

Investigation of alanine dosimeter for output measurement in radiotherapy: Results from multicenter in Thailand

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ABSTRACT

Background: Alanine dosimeters are generally used in high-dose industrial applications (kGy). Later, research into employing alanine as a dosimeter in radiotherapy (1-20 Gy) has increased, since alanine may be an alternative transfer dosimeter for quality control, postal audit, and intercomparison between laboratories. However, several factors such as the dosimeter's characteristic should be investigated while utilizing alanine in radiotherapy. In addition, the optimal electron paramagnetic resonance (EPR) reader should be configured to match the absorbed dose range.

Objectives: This study aims to optimize the EPR setting parameters, study the characteristics of alanine dosimeters, and estimate the uncertainty of the 6MV-FFF linear accelerator in a dose ranging from 1 to 20 Gy. The output measurements from different facilities were also investigated.

Materials and methods: The alanine dosimeters were irradiated with a 6MV-FFF beam using linear accelerator, Varian TrueBeam (Varian Medical Systems, Inc, CA, USA), 100 cm SSD, with a field size of 10x10 cm² at 1 to 30 Gy. The EPR operation parameter has been optimized for these dose ranges. The characteristics of alanine dosimeters were then investigated, along with the estimation of uncertainty in using alanine. Finally, the alanine dosimeter proficiency was validated using 9 distinct linear accelerator machines.

Results: The EPR parameters were found to be optimized at 1.589 mW of MP, 7.018 G of MA, and 40.96 ms of TC. The expanded uncertainty (k=2) was reported at 2.68% in the 1-20 Gy dose range. The alanine dosimeters' characteristics were found to have good uniformity and reproducibility, low fading, and angle-and dose-independence. Although the investigation was performed in 9 different linear accelerator machines, the difference of delivered dose output was measured and reported with difference percentages within $\pm 1\%$.

Conclusion: This study reports the feasibility of using alanine dosimeters in radiotherapy. The important EPR parameter setting, and alanine dosimetry characteristics were

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investigated, whose results suggest that alanine can be used at a dose range of 1-30 Gy. This especially benefits the SRS treatment which uses a high dose per fraction, and this dosimeter can be an alternative transfer dosimeter. Nonetheless, various factors should be explored using an appropriate phantom prior to clinical application.

Introduction

Alanine is a non-polar neutral amino acid that is commonly used as a dosimeter in radiotherapy operated based on the radiation-induced free radical principle. The advantage of alanine is that it is more human tissue equivalent than other transfer dosimeters, such as the optically stimulated dosimeter (OSL) and the radio photoluminescence (RPL) glass dosimeter. Alanine also has a low fading rate in long-term storage (5 % over a year).¹ Dry storage should be considered as it affects the measurement findings. Alanine has two structural forms: α ($\text{CH}_3\text{-CH}(\text{NH}_2)\text{-COOH}$) and β ($\text{CH}_2(\text{NH}_2)\text{CH}_2\text{-COOH}$). α has higher stability than β , therefore the α form is popularly used for radiation detection. The alanine signal is recorded using electron paramagnetic resonance spectroscopy (EPR). Following irradiation, free radicals are created from amino acids (NH_2). Concentration of free radicals is proportional to the absorbed dose, which is measured by EPR. In the reading process, the microwave bridge generates and adjusts the magnetic field to supply in the cavity containing the irradiated alanine. The optimal magnetic field can be adjusted by microwave power (MP) and modulation amplitude (MA) to achieve a good sensitivity, as well as high resolution spectrum shape and amplitude, while time constant decreases noise in the system. Therefore, these three parameters are the key to approach accurate results. Although the key parameters (MA, MP, and TC) have been discovered in different samples and reported in various research,^{2,3} the origin of the key parameters should be investigated in specific situations.

Alanine dosimeters are commonly used in industrial applications, such as food irradiation and medical device sterility, with doses ranging from 10-1000 kGy.² In fact, its sensitivity decreases when used in the dose of 1-10 Gy.² The alanine and EPR technique was established by several metrology institutes as a secondary standard for absorbed dose to water in the kGy dose range.⁴⁻⁶ Previous studies (by IAEA, NPL) demonstrated the use of alanine to measure delivered dose to patients in radiotherapy (usually in the range of 1-30 Gy) compared to conventional dosimeters in end-to-end tests, such as TLD, OSL, and RP glass dosimeters. The findings indicate that the alanine dosimeter can be used efficiently in end-to-end tests. Since alanine has a good response at high doses, it is beneficial to use alanine in stereotactic radiosurgery (SRS), which is an intracranial treatment using radiation dose of 15-24 Gy.⁷ In Thailand, there is no study on the use of alanine dosimeters for end-to-end measurement.

Accordingly, this study investigated the feasibility of using alanine dosimeters in the end-to-end test for SRS. This is the pioneer in investigating the optimal key parameters in EPR for readout process (MA, MP, and TC) for

the dose range of 1-20 Gy subjected to 6 MV-FFF, followed by exploring the characteristics of alanine dosimeter which include sensitivity, linearity, energy dependence, and fading. Finally, the accuracy of delivery dose in linear accelerator using alanine dosimeter was evaluated among eight radiotherapy centers in Thailand with nine linear accelerator machines.

Material and methods

Materials

Alanine dosimeter

The Harwell alanine dosimeter batch number BY616 was used in this study. Each dosimeter was a pellet with 4.8 ± 0.1 mm diameter, 2.8 ± 0.1 mm height, and 60 ± 2 mg mass. It consists of 90.9% L-alpha-alanine and 9.1% paraffin wax as a binder. Five alanine dosimeters were packed in a plastic bag during irradiation, transportation, and kept in a dry cabinet before the readout.

Electron paramagnetic resonance (EPR) spectroscopy

EPR spectroscopy is an X-Band machine, Bruker EMXmicro, installed with a standard ER 4119HS resonator (Bruker BioSpin Corporation).

Linear accelerator machine

Delivery dose was performed using nine linear accelerator machines from eight radiotherapy centers, consisting of eight linear accelerators from Varian Medical Systems, Inc. and one from Elekta.

Solid water phantom

Solid water phantom (GAMMEX RMI, Wisconsin, USA) with a density and average atomic number of 1.03 g/cm^3 and 5.96, respectively, was used in this study. The dimension was $30 \times 30 \text{ cm}^2$, with a range of thicknesses from 0.2 to 5.0 cm.

Method

Irradiation setup

In the study of parameters optimization, the irradiation of alanine dosimeters was performed with a 6MV-FFF (Flattening filter free) beam generated by a linear accelerator, Varian TrueBeam (Varian Medical Systems, Inc, CA, USA), 100 cm source to surface distance (SSD), with a field size of $10 \times 10 \text{ cm}^2$ at 1 to 20 Gy. The 6 MV was chosen because it provides a good beam profile with less transmission penumbra than 10 MV, and FFF is a common technique to reduce irradiation time during patient treatment. Beam size $10 \times 10 \text{ cm}^2$ can ensure that all dosimeters are irradiated. Five alanine dosimeters in a plastic bag represent a set of each dose. A package was placed between 1 cm bolus thickness to reduce the air gap effect in the solid water phantom as illustrated in Figure 1.

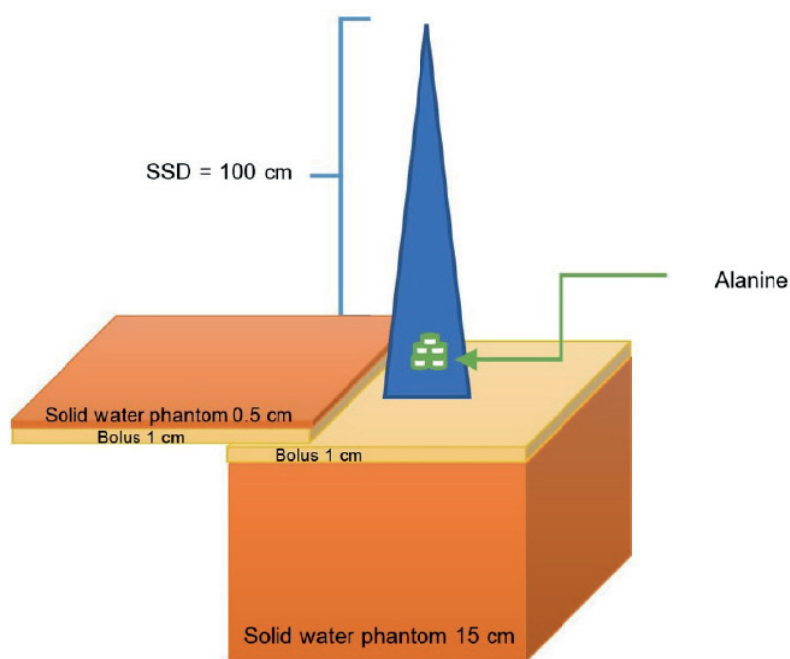


Figure 1. Alanine dosimeter irradiation setup.

For the study of alanine characteristics to test uniformity and reproducibility, 2 packs (10 dosimeters) were irradiated at the same time using the same technique as mentioned above. Whereas the alanine for fading study, 60 dosimeters were irradiated at a time. For delivery dose measurement, 3 packs of 5 dosimeters were sent to each radiotherapy center, where set A and B were irradiated at 10 Gy (same technique as mentioned above), and set C was a control set.

Optimization of EPR operation parameter

The EPR operation parameter was optimized for alanine readout at dose 1, 3, 5, 10, and 20 Gy. To achieve a clear signal, microwave power (MP) was firstly investigated, followed by modulation amplitude (MA) and

time constant (TC), respectively. The difference between maximum and minimum EPR spectrum for dose estimation was performed using the height method (peak-to-peak amplitude).⁸

Microwave power (MP)

To find MP, MA was fixed at 7.018 G following the previous study and TC was fixed at the minimum of 0.01 msec.⁹ Subsequently, MP was varied from minimum to maximum (5 to 35 dB, by increasing 1 dB in each step). The spectrum from EPR signal was observed until a clear spectrum was observed, as shown in Figure 2 (red line). At this step, the optimal MP was recorded for each dose. Eventually, the MP square of all doses against the EPR intensity graph was plotted.

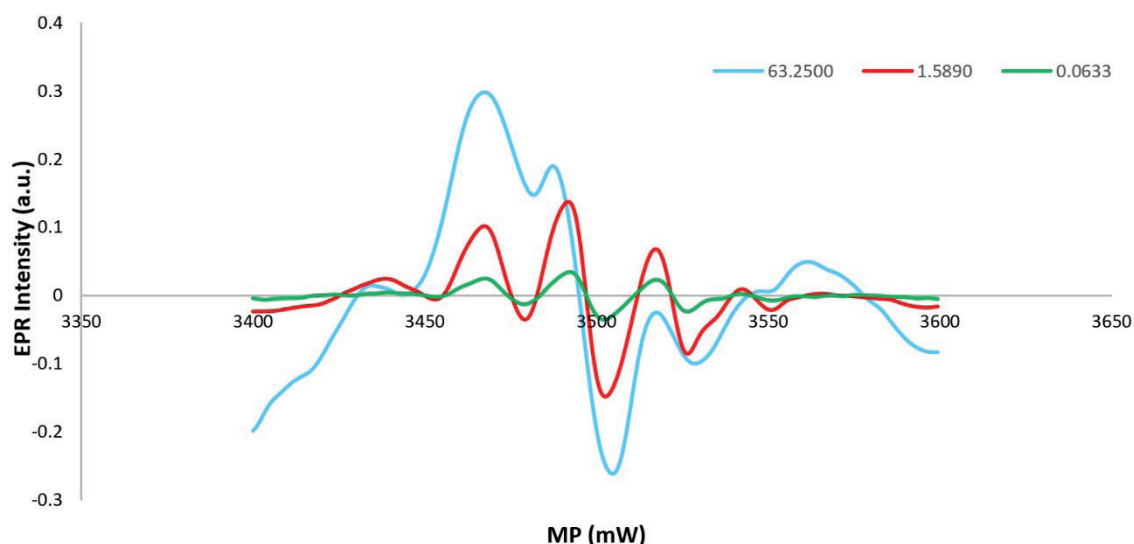


Figure 2. Spectrum from EPR signal at dose delivery of 1 Gy was set at 5 dB (0.0633 mW), 21dB (1.589 mW), and 35 dB (63.250 mW). MA and TC were fixed at 7.018 G and 0.01 ms, respectively. Clear spectrum of alanine was present in the red line.

Modulation amplitude (MA)

The optimal MP found in 2.2.1.1 for each dose was used as a fixed parameter, TC was fixed at the minimum of 0.01 msec. MA was set at 1.000, 2.000, 2.999, 4.000, 5.000, 6.006, 6.579, 7.018, 7.576, 8.032, 8.584, 9.050, 9.569, and 10.050 G (this is a fixed MA step of EPR machine which user cannot adjust). The spectrum from EPR signal was observed until a clear spectrum was observed as shown in Figure 3 (red line). At this step, the optimal MA was recorded for each dose. Eventually, the MA in units of G for all doses were plotted against the EPR intensity.

Time constant (TC)

The optimal MP and MA from 2.1.1.1 and 2.1.1.2, respectively, were used as fixed parameters to set the time constant at 0.01, 0.02, 0.04, 0.08, 0.16, 0.32, 0.64, 1.28, 2.56, 5.12, 10.24, 20.48, 40.96, 81.92, 163.84, 327.68, 655.36, 1310.72, 2521.44, and 5242.88 msec (this is a fixed TC step of EPR machine which user cannot adjust). The EPR signal was observed and peak-to-peak width (ΔB_{pp}) was measured as shown in Figure 4. Each ΔB_{pp} was normalized to ΔB_{pp} of TC 0.01 msec.

Alanine characteristics

After optimization of the EPR operation parameters possessed from the first section, this section was performed to explore the characteristics of alanine. Measurements were conducted in seven characteristics, namely uniformity, reproducibility, linearity, repetition rate, energy dependence, directional dependence, and fading. The data was employed to estimate the uncertainty of alanine.

Uniformity

EPR intensity was measured at each alanine pellet for readout. The average EPR intensity of 10 alanine pellets were used to determine the batch uniformity of all alanine dosimeters.

Reproducibility

Ten alanine pellets were read one at a time and repeated for five times each. The reproducibility was determined by the average of readout repeatability.

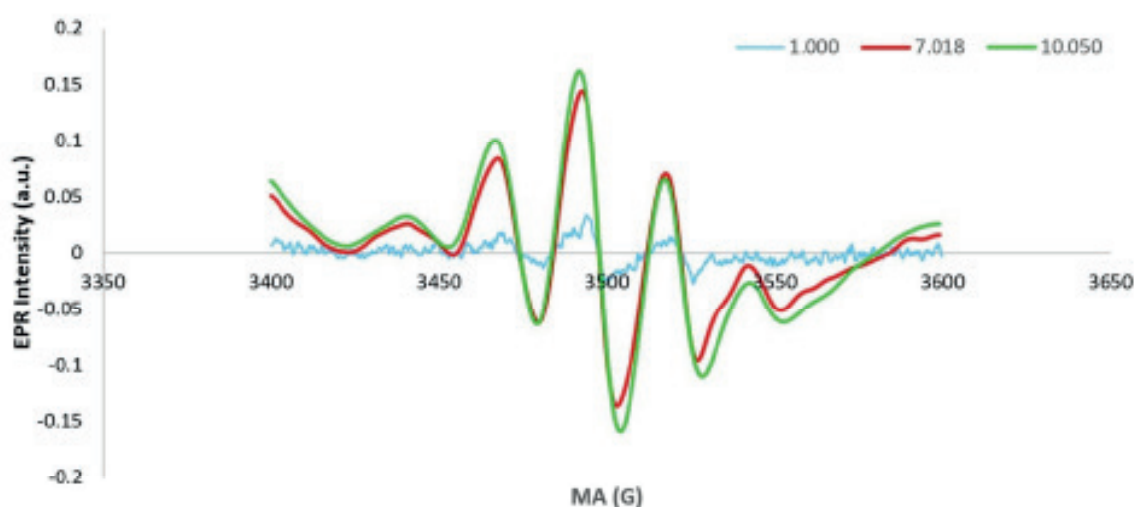


Figure 3. Spectrum from EPR signal at dose delivery of 1 Gy was set at 1.000, 7.018, and 10.050 G. Optimal MP was 1.589 mW and TC was fixed at 0.01 ms. Clear spectrum of alanine was present in the red line.

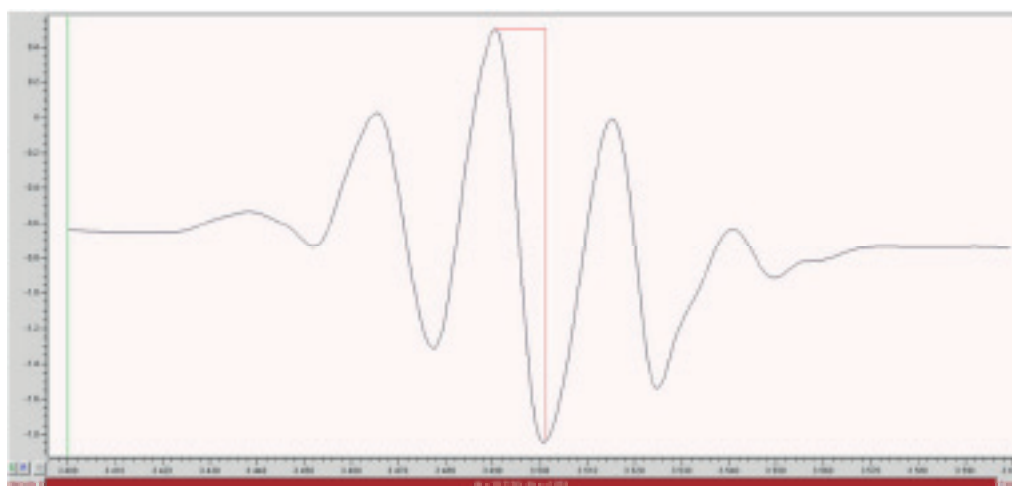


Figure 4. Measured EPR signal shown in red line for peak-to-peak width (ΔB_{pp}) at TC=40.96 ms.

Linearity

Ten alanine pellets were irradiated at 1, 2, 5, 10, 15, 20, and 30 Gy from 6MV-FFF, 100 cm SSD, with a 10x10 cm² field size at 1.5 cm depth. The calibration curve was established according to the International Code of Practice IAEA TRS-398. The readout was averaged from ten alanine for each dose.

Repetition rate

To study the response of alanine against high MU rate, five alanine pellets were irradiated with 10 Gy from 6MV-FFF, 100 cm SSD, with a 10x10 cm² field size at 1.5 cm. Repetition rates were performed at 400, 800, 1200, and 1400 MU/min. The readout of alanine pellets was averaged from EPR intensity of five alanine pellets at each repetition rate. Finally, the repetition rate in each measurement was normalized to 1400 MU/min.

Energy dependence

Five alanine pellets were irradiated with 10 Gy, 100 cm SSD, with a 10x10 cm² field size at 6 MV, 6 MV-FFF, 10 MV, and 10 MV-FFF. Readout of alanine pellets were averaged from EPR intensity of five alanine pellets in each measurement and was normalized to 6MV-FFF.

Directional dependence

Five alanine pellets were irradiated with 10 Gy, SSD 100 cm, with a 10 x 10 cm² field size at 1.5 cm depth from 6 MV-FFF for directional dependence. This was performed in two directions, perpendicular and parallel (Figure 5), where parallel measurements were normalized to perpendicular direction.

Fading

To examine the fading of alanine, 60 alanine pellets were exposed to 10 Gy from 6MV-FFF SSD 100 cm, with a field size of 10x10 cm². Five alanine pellets were separated for measurement readout for 12 consecutive weeks. The other alanine pellets were stored in the dry cabinet at room temperature. The fading determination was defined

as the response of EPR intensity to the initial EPR intensity readout. Consecutively, the uncertainty of alanine was calculated following the “Guide to the expression of uncertainty in measurement”.¹⁰

Output measurement survey

Three sets of alanine were sent to each radiotherapy center and were irradiated at 10 Gy. The delivery dose was at 10 Gy of 6 MV-FFF and the field size was 10x10 cm² at a depth of D_{max} . The alanine dosimeter was placed between 1 cm of bolus to reduce the air gap effect in the solid water phantom.

Results and discussion

Optimization of EPR operation parameter

Microwave power (MP) and Modulation amplitude (MA)

Optimal MP was obtained by plotting a graph between $MP^{1/2}$ setting and EPR intensity, as shown in Figure 6. The Intensity grows linearly as $MP^{1/2}$ increases in the beginning and has the maximum value of this linear $MP^{1/2}$ of approximately 1.26. Then, the graph shows a peak shape. The maximum value of the linear $MP^{1/2}$ of 1.26 represents the optimum MP at 1.589 mW for alanine readout of 1-20 Gy subjected to 6 MV-FFF linear accelerator. Meanwhile, the optimal MA can be determined with the same condition. Figure 7 displays the relationship of MA and EPR intensity, where EPR increases as MA is being raised. The linear trend ended at 7.018, and the optimal MA is determined at 7.018 G. Therefore, for the alanine dosimeter readout at dose of 1-20 Gy subjected to 6 MV-FFF linear accelerator, the optimal MP and MA in EPR is 1.589 mW and 7.018 G, respectively. Garcia *et al.*² and Gago-Arias *et al.*⁹ reported the optimal MP and MA parameters in the EPR setting as 1.589 mW (attenuation to 21 dB) and 7.018 G, respectively. While MA of this study coincides with the previous studies, the MP value is slightly less. This may be caused by human error when the user considers the clearest spectrum shape as previously described.

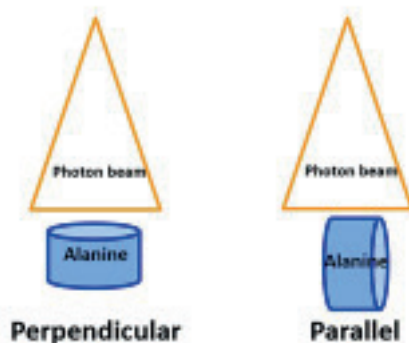


Figure 5. Measurement of alanine in two directions.

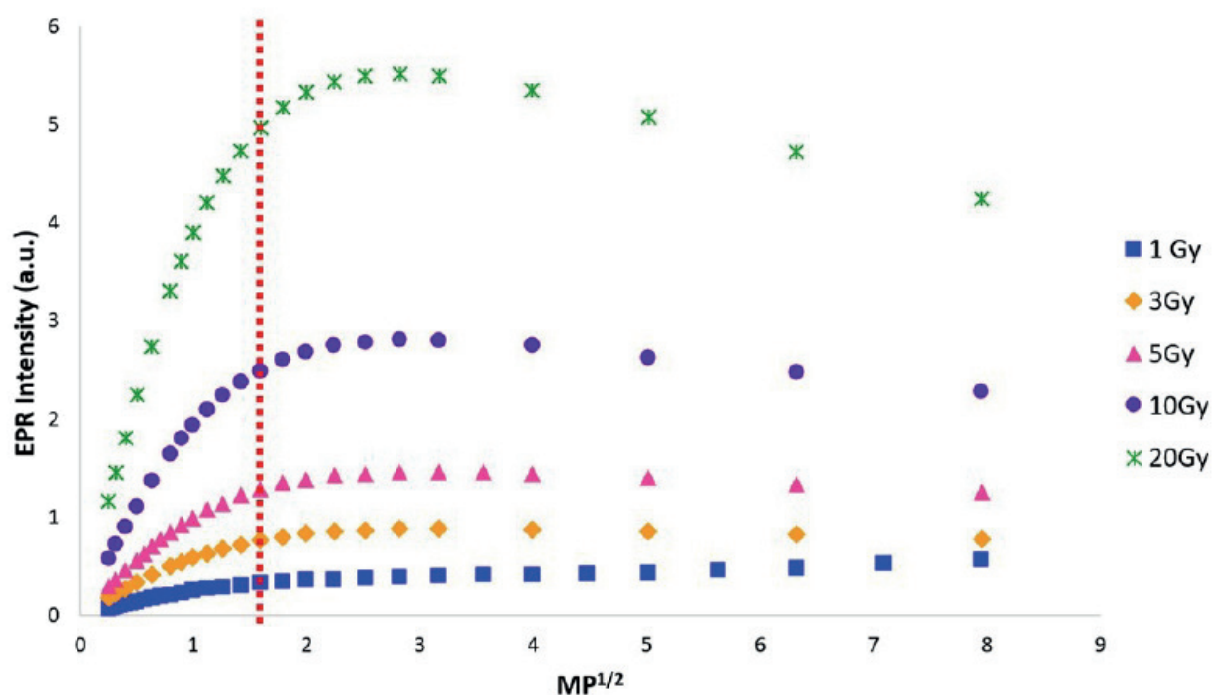


Figure 6. Relationship between $MP^{1/2}$ setting and EPR intensity. Red line represents the maximum value of the linear $MP^{1/2}$ for an alanine readout of 1-20 Gy subjected to a 6 MV-FFF linear accelerator.

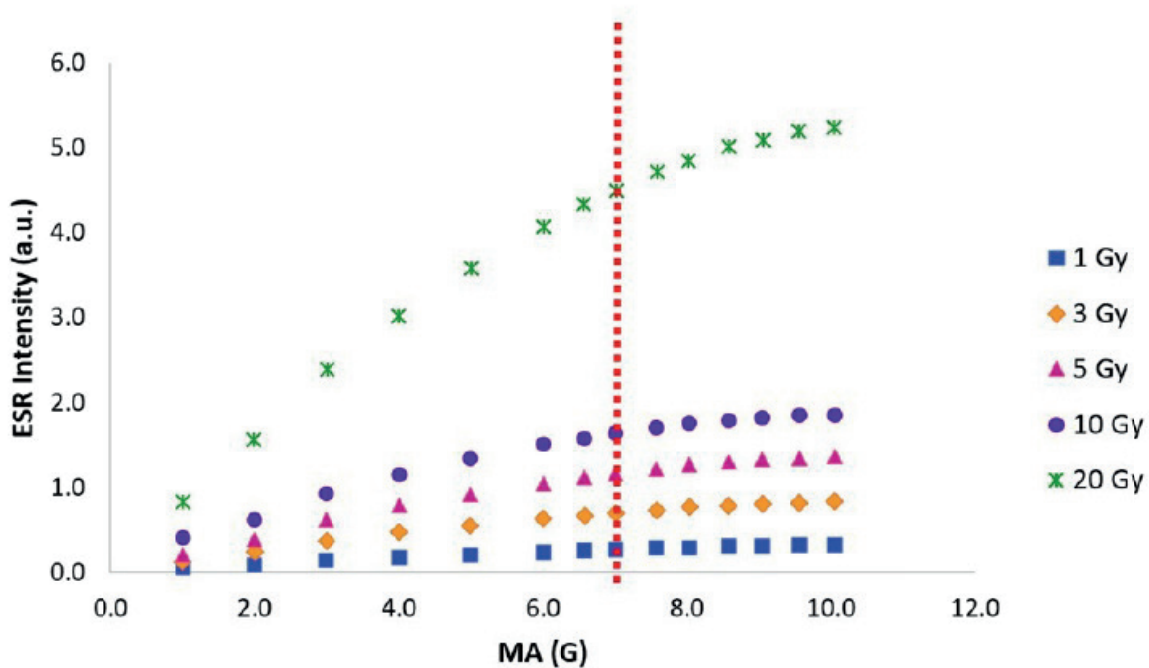


Figure 7. Relationship between MA setting and EPR intensity. Red line represents the maximum value of the linear MA for an alanine readout of 1-20 Gy subjected to a 6 MV-FFF linear accelerator.

Time constant or TC

Table 1 shows peak-to-peak width or ΔB_{pp} and relative intensity (after normalized to TC at 0.01 msec), where ΔB_{pp} represents a high intensity of signal and relative intensity shows the resolution. Both values are not significantly different with varying TC from 0.01 to 5342.88 msec. To achieve both high intensity and better resolution, the optimal TC was determined at 40.96 msec.

Uniformity and reproducibility of alanine dosimeter

Uniformity of the alanine dosimeter was explored in 10 alanine dosimeters as shown in Figure 8. The uniformity of alanine was considered by the standard deviation over 10 dosimeters and reports as $\pm 0.22\%$. This confirms that the alanine dosimeter has a good uniformity within the same batch.

Table 1 Time constant on resolution and intensity of the spectra for 1-20 Gy.

Time constant (ms)	ΔB_{pp} (G)*	Relative intensity
0.01	10.014	1.000
0.02	10.049	0.998
0.04	10.049	1.002
0.08	10.049	0.997
0.16	10.049	1.000
0.32	10.049	1.003
0.64	10.049	0.999
1.28	10.154	1.001
2.56	10.183	1.001
5.12	10.049	0.996
10.24	10.049	0.998
20.48	10.049	0.999
40.96	10.719	0.996
81.92	10.173	0.998
163.84	10.052	0.988
327.68	10.479	0.974
655.36	11.388	0.908
1310.72	12.460	0.740
2521.44	13.815	0.558
5242.88	16.144	0.574

Note: ΔB_{pp} (G)*: the peak-to-peak width

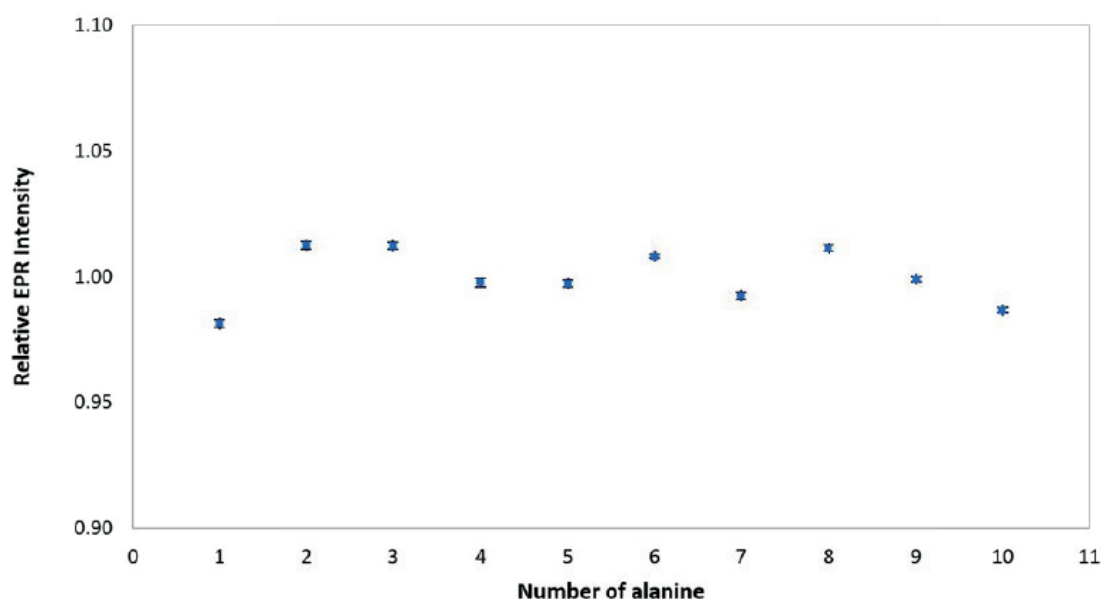


Figure 8. Uniformity of 10 alanine for 6MV-FFF. The readout of alanine dosimeters was normalized to the average of 10 alanine dosimeters. Error bars show the standard deviation for 5 times.

Linearity

Figure 9 shows the dose response of alanine dosimeter with overdose of 1-30 Gy. The graph shows a linear response with $R^2=0.9998$. The result agrees with a study by Mansour (2018)¹¹ and Garcia *et al.*² This contributes to the feasibility of using alanine dosimeters in radiotherapy dose range (1-30 Gy).

Repetition rate

The response of alanine dosimeter subjected to a varying repetition rate delivered by linear accelerator was investigated. The result is shown in Table 2 using the relative response by normalizing all repetition rates to 1400 MU/min. The deviation of repetition rate over 400 to

1400 MU/min is 0.80%, this means that the high repetition rate did not affect the readout of the alanine dosimeter. Monitor unit (MU) is a measure of machine output from a clinical linear accelerator.

Energy dependence

Energy dependence of alanine dosimeter was investigated in 6 and 10 MV with and without flattening filter. Table 3 shows the relative result of beam energy with different filters, $TPR_{20,10}$ is the IAEA TRS-398 photon beam quality index for megavoltage clinical photons produced by linear accelerator and relative response to 6 MV-FFF. The maximum difference of relative response to 6MV-FFF was 0.80%, indicating that the dosimeter is energy independent.

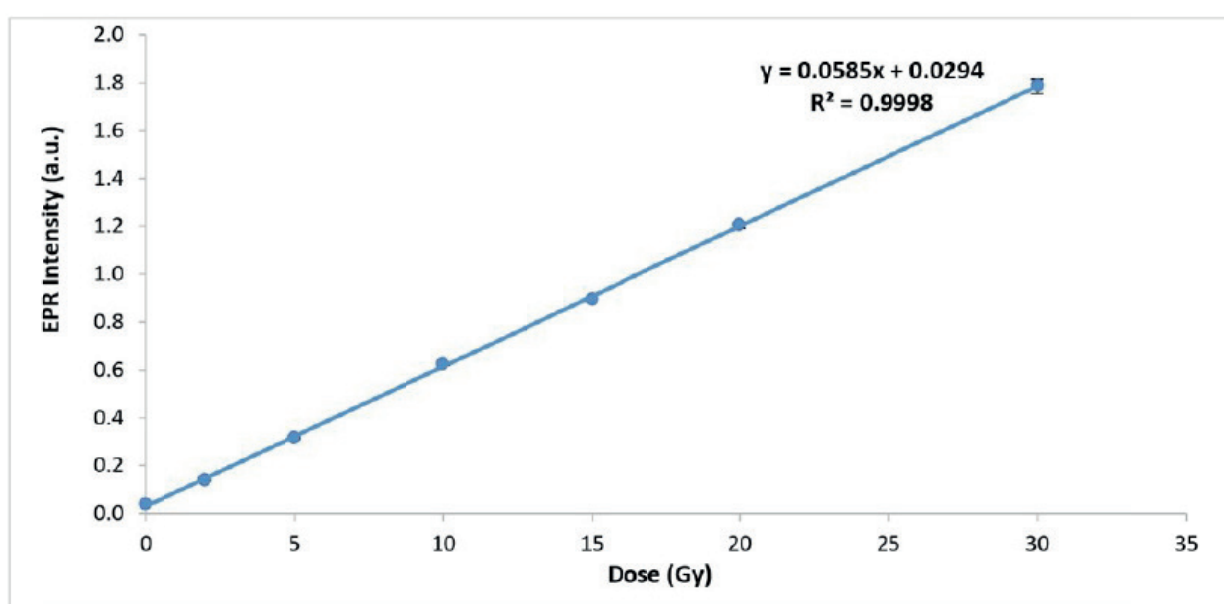


Figure 9. Linearity response of alanine dosimeter.

Table 2 Repetition rate of the alanine dosimeter was normalized to 1400 MU/min.

Repetition rate (MU/min)	Relative response to 1400 MU/min
400	1.008
800	0.999
1200	0.998

Table 3 Energy dependence of the alanine dosimeter from varied photon beams was normalized to 6 MV-FFF.

Photon beam	$TPR_{20,10}$	Relative response to 6 MV-FFF
6 MV-FFF	0.63	1.000
6 MV	0.67	1.005
10 MV-FFF	0.71	0.997
10 MV	0.74	0.992

Directional dependence

The directional dependence of alanine dosimeter was tested in two directions, perpendicular and parallel to the beam axis. The result after normalization to the perpendicular side shows that the difference is only 0.03% (Table 4). This confirms that the irradiation angular did not affect the alanine dosimeter.

Fading

The fading effect was examined for 12 consecutive weeks. As shown in Figure 10, the relative response to the first readout varies from 0.983 to 1.003. This fading over three months was 0.98% which agrees with Zeng *et al.*¹ This benefits in readout of alanine with low fading

after long term storage. This study did not apply fading correction factors, the readout process was within two weeks after irradiation.

Uncertainty of alanine dosimeter

The uncertainty of alanine dosimeter is presented in Table 5. The list of uncertainty sources comes from the alanine characteristics in this study, mechanical of Varian TrueBeam, and the mass of alanine (from manufacturer). Overall, the expanded uncertainty was 2.68% at 95% confidence interval. The uncertainty from previous studies by Mansour¹¹ reported at 1.52% for 10 Gy, and Garcia *et al.*² reported at 4.9% for 2 Gy and 1.4% for 10 Gy.

Table 4 Directional dependence of the alanine dosimeter in two directions.

Directional	Normalization
Perpendicular	1.000
Parallel	0.997

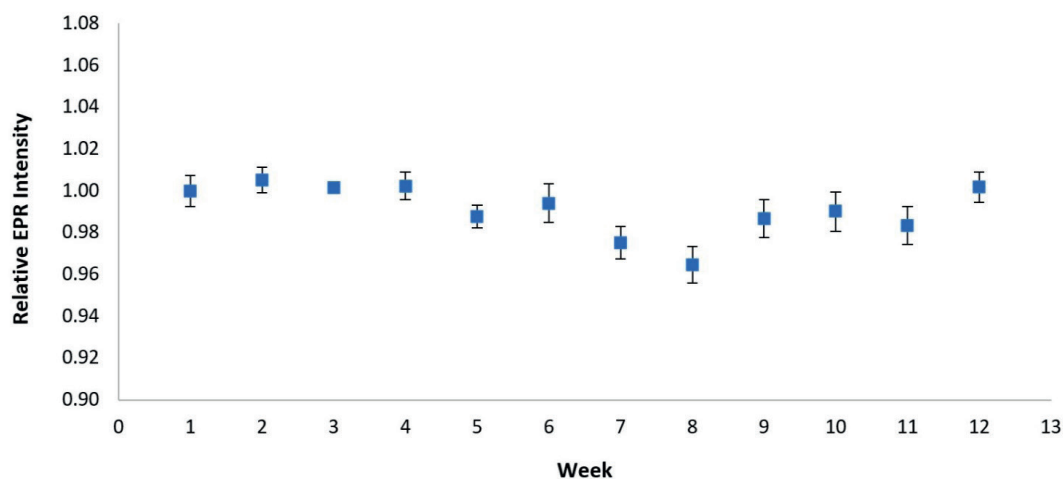


Figure 10. Fading of alanine dosimeter over 12 weeks. Error bars represent standard deviation of relative response from 5 alanine dosimeters.

Table 5 Uncertainty of alanine following “Guide to the expression of uncertainty in measurement”¹¹

Source of uncertainty	Type	U (%)
Uniformity	A	0.3671
Reproducibility	A	0.0315
Linearity	A	0.4469
Energy response	A	0.1933
Repetition rate	A	0.1890
Fading	A	0.0958
Directional	A	0.3619
Alanine mass	B	0.0144
Mechanical of machine	B	0.5000
Calibration factor ($N_{D,w}$)	B	1.0000
Correction for irradiation Temperature	B	0.0004
Combined uncertainty (Uc)		1.3414
Coverage factor (k)		2.0
Expanded uncertainty		2.68

Output measurement survey

All radiotherapy centers participating in this study regularly calibrate their routine dosimeters and validate the dose output. All results can be traced to the SI unit with reliable uncertainty. This ensures that the delivered dose from the linear accelerator machines is accurate. Figure 11 shows the output measurement of 6MV-FFF using alanine dosimeters from nine different linear accelerator machines at a dose of 10 Gy. The difference of output is within $\pm 1.0\%$. This contributes to feasibility of using the alanine dosimeter in quality audit programs and intercomparison between laboratories.

Conclusion

This study determined the optimal EPR operation key parameters for alanine dosimeter readout subjected to 6 MV in dose of 1-20 Gy usually applied in radiotherapy. Both key parameters (MA and TC) agree with the previous reports, only MP is slightly different which may be due to human error. These parameters could be applied in future studies for the use of alanine dosimeters in radiotherapy. Additionally, characteristics of the alanine dosimeter have been investigated. The result showed that

this dosimeter can be an alternative transfer dosimeter in quality control, postal audit, and intercomparison. The dosimeter has shown a good radiation response in dose of 1-20 Gy, which is largely lower than its usual application (kGy), good uniformity, linearity response, angle and energy independence, low fading, and the uncertainty of measurement is reported at 2.68%. The dose output comparison between nine linear accelerator machines (from 8 radiotherapy centers) revealed that the different result measured by alanine dosimeter is within $\pm 1.0\%$. These results contribute to the feasibility of using alanine dosimeters in radiotherapy, especially in SRS (15-30 Gy). However, further study in SRS with an appropriate phantom should be accompanied with alanine to verify the potential of this dosimeter prior to clinical applications.

Conflicting interests

The authors declare no conflict of interest.

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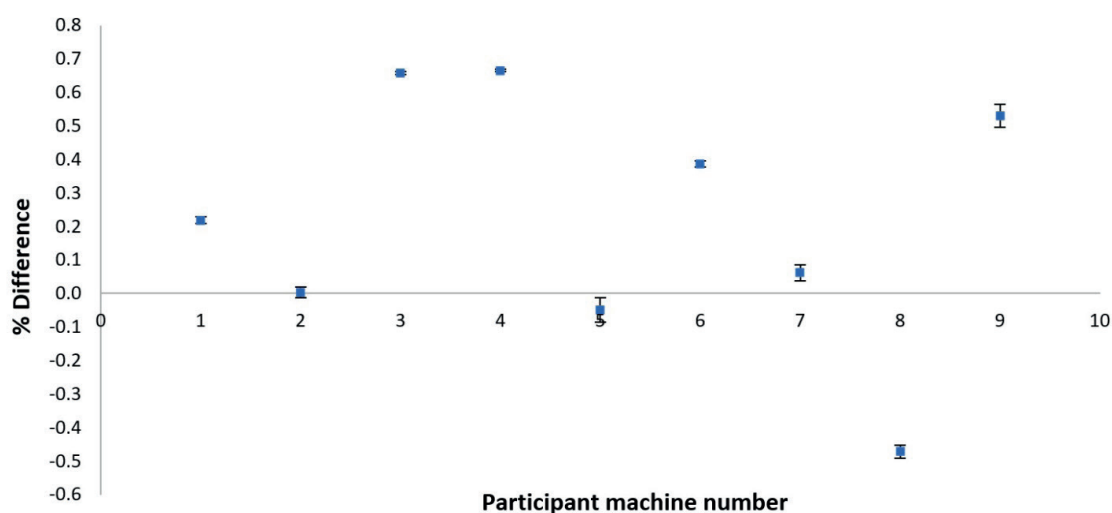


Figure 11. Percent difference of output survey in each participant.

References

- [1] Zeng GG, McEwen MR, Rogers DW, Klassen NV. An experimental and Monte Carlo investigation of the energy dependence of alanine/EPR dosimetry: I. Clinical x-ray beams. *Phys Med Biol*. 2004; 49(2): 257-70.
- [2] Garcia T, Lin M, Pasqu   I, Louren  o V. A methodology for choosing parameters for ESR readout of alanine dosimeters for radiotherapy. *Radiat Phys Chem*. 2009; 78(9): 782-90.
- [3] Goodman BA, Worasith N, Ninlaphruk S, Mungpayaban H, Deng W. Radiation Dosimetry Using Alanine and Electron Paramagnetic Resonance (EPR) Spectroscopy: A New Look at an Old Topic. *Appl Magn Reson*. 2017; 48(2): 155-73.
- [4] Regulla D and Deffner U. Dosimetry by ESR spectroscopy of alanine. *Int J Appl Radiat Isot*. 1982; 33(11): 1101-14.
- [5] McLaughlin WL and Desrosiers MF. Dosimetry systems for radiation processing. *Radiat Phys Chem*. 1995; 46(4, Part 2): 1163-74.
- [6] Sharpe PHG, Rajendran K, Sephton JP. Progress towards an alanine/ESR therapy level reference dosimetry service at NPL. *Appl Radiat Isot*. 1996; 47(11): 1171-5.
- [7] Buatti JM, Friedman WA, Meeks SL, Bova FJ. RTOG 90-05: the real conclusion. *Int J Radiat Oncol Biol Phys*. 2000; 47(2): 269-71.
- [8] Sharpe PHG, Sephton JP. Alanine dosimetry at NPL - the development of a mailed reference dosimetry service at radiotherapy dose levels. International Atomic Energy Agency (IAEA); 1999. Report No.: 1011-4289 Contract No.: IAEA-TECDOC--1070.

- [9] Gago-Arias A, González-Castaño DM, Gómez F, Peteiro E, Lodeiro C, Pardo-Montero J. Development of an alanine dosimetry system for radiation dose measurements in the radiotherapy range. J Instrum. 2015; 10(08): T08004-T.
- [10] JCGM member organizations. Evaluation of measurement data - Guide to the expression of uncertainty in measurement. JCGM guidance document. JCGM 100: 2008.
- [11] Mansour I. Development of mailed dosimetric audit for external beam radiation therapy using alanine dosimeters [dissertation]. Canada: Carleton University; 2018.