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Effects of dose fractionation on the response of alanine dosimetry

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H I G H L I G H T S

- Fractioning effects signaled in electron beam using an ANOVA at 6 equal increments.
- Fractioning effects not signaled in gamma using an ANOVA up to 7 equal increments.
- Insensitivity of alanine to dose fractioning indicates nominal impact on calibration.

A R T I C L E I N F O

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Alanine dosimetry is well established as a transfer standard and is becoming more prevalently used in routine dosimetry systems for radiation processing. Many routine measurement applications in radiation processing involve absorbed dose measurements resulting from fractionated exposures to ionizing radiation. Fractioning of absorbed dose is identified as an influence quantity (ISO/ASTM, 2013). This paper reports on study results of absorbed dose fractioning characteristics of alanine for gamma and high energy electron beam radiation sources. The results of this study indicate a radiation response difference due to absorbed dose fractioning in response can be observed after four fractionations for high-energy electron beams and no difference up to seven fractions for gamma rays using an ANOVA evaluation method.

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1. Introduction

Alanine dosimetry has experienced significant growth in use in routine dosimetry systems. Routine dosimetry system use in radiation processing typically involves absorbed dose measurements of processes where exposure to ionizing radiation is fractionated. Dose fractionation is considered a dosimetry influence quantity (ISO/ASTM, 2013) and may affect the response of a dosimeter. This influence quantity was studied to determine and characterize the effect, if any, on the response of alanine dosimeters and the corresponding dose measurement. Two to three fractions are the most prevalent; two in the case of some gamma irradiators and a two-sided process in electron beam, and in some gamma irradiators can be as many as three or four fractions. In each case the fractionated exposure can represent as much as half the absorbed dose resulting from the radiation processing in the case of two fractions. Characterization of this influence quantity is critical for accurate and traceable dose measurements. Fractioning study data are presented for routine alanine systems in high

energy electron beam and gamma rays and for a transfer standard system with gamma rays.

2. Background

2.1. Experimental design

The objective of this study was to identify the effect on absorbed dose measurements resulting from irradiating alanine dosimeters in both a 10 MeV electron beam irradiator and a gamma cell irradiator in multiple increments and to compare the measured estimates of absorbed dose to the absorbed dose estimates from single irradiation events at pre-determined absorbed dose levels. Absorbed dose estimates were evaluated using a one-way ANOVA at a 95% confidence level comparing the average absorbed dose estimates. The ANOVA treatment categories represented the fractionated state of each set of samples, i.e. $1 \times$, $2 \times$, $3 \times$, etc. Each fractionated sample set consisted of four pellets providing four replicates for each set. Alanine dosimeters used both in the transfer standard system and routine system were the FWT-50 dosimeter from manufacturing batch T030901. Alanine dosimeters for the routine system were irradiated in Delrin discs and alanine dosimeters for the transfer

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standard system were irradiated in Polystyrene discs. Irradiation temperatures were measured before and after each electron-beam fractionation and used to apply a response correction to the alanine radiation response as a maximum temperature correction (Lundahl and Logar, 2012).

2.2. Transfer standard dosimetry system

The alanine transfer standard dosimetry measurements completed in conjunction with both the TT-300 Rhodotron 10 MeV electron beam source and a GC220 gamma source were conducted at NIST in Gaithersburg, MD, USA. The transfer standard dosimeter was the FWT-050 alanine dosimeter. Absorbed dose was measured with a Bruker ECS106 EPR spectrometer that was calibrated to the national standard for absorbed dose (the calibration irradiations consisted of single exposures). The NIST EPR measured response is corrected for irradiation temperature using a maximum temperature correction method (Lundahl, Logar, 2012) with a temperature coefficient of 0.11% and is normalized to dosimeter mass and an in situ ruby EPR reference standard.

2.3. Routine dosimetry system

The routine alanine dosimetry measurements completed in conjunction with a gamma irradiation source (gamma cell GC207) were conducted at a constant temperature of 24 °C. The routine dosimeter was the FWT-050 measured with a Bruker e-scan EPR spectrometer. An absorbed dose calibration curve was developed using the NIST calibration irradiation service and dosimeters irradiated to a temperature of 24 °C. The calibration curve was fitted with the following function form with fit coefficients of $a = \times 1$, $b = \times 2$, and $c = \times 3$

$$R = a - [a(e^{-(b+D)/c})] \quad (1)$$

where R is the ratio of mass corrected alanine signal to marker signal, D is certified absorbed dose from the calibration laboratory and 'a', 'b', and 'c' are fit coefficients. Irradiation temperature

correction used a maximum temperature correction method (Lundahl and Logar, 2012) and a temperature coefficient of 0.15%.

3. Method

The study method consisted of exposing sample groups to target approximately 10 kGy exposures (exposures 1 through 7). Each sample group consisted of 4 individual dosimeters. Thirteen sample groups labeled A through M were exposed to the source of ionizing radiation in accordance with the fraction schedule identified in Table 1. Sample groups A, H, I, J, K, L, and M received a single exposure while sample groups B, C, D, E, F, and G received sequentially larger fractioned exposures.

4. Results and interpretation of data

4.1. Study 1

Study 1 consisted of irradiation of the routine dosimetry system alanine in 10 MeV electron beam. Each fraction targeted an 11 kGy dose to the samples. The irradiation parameters for each exposure were:

Energy: 10 MeV.
Beam current: 2 mA.
Conveyor speed: 9.3 ft/min (2.83 m/min).
Beam scan: 1 m.

Seven irradiations were completed in accordance with the irradiation schedule identified in Table 1. The irradiation temperature was measured prior to and immediately following each irradiation fraction. Temperature correction of the alanine response used the maximum temperature increase for each sample group. The maximum temperature increase for each sample group is shown in Table 2. The doses for replicate of each sample group are shown in Table 3. The time interval between all fractions of study 1 did not exceed 10 min between irradiation events.

The dose data was normalized for the number of fractions by dividing the measured dose by the number of fractions thus providing an estimate for the incremental dose per exposure. The normalized data was analyzed using a one-way ANOVA with a null hypothesis of no difference in normalized dose estimate between treatments where each fraction sample group represented a different treatment. The single exposure sample groups (A, H, I, J, K, L, and M) were grouped as a single treatment group. Treatments were removed from the ANOVA analysis sequentially from the highest fractioned group to the lowest until the ANOVA result indicated no statistical significance. The point at which the ANOVA analysis identified confirmation of the null hypothesis was the reported threshold at which the absorbed dose response was not impacted by the fractioned exposure.

The ANOVA analysis of the study 1 data set identified no treatment difference up to five fractions. The five fraction ANOVA had an F -test value of 2.147 compared to a F -critical value

Table 1
Absorbed dose fraction schedule.

Sample group	Sequence of exposures							Number of fractions
	1st	2nd	3rd	4th	5th	6th	7th	
A	x	–	–	–	–	–	–	1
B	x	x	–	–	–	–	–	2
C	x	x	x	–	–	–	–	3
D	x	x	x	x	–	–	–	4
E	x	x	x	x	x	–	–	5
F	x	x	x	x	x	x	–	6
G	x	x	x	x	x	x	x	7
H	–	x	–	–	–	–	–	1
I	–	–	x	–	–	–	–	1
J	–	–	–	x	–	–	–	1
K	–	–	–	–	x	–	–	1
L	–	–	–	–	–	x	–	1
M	–	–	–	–	–	–	x	1

Table 2
Study 1—Maximum irradiation temperature increase.

	Sample group												
	A	B	C	D	E	F	G	H	I	J	K	L	M
Temperature (°C)	27.4	27.8	28.9	30.8	30.6	29.9	30.4	27.6	28.8	28.9	29.7	30.4	27.6

($F_{4,39,95}$) of 2.61. This represents a 1.5% difference in the fractioned normalized average dose of the 6th fraction to the average of a single exposure.

4.2. Study 2

Study 2 consisted of irradiation of the transfer standard dosimetry system alanine in 10 MeV electron beam. Each fraction targeted an 11 kGy dose to the samples. The irradiation parameters for each exposure were:

Energy: 10 MeV.
 Beam current: 2 mA.
 Conveyor speed: 9.3 ft/min.
 Beam scan: 100 cm.

Seven irradiations were completed in accordance with the irradiation schedule identified in Table 1. The irradiation temperature was measured prior to and immediately following each irradiation fraction. Temperature correction of the alanine response used the maximum temperature increase for each sample group. The maximum temperature increase for each sample group is shown in Table 4. The doses for replicate of each sample group are shown in Table 5. The time interval between all fractions of study 2 did not exceed 10 min between irradiation events.

The dose data was normalized for the number of fractions by dividing the measured dose by the number of fractions thus providing an estimate for the incremental dose per exposure. The normalized data was analyzed using a one-way ANOVA with a null hypothesis of no difference in normalized dose estimate between treatments where each fraction sample group represented a different treatment. The single exposure sample groups (A, H, I, J, K, L, and M) were grouped as a single treatment group. Treatments were removed from the ANOVA analysis sequentially from the highest fractioned group to the lowest until the ANOVA

result indicated no statistical significance. The point at the ANOVA analysis identified confirmation of the null hypothesis was the reported threshold at which the absorbed dose response was not impacted by the fractioned exposure.

The ANOVA analysis of the study 2 data set identified no treatment difference up to four fractions. The four fraction ANOVA had an F -test value of 1.81 compared to a F -critical value ($F_{3,36,95}$) of 2.87. This represents a 1.1% difference in the fractioned normalized average dose of the 5th fraction to the average of a single exposure.

4.3. Study 3

Study 3 consisted of irradiation of the transfer standard dosimetry system alanine in GC220 gamma cell. Each fraction targeted an 11 kGy dose to the samples. Seven irradiations were

Table 5
Study 2—temperature corrected sample doses.

Sample	Sample group replicates				Average	Normalized average dose
	1	2	3	4		
A	10.66	10.71	10.71	10.68	10.69	10.69
B	21.33	21.44	21.50	21.43	21.43	10.72
C	32.71	31.78	31.67	31.67	31.71	10.57
D	42.54	42.65	42.59	42.13	42.48	10.62
E	54.09	54.03	54.10	54.02	54.06	10.81
F	65.57	65.41	66.52	65.78	65.57	10.93
G	76.48	76.54	76.49	77.06	76.64	10.95
H	10.64	10.66	10.61	10.67	10.64	10.64
I	10.64	10.63	10.64	10.66	10.64	10.64
J	10.65	10.63	10.65	10.62	10.64	10.64
K	10.76	10.74	10.79	10.77	10.76	10.76
L	10.79	10.76	10.73	10.72	10.75	10.75
M	10.74	10.74	10.77	10.76	10.75	10.75

Table 6
Study 3.

Sample	Sample group replicates				Average	Normalized average dose
	1	2	3	4		
A	10.42	10.47	10.41	10.40	10.42	10.42
B	20.60	20.78	20.71	20.71	20.70	10.35
C	30.99	30.98	31.00	30.80	30.94	10.31
D	41.51	40.44	41.19	40.99	41.28	10.32
E	51.70	51.73	51.95	51.53	51.73	10.35
F	62.39	62.56	62.45	62.13	62.38	10.40
G	72.73	72.61	73.12	73.05	72.88	10.41
H	10.32	10.31	10.38	10.31	10.33	10.33
I	10.33	10.36	10.33	10.31	10.33	10.33
J	10.36	10.41	10.36	10.27	10.35	10.35
K	10.45	10.47	10.42	10.37	10.43	10.43
L	10.37	10.28	10.37	10.26	10.32	10.32
M	10.29	10.37	10.38	10.36	10.35	10.35

Table 3
Study 1—Temperature corrected sample doses.

Sample	Sample group replicates				Average	Normalized average dose
	1	2	3	4		
A	10.85	10.85	10.94	10.87	10.87	10.87
B	21.74	21.66	21.82	21.57	21.70	10.85
C	32.32	32.31	32.24	32.22	32.27	10.76
D	43.25	42.92	42.88	43.41	43.12	10.78
E	54.67	54.47	54.77	53.91	54.46	10.89
F	65.52	66.36	66.39	65.95	66.06	11.01
G	78.34	78.55	77.64	78.13	78.17	11.17
H	10.71	10.77	10.75	10.67	10.73	10.73
I	10.73	10.84	10.75	10.90	10.81	10.81
J	10.69	10.75	10.88	10.84	10.79	10.79
K	10.93	10.91	10.94	10.94	10.93	10.93
L	10.94	10.82	10.91	10.87	10.89	10.89
M	10.87	10.87	10.90	10.88	10.88	10.88

Table 4
Study 2—maximum irradiation temperature increase.

	Sample group												
	A	B	C	D	E	F	G	H	I	J	K	L	M
Temperature (°C)	27.4	27.8	28.9	30.8	30.6	29.9	30.4	27.6	28.8	28.9	29.7	30.4	27.6

completed in accordance with the irradiation schedule identified in Table 1. The irradiation temperature was measured prior to and immediately following each irradiation fraction. The temperature of each irradiation event was 24 °C, the same temperature as the dosimeter calibration, thus no corrections were made. The doses for replicate of each sample group are shown in Table 6. The time interval between all fractions of study 3 did not exceed 10 min between irradiation events.

The dose data was normalized for the number of fractions by dividing the measured dose by the number of fractions thus providing an estimate for the incremental dose per exposure. The normalized data was analyzed using a one-way ANOVA with a null hypothesis of no difference in normalized dose estimate between treatments where each fraction sample group represented a different treatment. The single exposure sample groups (A, H, I, J, K, L, and M) were grouped as a single treatment group. Treatments were removed from the ANOVA analysis sequentially from the highest fractioned group to the lowest until the ANOVA result indicated no statistical significance. The point at the ANOVA analysis identified confirmation of the null hypothesis was the reported threshold at which the absorbed dose response was not impacted by the fractioned exposure.

The ANOVA analysis of the study 3 data set identified no treatment difference up to seven fractions. The seven fraction ANOVA had an *F*-test value of 2.09 compared to a *F*-critical value (*F*,6,45,.95) of 2.32.

5. Conclusions

Within the context of the fractionation schedule of these studies; 7 fractionations of approximately equal 11.0 kGy increments:

- 1 The fractioned absorbed dose response for the alanine transfer standard and routine dosimetry systems do not appear to be impacted up to four or five fractions irradiated in a 10 MeV electron beam.
- 2 The fractioned absorbed dose response for the alanine transfer standard dosimetry system does not appear to be impacted up to seven fractions irradiated with gamma rays.
- 3 The relative fractioning insensitivity in absorbed dose response of the alanine dosimeter would appear to indicate that differences in calibration irradiation and routine use fractioning would not impact calibration of an alanine dosimetry system and the routine measurement of absorbed dose in most if not all routine radiation processes.

References

- ISO/ASTM 2013, Standard Guide for Performance Characterization of Dosimeters and Dosimetry Systems for Use in Radiation Processing.
- Lundahl, B., Logar, J., 2012. Use of maximum temperature for correction of alanine dosimetry in electron beams. *Radiat. Phys. Chem.* 81 (8), 1266–1269.