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An experimental and Monte Carlo investigation of the energy dependence of alanine/EPR dosimetry: I. Clinical x-ray beams

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Abstract

The energy dependence of alanine/EPR dosimetry, in terms of absorbed doseto-water for clinical 6, 10, 25 MV x-rays and 60 Co γ -rays was investigated by measurements and Monte Carlo (MC) calculations. The dose rates were traceable to the NRC primary standard for absorbed dose, a sealed water calorimetry. The electron paramagnetic resonance (EPR) spectra of irradiated pellets were measured using a Bruker EMX 081 EPR spectrometer. The DOSRZnrc Monte Carlo code of the EGSnrc system was used to simulate the experimental conditions with BEAM code calculated input spectra of x-rays and γ -rays. Within the experimental uncertainty of 0.5%, the alanine EPR response to absorbed dose-to-water for x-rays was not dependent on beam quality from 6 MV to 25 MV, but on average, it was about 0.6% lower than its response to 60 Co γ -rays. Combining experimental data with Monte Carlo calculations, it is found that the alanine/EPR response per unit absorbed dose-to-alanine is the same for clinical x-rays and ⁶⁰Co γ -rays within the uncertainty of 0.6%. Monte Carlo simulations showed that neither the presence of PMMA holder nor varying the dosimeter thickness between 1 mm and 5 mm has significant effect on the energy dependence of alanine/EPR dosimetry within the calculation uncertainty of 0.3%.

1. Introduction

There is considerable literature on the use of alanine/EPR dosimetry for ionizing radiation (Regulla 2000, Regulla and Deffner 1982). The radiation-induced free radicals trapped in alanine crystals are stable under normal storage conditions (Sleptchonok *et al* 2000) and their electron paramagnetic resonance (EPR) signal can be measured using a non-destructive procedure (Raymond 1968). Alanine response per unit dose-to-water for ⁶⁰Co γ -rays is linear over a broad dose range from 1 Gy to 10 kGy (Nagy 2000). Dosimeters can be made in

many forms, rod, pellet, cable and even thin film, and are easily handled. Alanine/EPR dosimetry has been used in food irradiation and medical sterilization for more than 20 years. More recently, there has been an increasing interest in its use for radiation therapy dosimetry (Regulla 2000).

A number of studies have been published, dealing with the applications of alanine dosimetry to radiation therapy (Olsson *et al* 2002, Nagy *et al* 2002, Fainstein *et al* 2000, De Angelis *et al* 2000, 1999, Hayes *et al* 1999, Sharpe and Sephton 1999, Onori *et al* 1997, Mehta and Girzikowsky 1996, Ruckerbauer *et al* 1996, Gao and Zaiyong 1996). The applications range from quality assurance of external beams to dose determination in brachytherapy. The radiation sources include photons, electrons and protons. For example, The National Physical Laboratory in the United Kingdom developed a mailed reference dosimetry service using alanine/EPR to check clinical doses derived from ion chamber measurements (Sharpe and Sephton 1999); Olsson *et al* (2002) used alanine gel and alanine film to measure the absorbed dose around a high dose rate (HDR) ¹⁹²Ir source; Onori *et al* (1997) applied alanine pellets to map the depth dose distributions of proton beams in water.

A few papers focused on the alanine response to dose-to-water for different high-energy photons. Among them, Olsen *et al* (1990) suggested that mass energy absorption coefficient be used to correct the alanine response to x-rays, Sharpe's study (2003) indicated that the response for 4–12 MV x-rays was 0.6% lower than that for ⁶⁰Co γ -rays. Bergstrand *et al* (2003) used Bruker alanine pellets with 10–30 MV x-rays from the NRC Vickers accelerator compared to ⁶⁰Co γ -rays and concluded that the alanine response per unit absorbed dose-to-water for x-rays is slightly lower than that for ⁶⁰Co γ -rays and recommended a correction factor of 0.992 ± 0.005.

In this study we have investigated the energy dependence of our recently established alanine/EPR dosimetry system to strictly clinical beams from an Elekta medical accelerator and to 60 Co γ -rays from an Eldorado therapy unit. For this purpose, we developed a method for doing alanine/EPR measurements rapidly and with a standard deviation better than 0.5% for doses higher than 10 Gy. This enabled us to carry out the EPR measurements for the calibration curves for two beam qualities in the same day in order to improve the accuracy of measuring relative responses. Alanine pellets were irradiated in PMMA sleeves to several doses between 20 and 50 Gy in a water phantom for 6 MV, 10 MV and 25 MV x-rays and 60 Co γ -rays. We measured the alanine relative response for each x-ray beam to 60 Co γ -rays.

For chemical dosimeters, the energy dependence is caused by variations in stopping power or mass energy coefficient as well as in radiation yield (Olka 2002), a concept describing the production of the measurable value per unit absorbed energy to dosimeter. For example, it was found that for a Fricke dosimeter the production of Fe³⁺ per unit absorbed energy in Fricke solution increases by 0.7% on going from ⁶⁰Co to 30 MV x-rays (Klassen *et al* 1999). So in this study, we investigated the alanine/EPR signal per unit absorbed dose-to-alanine for x-rays relative to that for ⁶⁰Co γ -rays. We used Monte Carlo simulations to calculate the ratio of absorbed dose-to-alanine to absorbed dose-to-water.

Monte Carlo simulations were also performed to analyse the effect of the PMMA sleeves and the dosimeter size on alanine response.

2. Methods and definitions

In radiation therapy, dose-to-water, D_{water} , is the quantity of interest (IAEA 2000). For alanine dosimetry, one measures the alanine/EPR intensity, which is the signal amplitude per unit dosimeter mass. Alanine/EPR intensity is proportional to the number of free radicals produced by the irradiation (Regulla and Deffner 1982). Alanine/EPR response to absorbed

dose-to-water for a given beam quality Q, denoted as $(\text{Slope})_Q$ in this paper, is defined as the signal intensity per unit absorbed dose-to-water. Experimentally, $(\text{Slope})_Q$ 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. The alanine energy dependence is the variation of $(\text{Slope})_Q$ versus energy for a particular beam modality. The comparison of several beam qualities is best done by normalizing them to a reference beam quality, which we took as ⁶⁰Co in this study. We did the EPR measurements for two calibration curves on the same day, one for an x-ray beam quality and the other for ⁶⁰Co.

Let the radiation yield, G_Q , be the number of the free radicals produced by unit absorbed energy in alanine for a beam quality Q. The EPR amplitude is equal to the product of G_Q times the absorbed energy times a proportionality factor K,

$$(1)$$
(1)
(1)
(1)

Dividing each side of the equation by the mass of the dosimeter we have

$$(Intensity)_Q = KG_Q(D_{alanine})_Q.$$
 (2)

Here, D_{alanine} is the absorbed energy per unit mass, i.e., the absorbed dose-to-alanine. A calibration curve for a beam quality Q is the (Intensity)_Q versus absorbed dose-to-water, hence,

$$(\text{Slope})_Q = KG_Q(D_{\text{alanine}}/D_{\text{water}})_Q \tag{3}$$

where $(D_{\text{alanine}}/D_{\text{water}})_Q$ presents the ratio of the absorbed dose-to-alanine to the absorbed dose-to-water for beam quality Q.

K is not dependent on beam quality, only dependent on the individual EPR spectrometer, the dosimeters and the recording parameters and environmental conditions (Nagy *et al* 2000a, 2000b). If we use 60 Co as a reference beam and do the Slope under the same measurement conditions, we have

$$\frac{(\text{Slope})_{Q}}{(\text{Slope})_{Co}} = \frac{G_{Q}}{G_{Co}} \frac{(D_{\text{alanine}}/D_{\text{water}})_{Q}}{(D_{\text{alanine}}/D_{\text{water}})_{Co}}.$$
(4)

Equation (4) indicates that the energy dependence of alanine/EPR dosimetry comes about in two ways: the variation in radiation yield and the variation in the ratios of stopping powers or mass energy absorption coefficients. By experiment, we can measure $(\text{Slope})_Q/(\text{Slope})_{\text{Co}}$, while by Monte Carlo simulations, we can calculate $(D_{\text{alanine}}/D_{\text{water}})_Q/(D_{\text{alanine}}/D_{\text{water}})_{\text{Co}}$, so from equation (4), we can obtain the relative radiation yield

$$\frac{G_Q}{G_{\rm Co}} = \frac{({\rm Slope})_Q}{({\rm Slope})_{\rm Co}} \bigg/ \frac{(D_{\rm alanine}/D_{\rm water})_Q}{(D_{\rm alanine}/D_{\rm water})_{\rm Co}}.$$
(5)

3. Experiment

3.1. Alanine/EPR dosimetry at NRC

Alanine dosimeters were obtained from Gamma-Service Produktbestrahlung GmbH, Germany, Lot T020604. The composition was stated to be 96% L-alpha-alanine and 4% other binder material, and the density to be 1.22 g cm⁻³. The pellets were 5 mm in diameter and 3 mm in height and weighed 64.5 ± 0.5 mg.

A Bruker EMX 081 spectrometer was used for spectrum acquisition. The pellet was held in a quartz tube in the EPR cavity of the spectrometer. A Teflon support was used to position the pellet at the centre of cavity where the uniform electromagnetic field minimizes the effect of different sample shapes on signal acquisition. To change pellets, the quartz tube had to be

Parameters	Alanine	Reference ruby
Microwave power (mW)	0.25	0.25
Modulation amplitude (mT)	0.8	0.8
Receiver gain	2.0×10^5	2.0×10^{3}
Time constant (ms)	1311	1311
Conversion (ms)	82	82
Sweep time (s)	42	42
Sweep width (mT)	1.2	5
Resolution	512	512
Number of scans	2	1

 Table 1. EPR recording parameters used in measurements with the EMX 081 spectrometer.

removed and replaced. A reference ruby crystal was permanently fixed near the bottom of the cavity. By normalizing the alanine signal to the ruby signal, variations due to spectrometer instability and humidity changes are substantially reduced. Nagy *et al* (2000b) described in detail the usefulness of an adjacent reference sample.

For the EPR measurements, the peak-to-peak height of the central line of the alanine EPR spectrum was taken as the alanine signal amplitude (Ahlers and Schneider 1991). Alanine/EPR signal amplitude may be affected by the crystal orientation in the magnetic field (Haskell *et al* 1997). In order to correct for any non-random orientation of the micro-crystals in the dosimeters, each pellet was recorded in three orientations differing by 60° . The amplitude of the alanine signal was normalized to the ruby signal in each orientation. The signals of the three orientations were averaged and normalized to the mass of pellet to obtain the intensity.

The recording parameters used for EPR measurements in this study are listed in table 1. The scan width for pellets was 1.2 mT centred at 3508 Gauss, with 2 scans for each orientation. The ruby scan width was 5 mT centred at 2670 Gauss and only one scan was run. These parameters had been optimized to get the most reproducible and precise measurement in a reasonable recording time. We did not use higher microwave power or modulation amplitude, often suggested as a way to increase the signal amplitude for low doses measurement, because these lead to a less stable machine performance. The Bruker EMX 081 is a single cavity spectrometer. The spectrum of the dosimeter and the reference were run separately. We shortened the time between the two by doing only two scans of alanine, in order that the conditions during the alanine and ruby measurements should be similar.

The production of free radicals in alanine is affected by the irradiation temperature (Nagy *et al* 2000a, Weiser *et al* 1989). In this work we corrected the alanine/EPR intensity to T_0 by using the correction factor k_T suggested by Nagy *et al* (2000a),

$$k_T = 1 - 0.0017 \left(T - T_0 \right). \tag{6}$$

Here, T refers to the irradiation temperature and T_0 was taken to be 21 °C, the temperature to which the room was controlled.

As well as using a ruby reference, we further reduced environmental (temperature, humidity) day-to-day differences by doing the measurements of pellets for a particular beam in the same day as for the pellets irradiated using ⁶⁰Co. Our preliminary investigations at NRC showed that, for a single set of pellets, the standard deviation (nine measurements) from day-to-day could be as high as 0.4%, but the ratio of EPR readings for two sets varied by less than 0.15% from day-to-day. Thus, measuring two beams in the same day improved the accuracy of measuring the relative EPR response.



Figure 1. Positioning of alanine dosimeters in the water phantom relative to the beam direction. Six pellets were stacked in a 1 mm inner PMMA sleeve and sealed by a PMMA rod to press all pellets firmly together. The beam direction is perpendicular to the curved surface of the pellets.

3.2. Irradiations

The NRC Elekta Precise linac delivers three clinical x-ray beams, 6, 10 and 25 MV. The accelerator head was 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 10×10 cm at the phantom surface. Six pellets were stacked in a 1 mm PMMA sleeve and sealed by a PMMA rod and then put into an outer waterproof PMMA sleeve holder with a 1 mm wall. The geometry of the inner sleeve is similar to the NE2571 Farmer-type chamber used to determine the dose rate at the reference point, and the same outer sleeve was used for the ion chamber. The beam direction was perpendicular to the curved surface of the pellets, as depicted in figure 1. The centre of the stack of alanine pellets was placed at the reference depth of 10 cm taking into account the 2 mm phantom window. The positioning precision was 0.1 mm. Alanine was irradiated in steps of 10 Gy at a nominal dose rate of 3 Gy min⁻¹.

For measurements in linac beams, the dose-to-water at the reference depth was determined by an NE2571 Farmer-type chamber, that had been calibrated in terms of absorbed dose-towater in the NRC Eldorado ⁶⁰Co beam (Seuntjens *et al* 2000). The k_Q factors for the three linac beams were derived from the experimental data given by Seuntjens *et al* (2000). The chamber was irradiated with fixed doses of 1 Gy and ten irradiations were given, yielding a typical standard deviation of 0.06%. Two NE2571 chambers were used at each energy to check chamber performance. Agreement between the two chambers was better than 0.2% at all energies. All ion chamber data were corrected for temperature, pressure, ion recombination and polarity. No correction for beam non-uniformity was required as the irradiated volumes of the chamber and alanine were the same. The chamber measurement was repeated regularly to monitor any drift in linac output, the largest of which was found to be 0.12%.

Measurements were made to correct for differences between the 10 Gy alanine irradiations and the 1 Gy chamber irradiations caused by a beam start-up effect. The largest was found for the 25 MV beam where the correction was 0.18% at the nominal dose rate of 3 Gy min⁻¹. An external transmission ion chamber was used as a secondary beam monitor in addition to the internal linac monitor. Measurements showed that this monitor had no effect on the NE2571 chamber reading at the 0.03% level. The difference in the doses determined using the external and internal monitor chambers was about 0.15%. This difference is probably due to the fact that the two monitors sample different areas of the x-ray beam. The mean reading from the two monitors was used to determine the delivered dose to dosimeters.

For irradiations with ⁶⁰Co, a PTW MP-3 water phantom was used. The beam was horizontal and incident on the surface of a 3 mm thick PMMA window. The distance between

	Standard uncertainties (%)			
Energy	6 MV	10 MV	25 MV	
Components of uncertainty	Type A			Type B
Monitor calibration (chamber reading)	0.07	0.09	0.03	
Repeatability (linac drift)	0.12	0.08	0.03	
Run length variation	0.07	0.15	0.10	
Polarity correction	0.03	0.03	0.03	
Recombination correction				0.05
Beam uniformity	0.02	0.02	0.02	
k_Q factors	0.20	0.20	0.20	0.32
Overall	0.25	0.28	0.23	0.32
Overall uncertainty in relative dose	0.41	0.43	0.40	

Table 2. Uncertainties in the determination of relative absorbed dose-to-water. Chamber NE2571.

the source and entrance window was 100 cm and field size was 10×10 cm at the reference depth. The dose rate at the reference depth of 5 cm was about 0.5 Gy min⁻¹, based on the NRC sealed water calorimetry, and had a standard uncertainty of 0.4% (Seuntjens *et al* 1999). However, this uncertainty does not affect the uncertainty ratio of the alanine response for x-rays to the response for ⁶⁰Co. Because the ion chamber for x-rays dose measurements was calibrated by water calorimetry, only the relative uncertainties in dose determination from x-rays to ⁶⁰Co should be counted.

The uncertainties in the determinations of relative absorbed dose-to-water for three x-ray beams, expressed as standard uncertainties (ISO 1995), are given in table 2.

For each beam quality, four dose points, 20, 30, 40, 50 Gy, were given and six pellets were irradiated at each point. The order of doses was randomly chosen to minimize possible systematic effects. The irradiation temperature was carefully controlled. The maximum change in water temperature during the irradiations was $0.25 \,^{\circ}$ C for linac irradiations and $1 \,^{\circ}$ C for ⁶⁰Co irradiations. All the irradiations on the linac and ⁶⁰Co were carried out over a span of seven days.

3.3. Experimental data processing and statistical evaluation

Nagy and Desrosiers (1996) found that rapid changes of alanine EPR intensity take place shortly after irradiation but the signal is stable after 24 h, so pellets were measured at least two days after being irradiated and the radiation produced radicals were assumed to be stable over the measurement period. Sleptchonok *et al* (2000) found that alanine pellets of the NIST recipe exhibit a very slow decay for doses less than 1 kGy, the decay being less than 3% over one year if the relative humidity is kept below 50%. Our preliminary data indicate that the EPR signal for our pellets, for doses below 100 Gy, decays less than 2% over six months under NRC room conditions. The ⁶⁰Co and x-ray irradiations were completed in seven days, so the decay correction was ignored. Dose rate has no influence on the free radical production, according to Regulla and Deffner (1982), so no correction was needed between ⁶⁰Co and linac irradiations.

For each dose point, the EPR measurements of six pellets were averaged. For the dosimeters of Gamma-Service manufacture, the standard deviation of EPR measurements for six pellets under the same irradiation and storage conditions was between 0.5-0.2% over the 10–100 Gy dose range, which yields a standard uncertainty between 0.2-0.1% (1 σ) for the mean value. For each beam quality, a calibration curve of EPR intensity versus absorbed



Figure 2. Ratios of mass energy absorption coefficients, μ_{en}/ρ , obtained from MassEn program (http://dax.northgate.utah.edu/MassEn.html) based on NIST cross sections (Hubbell and Seltzer 1995); ratios of restricted mass collision stopping powers, $dT/\rho dx$, obtained using the EXAMIN code in the EGSnrc system. The solid lines are the ratio of alanine to water and the dotted lines are the ratio of dosimeter material to water.

dose-to-water was plotted. A least squares linear regression was applied to get the Slope of the calibration curve which gives the alanine EPR response, defined as alanine EPR intensity per unit absorbed dose-to-water. The uncertainty of a Slope was determined by taking into account the uncertainties of EPR measurements (Rogers 1978), for x-ray beams, as well as the uncertainty in the dose determinations using the ion chamber. For ⁶⁰Co, the uncertainty in dose determination by water calorimetry was not considered, since the ion chamber was calibrated by water calorimetry, which means the uncertainty does not apply to the relative response, i.e., the Slope ratio for a given x-ray beam to ⁶⁰Co. For the calculation of a Slope uncertainty from the EPR measurements, equal uncertainties were assigned to give EPR data of each point an internal error, typically about 0.1–0.2% in our measurements, and all points were equally weighted. The overall uncertainty of a Slope was calculated according to error propagation (Bevington and Robinson 1992), using the root-sum-of-squares of uncertainties in the *x*-axis and the *y*-axis. In general, by this method, the uncertainty of a Slope is larger than the value of a simple least squares fit that ignores the uncertainty of the input data. The uncertainty of the Slope ratio was also evaluated by error propagation theory.

4. Monte Carlo simulations

The simulations were performed using the DOSRZnrc Monte Carlo code in the EGSnrc system (Kawrakow and Rogers 2000, Rogers *et al* 2001). We used the NIST ESTAR code (Berger *et al* 1996) to calculate the density effect corrections and PEGS4 for cross section data used in calculations with AE = 0.521 MeV, AP = 0.001 MeV. Figure 2 shows the ratios of stopping powers obtained by EXAMIN code in the EGSnrc system and the ratios of mass energy absorption coefficients obtained from the MassEn program¹ based on NIST cross sections (Hubbell and Seltzer 1995). The spectra of x-rays at the phantom surface (Blake Walters, private communications) generated by the BEAM code (Rogers *et al* 1995) are plotted in figure 3. Calculations were done with parallel beams incident on the water

¹ http://dax.northgate.utah.edu/MassEn.html.



Figure 3. Spectra of x-rays at the phantom surface from the Elekta accelerator, $10 \times 10 \text{ cm}^2$ field size and 100 cm SSD (Blake Walters, private communications) generated by BEAM code (Rogers *et al* 1995).

surface with no lateral variations in spectra. For each beam quality, absorbed dose-to-alanine in pellets in the water phantom for the experimental geometry, D_{alanine} , was calculated as well as the absorbed dose-to-water at reference depth when the pellets were replaced by water and no holder material was present, D_{water} .

To investigate the effects of the dosimeter holder, the absorbed dose-to-alanine without the presence of the PMMA holder was simulated. To investigate the effect of dosimeter volume, a simple model was used in which the flat surface of the pellets was facing the beam direction. Pellets with three different thickness, 1, 3 and 5 mm were sampled. Their centres were placed at the reference point.

5. Results and discussion

5.1. Experimental calibration curves

Figure 4 gives a typical calibration curve and the residuals of linear fit, plotted in pairs with the reference ⁶⁰Co. The Slope of each linear fit for each beam and the standard uncertainty are given in table 3. The residuals on the linear fit are about 0.1%, which confirms that the EPR reading is proportional to the dose delivered. The standard deviation of EPR measurements of six pellets was typically 0.2–0.3% with the largest being 0.45%. The spread in EPR readings among pellets could be caused by the variation of pellet shape, anisotropy of crystalline orientation and uncontrollable changes of machine conditions.

5.2. Energy dependence of alanine/EPR for x-rays and $^{60}Co \gamma$ -rays

The experimental energy dependence of alanine is shown in figure 5. We designate the nominal energy of each beam using the beam-quality specification recommended by TG-51 (Almond *et al* 1999). The response for x-rays is normalized to a ⁶⁰Co reference beam, 58.7 in terms of %dd(10)_x. The Slopes of linear fit and their uncertainties are listed in table 3. Given the uncertainties of Slope ratios listed in table 4, figure 5 indicates no trend of energy dependence for the three investigated clinical x-rays. However, the alanine response to dose-to-water for x-rays is slightly lower than unity, 0.996 ± 0.005 for 6 MV, 0.992 ± 0.006 for



Figure 4. Typical experimental calibration curves and the residuals of linear fit. The regression coefficient for both lines is 1.000. Pellets for the investigated energy were measured pairwise on the same day with those of 60 Co to avoid day-to-day differences of the EPR spectrometer. The residuals for linear fit are less than 0.1%, which confirms that the intensity of the alanine EPR signal is linear with the dose delivered.

Table 3. Slopes of linear fitting and their uncertainties as percentages for x-rays and ⁶⁰Co γ -rays. The uncertainty of a slope was calculated by taking into account the measurement uncertainty of EPR readings, for x-rays, as well as the uncertainties in the determinations of absorbed dose-to-water relative to the water calorimetry.

Beams	$(Slope)_Q$	Uncertainty (%)	(Slope) _{Co}	Uncertainty (%)
6 MV	1.882	0.43	1.889	0.15
10 MV	1.870	0.63	1.886	0.15
25 MV	1.881	0.43	1.890	0.21

10 MV and 0.995 \pm 0.005 for 25 MV with an average of 0.6% (\pm 0.5%) lower than for γ -rays. The ion chamber determination of delivered dose for x-rays carried an uncertainty of 0.4% shown in table 2, which has been taken into account. These results agree with the work of Bergstrand *et al* (2003) and Sharpe (2003). The results of Bergstrand *et al* are added in figure 5 for comparisons. Bergstrand reported a relative alanine/EPR response for x-rays to ⁶⁰Co γ -rays of 0.987 \pm 0.005, 0.994 \pm 0.005 and 0.996 \pm 0.006 for 10, 20 and 30 MV x-rays of the NRC Vickers accelerator respectively, and suggested an average of 0.8% \pm 0.5% reduction. Their experimental geometry and analysis method, obtaining the EPR response to dose-to-water by using the gradient of EPR intensity versus absorbed dose-to-water, were similar to ours. Their slightly lower result at 10 MV might be due to experimental uncertainty. Sharpe's work (2003) also indicated a 0.6% lower response for 4–12 MV x-rays than for ⁶⁰Co. They used a side-by-side geometry to irradiate the alanine and an ion chamber in a phantom plate and a fixed dose for linac beam qualities being checked back to a ⁶⁰Co beam. All the independent investigations, different in beam quality, experimental set-up and analysis method, conclude



Figure 5. Experimental results of alanine response for clinical x-rays relative to 60 Co γ -rays. The full diamonds are the results of this study. The nominal energy of beam qualities is designated by using beam quality specifier recommended by TG-51, with 60 Co, 6 MV, 10 MV and 25 MV being 58.7, 67.8, 73.0, 84.1, respectively. The data are normalized to the response at 60 Co. The solid line drawn at 0.994 on the *y*-axis indicates the average lower response of 0.6% for x-rays relative to 60 Co. For comparison, the results of the Bergstrand *et al* study for Vickers linac x-rays are shown as open triangles.

Table 4. The radiation yield obtained by equation (5) in section 2. The percentage uncertainties were determined by error propagation. It can be seen that within the uncertainty of 0.6%, G_Q/G_{Co} does not change with beam quality. This indicates that the radiation yield of free radicals in alanine is the same for ⁶⁰Co γ -rays and 6, 10, 25 MV x-rays.

]		asurement	Monte Carlo		Relative radiation yield	
Beam	$(\text{Slope})_Q/$ $(\text{Slope})_{Co}$	Uncertainty (%)	$\frac{(D_a/D_w)_Q}{(D_a/D_w)_{\rm Co}}$	Uncertainty (%)	GQ/ GCo	Uncertainty (%)
⁶⁰ Co	1.000		1.000		1.000	
6 MV	0.996	0.45	0.997	0.32	0.999	0.55
10 MV	0.992	0.65	0.995	0.30	0.997	0.72
25 MV	0.995	0.48	0.994	0.31	1.001	0.57

that alanine has no significant energy dependence for linac x-rays and a small beam quality correction, less than 1%, relative to 60 Co for most beam qualities.

5.3. Radiation yield of alanine for x-rays and $^{60}Co \gamma$ -rays

Combining Monte Carlo calculations and measurements offers a way to investigate the radiation yield of free radicals in our alanine dosimeters. Radiation yield describes the efficiency of free radical production per unit mass by absorbed dose-to-alanine. In table 4, the measured relative alanine/EPR response to dose-to-water is compared with the ratios of dose-to-alanine to dose-to-water obtained by Monte Carlo calculations. The relative radiation yield was obtained by using equation (5) in section 2. It can be seen that G_E/G_{Co} does not change with beam quality well within the 0.6% uncertainty. This indicates that the radiation yield of free radicals in alanine is the same for ⁶⁰Co γ -rays and 6, 10, 25 MV x-rays.



Figure 6. Monte Carlo simulations of the effect of dosimeter size on alanine relative response for x-rays to ⁶⁰Co γ -rays. The thickness of dosimeter varies from 1 mm to 5 mm, with the beam incident on the flat surface of the dosimeters. Within calculation statistics of 0.3%, varying the size of dosimeter has no significant effect on alanine relative response to ⁶⁰Co.

5.4. Discussion of the energy dependence of alanine/EPR

Based on the results of section 5.3 and equation (5) in section 2, we can now interpret the energy dependence of alanine EPR dosimetry by looking at the ratios of mass collision stopping powers $dT/\rho dx$ and mass energy absorption coefficients μ_{en}/ρ . For a medium-size dosimeter there is a lack of secondary electron equilibrium, which means that the energy is deposited by electrons produced in the surroundings as well as by those produced inside the dosimeter. Therefore, the stopping power of secondary electrons and the mass energy absorption coefficient of incident photons play a role in the alanine response to a beam quality. Clinical x-ray beams have relatively broad spectra, so the spectra of secondary electrons are complicated. It is difficult to give a quantitative explanation. However, a qualitative explanation of the effect of different spectra is possible. As shown in figure 2, the most probable energy of the three x-rays spans from 0.6 to 3 MV, where the variation of μ_{en}/ρ ratio of alanine to water is very small. The average secondary electron energies for 0.6–3 MV photons are roughly 200 keV to 700 keV where the stopping power ratio in that range changes by 0.7%, it may not cause observed variations in energy dependence. The small decrease of alanine response to clinical beams compared to ⁶⁰Co might be explained in the following way. The spectrum of ⁶⁰Co is narrower than the x-ray spectra. The higher energy portions of the x-ray spectra have a lower μ_{en}/ρ ratio and they produce secondary electrons with higher energies whose stopping power ratio is slightly lower.

5.5. Wall effects on alanine response

In order to see if the PMMA sleeves have an effect on the alanine dose response, Monte Carlo simulations were done for alanine pellets sitting directly in water, i.e without the PMMA sleeves. The wall effect is calculated in terms of $D_{wall}/D_{without}$. Here D_{wall} refers to the dose-to-alanine with 2 mm wall PMMA sleeves and the PMMA rod in the sleeve, while $D_{without}$ is without PMMA. For all four beam qualities, our calculations indicate no wall effect within the calculation statistical uncertainty of 0.3%.

5.6. The size of dosimeters on alanine energy dependence

Because alanine dosimeters can be supplied in a variety of forms, we simulated the effect of varying the dosimeter thickness on the energy dependence for the beams in this study using a model where the flat surface of the pellet was facing the beam direction. The results are shown in figure 6. It is concluded that varying the size of the alanine dosimeter from 1 mm to 5 mm has no significant effect on alanine relative response to ⁶⁰Co within the calculation statistics of 0.3%. This means that the results in section 5.2 may apply to other forms of dosimeters. Burlin theory states that if the μ_{en}/ρ ratio and the $dT/\rho dx$ ratio are the same for cavity material to medium, the cavity size no longer affects the dose in cavity (Attix 1986). As seen in figure 2, for alanine, $(\mu_{en}/\rho)_a/(\mu_{en}/\rho)_w$ is about 0.97 while $(dT/\rho dx)_a/(dT/\rho dx)_w$ is between 0.964–0.977. Hence, it is reasonable that the size of the alanine dosimeters has no effect on energy dependence.

6. Conclusions

We investigated the energy dependence of alanine/EPR dosimetry at NRC at a level of overall measurement uncertainty of 0.5%. It was found that alanine EPR response versus dose-towater for three clinical beams is basically flat but about 0.6% lower than that for 60 Co. The experimental data and Monte Carlo simulations were used to calculate the alanine radiation yield, alanine EPR response to dose-to-alanine, and it was shown that the radiation yield does not change within the uncertainty of 0.6% on going from ⁶⁰Co γ -rays to 6, 10, 25 MV x-rays. Monte Carlo simulations showed that the PMMA sleeves and the PMMA rod used in our study had no effect within 0.3% on the alanine response and dosimeter size had no significant impact either. Compared with published experimental studies on non-clinical highenergy x-rays, it can be concluded that alanine/EPR dosimetry has no energy dependence for linac x-rays, but that the response is slightly lower than for ⁶⁰Co beams. The small energy dependence is encouraging for applying alanine/EPR dosimetry to radiation therapy, as a dosimetry for quality assurance, or as a dosimeter to deal with problems in build-up, interface and inhomogeneous regions if thinner dosimeters are available. At NRC, investigation of alanine/EPR dosimetry for clinical therapy electron beams is underway and for future work an investigation of lower energy x-rays has been planned.

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References

Ahlers F J and Schneider C C J 1991 Alanine ESP dosimetry: an assessment of peak-to-peak evaluation Radiat. Prot. Dosi. 37 117–22

Almond P R, Biggs P J, Coursey B M, Hanson W F, Huq M S, Nath R and Rogers D W O 1999 AAPM's TG-51 protocol for clinical reference dosimetry of high-energy photon and electron beams *Med. Phys.* 26 1847–70

Attix A F 1986 Introduction to Radiological Physics and Radiation Dosimetry (New York: Wiley) Berger M L Coursey LS and Zucker M A 1996 Stopping power and range tables for electrons, prof

Berger M J, Coursey J S and Zucker M A 1996 Stopping-power and range tables for electrons, protons, and helium ions http://physics.nist.gov/PhysRefData/Star

- Bergstrand E S, Shortt K R, Ross C K and Hole E O 2003 An investigation of the photon energy dependence of the EPR alanine dosimetry system *Phys. Med. Biol.* **48** 1753–71
- Bevington P R and Robinson D K 1992 Data Reduction and Error Analysis for the Physical (New York: McGraw-Hill)
 De Angelis C, Mattacchioni A, Onori S, Aragno D, de Paula U and Panichelli V 2000 Electron arc therapy treatment planning verification with alanine/EPR dosimetry Appl. Radiat. Isot. 52 1203–7
- De Angelis C, Onori S, Petetti E and Piermattei Azario L 1999 Alanine/EPR dosimetry in Brachytherapy *Phys. Med. Biol.* **44** 1181–91
- Fainstein C, Winkler E and Saravi M 2000 ESR/alanine gamma-dosimetry in the 10–30 Gy range Appl. Radiat. Isot 52 1195–96
- Gao J and Zaiyong W 1996 The extension of the range of NIM alanine/EPR dosimetric system to therapy level Appl. Radiation. Isot. 47 1193–6
- Haskell E H, Hayers R B and Kenner G H 1997 Improved accuracy of EPR dosimetry using a constant rotation goniometer *Radiat*. *Meas*. **27** 325–9
- Hayes R B, Haskell E H, Wieser A, Roamanyukha A A, Hardy B L and Barrus J K 1999 Assessment of an alanine EPR dosimetry technique with enhanced precision and accuracy *Nucl. Instrum. Methods Phys. Res.* A 440 453–61
- Hubbell J H and Seltzer S M 1995 Tables of x-ray mass attenuation coefficients and mass energy-absorption coefficients http://physics.nist.gov/PhysRefData/XrayMassCoef/
- IAEA 2000 Absorbed dose determination in external beam radiotherapy: An international code of practice for dosimetry based on standards of absorbed dose to water *Technical Report Series No. 398 (IAEA Vienna 2000)*
- ISO: International Organisation for Standardisation 1995 *Guide to the Expression of Uncertainty in Measurement* 2nd edn (Geneva: ISO)
- Kawrakow I and Rogers D W O 2000 NRC Report PIRS-701 (Ottawa) http://www.irs.inms.nrc.ca/inms/irs/ EGSnrc/EGSnrc.html
- Klassen N V, Shortt K R, Seuntjens J and Ross C K 1999 Fricke dosimetry: the difference between G(Fe³⁺) for ⁶⁰Co γ-rays and high energy x-rays *Phys. Med. Biol.* **44** 1609–24
- Mehta K and Girzikowsky 1996 Alanine-ESR dosimetry for radiotherapy IAEA experience *Appl. Radiat. Isot.* **47** 1263–68
- Nagy V 2000 Accuracy considerations in EPR dosimetry Appl. Radiat. Isot. 52 1039-50
- Nagy V Y and Desrosiers M F 1996 Complex time dependence of the EPR signal of irradiated L-α-alanine *Appl. Radiat. Isot.* **47** 789–93
- Nagy V, Puhl J M and Desrosiers M F 2000a Advancements in accuracy of the alanine dosimetry system: II. The influence of the irradiation temperature *Radiat*. *Phys. Chem* **57** 1–9
- Nagy V, Sholom S V, Chumak V V and Desrosiers M F 2002 Uncertainty in alanine dosimetry in the therapeutic dose range *Appl. Radiat. Isot.* **56** 917–29
- Nagy V, Sleptchonok O F, Desrosiers M F, Weber R T and Heiss A H 2000b Advancements in accuracy of alanine dosimetry system: III. Usefulness of an adjacent reference sample *Radiat. Phys. Chem.* 59 429–41
- Olka P 2002 The microdosimetric one-hit detector model for calculating the response of solid state detectors *Radiat*. *Meas.* **35** 255–67
- Olsen K J, Hensen J W and Wille M 1990 Response of the alanine radiation dosimeter to high-energy photon and electron beams *Phys. Med. Biol.* **35** 43–52
- Olsson S, Bergstrand E S, Carlsson A K, Hole E O and Lund E 2002 Radiation dose measurements with alanine/ agarose gel and thin alanine films around a ¹⁹²Ir brachytherapy source, using ESP spectroscopy *Phys. Med. Biol.* 47 1333–56
- Onori S, d'Errico F, De Angelis C, Egger E, Fattibene P and Janovsky I 1997 Alanine dosimetry of proton therapy beams *Med. Phys.* **24** 447–52
- Raymond S A 1968 Electron Paramagnetic Resonance: Techniques and Applications (New York: Interscience)
- Regulla D 2000 From dating to biophysics-20 years of progress in applied ESR spectroscope *Appl. Radiat. Isot.* **52** 1023–30
- Regulla D F and Deffner U 1982 Dosimetry by ESP spectroscopy of alanine Int. J Appl. Radiat. Isot. 33 1101-14
- Rogers D W O 1978 FITTER, a fortran non-linear least squares fitting package for the PDP-11 NRC Report PXNR 2477 (Ottawa)
- Rogers D W O, Faddegon B A, Ding G X, Ma C-M, Wei J and Mackie T R 1995 BEAM: a Monte Carlo code to simulate radiotherapy treatment units *Med. Phys.* 22 503–24
- Rogers D W O, Kawrakow I, Seuntjens J P and Walters B R B 2001 NRC Report PIRS-702 (Ottawa) http://www.irs.inms.nrc.ca/inms/irs/EGSnrc/EGSnrc.html
- Ruckerbauer F, Sprunck M and Regulla D F 1996 Numerical signal treatment for optimized alanine/ESR dosimetry in the therapy-level dose range *Appl. Radiat. Isot.* **47** 1263–8

- Seuntjens J P, Ross C K, Klassen N V and Shortt K R 1999 A status report on the NRC sealed water calorimeter NRC Report PIRS-0584 (Ottawa)
- Seuntjens J P, Ross C K, Shortt K R and Rogers D W O 2000 Absorbed-dose beam quality conversion factors for cylindrical chambers in high-energy photon beams *Med. Phys.* **27** 2763–79

Sharpe P 2003 Progress report on radiation dosimetry at NPL BIPM Report CCRI(1)-03-14 (Sèvres)

- Sharpe P and Sephton J 1999 The development of a mailed reference dosimetry service at radiotherapy dose levels *Techniques for High-Dose Dosimetry in Industry, Agriculture and Medicine IAEA, Vienna* IAEA-SM-356 183–190
- Sleptchonok O F, Nagy V and Desrosiers M F 2000 Advancements in accuracy of alanine dosimetry system: I. The effects of environmental humidity *Radiat. Phys. Chem.* **57** 115–33
- Weiser A, Siegele R and Regulla D F 1989 Influence of the irradiation temperature on the free-radical response of alanine *Appl. Radiat. Isot.* **40** 957–9