DEVELOPMENT OF MAILED DOSIMETRIC AUDIT FOR
EXTERNAL BEAM RADIATION THERAPY USING ALANINE
DOSIMETERS

by

Iymad Mansour

Submitted in partial fulfillment of the requirements
for the degree of Master of Science

at

Carleton University
Faculty of Physics
Ottawa, Ontario
July 2018

© Copyright by Iymad Mansour, 2018

Table of Contents

List of Tables	v
List of Figures	vii
Abstract	viii
List of Abbreviations and Symbols Used	ix
Acknowledgements	x
Chapter 1 Introduction	1
1.1 Historical developments	1
1.1.1 Ionizing radiation	1
1.1.2 Radiation therapy	1
1.2 The Calibration Chain	2
1.3 Primary Standard Realization of Dose	3
1.4 Motivation for development of a mailed audit dosimetry system traceable to the National Research Council using alanine	4
Chapter 2 Theory	6
2.1 Radiation Dosimetry	6
2.1.1 Definitions and Notation	6
2.1.2 Electron and Photon Detectors	8
2.1.3 Electron Detectors	8
2.1.4 Photon Detectors	9
2.2 Dose-Rate Dependence	9
2.3 Environmental Corrections	9
2.4 Intrinsic Linearity	10
2.5 Energy Dependence	10
2.6 Dosimetry Summary	11
2.7 Tissue Equivalence	11
2.8 Estimation of uncertainties	12

Chapter 3	Alanine Dosimetry	14
3.1	Alanine	14
3.2	Electron Paramagnetic Resonance (EPR) spectroscopy	16
3.2.1	EPR Theory	16
3.2.2	Practical Implementation	17
3.3	Environmental Corrections	23
3.3.1	Temperature Dependence	23
3.3.2	Cavity quality variations	23
3.3.3	Background Correction	24
3.4	Dose-Rate Dependence	25
3.5	Intrinsic Linearity	25
3.6	Energy Dependence	26
3.7	Anisotropy	27
3.8	Signal Fading	27
3.9	Summary	29
Chapter 4	Materials and Methods	30
4.1	Equipment used	30
4.1.1	Alanine dosimeters	30
4.1.2	Bruker EPR spectrometer	31
4.1.3	Scale	32
4.2	Irradiations	33
4.2.1	Irradiation holders	33
4.2.2	Cobalt-60 Irradiations	34
4.2.3	Linear Accelerator Irradiations	35
4.3	Alanine Readout	36
4.3.1	Pellet holder within EPR cavity	36
4.3.2	Reference sample	38
4.3.3	Signal acquisition	40
4.4	Spectrum analysis	41
4.4.1	High-Dose spectrum analysis	42
4.4.2	Low-Dose spectrum analysis	43
4.4.3	Distinction between low and high dose alanine dosimetry	47
4.5	Determination of absorbed dose calibration curve	48

Chapter 5	Results	51
5.1	Environmental effects	51
5.1.1	Environmental effects on spectrometer	51
5.1.2	Humidity effects on alanine dosimeters	52
5.2	Comparison of Alanine and Far West pellets	55
5.3	Energy dependence	57
5.4	Uncertainty budget	58
5.4.1	Example	59
5.4.2	Description	59
5.5	Local audits	60
Chapter 6	Discussion	65
6.1	Suitability of alanine as a clinical audit dosimeter	65
6.2	Audit methodology	65
6.3	Forward capabilities	66
Chapter 7	Conclusion	68
Bibliography		69
Appendices		71
Appendix A	Spectrometer parameter optimization	72
A.1	Spectrometer parameter optimization	72
A.1.1	Microwave Power	72
A.1.2	Modulation Amplitude	72
Appendix B	Using AlCal	75
Appendix C	Proposed Audit Worksheet	81

List of Tables

3.1	Chemical bonds within α -Alanine and their strength ^[13]	15
4.1	Commercially available alanine dosimeters	31
4.2	Spectrometer settings	32
4.3	NRC clinical LINACs	35
4.4	Automated alanine scanning algorithms	41
5.1	Pellets storage prior and post irradiation for humidity study	53
5.2	Comparison of calibration generated using ^{60}Co with Harwell and Far West pellets	56
5.3	Comparison of clinically applicable LINAC nominal energies to that of ^{60}Co using Far West dosimeters	57
5.4	Alanine uncertainty budget for 10 Gy irradiation using 6 pellets at $k = 1$. The total uncertainty is the quadrature sum of the individual components of the budget.	59
5.5	Uncertainty Breakdown on determining the dose delivered	61
5.6	Audit conducted at the Ottawa Hospital using Elekta Synergy clinical LINAC using a nominal energy of 6 MV	62
5.7	Audit conducted at the Ottawa Hospital using Elekta Synergy clinical LINAC using a nominal energy of 10 MV	62

List of Figures

1.1	Basis of radiation therapy	2
3.1	α alanine	15
3.2	Alanine production of free radicals	15
3.3	EPR Spectrometer block diagram	17
3.4	Zeeman Effect	18
3.5	Microwave bridge block diagram	19
3.6	EPR signal for single molecule	21
3.7	60 Gy alanine EPR spectrum	22
3.8	Environmental stability of NRC laboratory housing spectrometer .	24
3.9	Alanine calibration data set measured at the National Physical Laboratory in Teddington, courtesy of NPL UK	26
4.1	Alanine pellet dosimeter with dimensions	30
4.2	Bruker EPR spectrometer at the NRC	31
4.3	Sartorius Quintix scale used for alanine mass determination . . .	33
4.4	Alanine irradiation holder	34
4.5	Irradiation Geometry	35
4.6	Alanine quartz tube holder	36
4.7	Pellet positioning QA	37
4.8	Effect of varied pellet position within cavity on measured peak-to- peak value of spectrum	37
4.9	Reference ruby permanently fixed within the EPR cavity	39
4.10	Separation between ruby and 35 kGy alanine EPR signal	39
4.11	Ruby signal determination	40
4.12	Comparison of irradiated alanine dosimeters on the range from 2 Gy to 10 kGy	42
4.13	Calculation of the peak-to-peak height using a 60 Gy spectra . . .	43

4.14	Comparison of different unirradiated pellet measurements	44
4.15	Peak to Peak intensity variation using different background measurements for a 10 Gy sample	45
4.16	Low-dose alanine subtraction example	47
4.17	Comparison of high and low dose algorithm	48
4.18	Alanine calibration curve using reference irradiations in NRC ^{60}Co beam to relate the absorbed dose to the peak to peak EPR signal intensity	50
5.1	Effectiveness of reference normalization to remove enviromentaly induced variation in spectrometer	52
5.2	Inter-day spectrometer reproducibility	52
5.3	Pellet storage both prior and post irradiation to monitor for humidity induced fading	54
5.4	Comparing conditioned and unconditioned pellets response over a month as they are subjected to different environmental conditions	55
5.5	Comparison of Harwell and Far West calibration curves	56
5.6	Energy dependence of the alanine pellets for different beam qualities	57
5.7	Consolidated literature comparison of Alanine energy dependence	58
5.8	Residuals from TOH 6 MV and 10 MV audit	62
5.9	Alanine calibration curve generated with an emphasis on below 5 Gy measurements	63
A.1	Saturation behavior of alanine EPR signal as a result of increased microwave power using 60 Gy alanine pellet as sample	72
A.2	Changing modulation amplitude	73
A.3	Distortion affect of EPR signal ^[36]	73
A.4	Increasing modulation amplitude beyond linewidth	74

Abstract

This projects aim is to provide the basis for an on-demand dosimetry service at the NRC for the independent check of dose delivery in external beam radiation therapy in Canadian cancer centres. The service will use mailed alanine dosimeters, and therefore the main focus of the project was to develop a low-dose, clinically applicable, alanine dosimetry protocol. Alanine dosimetry was originally developed for industrial uses of radiation (kGy dose levels) and there are a series of hurdles that have to be overcome to achieve acceptable accuracy at clinically realistic doses (a few Gy). Techniques for the correct readout procedure, choice of dosimeter, sample handling and detector operation were developed and/or adopted from the literature with the aim of obtaining dose measurements with an overall uncertainty below 1 %.

Monitoring for changes in measured alanine EPR signals attributed to varied environmental conditions, both in terms of storage of the pellets as well as the laboratory housing the spectrometer were investigated. It was observed that the manufacturing procedure of the dosimeters includes a sufficient *pre-conditioning* protocol, such that humidity effects become statistically insignificant. Permanently fixing a reference sample to the base of the spectrometer cavity, for signal normalization, was sufficient in mitigating spectrometer based signal variation.

The relative absorbed dose sensitivity of the dosimeter in several clinically relevant beam modalities relative to Cobalt-60 was measured. It was seen that in 6, 10 and 18 MV photon beams alanine has no significant energy dependence, and a small beam quality correction, less than 1%, relative to Cobalt-60 for most beam qualities.

The first NRC external beam audit was performed as an end-to-end test with the help of The Ottawa Hospital. The test, looking primarily at the efficacy of implementing the protocol, verified the use of alanine as an audit dosimeter on the range from 5 Gy and above; with an overall uncertainty below 1 %.

List of Abbreviations and Symbols Used

$\left(\frac{\bar{S}}{\rho}\right)_{det}^{med}$	Ratio of the mass electronic stopping powers of the medium to the detector
$\%dd(10)_x$	Percentage depth-dose at 10 cm depth in a 10 x 10 cm ² field on the surface of a water phantom with an SSD of 100 cm
CPE	Charged Particle Equilibrium
EPR	Electron Paramagnetic Resonance
ESR	Electron Spin Resonance
Gy	gray, SI unit for absorbed dose
Kerma (K)	Kinetic Energy Released per Mass
linac	Linear Accelerator
NPL	National Physical Laboratory
NRC	National Research Council, the national metrology institution of Canada
PSDL	Primary Standards Dosimetry Laboratory
Q	Beam Quality
Q_{cav}	Quality factor of EPR cavity
QA	Quality assurance
SSD	Source to Surface Distance

Acknowledgements

Malcolm McEwen: The list of things which you deserve acknowledgments and recognition for is far too long (and way too cheesy!) to account for independently. All I can really say thank you for being an absolutely incredible supervisor; in every sense of how that word can be interpreted.

Bryan Muir: It goes without saying this project would not have been possible without your help, guidance, and patience. Thank you for the countless hours of help both with irradiations and discussions you provided to meet the seemingly unrealistic goals I had for this project.

Justin Sutherland: It is strange to think, but if it wasn't for you coming to Halifax I might not be writing this thesis as a general statement. Thank you not only for your help with establishing the audit framework, but for your help in putting me on this path.

Kim Moore: The work you did behind the scenes of this project was paramount. Thank you for being not only approachable, but the peace of mind you provided knowing that if I needed anything to make this project work - you'd be able to make it so.

Peter Sharpe and NPL: Thank you for not only being a forerunner in establishing clinical alanine dosimetry on the world stage, but thank you for being so approachable and helpful throughout this project.

Chuck Hanson and Ralph Weber: A huge thank you for you two for all the help provided with getting the spectrometer running and troubleshooting the seemingly never ending series of hurdles with this project. You two were so kind when answering my questions (regardless of their nature), even when they were incredibly remedial.

I'd also like to thank every group member in building M35 at the NRC not listed here for being so welcoming and approachable while I was working on my thesis. Having such a wonderful team made all the difference in the world.

Chapter 1

Introduction

1.1 Historical developments

1.1.1 Ionizing radiation

At the tail end of the nineteenth century one of the most influential discoveries in the field of, what would become, modern medicine happened almost completely by accident. Wilhelm Roentgen, studying the effects of cathode ray tubes, noticed that if the tube was covered in a fluorescent material it would be illuminated without the presence of any external power source. At that moment he discovered what he called *X Rays* and this was the scientific community's first introduction into the world of ionizing radiation.

The applications of this finding grew quickly from the moment of discovery. One of the first effects observed was radiation-induced cutaneous burns, or in other words, it was noticed that ionizing radiation could be applied for biological applications to kill cells. This was almost immediately applied in the field of medicine, forming what would become *radiation therapy* treatment.

1.1.2 Radiation therapy

Radiation therapy is a locoregional treatment modality which relies on accurate delivery of radiation to a target while minimizing damage to surrounding healthy structures to remove unhealthy cells. The metric of concern in radiation therapy is *dose*, and is defined as the energy deposited per unit mass. It has the SI unit of the *gray* (Gy), and ultimately the dose to unhealthy (or healthy) tissue is what results in cell death.

The most common application of radiation therapy is in cancer treatment, the underlying basis for which is illustrated in figure 1.1. The required accuracy for dose delivery to the target tissue is typically quoted as being within $\pm 5\%$ of the prescribed dose^[1]. To that end, the goal behind this thesis, the development of a mailed audit system, is

to help facilitate optimal treatment by providing an independent check on dose delivery accuracy.

Figure 1.1: Example cell survival curve, which is the underlying principal of radiation therapy; radiation induces cell death. The goal within a cancer clinic is to minimize dose to healthy tissue, while maximizing dose to unhealthy tissue.

Most commonly, photons are used as the primary treatment modality in radiation therapy. They can be generated in a number of ways, including exploitation of radioactive material, but are typically generated through bremsstrahlung emission of decelerated electrons which have been accelerated by a linear accelerator (linac). Due to the overwhelming presence of photon usage within radiation therapy, the focus of this thesis will be to develop the audit framework needed to verify such modalities.

1.2 The Calibration Chain

The calibration chain is the basis for standardization and consistency in radiation therapy; the expectation being that there is no suffering of quality within a treatment simply based on geography. The importance of consistency within radiation therapy cannot be overstated - both from a medical standpoint to ensure the best quality of care, but also from a scientific standpoint so that different treatments may be objectively evaluated and compared.

The calibration chain itself is defined as the traceable link between a measurement made in the field to that made at the Primary Standards Dosimetry Laboratory (PSDL).

A PSDL is usually a national laboratory designated by the government for the purpose of developing, maintaining, and improving primary standards in radiation dosimetry. Within Canada the primary laboratory is also the national metrology institute, the National Research Council (NRC); and is responsible for disseminating (propagating) primary standards by calibrating secondary standards for users such as hospitals, laboratories, and industry^[2].

1.3 Primary Standard Realization of Dose

A primary standard measurement is the foundation for the calibration chain conducted at the PSDL, and is vital for accuracy within the medical physics domain. The basis for a primary standard measurement has a few characteristics:^[2]

1. Based on well established physical principals
2. No reliance on consensus data
3. Relative uncertainty is small
4. Validated and peer reviewed

With these four characteristics, accuracy and precision of a measurement are maximized. Within Canada there exists primary standards for different forms of measurements; in the context of absorbed dose the primary standard is water calorimetry. Stripping away the layers of complexities and difficulties associated with calorimetry, at its very core, it is a measurement of temperature change; which is directly related to the absorbed dose. Using the relation that absorbed dose will cause a temperature change in a medium you can relate radiation-induced temperature rise in a material via the specific heat capacity:

$$D = \frac{\Delta E}{\Delta m} = c_p \Delta T \quad (1.1)$$

Where D is the absorbed dose to the material, c_p is the specific heat capacity at constant pressure (units of J/K), and ΔT is the temperature rise due to absorbed radiation. This measurement technique is capable of giving directly the absorbed dose at a point^[3].

Other dosimeters are calibrated using the calorimetry primary standard to convert that detector's reading into absorbed dose, typically through a series of correction coefficients and factors, and are known as *secondary standards*. This process can continue further, calibrating dosimeters against the secondary standard, defining tertiary standard dosimeters. The focus of this thesis will be the use of alanine as both secondary and tertiary standards for dose determination.

1.4 Motivation for development of a mailed audit dosimetry system traceable to the National Research Council using alanine

The concept of alanine dosimetry, or specifically a mailed audit using alanine dosimetry is not novel. The goal behind this project was not necessarily to challenge the topic, but to thoughtfully review the different approaches historically applied to develop a suitable adaptation for NRC and, applicable to the needs of Canadian cancer centres.

The largest two dosimetric audit networks available in North America are operated by the International Atomic Energy Agency (IAEA) in Vienna Austria*, and the Imaging and Radiation Oncology Core (IROC) in Houston USA†. Few centres in North America use the IAEA service, overwhelmingly they use IROC, as an IROC audit is required for participation in clinical trials within North America. IROC uses OSLD‡ and the IAEA used TLD§ but has moved to RPLD¶ in the last year or so, the advantages of this transition were shown by Wesolowska et. al^[4]. Both IAEA and IROC audits are performed using dosimeters which have high atomic Z value, which is less than ideal in the context of clinical dosimetry. The significance of the high atomic Z value is that this introduces an additional dimension of uncertainty when the quantity of interest in a clinic is absorbed dose to water, a material with a relatively low effective atomic number, and you have to correct for that difference. This will be elaborated more in section 2.7, but using alanine which has a similar effective atomic number, and density, to that of water makes it an ideal clinical dosimeter. In addition having the dosimetry service traceable

---

*<https://www.iaea.org/>

†<http://rpc.mdanderson.org/RPC/home.htm>

‡Optically stimulated luminescent dosimeter

§Thermoluminescent dosimeter, made of many materials one of the most common is Lithium Fluoride

¶Radiophotoluminescent glass dosimeter

to the National Research Council means the audit service can be directly traceable to the primary standard realization of dose within Canada. Any facility being audited, which has a calibration traceable to the Canadian primary standard, will benefit from a large reduction in the total uncertainty due to the correlation between the measurements.

This thesis describes my work to develop the framework required of the NRC clinical mailed audit protocol. Chapter 2 is a consolidated literature review on dosimetry, not necessarily specific for alanine dosimetry; but each of the components one has to address when trying to perform accurate dosimetry. Chapter 3 is the expansion of chapter 2, but addressing each component systematically as they relate to alanine dosimetry. Chapter 4 is a detailed outline on the equipment used to test the alanine dosimeters, and ultimately the methodology framework developed for the purposes of the audit. Chapters 5 and 6 summarize the work I've done at the NRC to develop the framework for clinically applicable mailed dosimetry service. For additional information on practical procedures, such as custom software which was developed at the NRC for use with alanine dosimetry usage - which will be applicable for individuals wanting to continue the program - an appendix has been provided outlining some of the best practices.

Chapter 2

Theory

2.1 Radiation Dosimetry

The focus of this section is to outline the basis of dosimetry, defining some basic quantities and their dependencies on influence factors. The notation, and underlying theory, comes universally from Rogers^[5]. This section is designed to be a concise review of the general dosimetric definitions and quantities, and not necessarily those which are specific to alanine.

2.1.1 Definitions and Notation

Reference conditions:

For the purposes of this work reference conditions will be identical to that put forward in AAPM's TG-51^[6] specifying a set of irradiation conditions and geometries.

Beam Quality (Q):

Beam quality is an all encompassing term which describes the radiation coming from a source, and is used in calibration protocols such as AAPM's TG-51^[6] to select values for specific circumstances. The quality of a radiation therapy beam is only fully specified by knowing the incident energy spectrum and the angular and spatial distributions of the fluence along with the charge of the different incident particles. In practice, it is specified by beam quality specifiers such as $\%dd(10)_x$ which is the percentage depth-dose at 10 cm depth in a 10 x 10 cm² field on the surface of a water phantom with an SSD of 100 cm.

Kerma (K):

Kinetic Energy Released per Mass (KERMA) is the expectation value of the energy transferred to charged particles per mass at a point of interest by uncharged

particles incident on a small mass dm of that material. By definition Kerma is only applicable to either photons or neutrons (indirectly ionizing forms of radiation).

$$K = \frac{\langle d\epsilon_{tr} \rangle}{dm} = \psi \left(\frac{\mu_{tr}}{\rho} \right) \quad (2.1)$$

Where $\frac{\langle d\epsilon_{tr} \rangle}{dm}$ is the expectation value for the net energy transferred to charged particles per unit mass, ψ is particle fluence and $\frac{\mu_{tr}}{\rho}$ is the mass energy absorption coefficient.

D : Absorbed dose to the medium.

$\dot{D}$: Absorbed dose rate.

θ, ϕ : The angular orientation of the detector with respect to the radiation source and geometry.

M_{det} :

Reading of the detector, can be referring to the *raw* or *corrected* version of the detector reading. When referring to the raw reading from the detector it will be specified with the superscript *raw*, and if not specified will be referring to the fully corrected reading from the detector.

D_{det} :

Average absorbed dose to the material of the detector, the SI unit of measurement is the gray (Gy). This quantity is related to the composition of the *active material* of the detector; the component of the detector which elicits the dosimetric response.

D_{med} :

Absorbed dose to the medium at the point of measurement in the absence of the detector.

$S_{AD,med}$:

Detector's absorbed dose sensitivity defined as

$$S_{AD,med} = \frac{M_{det}}{D_{med}} \quad (2.2)$$

The absorbed dose sensitivity is the detector's reading divided by the absorbed dose to the medium at the point of measurement of the detector, in the absence of the detector to determine how the detector's response relates to the delivered dose.

2.1.2 Electron and Photon Detectors

All energy deposition in the sensitive region of a detector is due to electrons or positrons. That being said it can be beneficial to form a distinction between an electron and photon detector by referring to *what* the detector is responding to.

2.1.3 Electron Detectors

For the case of an electron detector the dose to the detector is attributed solely from charged particles passing through the detector. An ideal electron detector follows Bragg-Gray cavity theory, such that the dose to the sensitive region of the detector may be related to the dose to the material through the ratio of the stopping powers of both the detector material as well as the medium in question.

$$D_{med} = D_{det} \left(\frac{\bar{S}}{\rho} \right)_{det}^{med} \quad (2.3)$$

Where $\left(\frac{\bar{S}}{\rho} \right)_{det}^{med}$ is the ratio of the mass electronic stopping powers of the medium to the detector.

In practice Bragg-Gray cavity theory fails in modeling dose because it does not account for secondary electron production. To combat this problem Spencer and Attix^[7] formulated a theory which takes these secondary electrons into account. The theory which they developed parallels Bragg-Gray, except for the introduction of the *restricted electronic stopping power* $\bar{L}$. The significance of $\bar{L}$ is that it assumes that all particles with energy below some threshold, Δ , are deposited locally. With this consideration equation 2.3 becomes:

$$D_{med} = D_{det} \left(\frac{\bar{L}}{\rho} \right)_{det}^{med} \quad (2.4)$$

Where $\left(\frac{\bar{L}}{\rho} \right)_{det}^{med}$ is the ratio of the restricted mass electronic stopping powers of the medium to the detector.

2.1.4 Photon Detectors

For the case of photon detectors, and in the case of CPE, dose to the medium is equal to the kerma, and hence the relationship between dose to the detector and that of the medium can be related through the ratio of mass energy absorption coefficients:

$$D_{med} = D_{det} \left(\frac{\mu_{en}}{\rho} \right)_{det}^{med} \quad (2.5)$$

2.2 Dose-Rate Dependence

A detector's reading may be dependent on the dose rate being measured, giving an additional dependence of the form:

$$M'_{det}(\dot{D}) = k_{dr}(M_{det}^{raw}(\dot{D})) M_{det}^{raw}(\dot{D}) \quad (2.6)$$

Where $k_{dr}(M_{det}^{raw}(\dot{D}))$ is the *dose-rate dependence* which by definition equals 1.00 for reference conditions.

2.3 Environmental Corrections

If a detector's reading is sensitive to environmental and measurement conditions, namely temperature pressure and humidity (T, P and H respectively), then the convention is to correct the detector reading to that of a reference set of conditions using an environmental correction factor, k_{env} , and dose-rate correction k_{dr}

$$M_{det}(T_0, P_0, H_0) = k_{env}(T, P, H) k_{dr}(M_{det}^{raw}(\dot{D})) M_{det}^{raw}(T, P, H, \dot{D}) \quad (2.7)$$

Another component of the environmental correction is the subtraction of the background reading, measured from unirradiated dosimeters. The background component is given by:

$$k_{env}^{bkgd} = \left(1 - \frac{M_{det}^{bkgd}}{M_{det}}\right) \quad (2.8)$$

where M_{det}^{bkgd} is the detectors background reading during the measurement of M_{det} .

2.4 Intrinsic Linearity

This is simply the nature in which the detector reading, M_{det} , changes with increasing dose. In general:

$$D_{det}(D) = \alpha k_1[M_{det}(D)]M_{det}(D) \quad (2.9)$$

Where $k_1[M_{det}(D)]$ is the *intrinsic linearity* of the detector. By definition it equals 1.00 for a reference dose, D_0 , and α relates $M_{det}(D_0)$ to $D_{det}(D_0)$. If k_1 is **independent** of D , and M_{det} then the detector's response is linear. In other words, a factor of two increase in dose, will correspond to a factor of two increase in the detector's response.

2.5 Energy Dependence

The overall energy dependence or beam quality dependence of a detector's reading is broken into two components. The first relates the detector's reading to the average dose to the material of the sensitive detecting element. The second is the relationship between the dose to the detector material and the dose to the medium at the point of measurement of the detector.

Intrinsic Energy Dependence

The intrinsic energy dependence, k_{bq} , is the relationship between the reading from the dosimeter to the average dose to the sensitive detecting volume.

$$D_{det}(Q) = k_{bq}(Q)M_{det}(Q) \quad (2.10)$$

Absorbed-Dose Energy Dependence

The form of energy dependence which is widely recognized is that of the absorbed-dose energy dependence, f . It is the relationship between the dose to the detector material and the dose to the medium at the point of measurement (in the absence of the detector).

$$D_{med}(Q) = f(Q)D_{det}(Q) \quad (2.11)$$

2.6 Dosimetry Summary

Combining all of the previous correction factors it is possible to convert a detector reading (e.g., charge collected in the case of ionization chambers, EPR intensity for alanine) which was elicited by radiation, to the quantity of interest, absorbed dose to the medium.

$$D_{med}(Q) = f k_{bq} k_l M_{det} \left(Q, D, \dot{D}, \theta, \phi \right) = f k_{bq} k_l k_{env} k_{dr} M_{det}^{raw} \left(Q, D, \dot{D}, \theta, \phi, T, P, H \right) \quad (2.12)$$

This is intentionally cumbersome, as it is supposed to be representative of all the individual components which require consideration as one goes from a raw detector reading to the dose to the medium of question.

2.7 Tissue Equivalence

For the purpose of this thesis, the absorbed dose will be referring to the *absorbed dose to water*. In most clinical situations, because of its similarity to that of human soft tissue (which is composed almost completely of water) this is typically a reasonable assumption which reduces the complexity of the problem. Dosimeters are usually calibrated to specifically report the dose to water, although careful attention has to be made when making this conversion; namely because not all materials will respond to ionizing radiation in the same manner as water. Tabulated values exist for the response of electrons in materials, through the mass collisional stopping power^[8] and photons, through mass

energy absorption coefficient^[9], which allow corrections as shown in sections 2.1.3 and 2.1.4

2.8 Estimation of uncertainties

The definition of uncertainty and how it relates to a given measurement will follow exactly from the ISO:GUM^[10]. The uncertainties and errors in this thesis follows the definitions in which the error is the difference between measured value and the true value. If we knew the error, then we would know the true value. Uncertainties follow our lack of knowledge, often quantified by the standard deviation of the normal distribution. Uncertainties are classified into two groups: A and B. Type A uncertainties are those which are found through statistical analysis of repeated measurements, e.g the standard deviation of the mean after N measurements:

$$\sigma = \sqrt{\frac{1}{N} \frac{\sum_{i=1}^N (x - x_i)^2}{N - 1}} \quad (2.13)$$

The distinction between type A and B is that the uncertainty component for type B is not necessarily based on statistical analysis of the data.

In order to establish the uncertainty associated with a measurement, it is necessary to first identify and then quantify all possible sources of uncertainty. This is most easily done by considering, in turn, each step involved in the calculation of the quantity, and assessing what uncertainties are likely to be associated with each of these steps. The philosophy used is to ascribe to each component of uncertainty an effective standard deviation, known as a standard uncertainty, and it is these standard uncertainties that are then combined to produce the overall uncertainty. A tabulation of the individual components of uncertainty, along with their values and methods of estimation is often referred to as an “uncertainty budget^[11]”.

The combined uncertainty associated with a particular measurement is obtained from the quadrature sum of the individual component standard uncertainties:

$$u_c = \sqrt{\sum_{i=1}^N u_i^2} \quad (2.14)$$

Where u_c is the uncertainty on the measurement, and u_i represents individual components standard uncertainties.

Chapter 3

Alanine Dosimetry

3.1 Alanine

Alanine is a neutral non-polar amino acid which exists in two structural forms, α and β , and is one of the most common amino acids used by the human body for the synthesis of protein. In addition to its use in the human body, it can be used in radiation dosimetry. It was first described as a possible radiation dosimeter by Bradshaw *et. al* in 1963^[12]. The basis of alanine as a dosimeter is that ionizing radiation is capable of breaking the molecule, causing the formation of free radicals as a by-product of the deamination process. Determining the number of free radicals, which have been produced, will then be directly related to the absorbed dose.

To that end, α -alanine is the structure universally used for dosimetry because of the high stability of radiation induced free radicals^[13]. Due to the crystalline structure of the α -alanine molecule specifically, the free radicals which form are able to remain stable for long periods of time, numbering in years without recombination effects.

α -alanine has a density of 1.42 g/cm³ and an effective atomic number of 6.8; making it similar to water in its fundamental characteristics and therefore appealing in clinical dosimetry. α -alanine structure is shown in figure 3.1

Figure 3.1: α alanine

The chemical bond strengths within the alanine molecule are shown in table 3.1. The weakest bond is C-N and it is broken during the radiation induced radiolysis, this process is shown in figure 3.2. Although the other bonds within the molecule are not impervious to irradiation, they are not stable when broken and recombine after a short period of time. The NH_2 which is produced after irradiation is believed to remain stable within the matrix post irradiation.

Table 3.1: Chemical bonds within α -Alanine and their strength^[13]

Chemical Bond	Energy (eV)
C-H	4.3
N-H	4
C-O	3.6
C-C	3.5
C-N	3

Figure 3.2: Radiation induced production of free radicals within alanine.

α -alanine exists in different configurations D, and L. Both of which *can* be used for dosimetry. That being said, it is simply impractical to use D- α -alanine, due to the

drastically inflated price associated with the difficult method needed to produce it in high levels of purity required for dosimetry^[13]. This makes L- α -alanine the choice for dosimetric purposes.

3.2 Electron Paramagnetic Resonance (EPR) spectroscopy

Electron Paramagnetic Resonance, sometimes referred to as Electron Spin Resonance (ESR), is a spectroscopic method to determine the number of free electrons (and therefore radicals) within a sample. This section will be broken into two components, the first will cover the theory required for the basis of EPR, while the second will discuss the practical implications of EPR; specifically how the aforementioned theory is utilized to create one homogeneous system capable of relating the number of free radicals of a sample to a measurable quantity.

3.2.1 EPR Theory

The Zeeman effect

Electrons are spin one half particles, meaning that their angular momentum projected along an arbitrary direction will have one of two possible values:

$$\hat{S}_z = |\uparrow\rangle = \frac{\hbar}{2}, \quad \hat{S}_z = |\downarrow\rangle = -\frac{\hbar}{2} \quad (3.1)$$

In the presence of an external magnetic field, an electron has a state of lower energy when the moment is aligned with the magnetic field and a higher energy state when moment is aligned against the magnetic field. The two states are designated by the projection of the electron spin on the direction of the magnetic field. The difference between the energies of these two states caused by the interaction between the electron spin and the magnetic field is equal to:

$$\Delta E = g\mu_B B_0 \Delta m_S = g\mu_B B_0 \quad (3.2)$$

Where g is the Lande factor (≈ 2 for an electron), μ_B is the Bohr magneton, B_0 is the magnetic field strength and Δm_S is the difference of spin states ($=\hbar$ for an electron).

3.2.2 Practical Implementation

Quantitative EPR

Quantitative Electron Paramagnetic Spectroscopy is performed through the exploitation of the Zeeman effect with the use of three essential components:

Figure 3.3: EPR Spectrometer block diagram^[14], all components are explained below

1. Cavity - houses the sample of interest.
2. Magnet - produces a sweeping magnetic field.
3. Microwave bridge - produces a constant, tunable, mono-energetic energy source and serves as detector measuring the absorption of energy by the sample.

In principal, the microwave bridge produces a continuous energy supply to the cavity, which is in the presence of a magnetic field varying in strength. As a result, the absorption spectra of the sample is measurable, as illustrated in figure 3.4.

Figure 3.4: Separation of magnetic spin states (shown in blue) caused by addition of external magnetic field (top) and the absorption of energy by the sample (bottom)

The Microwave Bridge

The microwave bridge houses the microwave source and the detector. There are more parts in a bridge than shown in Fig. 3.5, but most of them are control, power supply, and security electronics that are not necessary to understand the basic operation of the bridge. The path of the microwaves start at the source which produces the microwaves used to probe the sample in the presence in the external field. After leaving the source the microwaves will cross the variable attenuator, a device which controls the flow of microwaves and allows for precise control of the microwave power reaching the sample. Most EPR spectrometers are reflection spectrometers, which means that they measure the amount of radiation leaking out of the cavity and not the absorption directly. The

circulator is a device which facilitates this, specifically, radiation entering from port one can only exit through port two, and radiation entering through port two can only exit through port three. This leads to the final component, the diode; which converts microwave power to an electrical, measurable, signal.

Figure 3.5: Simplified block diagram of EPR spectrometer block diagram illustrating the path of the microwaves, in blue, as they pass from the source to the detector with the wave guides illustrated in black. The bridge, and its main components, are shown in the large rectangle

The EPR cavity

The EPR cavity serves to house the sample of interest, and acts as a resonator for incoming microwaves produced in the bridge. What this means is that if the cavity is *critically coupled*, and at its *resonant frequency* it will store the microwave energy in the form of a standing wave within the cavity. In practice this is not possible to achieve as

most of the energy will be dissipated in the resistance of the resonator and thus EPR cavities are categorized by their Q_{cav} or *quality factor*; which is a quantitative measure of how well the cavity is storing microwave energy.

Simply put, as the Q_{cav} value increases, the sensitivity of the spectrometer also increases. This is defined as:

$$Q_{cav} = \frac{2\pi(\text{energy stored})}{\text{energy dissipated per cycle}} \quad (3.3)$$

The quality factor of a cavity is of vital importance for quantitative EPR spectroscopy. Many problems with the reproducibility of EPR intensities within a lab, or among labs, are due to different values of Q_{cav} . This makes in depth knowledge of an individual's spectrometer vital, and direct comparisons from lab-to-lab using raw measurements meaningless.

Q_{cav} can be expressed in a different form from what was shown in equation 3.3 as follows:

$$Q_{cav} = \frac{v_{res}}{\Delta v} \quad (3.4)$$

Where v_{res} is the resonant frequency of the cavity and Δv is the width at half height of the resonance. High Q means large peak with very narrow width, low Q means low peak but large width. The Q of a cavity also therefore has the concept of “capture” or “acceptance” - a high-Q cavity is going to give you a larger response (peak height) but it's acceptance window is much narrower than for a low-Q cavity.

The magnetic component of the microwave field drives the absorption in EPR; therefore, if the sample is placed in the microwave electric field minimum and the magnetic field maximum, the biggest signal and the highest sensitivity are achieved. The significance of this is that careful attention has to be placed on the sample position within the cavity to obtain the optimal signal output.

EPR Signal

The actual operation of the spectrometer is slightly more complex than the simple example of a free particle illustrated in figure 3.4. A smaller modulated field is applied to

the swept magnetic field and the resulting signal is the first derivative of the spectrum. This results in a higher signal to noise ratio, better peak identification, and less sensitivity to background signals.

The modulation amplitude should be small enough that it samples an approximately linear segment of the EPR absorption signal. Thus it is important to optimize the modulation amplitude for the measurements taking place; the general rule for best practice being that the modulation amplitude should be the same size as the distance between the peaks the operator is trying to resolve, ensuring linearity in the region of interest.

An advantage of derivative spectroscopy is that it emphasizes rapidly-changing features of the spectrum, thus enhancing resolution. Considering the simple free particle example the absorption and respective EPR spectrum will be of the form:

Figure 3.6: EPR signal for single free particle

As the species being examined strays away from the free particle example, the shape of the EPR spectra will become more complex. In the case of alanine, the EPR spectra

measured is from that of the radiation induced radicals - which are molecules. The difference being that the radical molecule being measured facilitates hyperfine interactions caused by spin interactions between adjacent hydrogen atoms. This leads to an EPR spectrum with at least five main peaks^[12]. An example of an irradiated alanine EPR spectrum is shown in figure 3.7.

Figure 3.7: 60 Gy alanine EPR spectrum

The Intensity is in arbitrary units (A.U) because the measured intensity is directly related to the spectrometer settings at the time of measurement. The magnetic field strength is in Gauss (G), which can be converted to the SI unit Tesla (T) via the relation $1 \text{ T} = 10^4 \text{ G}$

3.3 Environmental Corrections

3.3.1 Temperature Dependence

The radiation yield of alanine increases with irradiation temperature (specifically the temperature of the alanine as it is being irradiated). Over what would be considered non-extreme temperature conditions, between -20 and 55 °C this increase is well approximated as linear^[15]. A correction for temperature at the time of irradiation, k_T , needs to be applied to the measured EPR intensity to derive the EPR intensity that would correspond to a reference temperature, T_0 . This factor is defined as:

$$k_T = \frac{G_{Q,T_0}}{G_{Q,T}} = 1 - c_t(T - T_0) \quad (3.5)$$

where T is the temperature of irradiation, T_0 is an arbitrary reference temperature (usually taken to be room temperature, 21°C), and c_t is the temperature coefficient taking into consideration the alanine radical production efficiency.

For the two major suppliers of alanine pellet dosimeters, Far-West* and Harwell Dosimeters†, a result of multiple independent studies^[15–17] have shown that both L- α -alanine dosimeter's produce temperature correction factors in close agreement; the consensus values for c_t are 0.0017 and 0.0014 /°C for Far West and Harwell respectively.

3.3.2 Cavity quality variations

The spectrometer itself is susceptible to changes in readings associated with environmental conditions (gradients) within the laboratory housing the spectrometer. Subtle changes in both ambient temperature and relative humidity can cause unpredictable changes in the Q_{cav} ^[18]. Due to the unpredictable nature of the cavity changes, a direct response correction (analogous to what is applied to account for temperature of irradiation) is not feasible.

To combat this, there are two general approaches. The first, remove the issue entirely by maintaining constant environmental conditions within the laboratory. This is the seemingly intuitive approach, but does not come without difficulties. Maintenance of a

---

*Far-West alanine dosimeters: <http://www.fwt.com/racm/fwt50ds.htm>

†Harwell Dosimeters alanine pellets: <http://www.harwell-dosimeters.co.uk/harwell-alanine/>

laboratory to the level of stability required is not trivial. As a result, this is adopted by few facilities. The environmental stability of the laboratory housing the spectrometer at the NRC is shown in figure 3.8. With the exception of a few instances throughout the year which result in gross temperature increases, the stability of the temperature from month to month is within 1°C . That being said the humidity does not benefit from the same level of consistency. The relative humidity has gross levels of fluctuations from day-to-day. Short of redesigning the laboratory to facilitate the high level of environmental stability needed, a different approach needs to be adopted.

Figure 3.8: Environmental stability of NRC laboratory housing spectrometer

The second approach is to fix an adjacent reference sample that is permanently present in the cavity in a position different from that of test samples. This technique was introduced by Anderson and Weil (1959)^[19] and later applied to alanine dosimetry by Nagy *et. al*^[20]. After each measurement one would normalize the measured intensity to that of the reference sample, which should be reflective of environmental changes within the cavity.

3.3.3 Background Correction

Alanine background is often omitted for industrial dosimetry ($>1 \text{ kGy}$), but in the clinical domain is vital to account for, as it can comprise a significant component of the overall EPR signal. Depending on how low a dose the irradiation is, a significant amount of effort may need to be expended to account for the background component. This will be explained further detail in section 4.4.2.

3.4 Dose-Rate Dependence

No significant influence of dose rate on the alanine signal has been indicated. Regulla and Deffner (1982)^[21] varied the dose rate from 2 Gy min⁻¹ to 200 Gy min⁻¹ and saw no variation in the alanine response per unit dose delivered. For pulsed electron beam the ISO/ASTM standard 51607:2004 (ISO 2004) states that use up to 10⁷ Gy s⁻¹ is permitted.

3.5 Intrinsic Linearity

One of the major advantages of alanine is that it exhibits a linear response to the dose delivered over several orders of magnitude. At very high doses saturation becomes apparent and this is probably due to a form of species consumption, as the alanine crystal becomes damaged. The shape of the curve fits a one-hit model with saturation. “One hit” comes from the fact that the model of the passage of a single particle through a *sensitive target* is sufficient to produce an effect. For clinical dosimetry, alanine signal per unit dose may be regarded as linear, as no curvature in the response is exhibited until kGy doses. An example calibration curve, courtesy of the National Physical Laboratory in Teddington UK[‡], is shown in figure 3.9.

[‡]NPL Chemical dosimetry: <http://www.npl.co.uk/science-technology/radiation-dosimetry/research/chemical-dosimetry>

Figure 3.9: Alanine calibration data set measured at the National Physical Laboratory in Teddington, courtesy of NPL UK

3.6 Energy Dependence

For the purposes of a national cancer centre audit, it is vital to have a clear understanding of the alanine response in different beam qualities; it is not feasible to generate calibration data in every clinically applicable treatment modality. To that end, the ability to calibrate alanine response in a reference beam at the NRC, and accurately determine the dose to a dosimeter irradiated in a beam of a different quality is needed.

Although it is a useful learning exercise to break the overall energy dependence into intrinsic and absorbed dose energy dependence, as was shown in section 2.1, experimentally it is not especially helpful. The overall energy dependence (which is the product of the intrinsic and absorbed dose energy dependence) will need to be considered, and can be evaluated through the variation of the Alanine/EPR response irradiated using different beam qualities.

When considering alanine response in a clinically applicable dose region where the response is well approximated as linear, $(\text{Slope})_Q$ is the slope of the best straight line through the measured intensity versus absorbed dose-to-water points, i.e., the slope of

the calibration curve. As was initially shown by Zeng *et. al*^[22] the overall alanine energy dependence is simply the variation of $(\text{Slope})_Q$ versus energy for a particular beam modality.

3.7 Anisotropy

Inhomogeneities in the alanine-binder, which depend on the manufacturing process, are thought to be responsible for the dependence of the signal intensity relative orientation of the pellet within the cavity (referred to as anisotropy). The anisotropy of the alanine pellets is usually taken into account by averaging EPR spectra acquired at different orientations of the sample^[23].

The need to limit the number of acquisitions introduces an uncertainty in the signal measurement. Fortunately, a significant amount of research has been devoted to quantifying the relative difference in measured intensity attributed to the amount of rotations within a measurement. The signal can vary on the order of 0.1-0.2% based on the orientation of the pellet relative to the axis^[23]. The optimal number of orientations was three, as there was no significant decrease in the relative standard deviation beyond that^[23]. Beyond three rotations the relative standard deviation becomes so low that it is unresolvable from the spectrometer reproducibility itself.

3.8 Signal Fading

Alanine signal fading is the phenomena of the alanine intensity changing over time in one direction (rather than simply varying) and this can be attributed to radical recombination. This results in the reading of a decreased signal, and therefore an underestimation of the absorbed dose. Although in standard laboratory conditions the alanine itself is quite stable^[24], extreme environmental conditions can induce fading.

The effects of post irradiation temperature were studied by Sharpe *et. al*^[15] by subjecting pellets which were irradiated at 25°C, and then, post irradiation, heating up to 80°C for ~6 h. The result from the experiment was that there is little to no effect on the signal. The main environmental consideration is storage humidity, as improper storage can cause signal fading on the order of ~5% within a single year^[25]. It has

been shown that humidity is somewhat easy to combat through the adoption of a *pre-conditioning* technique, first proposed by Sharpe et. al^[25], which is simply the exposure of the dosimeter to highly humid environments (>70 % RH for minimum 6 weeks). The conditioning makes the dosimeter no longer vulnerable to humidity effects, lowering the rate of signal fading to $<1\%$ within a year^[25]. The experiment was performed using Harwell pellets and concluded that this was likely caused by the final component of the manufacturing process, which is to heat the pellets, causing the finished product to be essentially in a dry state. Furthermore, no significant variations in the pellet masses were observed, suggested that the fading observed was induced by increases in the dosimeter water content, rather than the absolute amount of water in the dosimeter.

3.9 Summary

Alanine dosimetry can therefore be contained in the simple relation:

$$D_{det} = \frac{c \cdot M_{det} \cdot k_T \cdot k_t}{m_{det}} \quad (3.6)$$

M_{det} :

Peak-to-peak intensity of the EPR spectrum in arbitrary units, fully corrected.

D_{det} :

Average absorbed dose to the pellet in gray (Gy).

m_{det} :

The mass of the dosimeter being used.

k_T : Temperature correction factor which needs to be considered at time of irradiation which effects the radical production efficiency, elaborated more in section 3.3.1.

k_t : Environmental correction factor which needs to be considered at time of readout. Determined through reference sample measurements and will be elaborated more in section 4.3.2.

c : Conversion coefficient which converts spectrum output to energy deposited. This is not a universal constant, and must be determined through regular calibration. This will be elaborated more in section 4.5. In this formalism, c also includes the impact of any holder required for the alanine pellets. When the calibration and user beams are the same, this effect obviously cancels out. Where the user beam differs from calibration beam (eg., 6 MV linac vs. ^{60}Co) the effect of the holder is generally folded into the measured energy dependence, elaborated in section 5.3.

Chapter 4

Materials and Methods

4.1 Equipment used

4.1.1 Alanine dosimeters

Alanine in its raw form is a powder but for dosimetric purposes, although it can be used as a powder, it is typically formed into some kind of geometry through the addition of a binding agent. The most common binders used are listed in table 4.1. The main consideration behind the choice of binder is that, upon irradiation, it will not introduce any species into the dosimeter that would effect the dose determination.

Dolo and Garcia^[26] investigated the effect of the binder and showed that all the commonly used binders have some post-irradiation signal, but that this usually has a fast decay. What this means is that directly after irradiation there will be some instability in the measured EPR signal caused by additional, unstable, radicals from the irradiation of the binding component. Fortunately the signal stabilizes quite quickly (i.e., within 24 hours), meaning most facilities have a wait period between time of irradiation and readout to ensure stable samples.

For the proceeding work, the dosimeter form of choice was *alanine pellets* with dimensions illustrated in figure 4.1.

Figure 4.1: Alanine pellet dosimeter with dimensions

Table 4.1: Commercially available alanine dosimeters

Producer	Binder	Diameter (mm)	Height (mm)	Pellet Mass (mg)	c_T (/ °C)
Harwell	9.1 % Paraffin	4.80 ± 0.1	2.80 ± 0.10	60 ± 2	$0.0014 \pm 2.9\%$ ^[16]
Far West	4.0 % Polyethylene	4.80 ± 0.04	3.00 ± 0.10	65.0 ± 0.5	$0.0017 \pm 2.8\%$ ^[17]

4.1.2 Bruker EPR spectrometer

The spectrometer used for this work is a Bruker EMX system. The microwave bridge is software controlled, and features automatic tuning. The cavity is the Bruker-made high sensitivity cavity model HS0105. The spectrometer has recently undergone the Xenon upgrade*. The bulk of the spectrometer equipment (magnet, cavity and bridge) were not changed during the upgrade, but it has modernized the processing and acquisition components of the spectrometer. The overall functionality of the spectrometer has therefore remained constant. The NRC EPR spectrometer is shown in figure 4.2.

Figure 4.2: Bruker EPR spectrometer at the NRC

---

*<https://www.bruker.com/products/mr/epr/epr-software/xenon/overview.html>

Spectrometer settings

The spectrometer settings shown in table 4.2 are specific for the NRC spectrometer running the Xenon upgrade. The parameters are somewhat different to the ones used by Zeng *et. al*^[22] (who used the NRC spectrometer prior to this work) because the individual parameters are dependent on the optimization process during equipment commissioning.

EPR measurement parameters have to be carefully optimized when measuring doses below and around 15 Gy. Both microwave power and modulation amplitude have to be increased compared to the values used for higher dose measurements. The parameters used in this work were chosen to provide the maximum signal-to-noise ratio consistent with the preservation of the major features of the alanine spectrum. A synopsis of the parameter optimization has been provided in the appendix, section A.1.

Table 4.2: Spectrometer settings

Parameters	Alanine	Reference Ruby
Microwave Power (mW)	2.97	2.97
Modulation amplitude (G)	8	8
Receiver gain (dB)	40	25
Time Constant (ms)	163.84	163.84
Sweep time (s)	20.97	20.97
Sweep Width (G)	250	150
Number of scans	6	1
Rotations	3	0
Spectrum Centre (G)	3508	2645

4.1.3 Scale

A Sartorius scale was used for alanine mass determination. Mass measurements occur directly before EPR measurements take place.

Figure 4.3: Sartorius Quintix scale used for alanine mass determination

The mass of the pellets needs to be considered for alanine dosimetry, as more mass will simply result in more radicals created upon irradiation; if not accounted for this could bias a measurement. The quantity of interest, in terms of dosimetry, is the EPR signal normalized to the mass of the pellet. That being said, the actual variation of mass between pellets is typically on the order of 0.1 mg, requiring a high resolution scale.

4.2 Irradiations

4.2.1 Irradiation holders

Irradiation holders were designed with two situations in mind, the irradiations within the NRC (calibrations) and irradiations in practice (audits). To meet both criteria, a waterproof alanine holder was constructed, in house, which was designed to replicate the outer dimensions of a standard NE2571 Farmer reference chamber^[27]. The reason for replication of the NE2571 dimensions is for easy integration of the audit protocol in clinical settings. Most clinics, as recommended by TG-51^[6], implement regular quality assurance with reference chambers that have the dimensions of a NE2571 chamber, making the integration of alanine dosimetry relatively seamless.

The holder itself is made out of Delrin[†] a plastic commonly used in ionizing radiation equipment, and has a density of $1.41 \left(\frac{g}{cm^3}\right)$, low water absorption, and excellent dimensional stability facilitating precision component fabrication. The holder is made of three parts, the base, cap and stem. The base (1) and cap (3) form a hermetically sealed compartment using a rubber o-ring (4) which houses six alanine pellets, and the stem (2) serves to resemble the structure of the NE2571 Chamber outer dimensions.

(a) Four piece alanine audit holder based on reference chamber geometries. The cavity has a wall thickness of 1 mm and a depth of 18.6 mm

(b) Physical copy of alanine holder

Figure 4.4: Alanine irradiation holder

4.2.2 Cobalt-60 Irradiations

The Co-60 Gammabeam X200 irradiator is set up to provide a horizontal beam. An in-house designed water phantom was used. The SSD was set at 100 cm and the field size was 10 x 10 cm at the phantom surface. The beam direction was perpendicular to the curved surface of the pellets, as depicted in fig 4.5. The centre of the stack of six alanine pellets was placed at the reference depth of 5.3 cm (taking into account the 3 mm PMMA window). The positioning precision was 0.1 mm. Alanine was irradiated at a nominal dose rate of 0.6 Gy min^{-1} . NRC Cobalt-60 reference irradiations are directly traceable to the Canadian primary standard realization of dose, water calorimetry, and have an overall uncertainty of 0.25% ^[28] on dose determination.

[†]Delrin being the trade name for polyoxymethylene, $(\text{CH}_2\text{O})_n$ referred to as POM

Figure 4.5: Irradiation Geometry

4.2.3 Linear Accelerator Irradiations

The NRC has two Elekta clinical linear accelerators with nominal energies outlined in table 4.3

Table 4.3: NRC clinical LINACs

Nominal Energy (MV)	%dd(10) _x	
	Precise	Synergy
6	67.3	67.7
10	72.3	73.1
18	–	79.1
25	81.5	–

The irradiation geometries are nearly identical to that of the ^{60}Co , using a dedicated NRC-made water phantom. SSD was set at 100 cm and the field size was 10 x 10 cm at the phantom surface. The beam direction was perpendicular to the curved surface of the pellets, as depicted in figure 4.5. The centre of the stack of six alanine pellets was placed at the reference depth of 10.2 cm (taking into account the 2 mm PMMA window). The positioning precision was 0.1 mm. The dose determination comes directly from a NRC-calibrated secondary standard and has an uncertainty of 0.35%^[28].

4.3 Alanine Readout

4.3.1 Pellet holder within EPR cavity

The pellet position within the cavity has a direct relationship to the measured spectra intensity, therefore a robust QA protocol must be maintained to ensure consistency in measurements. The pellet position can be varied through the use of a Teflon[‡] support which was made in house and is illustrated in figure 4.6a. This facilitates the precision needed to ensure reproducibility of the pellet positioning. The Teflon makes a friction seal with the quartz tube, and for further stability a Teflon screw was added. This setup is shown in figure 4.6a

(a) Quartz and Teflon support system to hold pellet within cavity

(b) Quartz tube loaded into spectrometer cavity

Figure 4.6: Alanine quartz tube holder

Positioning consistency is maintained through a micrometer and an in house designed clear plastic reference piece. The reference piece is designed to fit on the Teflon support and allow for measurement of the base of the quartz tube. Measurements are done daily, as the positional stability of the quartz tube once the Teflon screw has been tightened is sufficiently high.

[‡]Teflon being the trade name for PTFE

Figure 4.7: Pellet positioning QA

The effect varying the pellet position is illustrated in figure 4.8.

Figure 4.8: Effect of varied pellet position within cavity on measured peak-to-peak value of spectrum

The residuals shown in the subplot within figure 4.8 have a RMS deviation of 0.3%, with the largest deviations seen away from the “sweet spot” where the signal intensity is greatest. There appears to be no trend in the residuals and the RMS deviation is consistent with that seen for multiple measurements at the same position, suggesting the quadratic fit is appropriate. The fitted curve in figure 4.8 can be used to estimate

the additional uncertainty, beyond that due to readout repeatability, from the estimated uncertainty in positioning. Measurements with the micrometer system in figure 4.7 suggest a maximum variation in the position of the pellet within the cavity of 0.15 mm, which at the "sweet spot" corresponds to a standard uncertainty in the alanine signal of 0.05%.

4.3.2 Reference sample

The choice of a reference sample comes down to a few simple components, most important are stability and location. The reference sample of choice has to remain stable such that measured changes in the EPR spectra are attributed to spectrometer changes and not sample instability. The second is peak location, the reference spectra should be centred at a location far enough away along the B axis from the sample of interest that it will not bias either the reference or sample measurement.

Modern spectrometers facilitate the latter component with the use of automation routines for signal acquisition, allowing multiple scans to be performed autonomously with different spectrometer parameters without the need for operator intervention. This allows alanine and reference sample measurements to be measured, located at very different magnetic field strengths, in separate sequential scans.

A common choice for reference material, as recommended by the spectrometer producer, is synthetic ruby, a material which produces a constant EPR signal over long periods of time without any fading effects. The reference sample position within the cavity is illustrated in figure 4.9

Figure 4.9: Reference ruby permanently fixed within the EPR cavity

The synthetic ruby crystal contains about $10^{-2}\%$ chromium ($3+$)^[20]. Its EPR spectra is located at ~ 2800 G (~ 700 G lower than that of alanine). The separation between the alanine and reference ruby EPR spectra is shown in figure 4.10.

Figure 4.10: Separation between ruby and 35 kGy alanine EPR signal

The peak-to-peak of an individual spectrum is determined by measuring the distance between the global maxima and minima of the EPR spectra. These extrema are located automatically by fitting quadratics to the highest and lowest points within the spectrum, and then calculating the difference between the points. The basis for the algorithm is illustrated in figure 4.11.

Figure 4.11: Ruby signal determination

4.3.3 Signal acquisition

The use of integrated Python[§] scripting with the proprietary Bruker software makes complex spectrum acquisition automatable. There are two scripts written for the NRC alanine dosimetry readout; the first is designed for measuring irradiated alanine pellets while the other is designed for measuring unirradiated alanine pellets (for background measurements). The distinction between the two is the additional measurement of the reference sample used for normalization. Although the reference sample is not explicitly measured with the unirradiated pellets, it is considered being that the unirradiated

[§]Python programming language using version 3.6 - <https://www.python.org>

pellets are measured concurrently with the irradiated pellets. For both irradiated and unirradiated alanine measurements, the operator is required to rotate the sample within the cavity, ensuring successive scans at different angles relative to the cavity; this accounts for the anisotropy associated with the alanine pellets. Due to alanine's prevalence in industrial dosimetry, many independent investigations have studied the optimal number of scans and the separation between them^[23;29].

The consolidated scan procedure is shown in table 4.4:

Table 4.4: Automated alanine scanning algorithms

	Irradiated	Unirradiated
Scans	6	6
Angle between scans	60°	60°
Scans at each angle	2	2
Reference scan	yes	no

There are multiple scans at each angle to increase the signal to noise ratio, which is especially applicable for low dose measurements due to their weak signals. The signal will increase proportionally to N , the number of scans. If the noise is truly random, its increase will only be proportional to $\sqrt{N}$. The result is an enhancement of signal to noise proportional to $\sqrt{N}$.

4.4 Spectrum analysis

The inherent goal behind alanine spectrum analysis is to relate the alanine EPR spectrum to the absorbed dose. Alanine dosimetry is broken into two distinct categories. The simple *high dose* alanine dosimetry; which has a high signal to noise ratio making the relation of the EPR signal to deposited dose quite intuitive, and the more complex *low dose* alanine dosimetry which has a much lower signal to noise ratio requiring the adoption of a more complex analysis procedure. The need for this distinction between high and low dose alanine is evident from figure 4.12.

Figure 4.12: Comparison of irradiated alanine dosimeters on the range from 2 Gy to 10 kGy without the use of any background subtraction.

At low-doses, specifically sub 15 Gy, the alanine component of the EPR spectrum becomes unresolvable in comparison to their high-dose counterparts. In the region of 25 - 100 Gy, the alanine component is clearly resolvable with the presence of a small background component. In excess of 100 Gy subtraction of the background component has no effect on the measured alanine signal.

4.4.1 High-Dose spectrum analysis

At high-dose levels the EPR spectrum is very “clean” and the analysis straightforward; as a result alanine has historically been applied for use with high dose dosimetry in industrial applications. At high doses the alanine EPR spectrum will be outside of the range of background effects, specifically baseline distortion and noise, and the dose to the pellets can be easily determined directly from the EPR spectrum by measuring the peak-to-peak height of the global maximum and minimum.

Determination of peak-to-peak height

The peak-to-peak of an individual spectrum is determined using the same algorithm previously mentioned in section 4.3.2, this is illustrated for use with alanine in figure

4.13.

Figure 4.13: Calculation of the peak-to-peak height for a 60 Gy spectrum using quadratic peak determination

4.4.2 Low-Dose spectrum analysis

Low dose alanine dosimetry is more difficult than high dose due to the presence of a relatively large background signal. The simple peak-to-peak quantity of interest is no longer directly measurable. The data analysis method first proposed by Sharpe et al.^[30] is based on the assumption that only the amplitude of the EPR signal depends on the dose, but not the shape. The low dose signal can be considered as the linear combination of a series of different background components, from the cavity and the alanine, as well as the radiation induced radical signal itself (which is the quantity of interest).

Cavity Background

The background is measured by using a series of unirradiated pellets, and is measured daily. The significance of the daily background measurement is illustrated in figure 4.14.

The shape of the background measurement does not significantly change, but it is clear that there are subtle changes, likely due to subtle Q_{cav} changes, changes in tube height within the tolerance of daily QA, or spectrometer reproducibility itself.

Figure 4.14: Five alanine cavity background measurements (left) compared to fifteen alanine pellets made over three days (right). The width of the line corresponds to the standard deviation of the alanine intensity at each value in the magnetic field strength.

Comparing the single day vs. three day background measurements there is a 2.45 increase in point-to-point variability. What this would mean, for this example, would be a bias of $\sim 1\%$ for a 10 Gy measurement (or 0.1 Gy) would be introduced in the extreme cases if the multi-day background measurement was used. To compute the uncertainty associated with the cavity background for a days measurement, the variation in signal intensity is computed using all the different background measurements. An example is shown in figure 4.15 which uses background measurements which were all made on the same day.

Figure 4.15: Peak to Peak intensity variation using different background measurements for a 10 Gy sample

As one might infer the number of background measurements required is dependent on the dose being measured. To maximize accuracy in the below-15 Gy area a minimum of 8 measurements of the background typically take place; depending on how low the dose is, and the spread of the background measurements, can number in excess of a dozen.

Alanine Background

The second component, referred to as the alanine background, is distortion in the baseline of the spectrum. Baseline distortion can arise from several sources including: the cavity, the holder used to position the alanine, and the alanine sample itself^[30]; all of which can cause a variation in the Q_{cav} or the background signal - resulting in variable change in the spectrum baseline. This component of the background is not directly measurable but is obtained by using an iterative least squares approach for each individual pellet. By comparing the spectrum of interest to that of a high dose spectrum, which is free of background effects, and removing the portion of the signal not attributed from radiation induced species the corrected spectra can be obtained.

The algorithm works as follows: first the cavity background is subtracted from the raw spectrum. Then there is a least squares comparison between the low dose spectra of interest and the high dose template spectra. The result is a scaling factor used to normalize the template spectra. Upon normalization the difference between the two

spectra is computed, and smoothed by fitting a fourth order polynomial - the smoothed difference is then subtracted from the low dose spectra. This process continues iteratively until the difference in peak-to-peak height of the low dose spectra is less than 0.015% that of its previous version through the iteration. This iteration threshold comes from the recommendation of researchers who employ a similar algorithm in their facility. Upon testing, it was seen that this exit condition of 0.015% was an optimal choice as lowering the threshold caused oscillations in the measured intensity between iterations (around a convergence point), making the algorithm unable to converge.

This process of determining the alanine background, although reproducible, has little physical meaning, in the sense that it is impossible to predict the shape of the alanine background *a priori*. In comparing the raw 5 Gy spectrum in figure 4.12 to the equivalent in figure 4.16, it can be clearly seen that the gradient of alanine background is very different.

Subtraction Example

The entire goal behind the algorithm is to remove the background component of the spectra from the raw spectra to determine the corrected alanine spectrum, as shown in equation 4.1:

$$S_{Al} = S_{Raw} - S_{Bkg} \quad (4.1)$$

Where S_{Al} is the corrected alanine spectrum, S_{Raw} is the raw alanine spectrum, and S_{Bkg} is the background component of the alanine spectrum. The background component of the alanine spectra consists of two components, the cavity background (explained in section 4.4.2) and the alanine background (explained in section 4.4.2).

$$S_{Bkg} = S_{Bkg-Cav} + S_{Bkg-Al} \quad (4.2)$$

Where $S_{Bkg-Cav}$ is the cavity background, S_{Bkg-Al} is the alanine background. To determine S_{Bkg-Al} , a high-dose “template” function is used to separate the alanine from its background component. This is done by comparing the raw spectra (after being corrected for the cavity background component) to a high-dose using a least squares

method to determine a scaling factor, n . Once the scaling factor is determined, the two spectra are subtracted and smoothed using a fourth order polynomial. The smoothing is done to preserve the shape of the low-dose spectra, or worded somewhat differently, so that the template function is not what is recovered in the subtraction algorithm.

$$S_{Bkg-Al} = f^4(n \cdot S_{temp} - (S_{Raw} - S_{Bkg-Cav})) \quad (4.3)$$

Figure 4.16: Low-dose alanine subtraction example

Once the *corrected spectrum* is pulled from the raw spectrum, the same peak-to-peak algorithm demonstrated in section 4.4.1 can be applied.

4.4.3 Distinction between low and high dose alanine dosimetry

The transition from high to low dose alanine dosimetry is somewhat arbitrary. In principal, the low dose algorithm can be used in all contexts without any compromise on accuracy or precision. The only caveat being that it is more cumbersome to use, and completely unnecessary as you go to higher doses. To that end, a separation point can be

made between the different analysis procedures without any sacrifice in accuracy. The method by which this point was determined was through the comparison of the peak to peak height measured using both analysis algorithms. A large number of scans were analyzed and for each, the ratio of the peak-to-peak intensity obtained via the low and high-dose algorithms was determined. Figure 4.17 shows the results of this analysis.

Figure 4.17: Comparison of high and low dose signal calculation algorithm at a series of different doses. The uncertainty bars represent the standard uncertainty of the ratio values at each dose point.

From an analysis of figure 4.17, it is clear that below 10 Gy the algorithm is vital for reaching the targeted accuracy. As you increase the dose above 10 Gy the ratio of the algorithms approaches one. With that in mind, the threshold for what is considered *low dose* will be taken as irradiations below 15 Gy; 15 Gy is consistent with NPL recommendations of what is considered low dose alanine dosimetry^[31].

4.5 Determination of absorbed dose calibration curve

As outlined in equation 3.6, there is no “constant” relating alanine signal intensity to dose and therefore to calculate the dose, a calibration curve is generated from reference

irradiations in the NRC, typically in the ^{60}Co beam. The principal being that the calibration curve is able to relate the peak-to-peak value of the average reading from a set of pellets (irradiated concurrently in a single irradiation) to an absorbed dose value.

In the calibration curve shown in figure 4.18, each point is the average from six pellets irradiated together. The dose determination comes from reference irradiations traceable to the NRC primary standard water calorimeter. The low dose subtraction algorithm was used for all points below 20 Gy. Uncertainty of the measured intensity was propagated as the standard uncertainty for each set, and is too small to see. The line of best fit was calculated using a standard regression technique. Other, more sophisticated, regression algorithms are not necessary. This is because of the consistent uncertainty between measurements, combined with well modeled linear response of the detector for doses above 5 Gy and below any kind of saturation effects (>1 kGy).

The subtraction of the cavity background as outlined in section 4.4.2 implies the intercept of figure 4.18 will be zero. The determined intercept was consistent with this. This becomes a useful QA check, as inconsistencies would imply potential failure in the overall system.

Figure 4.18: Alanine calibration curve using reference irradiations in NRC ^{60}Co beam to relate the absorbed dose to the peak to peak EPR signal intensity

In principal, a batch calibration is a viable option, and is adopted by some facilities who employ an alanine dosimetry program. This method is certainly appealing in the sense that one can buy a large supply of pellets, store them in a controlled setting, and only calibrate once. Going forward, investigations can be mounted to investigate changes in the calibration data over long periods of time, to explore the efficacy of batch calibrations.

Chapter 5

Results

5.1 Environmental effects

The environmental effects of alanine dosimetry are broken into two distinct components: effect on the pellets, considering their storage prior and post irradiation, and effects on the spectrometer at the time of readout. Both of these were systematically investigated to try and determine optimal handling procedure for both the pellets and the spectrometer.

5.1.1 Environmental effects on spectrometer

Environmental effects at the time of readout are contingent on the spectrometer itself, and to what extent the reproducibility suffers from being housed in a less than optimal environmentally controlled laboratory. As mentioned in section 3.3.2, the cavity of the spectrometer is susceptible to quality changes associated with varying environmental conditions. The changes in the cavity, as shown by Nagy *et. al*^[18], are unpredictable and therefore simply adding a correction factor to account for environmental changes is not a practical option to combat this problem. The solution arrived at was in fixing a reference sample in the cavity to be used for signal normalization; the assumption being that changes in the reference sample measured intensity will be directly proportional to variations in the cavity.

The benefits of reference signal normalization are illustrated in figure 5.1. The study used a sample of five pellets irradiated to 60 Gy measured once per day to quantify the reproducibility of the spectrometer. Over the two week study the reproducibility both with and without signal normalization were compared. It can be seen that using the reference ruby caused a 2.6 fold reduction in the measured signal standard deviation.

Figure 5.1: Comparing the reproducibility of the spectrometer over two weeks of reading the same pellet both with and without the use of a stable reference sample, both are fitted with a Gaussian (in red) to determine the standard deviation

For comparison, the same experiment was conducted in a shorter one day time period to quantify the reproducibility of the spectrometer over the course of a day. Within a typical eight hour day, the same set of pellets were measured continuously nine times to monitor for the spread of the measurements. It is clear that there is no advantage to consolidating all of ones measurements into a single day, as the reproducibility of the spectrometer over the course of two weeks is consistent with the single day's measurements.

Figure 5.2: The reproducibility of the spectrometer over the course of an eight hour day by reading the same pellet with Gaussian fit (in red)

5.1.2 Humidity effects on alanine dosimeters

It is known that pre-conditioning alanine pellets prior to irradiation can remove alanine sensitivity to humidity effects^[25]. Being that the alanine pellets most commonly used are proprietary products, their manufacturing procedures are not readily available.

More specifically, whether the manufactures pre-condition their pellets, and to what extent, was not possible to ascertain. To that end, a study investigating the difference in signal response from NRC-pre-conditioned and un-conditioned pellets was carried out. To consider the effects of NRC-pre-irradiation storage using Far West pellets, one set of pellets was conditioned at a RH of 70%, as recommended by NPL, for six weeks and was compared to a set of pellets which was not conditioned in any way. Both sets of pellets were broken into four groups for irradiation, all nominally to 30 Gy. To monitor for any humidity-induced signal variation, both sets of irradiated pellets, conditioned and unconditioned, were stored in three separate environmental conditions to monitor for relative signal changes.

The first, for 85 % RH humidity storage, was the CSZ MCBH-1.2 unit* with a stated range of -73°C to 190°C ($\pm 0.5^{\circ}\text{C}$) and a stated humidity range of 10% to 98% RH ($\pm 2\%$)

The second, for 70% RH humidity storage, was a Nalgene [†] desiccator cabinet with the addition of an aqueous sodium bisulphate solution. The cabinet has no form of temperature control and is therefore at room temperature. The room housing the cabinet was maintained at 21°C ($\pm 1.0^{\circ}\text{C}$)

The third is an XDry cabinet[‡]. This cabinet actively removes humidity from the air and is maintained at 20 % RH ($\pm 2\%$). Similar to the desiccator cabinet, this cabinet had no form of independent temperature control; and therefore maintained at room temperature. The room was maintained at 21°C ($\pm 1.0^{\circ}\text{C}$).

Table 5.1: Pellets storage prior and post irradiation for humidity study

Pellet set	Pre-conditioning	Post irradiation storage
H1-C	yes	70% RH
H2-C	yes	85 % RH
Dry-C	yes	20% RH
H1-UC	no	70% RH
H2-UC	no	85% RH
Dry-UC	no	20% RH

The storage of the pellets both pre and post irradiation are illustrated in figure 5.3.

---

*Cincinnati Cub Zero Inc., Cincinnati Oh

[†]Nalge Nunc International

[‡]Auto-Recycling Desiccant Dry Box: <http://www.xdry.com/>

The index is referring to the individual irradiations (each with six pellets, illustrated by the coloured circles) while the colours serve to illustrate the difference in storage for the sets of pellets used in each irradiation both for prior and post irradiation storage.

Figure 5.3: Pellet storage both prior and post irradiation to monitor for humidity induced fading

Each week every set of pellets was measured and normalized by the reading from the dry samples, giving a relative measurement of environmentally induced signal change. It is evident from figure 5.4 that there is no discernible difference between the conditioned and the unconditioned pellets - effectively a null result was seen. Additionally since no statistically significant deviation was seen in the three week period of the study, which is long enough to cover any shipments within Canada, we can confidently ship the pellets within Canada without having to worry about humidity effects. This could be a point of interest for further study, to mount a larger study to more precisely analyze the effects of fading, or specifically humidity induced fading. For the purposes of this work, the result showed that no additional preconditioning is needed beyond what the producers are presumed to be doing.

Figure 5.4: Comparing conditioned and unconditioned pellets response over a month as they are subjected to different environmental conditions

5.2 Comparison of Alanine and Far West pellets

A comparison of Harwell and Far West pellets calibration curves is shown in figure 5.5, with the fit parameters in table 5.2. It is important to note that for the comparison the signal measurements are normalized to alanine, and not the pellet.

Figure 5.5: Comparison of Harwell and Far West calibration curves

Table 5.2: Comparison of calibration generated using ^{60}Co with Harwell and Far West pellets

Curve	Slope	Intercept
Far West	2.389 ± 0.002	-0.291 ± 0.050
Harwell	2.340 ± 0.008	-0.576 ± 0.250

The difference in the measured gradient between the two pellet suppliers pellets (2%) is outside of the expected reproducibility of calibration data which is typically on the order of 0.5%. This difference is likely attributed to the uncertainty component attributed to the percentage composition of alanine in each pellet, which is not provided from the manufacturer. Individual batches are, however, guaranteed to be consistent from pellet to pellet. What this means is that a general correction based on quoted composition would not be an optimal approach to perform inter-provider measurements, as the correction should be corroborated based on the batch being used.

5.3 Energy dependence

The method for determination of alanine energy dependence was outlined in section 3.6. The alanine energy dependence is the variation of Slope_Q versus energy for a particular beam modality.

The experimentally determined energy dependence, for use in commonly used clinical treatment modalities relative to cobalt-60, is shown in table 5.3. This experiment used the NRC Synergy clinical linac with nominal beam energies of 6, 10 and 18 MV. Each calibration curve was generated using four irradiations (consisting of five pellets each) on the dose range from 20 to 60 Gy ensuring linearity. The bulk of the uncertainty comes from the primary standard realization of dose, which is almost completely correlated and therefore cancels to a large degree. Based on the small change in response, no trend of energy dependence was seen in the measurements made in 6, 10, or 18 MV.

Table 5.3: Comparison of clinically applicable LINAC nominal energies to that of ^{60}Co using Far West dosimeters

Beam	$\%dd(10)_x$	Slope	Ratio to Cobalt
Cobalt	58.4	2.226 ± 0.004	1.000
6 MV	67.7	2.217 ± 0.004	0.996 ± 0.004
10 MV	73.1	2.215 ± 0.006	0.995 ± 0.005
18 MV	79.1	2.212 ± 0.004	0.994 ± 0.004

Figure 5.6: Energy dependence of the alanine pellets for different beam qualities

These results agree with the work of Bergstrand et al (2003)^[32], Zeng (2004)^[22] and Anton (2015)^[33]. All the independent investigations, different in beam quality, experimental set-up and analysis method, conclude alanine has a small beam quality correction, less than 1%, relative to Cobalt-60 for most linac x-rays beam qualities.

Figure 5.7: Consolidated literature comparison of Alanine energy dependence

5.4 Uncertainty budget

This section will be broken into two components, the first will be an *example* uncertainty budget for a 10 Gy irradiation using both Cobalt as well as an MV beam. The word example is stressed because many components within the budget are subject to variation, and therefore this cannot be applied in all contexts. The second section will be a more in depth breakdown of the different components and where they come from.

5.4.1 Example

Table 5.4: Alanine uncertainty budget for 10 Gy irradiation using 6 pellets at $k = 1$. The total uncertainty is the quadrature sum of the individual components of the budget.

Component	Relative standard uncertainty for ^{60}Co (%)	Relative standard uncertainty for MV (%)
Realization of Dose	0.25	0.35
Signal Measurement	0.2	0.2
Mass of pellet	0.05	0.05
Temperature	0.05	0.05
Calibration Fit	0.3	0.3
Spectrometer Reproducibility	0.24	0.24
Energy dependence	—	0 - 0.5
Background	0.1	0.1
<u>Total</u>	<u>0.52</u>	<u>0.57 - 0.76</u>

5.4.2 Description

Not many facilities worldwide employ a clinically applicable alanine dosimetry service. It is difficult to do a direct comparison of uncertainty budgets, but the work to date is consistent with Anton *et. al*^[34] who developed a clinically applicable alanine dosimetry service for the Physikalisch-Technische Bundesanstalt (PTB) in Germany.

Realization of Dose:

Comes from the primary standard measurement of the gray. Traceable directly to the NRC primary standard realization of dose, using water calorimetry, and has an overall uncertainty on dose determination of 0.25 % and 0.35% for Cobalt and MV respectively^[28].

Signal Measurement:

The variation in the signal intensity from measurement to measurement. Taken as the standard uncertainty of the measured peak-to-peak signal for a set of pellets.

Mass:

The uncertainty on the mass measurement. Taken to be as 0.03 mg (and therefore 0.05% of 60 mg, the nominal mass of the pellets). This is slightly higher than the quoted uncertainty by the scale manufacturer, to account for changes in reading

associated with room pressure changes, as well as the potential for slight dust build up during measurements.

Calibration Fit:

Taken as the residual RMS from the linear calibration curve.

Spectrometer Reproducibility:

This is elaborated in section 5.1.1.

Energy dependence:

Taken as the energy dependence correction factor. Can be avoided entirely of course by calibrating in the same beam quality as the audit irradiations. The range of values quoted come from my measurements and are elaborated in section 5.3.

Background:

The possible bias which is introduced from the background subtraction. The bias which can be introduced will have a larger effect as you go to lower doses which have a lower signal intensity. A full example is shown in section 4.4.2 for a 10 Gy sample.

5.5 Local audits

To date, two audits have been conducted using alanine dosimeters, both of which have been at the Ottawa Hospital[§] using their Elekta Agility clinical linear accelerator. The goal of these initial audits were to field test the alanine system and therefore were conducted by the clinic without any oversight from myself.

The accelerator is capable of nominal energies of 6 and 10 MV. The irradiations were performed using a vertical irradiation geometry, in their dedicated TG-51 water phantom. The SSD was set at 100 cm and the field size was 10 x 10 cm at the phantom surface. A crosshair on the phantom was aligned by a set of lasers what are coincident with the isocentre. This was shifted so that the SSD was 100 cm. The water level was adjusted to ensure the depth of the chamber holder was at 5 cm.

[§]The Ottawa Hospital, 501 Smyth Rd, Ottawa, ON K1H 8L6

The beam direction was perpendicular to the curved surface of the pellets and the centre of the stack of six alanine pellets was placed at the reference depth of 5 cm. The delivered dose was measured using their dedicated reference ionization chamber (an IBA FC65-G with a Fluke 35040 electrometer); it is a secondary standard ionization chamber, which was calibrated at the NRC. The uncertainty on delivered dose is 0.98% at $k = 1$ [35], the full breakdown of the uncertainty budget is outlined in table 5.5.

Table 5.5: Uncertainty Breakdown on determining the dose delivered

Component of uncertainty	Value (%)
<u>Measurements</u>	
SSD setting	0.4
depth setting	0.17
Field-size setting	0.2
Charge Measurement	0.23
Ptp correction	0.1
Humidity	0.05
<u>Calibration data</u>	
^{60}Co N_{DW}	0.5
k_Q Factor	0.4
Assignment of K_Q	0.3
Stability of reference	0.2
<u>Influence Quantities</u>	
P_{pol}	0.2
P_{ion}	0.1
Preirradiation history	0.1
Leakage current	0.05
Linac Stability	0.05
P_{ele}	0.07
P_{rp}	0.25
Total:	0.98

Tables 5.6 and 5.7 show the results of first and second audit respectively. The uncertainty on the measured dose follow the uncertainty budget outlined in table 5.4. Both audits used calibration data sets, generated at the NRC using their Elekta Synergy clinical linac (which has been retrofitted to be identical to the Elekta Agility linac used by the clinic), under the same beam quality, removing any energy dependence effects. Considering that the alanine was irradiated without any changes to the irradiation geometries, and that The Ottawa Hospital is directly traceable to the NRC for its calibration, many

components of the uncertainty in both the *measurements* and *calibration* drop out when considering the ratio of the dose delivered to the dose determined.

Table 5.6: Audit conducted at the Ottawa Hospital using Elekta Synergy clinical LINAC using a nominal energy of 6 MV

Delivered Dose using IC (Gy)	Measured Using Alanine (Gy)	Residual
3.016	$2.970 \pm 0.86\%$	$1.52\% \pm 0.97\%$
5.017	$4.952 \pm 0.72\%$	$1.31\% \pm 0.80\%$
7.014	$7.020 \pm 0.75\%$	$-0.08\% \pm 0.83\%$
8.020	$8.023 \pm 0.50\%$	$-0.04\% \pm 0.61\%$
10.017	$10.031 \pm 0.54\%$	$-0.14\% \pm 0.64\%$
12.015	$12.018 \pm 0.57\%$	$-0.02\% \pm 0.67\%$
20.019	$20.186 \pm 0.49\%$	$-0.83\% \pm 0.60\%$

Table 5.7: Audit conducted at the Ottawa Hospital using Elekta Synergy clinical LINAC using a nominal energy of 10 MV

Delivered Dose using IC (Gy)	Measured Using Alanine (Gy)	Residual
3.010	$2.925 \pm 1.4\%$	$2.83\% \pm 1.46\%$
5.011	$4.956 \pm 0.63\%$	$1.11\% \pm 0.72\%$
8.008	$8.011 \pm 0.64\%$	$-0.04\% \pm 0.73\%$
10.004	$10.009 \pm 0.65\%$	$-0.05\% \pm 0.74\%$
12.003	$11.997 \pm 0.56\%$	$0.05\% \pm 0.66\%$
19.999	$20.035 \pm 0.49\%$	$-0.18\% \pm 0.61\%$

Figure 5.8: Residuals from TOH 6 MV and 10 MV audit

The difference-RMS, considering all of 6 MV and 10 MV audit data, is 0.82% and 1.24% respectively. Considering the gross increase in the residual as you go below a 5 Gy delivered dose, it is apparent that we require all irradiations to be greater than 5 Gy, so that the targeted level of accuracy can be met. The reason for the increase is attributed to the difficulties associated with removing the alanine signal from the background signal at such low dose levels, even with the low dose background subtraction algorithm. Only considering irradiations which have a delivered dose higher than 5 Gy, the residual RMS lowers to 0.38% and 0.1% for 6 and 10 MV respectively.

The purpose of pushing the audit below 5 Gy came from trying to make the alanine dosimetry program more convenient for clinical dosimetry. In terms of an audit, it would be preferable to irradiate to lower dose from the view of the clinic. To investigate these apparent deviations at lower doses, a set of measurements were carried out, using identical procedure to that of the audit, but using the 6 MV beam from the NRC Synergy linac. Doses down to 2 Gy were delivered, and the results are shown in figure 5.9.

Figure 5.9: Alanine calibration curve generated with an emphasis on below 5 Gy measurements

The residual sub-plot in figure 5.9 shows increased deviations below 5 Gy, but there is no obvious trend with dose. This suggests that the linear fit for the calibration curve is appropriate, and a minimum of 5 Gy is required to maintain the targeted accuracy level. Lower doses in the sub-5 Gy region are certainly possible, and may be preferable depending on the application, but come with the higher level of uncertainty.

Chapter 6

Discussion

6.1 Suitability of alanine as a clinical audit dosimeter

The aim of this thesis was to determine if alanine would be suitable as a clinical audit dosimeter, and if that was a possibility, what conditions would have to be met such that the targeted level of below 1% accuracy could be met. The susceptibility of environmental induced changes in the EPR signals post irradiation was investigated and no significant changes were measured within the uncertainty budget of the experiment. This suggest that the major producers of alanine dosimeters employ a sufficient pre-conditioning component during their manufacturing procedure. The work investigating alanine energy dependence in some of the most common clinically applicable treatment modalities is consistent with previous, independent, studies suggesting little to no energy dependence relative to ^{60}Co .

The work to date has confirmed that the NRC alanine dosimetry system has the capability to offer an audit service with the targeted accuracy of sub 1%. Based on the results of the first successful audits which were conducted at the Ottawa hospital, it is recommended to have a lower limit on the delivered doses of 5 Gy, such that the accuracy of the program can be maintained.

6.2 Audit methodology

The basis for the audit methodology has been established specifically for TG-51 reference dosimetry verification. This is not suggesting that reference dosimetry within Canada is poorly done, but precisely the opposite of that. The underlying assumption of the initial work to develop a mailed audit framework is that clinics within Canada do reference dosimetry well - which will highlight the strengths of alanine. Once the initial program has been established it can grow in the directions that it needs to, or

worded somewhat differently, it can be used for whatever the medical physics community requires.

An in-house designed and fabricated alanine holder was designed to replicate the dimensions of a Farmer style chamber, as recommended by TG-51^[6] to be used for reference dosimetry. Currently there exists thirteen holders capable for use, specifying the number of irradiations which can be conducted at any one time.

The equipment which will be sent out for initial audits are is follows:

1. Alanine - the dosimeters will be hermetically sealed in the holders such that from the time they leave the NRC to the time they return, they will not be exposed to any potential contaminants which will bias the EPR measurement. There will include controls, which will remain un-irradiated for the duration of the audit.
2. Audit worksheet - The worksheet consists of three components, a beam quality questionnaire, alanine irradiation instructions, and irradiation records (reporting both temperature of irradiation as well as delivered dose)

Once returned to the NRC, the audit dosimeters will be measured at the same time as a series of *check* irradiations. The check irradiations will serve to measure the stability of the calibration data set. They are simply a series of pellet sets irradiated at the NRC, which are then measured concurrently with the audit data. Check irradiations, therefore, will be generated at a much higher frequency than that of calibration data. An example of the audit worksheet is provided in appendix C.

6.3 Forward capabilities

At this date the potential for a mailed audit service has been verified, and a TG-51 verification audit is possible. Currently there exists a lower limit of 5 Gy to maintain the targeted level of below 1% accuracy on dose determination. After speaking with the Advisory Committee on Quality Assurance and Protection (QARSAC)* at the 2017 Canadian Association for Medical Physics (COMP) Annual Scientific Meeting (ASM)[†], the beginning stages of an alanine dosimetry service were discussed. Upon establishing

---

*<https://www.comp-ocpm.ca/francais/news/representants-du-qarsac-aux-audiences-de-la-ccsn.htm>

[†]<https://www.comp-ocpm.ca/english/>

and testing the framework (the work to date) the next step will be to conduct a mailed audit for every province in Canada.

Air-filled ion chambers have been the workhorses of radiation dosimetry for a century but new technologies such as SRS/SBRT or MRI-linacs have demonstrated their weaknesses. A different kind of dosimetry is needed for the future, something close to unit density and effective atomic number close to that of water. Alanine can do this, and the work thus far on reducing the minimum dose that can be delivered opens up the possibility of using alanine for many of these challenging dosimetric situations.

Chapter 7

Conclusion

This study has successfully validated alanine as an audit dosimeter by investigating and minimizing the potential sources of inaccuracy associated with alanine dosimetry: environmental sensitivity, background effects and energy dependence. Monitoring for changes in measured alanine EPR signals attributed to varied environmental conditions, both in terms of storage of the pellets as well as the laboratory housing the spectrometer were investigated. It was observed that the manufacturing procedure of the dosimeters includes a sufficient *pre-conditioning* protocol, such that humidity effects become statistically insignificant. Permanently fixing a reference sample to the base of the spectrometer cavity, for signal normalization, was sufficient in mitigating spectrometer based signal variation. A template based background subtraction algorithm was developed, based on the literature, allowing irradiations in excess of 5 Gy to be measured without any significant loss in accuracy or reproducibility. The response of the dosimeter in several clinically relevant beam modalities relative to ^{60}Co was measured. It was seen that in 6, 10 and 18 MV alanine has no significant energy dependence, and a small beam quality correction, of less than 1%, relative to ^{60}Co .

The framework has been tested by performing an end-to-end TG-51 verification at a local cancer centre. The results from the first audits, covering 6 MV and 10 MV beams, are more than encouraging. The differences between the dose delivered and the dose determined had a RMS deviation better than 0.4%, for doses of 7 Gy and above.

Bibliography

- [1] “Report 24,” *Journal of the International Commission on Radiation Units and Measurements*, vol. os13, pp. NP–NP, 09 1976.
- [2] J. Seuntjens and M. McEwen, “The calibration chain: Role of BIPM, PSDLs and ADCLs,” in *Clinical Dosimetry Measurements in Radiotherapy* (D. W. O. Rogers and J. E. Cygler, eds.), ch. 17, pp. 567 – 576, Madison, Wisconsin: Medical Physics Publishing, 2009.
- [3] J. P. Seuntjens, C. K. Ross, N. V. Klassen, and K. R. Shortt, “A status report on the NRC sealed water calorimeter,” tech. rep., National Research Council, Ottawa, Canada, 1999.
- [4] P. E. Wesolowska, A. Cole, T. Santos, T. Bokulic, P. Kazantsev, and J. Izewska, “Characterization of three solid state dosimetry systems for use in high energy photon dosimetry audits in radiotherapy,” vol. 106, pp. 556–562, 2017.
- [5] D. W. O. Rogers, “General characteristics of radiation dosimeters and a terminology to describe them,” in *Clinical Dosimetry Measurements in Radiotherapy* (D. W. O. Rogers and J. Cygler, eds.), ch. 4, pp. 137–145, Madison, Wisconsin: Medical Physics Publishing, 2009.
- [6] P. R. Almond, P. J. Biggs, B. M. Coursey, W. F. Hanson, M. S. Huq, R. Nath, and D. W. O. Rogers, “AAPM’s TG-51 protocol for clinical reference dosimetry of high-energy photon and electron beams,” *Medical physics*, vol. 26, no. 9, pp. 1847–1870, 1999.
- [7] L. V. Spencer and F. H. Attix, “A theory of cavity ionization,” *Radiat. Res.*, vol. 3, pp. 239–254, 1966.
- [8] M. J. Berger, M. Inokuti, H. H. Anderson, H. Bichsel, J. A. Dennis, D. Powers, S. M. Seltzer, and J. E. Turner, “Report 37,” vol. os19, no. 2, p. NP, 1984.
- [9] M. J. Berger, J. H. Hubbell, S. M. Seltzer, J. S. Coursey, and D. S. Zucker, “XCOM: Photon cross section database (version 1.2),” no. NBSIR87-3597, 1999, see <http://physics.nist.gov/xcom>.
- [10] R. E. Bentley, *Uncertainty in Measurement: The ISO Guide*. 6th ed, National Measurement Laboratory CSIRO, Australia, 2003.
- [11] P. Sharpe and A. Miller, “Guidelines for the calibration of routine dosimetry systems for use in radiation processing,” tech. rep., National Physical Laboratory, Teddington, United Kingdom, 2009.
- [12] W. W. Bradshaw, D. G. Cadena, G. W. Crawford, and H. A. W. Spetzler, “The use of alanine as a solid dosimeter,” *Radiation Research*, vol. 17, no. 1, pp. 11–21, 1962.
- [13] Z. Stuglik. IAEA Training Course, December 2007.
- [14] G. R. Eaton, S. S. Eaton, D. P. Barr, and R. T. Weber, *Quantitative EPR*. Springer Vienna, 2010.

- [15] P. Sharpe, A. Miller, J. Sephton, C. Gouldstone, M. Bailey, and J. Helt-Hansen, "The effect of irradiation temperatures between ambient and 80C on the response of alanine dosimeters," *Radiation Physics and Chemistry*, vol. 78, no. 7, pp. 473–475, 2009.
- [16] M. F. Desrosiers, S. L. Cooper, J. M. Puhl, A. L. McBain, and G. W. Calvert, "A study of the alanine dosimeter irradiation temperature coefficient in the -77C to +50C range," *Radiation Physics and Chemistry*, vol. 71, no. 1, pp. 365–370, 2004.
- [17] P. J. M. Nagy V and D. M. F, "Advancements in accuracy of the alanine dosimetry system: II. the influence of the irradiation temperature," *Radiat. Phys. Chem.*, vol. 57, pp. 1–9, 1999.
- [18] O. F. Sleptchonok, V. Nagy, and M. F. Desrosiers, "Advancements in accuracy of the alanine dosimetry system. part 1. the effects of environmental humidity," *Radiation Physics and Chemistry*, p. 19, 2000.
- [19] J. Anderson and J. Weil, "Paramagnetic resonance of color centers in germanium-doped quartz.," *Chem. Phys.*, vol. 31, pp. 427–434, 1959.
- [20] V. Nagy, O. F. Sleptchonok, M. F. Desrosiers, R. T. Weber, and A. H. Heiss, "Advancements in accuracy of the alanine EPR dosimetry system part III: Usefulness of an adjacent reference sample," *Radiation Physics and Chemistry*, p. 13, 2000.
- [21] D. F. Regulla and U. Deffner, "Dosimetry by ESR spectroscopy of alanine," *The International Journal of Applied Radiation and Isotopes*, vol. 33, no. 11, pp. 1101–1114, 1982.
- [22] G. G. Zeng, M. R. McEwen, D. W. O. Rogers, and N. V. Klassen, "An experimental and Monte Carlo investigation of the energy dependence of alanine/EPR dosimetry: I. Clinical x-ray beams," *Physics in Medicine & Biology*, vol. 49, no. 2, p. 257, 2004.
- [23] A. Gago-Arias, D. Gonzalez-Castao, F. Gmez, E. Peteiro, C. Lodeiro, and J. Pardo-Montero, "Development of an alanine dosimetry system for radiation dose measurements in the radiotherapy range," *Journal of Instrumentation*, vol. 10, no. 8, 2015.
- [24] M. Anton, "Postirradiation effects in alanine dosimeter probes of two different suppliers," *Physics in Medicine and Biology*, vol. 53, no. 5, pp. 1241–1258, 2008.
- [25] J. M. Arber and P. H. G. Sharpe, "Fading characteristics of irradiated alanine pellets: the importance of pre-irradiation conditioning," *Applied Radiation and Isotopes*, vol. 44, no. 1, pp. 19–22, 1993.
- [26] Dolo, J. M., and T. Garcia., "Composition of alanine pellet dosimeters: background study for low doses applications," *Proceedings of the PTB Workshop PTB-Dos-51 on Alanine dosimetry for clinical applications (Braunschweig: Physikalisch-Technische Bundesanstalt)*, pp. 15 – 20, 2006.
- [27] E. G. A. Aird and F. T. Farmer, "The design of a thimble chamber for the farmer dosimeter," *Physics in Medicine and Biology*, vol. 17, no. 2, 1972.
- [28] M. R. McEwen, "Measurement of ionization chamber absorbed dose kQ factors in megavoltage photon beams: Measurement of photon kQ factors," *Medical Physics*, vol. 37, no. 5, pp. 2179–2193, 2010.

- [29] T. Garcia and J. Dolo, “Study of the influence of grain size on the esr angular response in alanine radicals,” *Radiat. Meas*, vol. 42, 2007.
- [30] P. H. G. Sharpe, K. Rajendran, and J. P. Sephton, “Progress towards an alanine/ESR therapy level reference dosimetry service at NPL,” *Applied radiation and isotopes*, vol. 47, no. 11, pp. 1171–1175, 1996.
- [31] M. McEwen, P. Sharpe, and S. Vrs, “Evaluation of alanine as a reference dosimeter for therapy level dose comparisons in megavoltage electron beams,” *Metrologia*, vol. 52, no. 2, pp. 272–279, 2015.
- [32] E. S. Bergstrand, K. R. Shortt, C. K. Ross, and E. O. Hole, “An investigation of the photon energy dependence of the EPR alanine dosimetry system,” *Physics in Medicine and Biology*, vol. 48, no. 12, pp. 1753–1771, 2003.
- [33] M. Anton, R.-P. Kapsch, A. Krauss, P. von Voigts-Rhetz, K. Zink, and M. McEwen, “Difference in the relative response of the alanine dosimeter to megavoltage x-ray and electron beams,” *Physics in Medicine and Biology*, vol. 58, no. 10, pp. 3259–3282, 2013.
- [34] M. Anton, “Uncertainties in alanine/ESR dosimetry at the physikalisch-technische bundesanstalt,” *Physics in Medicine and Biology*, vol. 51, no. 21, pp. 5419–5440, 2006.
- [35] M. McEwen, L. DeWerd, G. Ibbott, D. Followill, D. W. O. Rogers, S. Seltzer, and J. Seuntjens, “Addendum to the AAPMs TG-51 protocol for clinical reference dosimetry of high-energy photon beams: TG-51 photon addendum,” *Medical Physics*, vol. 41, no. 4, 2014.
- [36] R. T. Weber, “Xenon users guide.” Spectrometer user manual, 2011.

Appendix A

Spectrometer parameter optimization

A.1 Spectrometer parameter optimization

A.1.1 Microwave Power

It is clear that there is a direct relationship between microwave power and measured intensity, this is shown in figure A.1. Although it may be tempting to drastically increase the microwave power, it is important not to increase the microwave power into the point of saturation.

Figure A.1: Saturation behavior of alanine EPR signal as a result of increased microwave power using 60 Gy alanine pellet as sample

A.1.2 Modulation Amplitude

Varying the modulation amplitude has one of the largest effects on an EPR spectra. As we apply more magnetic field modulation, the intensity of the detected EPR signals increases. The increase in the signal is apparent in figure A.2 which varies the modulation

amplitude from 1 G to 10 G.

Figure A.2: Changing modulation amplitude

However, if the modulation amplitude is too large (larger than the linewidths of the EPR signal), the detected EPR signal broadens and becomes distorted.

Figure A.3: Distortion affect of EPR signal^[36]

This is apparent when looking at an alanine spectra as you increase the modulation amplitude past the line-width (~ 8 G).

Figure A.4: Increasing modulation amplitude beyond linewidth

Appendix B

1 Introduction

AlCal is a graphical user software designed for use in Low-Mid dose range alanine dosimetry. The software is designed to reduce the computational time post readout for quick and easy generation of calibration data, and dose interpolations/extrapolations.

2 Data organization

Data organization of AlCal is designed to integrate with the software used to run the spectrometer. Specifically, the organization of the input data is designed to read from the output of the spectrometer.

Figure 1: Organization structure of date file housing all alanine spectra and supporting data

Figure 2: Folder structure for tutorial data containing calibration data set

3 Calibration

For the calibration data set, the user needs to specify the location for both the parent directory, housing all the individual dose files, and a template directory, which is the directory pointing to the template dose file specifically. The template need only be specified if the user is doing low-dose dosimetry.

Once directories are specified, the user has the ability to populate the *Low Doses* and *High Doses* options. The user can use either the Low doses or high doses independently, or in combination by pressing, *Only Low*, *Only High* or *High and Low* respectively - all of which are illustrated in figure 3.

Alanine Calibration and Interpolation

Parent Find

Template Find

Low Doses: Use all points

High Doses: Use all points

Save Fit

High and Low

Only High

Only Low

Figure 3: Calibration data input menu. Parent points to directory containing calibration set, template points to directory template directory (only required if low-dose algorithm is being used), Low and High Doses are the folders containing all spectra for measurement set. The Low and High doses can be specified manually, or be automatically filled using the *Use all points function* (Which grabs all folders within the parent directory.)

The last component of user specified information required is the population of the *input file*, which contains the information on both delivered dose, and irradiation temperature.

The user has the capability to populate the low and high dose inputs individually by specifying dose folders, or by simply pressing the *Use all points* which will pull all folder names within the parent directory. Careful attention has to be used when inputting dose folders, as the order of the dose directory has to match the order of the input file.

4 Interpolation/Extrapolation

The interpolation/extrapolation functionality is quite similar to that of the calibration, the only major distinction being the nature of the supporting data; specifically in the case of interpolation a *temp* input file has to be provided. This is in the parent director and contains the temperature of irradiation of each set.

The program will determine both the average spectrum intensities as well as the standard uncertainty for each dose file provided. It will use the fit generated from the calibration set, or the user has the option to load in a fit manually using the *Import Fit*. Save files of calibration fits are able to be generated using the *Save fit* option on the calibration page.

The screenshot shows a window titled "Alanine Calibration and Interpolation". It contains several input fields and buttons:

- Parent Directory:** A text input field followed by a "Find" button.
- Template:** A text input field followed by a "Find" button.
- Folders with spectrums:** A text input field followed by a "Use all points" button.
- Low Dose:** A button.
- High Dose:** A button.
- Import Fit:** A button.
- Below Import Fit:** A large empty text area.

Figure 4: Interpolation data input

5 Saving and Loading Data

Saving files for both calibrations and dose determinations is possible under the file heading of the menu bar illustrated in figure 5.

Figure 5: Saving and loading data

6 Navigating

There are three pages within the program, the Graph, Calibration, and Interpolation. All of these different pages are accessible using the navigation menu option, illustrated in figure 6.

Figure 6: Navigating between Graph, Calibration and Interpolation

7 Graphing

Upon opening the program, the graphing page will be blank, illustrated in figure 7a. There is the option to either generate data to populate the graph through the calibration and interpolation page, or load data for plotting through the load calibration option. The load option simply being a quick way to use older calibration data. A plot populated with both calibration and interpolation/extrapolation data are illustrated in figure 7b.

(a) Blank graph which appears prior to data population

(b) Example calibration and dose determination

Figure 7: Plotting Data

Appendix C

NRC Postal Dose Quality Audit
☐ Co-60   ☐ Megavoltage X-Ray Beams

Data Sheet

Audit No.   **Dosimeter Set No.**

Contact Person:

Family Name
Given name
Position
Department
E-mail (individual)
Phone (individual)
Name of Institution

Specifications of irradiation unit:

The irradiation unit used for this audit is of type:

Manufacturer and Model
Serial Number
Production year

Installation year

The beam is

☐ With flattening filter
☐ Flattening filter free

 and is commissioned as ... beam.

The beam quality is characterized by:

☐ $dd(10)_x =$ (10 cm x 10 cm at SSD = 100cm)

Irradiation of Alanine Pellets

The Alanine pellets were irradiated on the following date

The Alanine pellets were irradiated   cm in water

Using a field   cm x   cm

At a distance of

☐ SSD
☐ SAD

With the following geometry arrangements: ... with water phantom and NRC holder
If non-standard, please explain:

For the different alanine dosimeter sets, the time/monitor settings, temperature, and dose delivered were:

Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy
Dosimeter ID	____ min ____ MU	°C	D =	Gy

Background ID

Calculation of time/monitor setting

Provide the data used for the calculation of time/monitor settings for alanine irradiation. Please provide factors such as beam output, any conversions/correction factors, etc.

Beam output as stated in your records is: ... on the date   (dd/mm/yyyy)

Please explain in detail the irradiation conditions for which beam output applies (depth, SAD/SSD, Field size):