Development of a mailed dosimetry audit system for radiation therapy in Canada

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ABSTRACT

The aim of this work was to develop and trial a mailed audit system for external beam radiation therapy, traceable to the Canadian National Metrology Institute, with an overall uncertainty comparable to calibrated secondary standard reference detectors.

Alanine was chosen as the dosimeter to be used for the audit system. After a detailed investigation of influence quantities, a complete uncertainty budget was constructed, indicating a relative standard uncertainty in the desired quantity – absorbed dose to water – of around 0.9 %.

The complete system was then validated by comparison with the standard maintained by the National Physical Laboratory in the UK. The comparison between the two alanine systems at the two laboratories showed agreement at the 0.5 % level.

A hermitically-sealed dosimeter holder was developed for simplicity of use and to reproduce the geometry of standard clinical dosimeters. Eleven cancer centres across Canada participated in the initial trial. The mean ratio of the dose measured using alanine, relative to the dose delivered was found to be 1.010 with a relative standard uncertainty of 0.6 %.

These investigations have confirmed the suitability of the alanine system, both in terms of ease-of-use and accuracy, for mailed audit dose measurements in Canada.

1. Introduction

For soft-tissue cancers, radiation therapy is used curatively in approximately 40 % of all treatments, either alone or in conjunction with surgery or chemotherapy. Successful radiation therapy depends directly on the accuracy of the delivered dose and the International Commission on Radiation Units and Measurements (ICRU) recommends an uncertainty of $\leq$5 % on the dose delivered to a target volume (i.e., the tumour) [1]. Given the steps in a typical radiation therapy workflow, this requirement implies that the output of the device used to deliver the ionizing radiation (typically an electron linear accelerator) should be known to better than 2 %, and ideally, 1 % (as a relative standard uncertainty). Over more than three decades, a robust calibration system has been set up in Canada to provide traceable measurements allowing clinical medical physicists to achieve this level of accuracy.

However, there is currently no national Canadian audit capability that can provide independent verification of this calibration procedure and that is traceable to the same national measurement standards. The aim of this work is to develop such a capability, which will provide a more stringent test of dose delivery than can be obtained with other, international audit services that are traceable to different national standards.

Alanine is a neutral non-polar amino acid with an effective atomic number of 6.8 and a density of 1.42 g/cm^3. Alanine forms a crystalline structure, allowing free radicals produced via ionizing radiation to exist for a long time (years) without recombination, and read out is via EPR spectroscopy. The free radical signal is proportional to the energy absorbed and alanine powder can be easily formed into small pellets (typically 5 mm diameter, 3 mm thick). This combination of properties makes it very attractive as a dosimeter for a mailed audit service.

A number of different passive dosimeters are currently in use worldwide for mailed dosimetry services. The National Physical laboratory, UK, has pioneered the use of alanine for radiation therapy audits [2]. The two largest providers, the IAEA and IROC-Houston use, respectively, radio-photoluminescent dosimetry (RPLDs) and optically stimulated luminescent dosimetry (OSLD) [3,4].

1.1. Performance specification

The target for the audit dosimetry system was that it would be able to measure absorbed dose to water with a standard uncertainty of better than 1 % for a delivered dose of around 15 Gy. In addition, the system should be immune to transport and environmental effects at the level of 0.5 %.

2. Methods and procedures

The alanine dosimetry system is a combination of the alanine pellet (dosimeter) and the read-out device (EPR spectrometer).

2.1. Alanine dosimeters

In developing the alanine dosimetry capability at NRC, two types of alanine pellets have been used, as shown in Table 1. These were provided by Far West Technology and Harwell Dosimeters and both consist of high-purity L-alpha-alanine combined with a binder to allow for

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Table 1
Commercially available alanine dosimeters. The tolerances shown are as given by the manufacturer.

Vendor	Binder	Diameter (mm)	Height (mm)	Mass (mg)
Harwell	9.1 % Paraffin	4.8 ± 0.1	2.8 ± 0.1	60 ± 2
Far West[a]	4.0 % Polyethylene	4.8 ± 0.04	3.0 ± 0.1	65 ± 0.5

[a] Far West Technology, Goleta, CA.

moulding into specific pellet shapes.

2.2. EPR spectrometer

The spectrometer used for this work is a Bruker EMX system, with HS0105 high sensitivity cavity and Xenon electronics upgrade. Spectrometer measurement parameters were carefully optimized for the measurement of doses in the 10 Gy to 20 Gy range (the target dose range for clinical measurements). Reference [5] details an investigation of spectrometer parameters and a similar procedure was followed here, but tailored to the specific needs of this project and the equipment being used.

An in-house built Teflon support is used to reliably position the alanine pellet at the centre of the cavity. A reference ruby is fixed to the base of the spectrometer cavity and does not move when changing pellets. The ruby signal is measured immediately after each alanine measurement and provides a way to the normalize the spectrometer response and reduce variations attributed to spectrometer instability [6].

2.3. Pellet holder for irradiations

A hermitically-sealed holder containing six alanine pellets (hereafter referred to as the "dosimeter") was developed to mitigate the effect of environmental changes during a transport and irradiation, since humidity, in particular, can affect the alanine free-radical signal. The holder shown in Fig. 1 is made out of Delrin® (polyoxymethylene, POM) and is designed to replicate the outer dimensions of a Farmer-type ionization chamber. This chamber type is the default reference dosimeter used in cancer centres worldwide, so matching dimensions should simplify the audit process.

2.4. Calibration methodology

The alanine signal intensity and the absorbed dose are not related by a universal constant and therefore a calibration curve has to be obtained using reference irradiations carried out in the NRC ^{60}Co beam. The ^{60}Co intensity has been previously determined using the NRC primary standard water calorimeter [7]. An example alanine calibration curve is shown in Fig. 2. The line of best fit was calculated using a standard unweighted regression technique.

Calibration of alanine dosimeters is carried out on a batch basis, whereby it assumed that a specific manufacturing batch exhibits the same response to ionizing radiation.

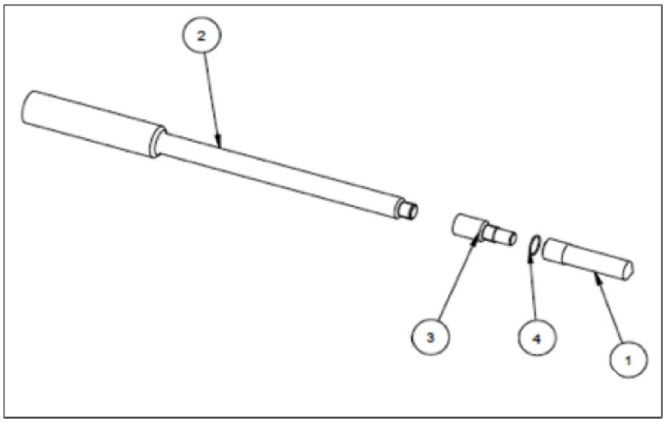

Fig. 1. Four-piece alanine dosimeter holder, based on reference ionization chamber geometry: 1) pellet cavity, 2) mounting stem, 3) plug, 4) O-ring. The cavity has a wall thickness of 1 mm, a depth of 18.6 mm, and can hold 6 alanine pellets.

2.5. Influence quantities

A number of influence quantities must be considered to ensure accurate application of the alanine/EPR method. Some are specific to the alanine dosimeter; others are related to the EPR spectrometer used for read-out.

2.5.1. Irradiation temperature

The free radical intensity per unit absorbed dose is dependent on the temperature at irradiation. A correction, as proposed by Nagy et al. [8] was used to correct the measured EPR intensity:

$$k_T = 1 - c_t(T - T_0) \quad (1)$$

where c_t is the temperature coefficient which has been previously reported [9,10], T refers to the irradiation temperature, and T_0 is an arbitrary reference temperature, taken to be 21 °C.

2.5.2. Energy dependence

Dosimeters generally show some energy dependence in their response and this has been investigated for alanine by several groups [11,12]. The literature data was confirmed through measurements in ^{60}Co and MV photon linear accelerator beams (*Elekta Synergy*) at the NRC, yielding a correction factor of 1.005, independent of energy in the range 6 MV–18 MV (the energy range of interest for this project).

2.5.3. Free radical stability

Although the free radicals produced in alanine due to the interaction with ionizing radiation have very long lifetimes (motivating its use as a mailed dosimeter), there is a degree of signal fading due to free radical recombination. This fading is dependent on environmental effects including pellet pre-treatment and storage, conditions during transport

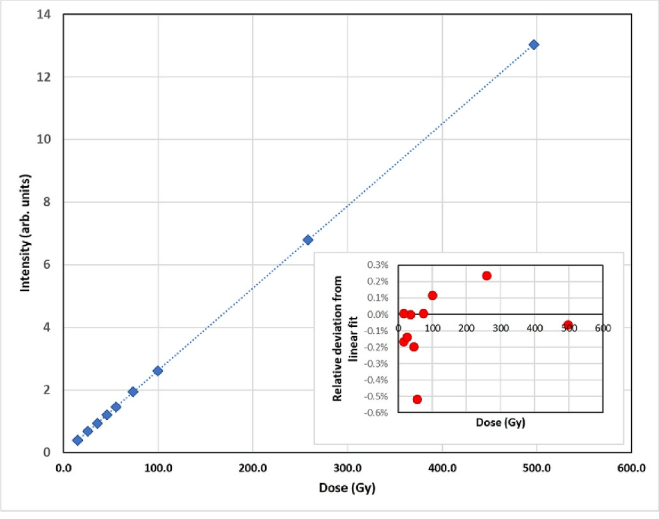

Fig. 2. Calibration data for alanine pellets irradiated at NRC. The inset plot shows the relative deviations of the linear fit, which are typically less than 0.2 %. The Type A relative standard uncertainty of the EPR signal of the five pellets in each irradiation was, on average, around 0.2 %.

and irradiation, and handling during read-out. This has been studied in detail [13] and with the adoption of best practice, signal fading can be limited to less than 1 % per year.

2.5.4. Spectrometer environment

A review of long-term QA data for reference pellets at the NRC indicated an annual cyclical variation in the measured dose, superimposed on the quasi-linear signal decay due to radical recombination. An extensive study of spectrometer performance indicated that temperature and humidity had a larger effect than had been expected. Improvements were made to both i) the physical environment, through dedicated, local HVAC control, and ii) measurement procedures, allowing increased time for thermal stabilization of the system, and this resulted in improved performance.

During this investigation, other aspects of the measurement procedure were reviewed to identify any impact on the alanine signal. These included the effect of the quartz tube required to hold the alanine pellet within the RF cavity and the impact of pellet anisotropy (i.e., the effect of position and/or rotation within the cavity).

2.6. Irradiation procedure for alanine dosimeters

A common irradiation procedure was developed, which can be used for internal research purposes as well as any external irradiation activities. The example is given for measurements at a clinical cancer centre.

Alanine pellets were loaded into a set of holders, as shown in Fig. 1, and sent to the participant. At the clinical site, the participant irradiated each dosimeter to a dose based on their local realization of the quantity. Typical 5–7 dosimeters (holders) were sent and each participant could choose how to use them (e.g., all at one beam energy, or spread across multiple beams). The only requirements were that the doses delivered should be in the range 12 Gy–20 Gy. The dosimeters were then returned to NRC for read-out, which was carried out in the same way as for the calibration data set described in section 2.4. In addition, at least two control dosimeters were sent – one a blank (unirradiated) and one pre-irradiated to an absorbed dose of around 15 Gy. The reading of these two controls were used to identify any effects of transport and correct the user-irradiated dosimeters accordingly. In addition to providing the delivered dose, the user must also record the irradiation temperature of dosimeters and the irradiation geometry (beam energy, phantom material, measurement depth, distance from the radiation source, *etc*) as these are all influence quantities.

The absorbed dose to water determined from the read-out of alanine pellets, $D_{w,al}$ is given by:

$$D_{w,al} = M_{EPR} N_{D,w}^{Co-60} f_{Co \rightarrow X} k_T \quad (2)$$

where M_{EPR} is the mean alanine signal for the set of pellets within a single dosimeter; $N_{D,w}$ is the calibration coefficient for the batch of pellets derived from irradiations in the NRC Co-60 beam; $f_{Co \rightarrow X}$ is the correction factor to convert from the calibration field (Co-60) to the irradiation field (X-rays); and k_T is the correction for irradiation temperature.

3. Results and discussion

3.1. Validation

Prior to any testing of the alanine dosimetry system for auditing Canadian cancer centres, a comparison was carried out with the National Physical Laboratory, UK, which has operated an alanine capability for more than two decades. This was a two-way comparison, testing both irradiation and read-out procedures at both laboratories, and is described in more detail in Ref. [14]. The results are summarized in Table 2, and demonstrate the equivalence of the two national capabilities.

3.2. Uncertainty budget

An uncertainty budget was constructed and is shown in Table 3. Each component is based on operation over several years. As can be seen, the target specification of 1 % from section 1.1 has been met. There is not a single, dominant uncertainty component and it is typical, in ionizing radiation standards, that the primary standard is one of the largest contributions to the overall uncertainty. The uncertainty in the signal measurement is approximately a factor of two smaller than prior to implementing improvements described in section 2.5.4.

3.3. Results from first audit

Seven Canadian cancer centres participated in the first trial of the audit system. The irradiations were all carried out in high-energy photon beams produced by linear accelerators, since the majority of radiation therapy treatments in Canada are delivered using this type of radiation beam. Irradiations covered the energy range 6 MV–18 MV and the doses delivered to the dosimeters were in the range 12–20 Gy. The results are summarized in Table 4 with the different cancer centres anonymized, since the intent is to test the dosimetry system, not clinical performance. In Table 4, "DEL" refers to the dose delivered, as determined by the clinical medical physicist and based on their standard calibration methodology; "MEAS" refers to the dose determined from the read-out of the alanine pellets, as given in Equation (2).

No significant impact due to transport was observed on the alanine readings, despite the trial covering cancer centres across four time zones (and therefore very different shipping durations/routes). However, it was identified through additional investigations that increasing the number of control dosimeters sent (i.e., 2 or 3 dosimeters irradiated to known doses) provided more confidence in the mailing process. The value given for the uncertainty component due to transport in Table 2 is a typical value but it shows the largest inter-participant variation and increasing the number of controls constrains this contribution.

The relative standard uncertainty for the pellets in a single dosimeter was typically 0.2 % to 0.3 %, consistent with Table 2. The standard deviation column in Table 3 indicates the spread on multiple dosimeters irradiated at each centre. In general, this is generally less than 0.5 % but approaches 1 % for two participants, possibly indicating challenges in following a new experimental procedure, or instabilities in the dose delivery system. There is a general trend that the dose measured by the alanine system is lower than the delivered dose, with a rms value of 1 %. However, the uncertainty in the dose delivery itself has been estimated to be around 1 % [15] and though of interest for further study, this difference is not considered to be statistically significant.

A review of participant experiences indicated that the procedure was suitable for implementation in the clinic and there was satisfaction with the process and outputs.

3.4. Extension to specialized delivery systems

The initial audit was carried out for standard linear accelerator conditions, as laid out in international dosimetry protocols [15,16]. This is a useful baseline, but alanine can be applied to more specialized radiation beams, where independent validation using an accurate passive dosimeter has increased value (i.e., to overcome challenges in these

Table 2
Summary of results of NPL/NRC comparison.

Irradiation lab	Read-out lab	D_{NPL}/D_{NRC}	Standard deviation[a]
NRC	NPL	0.9975	0.28 %
NPL	NRC	0.9934	0.34 %

[a] Multiple dosimeters were irradiated to doses in the range 10 Gy–1000 Gy. The standard deviation reflects the variation in the dose ratio for the complete set of dosimeters.

Table 3
Uncertainty budget for the determination of absorbed dose to water in high-energy photon beams from a linear accelerator, using alanine dosimeters.

Component	Standard uncertainty (%)	
	Type A	Type B
Realization of dose (primary standard)	0.1	0.39
Signal measurement – calibration	0.2	
Irradiation temperature – calibration		0.05
Mass of pellet	0.05	
Spectrometer reproducibility	0.2	0.25
Calibration fit[a]		0.35
Signal measurement – participant	0.2	
Irradiation temperature – participant		0.1
Energy dependence correction factor		0.25
Transportation of dosimeters		0.35
Total uncertainty (k=1)	**0.36**	**0.73**
Combined relative standard uncertainty	**0.82**	

[a] Includes goodness of fit and repeatability across a batch.

Table 4
Results of first trial of alanine audit system.

Centre	Difference D_{DEL} - D_{MEAS}	Standard deviation
A	1.1 %	0.6 %
B	2.3 %	0.8 %
C	−0.2 %	1.0 %
D	0.5 %	0.4 %
E	0.7 %	0.4 %
F	0.9 %	0.5 %
G	0.2 %	0.3 %
H	0.5 %	0.3 %
rms values	**1.0 %**	**0.6 %**

beams associated with performing dose measurements or delivery). This includes small-field dosimetry [17], hybrid MRI-linear accelerator treatment devices [18] and novel radiosurgery systems.

The NRC alanine system has recently been applied to the latter two radiation delivery systems [19,20], with sub-1 % accuracy, allowing the testing of other clinical dosimeters and providing added confidence in machine calibrations used for newer radiation therapy treatments.

4. Conclusions

A dosimetry system based on alanine dosimeters read-out using EPR spectroscopy has been extensively investigated for use in a Canada-wide mailed dosimetry audit capability. The system was validated by comparison with an existing capability at the UK National Metrology Institute and a detailed uncertainty budget indicated that absorbed dose to water could be determined with a relative standard uncertainty of less than 0.9 %. An initial trial of the audit procedure involved seven radiotherapy centres across Canada and demonstrated both the accuracy of the system and the feasibility of the process.

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