td>2.390</td>
<td>2.716</td>
<td>0.880</td>
<td>12.004</td>
</tr>
<tr>
<td>15</td>
<td>16.826</td>
<td>5.647</td>
<td>5.651</td>
<td>0.999</td>
<td>0.058</td>
</tr>
<tr>
<td>15</td>
<td>21.240</td>
<td>7.212</td>
<td>7.133</td>
<td>1.011</td>
<td>-1.110</td>
</tr>
<tr>
<td>n</td>
<td>x</td>
<td>y</td>
<td>z</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>----</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>15</td>
<td>19.610</td>
<td>6.611</td>
<td>6.586</td>
<td>1.004</td>
<td>-0.390</td>
</tr>
<tr>
<td>12</td>
<td>14.004</td>
<td>4.518</td>
<td>4.703</td>
<td>0.961</td>
<td>3.934</td>
</tr>
<tr>
<td>5</td>
<td>7.470</td>
<td>2.204</td>
<td>2.509</td>
<td>0.878</td>
<td>12.151</td>
</tr>
<tr>
<td>15</td>
<td>18.586</td>
<td>6.649</td>
<td>6.211</td>
<td>1.071</td>
<td>-7.054</td>
</tr>
<tr>
<td>15</td>
<td>17.323</td>
<td>6.095</td>
<td>5.789</td>
<td>1.053</td>
<td>-5.285</td>
</tr>
<tr>
<td>15</td>
<td>15.045</td>
<td>5.207</td>
<td>5.028</td>
<td>1.036</td>
<td>-3.553</td>
</tr>
<tr>
<td>12</td>
<td>12.460</td>
<td>4.165</td>
<td>4.164</td>
<td>1.000</td>
<td>-0.027</td>
</tr>
<tr>
<td>5</td>
<td>6.177</td>
<td>2.032</td>
<td>2.064</td>
<td>0.984</td>
<td>1.574</td>
</tr>
<tr>
<td>15</td>
<td>18.493</td>
<td>6.134</td>
<td>6.273</td>
<td>0.978</td>
<td>2.205</td>
</tr>
<tr>
<td>15</td>
<td>17.121</td>
<td>5.623</td>
<td>5.807</td>
<td>0.968</td>
<td>3.172</td>
</tr>
<tr>
<td>15</td>
<td>14.866</td>
<td>4.803</td>
<td>5.042</td>
<td>0.953</td>
<td>4.741</td>
</tr>
<tr>
<td>12</td>
<td>12.415</td>
<td>3.843</td>
<td>4.211</td>
<td>0.913</td>
<td>8.746</td>
</tr>
<tr>
<td>5</td>
<td>6.817</td>
<td>1.874</td>
<td>2.312</td>
<td>0.811</td>
<td>16.348</td>
</tr>
</tbody>
</table>
Figure 4.5: Manufacturer stated source strength versus electrometer reading corrected for temperature and pressure.

4.2 Discussions

In Figure 4.1, it was found that the sensitivity of the WTIC increases with the source position from the bottom to the top. The sensitivity was low at the chamber base and shifted to its maximum and uniform value at the sweet (calibration point) position where it showed a plateau response. The sensitivity started to fall down as one approaches the mouth of the chamber where it attained its lowest value. Similar chamber profile response to I-125 BT sources was also found by Calatayud et al. [52] while they were calibrating I-125 seeds by using the seed-selectron afterloader prior to seed implantation into the patient. Again, this profile was obtained by Otani et al. [46] while they were assaying the strength of I-125.
sources by using their designed novel jig. Furthermore, a similar chamber profile (Figure 4.6) response at different depths was obtained by Candela et al. [45] in their study of measuring the strength of multiple seeds of I-125 by using a new developed insert (Valencia-PTW insert) and a WTIC from PTW-Freiburg, Germany.

![Figure 4.6: Chamber response against the source position (from [45]).](image)

In Figure 4.7, the percentage deviation of measurements is represented with two horizontal dashed red lines indicating ±10% as the tolerance level recommended by AAPM task group reports and IAEA technical reports [13], [15]. In this study, there were found cases with high deviations up to 16% even though in most cases the deviations were within ±10%. These high deviations found are believed to result from uncertainty of dosimeter system
during measurements. The report by AAPM [13], [15] recommend that if the percentage deviation between manufacturer stated source strength and user measured one exceeds ±10%, the sources should not be used to treat the patient. In such case, there is a need of investigating the source of the error by qualified local medical physicists. The user must also report the abnormality to the source manufacturer. It can be seen from Figure 4.7 that four out of twenty eight measurements performed in this study requires further investigation and reporting the error to source manufacturer. Based on the observation, the study strongly recommends that patient should not be treated by using the sources that present a discrepancy exceeding the tolerance level until the difference is clearly justified and well understood. Abnormal (or dead) sources can either underdose the patient which may lead to further early/later biological complications. Even though some of the measurements performed in this study present deviations which are above 10% but the mean deviation obtained (2.588%) is within ±3 % recommended by AAPM report for low energy BT source calibration [16]. This report recommends that a mean deviation beyond 5% implies reporting the abnormality to source manufacturer.
During single seed measurements of various cartridges considered in this study, it was shown that the relation between number of seeds and chamber response is linear. As the number of seeds in the cartridge increases, the chamber response also increases linearly. The correlation coefficients of linear fitting were found to be above 0.9412 with 0.9955 being the highest. The lower correlation coefficient is associated with temperature and pressure fluctuations during measurements. This linearity response gives an implication that the source strength of a single seed can be obtained by dividing the total air kerma strength of the cartridge by the number of seeds packed in it. This finding of linearity response of WTIC is consistent with the study by Larry et al. [18] as shown in Figure 4.8.
while they were measuring the air kerma strength of Ir-192 by using a WTIC. Otani et al. [46] also found similar chamber response behavior with a correlation coefficient of 0.998.

Figure 4.8: Air Kerma strength of Ir-192 seeds measured in WTIC (from [18]).
CHAPTER FIVE

CONCLUSIONS AND RECOMMENDATIONS

5.1. Conclusions

Two source holders have been fabricated by using perpex materials successfully. One source holder, which has a mobile source positioning mechanism, was used to locate sweet point (calibration point) inside the WTIC for I-125 LDR seeds. The calibration point was found to be within 4.5 to 6 cm from the mouth of the WTIC. The other holder was designed and constructed based on the knowledge of the calibration point location. This source holder was used for source strength measurements within the WTIC at the calibration point. A comparison between the manufacturer stated source strength and the measured source strength has been performed. The lowest discrepancy of source strength was found to be 0.027% and the highest to be 16.348%. The mean discrepancy of measured source strength was found to be 2.588% which is within ±3% recommended by AAPM reports for low energy BT source calibration. Based on linear polynomial fitting and regression analysis of manufacturer stated source strengths and corrected electrometer readings, calibration coefficient of I-125 for the dosimeter system formed by locally constructed source holder was found to be \((3.372\pm0.200)\times10^{11}\) U/A. The batch source calibration method used maintains the sterility and integrity of I-125 sources and verifies that the mean manufacturer's stated source strength is accurate to within ±3%.
5.2. Recommendations

This study recommends that the methodology used for determination and validation of the air kerma source strength by inventing a new source holder fabricated from low cost locally available materials can be used in BT departments to calibrate sources of LDR I-125 seeds.

To ensure that the constructed source holder satisfies international standards, this study recommends that the holder should be sent to PSDL or SSDL for calibration.
REFERENCES


[21] M. Afsarigolshan, “Source Strength Verification and Quality Assurance of Sterile, Pre-loaded Iodine-125 seed Trains used for Prostate Brachytherapy,” no. April,
2014.


[33] British Institute of Radiology, “Recommendations for brachytherapy dosimetry,”


APPENDIX A: Calibration certificate of I-125 brachytherapy sources and traceability to NIST

**BrachySource® Seed Implants**

**Model Number:** STM1251

**Manufactured by:**

**Bard Brachytherapy, Inc.**

295 E. Lies Road
Carol Stream, IL 60188 USA

800-977-6733

**Customer:** MIN OF HEALTH

**Address:** KORLEBU TEACHING HOSPITAL ACCRA GH

**Certificate Number:** 425997SL

**Physician Name:** ACC185JA

**Reference Date:** 2018/10/06

**Implant Date:** 2018/10/13

<table>
<thead>
<tr>
<th>Lot Number</th>
<th>BBC000070</th>
<th>Quantity</th>
<th>51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparent Activity Range (mCi) on 2018/10/06</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min:</td>
<td>0.475 mCi</td>
<td>17.58 MBq</td>
<td></td>
</tr>
<tr>
<td>Midpt:</td>
<td>0.498 mCi</td>
<td>19.43 MBq</td>
<td></td>
</tr>
<tr>
<td>Max:</td>
<td>0.520 mCi</td>
<td>19.24 MBq</td>
<td></td>
</tr>
<tr>
<td>Total:</td>
<td>25.398 mCi</td>
<td>939.73 MBq</td>
<td></td>
</tr>
<tr>
<td>Range Midpoint on Implant Date</td>
<td></td>
<td>0.469 mCi (16.99 MBq)</td>
<td></td>
</tr>
</tbody>
</table>

| Air Kerma Strength Range (μGy/h) on 2018/10/06 | | | |
| Min: | 0.603 μGy/h |
| Midpt: | 0.632 μGy/h |
| Max: | 0.660 μGy/h |
| Total: | 32.232 μGy/h |
| Air Kerma Strength, Range on 2018/10/13 | | 0.583 μGy/h |

The enclosed sources consist of a radiosotope-coated cylindrical core pellet hermetically sealed within a titanium capsule. Each brachytherapy source is calibrated by measurement in a re-entrant ionization chamber with the measurement traceable to the National Institute of Standards and Technology (NIST) per the 1989 primary calibration standard. The uncertainty in the assay of the sources is ±5%. Bard Brachytherapy, Inc. certifies that the listed sources passed a leakage and contamination test meeting the requirements of ISO 9978:1992 (E), 5.1.1, Immersion Test (hot liquid), showing less than 0.005 microcuries (0.19 MBq) of removable Iodine-125 activity.

The total Air Kerma Strength or Apparent Activity is calculated by multiplying the midpoint by the number of sources. The midpoint is the middle of the range, not an average of the strength of the sources. The apparent activity and air kerma strength are measures of radiation output, not the contained activity. To calculate the contained activity, multiply the apparent activity by 1.7. The sources must be re-leak tested six months after the Leak Test Date before use or return to Bard Brachytherapy, Inc. If the source activity is greater than 100 microcuries (3.7 MBq). Iodine-125 has a half-life of 59.6 days and the principal photon emissions are 27.4 keV and 31 keV X-rays and a 35.5 keV gamma.

Quality Assurance

Reference: 1. NCRP Report No. 58

ISO Classification: ISO/99/C64221

Bard Brachytherapy Inc., Carol Stream, IL 60188 P: 800-977-6733 F: 888-383-3839

Authorized Representative: Bard Limited, Forest House, Brighton Road, Crawley, West Sussex, RH11 9BP UK

Bard and BrachySource are registered trademarks of C.R. Bard, Inc. or an affiliate. © 2003 All rights reserved.

PK0301513
### Bard® BrachySource® Seed Implants - 10% Assay Certificate

**Customer:** MIN OF HEALTH  
**Address:** KORLEBU TEACHING HOSPITAL, NATIONAL CENTER RADIOThERAPY AND NUCLEAR MEDICINE  
**Bard Tracking Number:** 425997SL  
**Independent Assay Date:** 10/3/2018  
**Leak Test Date:** 9/25/2018  
**Certificate Number:** 425997SL  
**Source Model:** STM1251  
**Independent Quality Assurance Ion Chamber ID:** 1643003  
**Ion Chamber NIST-Traceable Calibration:** Aug-2016

<table>
<thead>
<tr>
<th>Source Lot Number</th>
<th>Source Quantity</th>
<th>Bard's Stated Activity on Implant Date</th>
<th>Bard's Stated Total Activity on Implant Date</th>
<th>Bard's Stated Total Air Kerma Strength on Implant Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBCW0070</td>
<td>61</td>
<td>Min: 0.437 mCi</td>
<td>23.499 mCi</td>
<td>26.729 U</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Midpoint: 0.459 mCi</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max: 0.479 mCi</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Decay Factor (55.9 day half-life):**

<table>
<thead>
<tr>
<th>Day</th>
<th>Decay Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>1</td>
<td>0.988</td>
</tr>
<tr>
<td>2</td>
<td>0.977</td>
</tr>
<tr>
<td>3</td>
<td>0.966</td>
</tr>
<tr>
<td>4</td>
<td>0.955</td>
</tr>
<tr>
<td>5</td>
<td>0.944</td>
</tr>
<tr>
<td>6</td>
<td>0.933</td>
</tr>
<tr>
<td>7</td>
<td>0.922</td>
</tr>
<tr>
<td>8</td>
<td>0.911</td>
</tr>
<tr>
<td>9</td>
<td>0.901</td>
</tr>
<tr>
<td>10</td>
<td>0.890</td>
</tr>
</tbody>
</table>

### Test Data

<table>
<thead>
<tr>
<th>Assay Number</th>
<th>Assayed Activity (mCi) on 10/3/2018</th>
<th>Assayed Activity Corrected to Implant Date (mCi)</th>
<th>Bard's Stated Midpoint Activity on implant date (mCi)</th>
<th>Calculated Air Kerma (U) on Implant Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.502</td>
<td>0.448</td>
<td>0.459</td>
<td>0.566</td>
</tr>
<tr>
<td>2</td>
<td>0.503</td>
<td>0.447</td>
<td>0.459</td>
<td>0.557</td>
</tr>
<tr>
<td>3</td>
<td>0.502</td>
<td>0.446</td>
<td>0.459</td>
<td>0.557</td>
</tr>
<tr>
<td>4</td>
<td>0.504</td>
<td>0.448</td>
<td>0.459</td>
<td>0.558</td>
</tr>
<tr>
<td>5</td>
<td>0.496</td>
<td>0.444</td>
<td>0.459</td>
<td>0.553</td>
</tr>
<tr>
<td>6</td>
<td>0.493</td>
<td>0.438</td>
<td>0.459</td>
<td>0.556</td>
</tr>
<tr>
<td>7</td>
<td>0.495</td>
<td>0.440</td>
<td>0.459</td>
<td>0.558</td>
</tr>
<tr>
<td>8</td>
<td>0.500</td>
<td>0.445</td>
<td>0.459</td>
<td>0.555</td>
</tr>
<tr>
<td>9</td>
<td>0.501</td>
<td>0.445</td>
<td>0.459</td>
<td>0.555</td>
</tr>
<tr>
<td>10</td>
<td>0.497</td>
<td>0.442</td>
<td>0.459</td>
<td>0.551</td>
</tr>
</tbody>
</table>

Avg. = 0.446 mCi  
Avg. = 0.564 U  
Avg. = 16.432 mBq  
on 10/3/2018 on 10/13/2018

The average assayed activity error to mean is -3.2%.