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The measurement of radiation doses in brachytherapy using an alanine dosimeter

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ABSTRACT

Background: Brachytherapy involves the use of high radiation doses to treat cancer patients, making it essential to have appropriate dosimeter properties to confirm the accuracy and precision of the dose delivered to the patient.

Objectives: This study was to investigate the relationship between radiation dose and electron spin resonance (ESR) signal and to evaluate the optimal conditions for the ESR technique. Additionally, the radiation dose from brachytherapy was measured in a solid phantom using alanine in combination with the ESR technique.

Materials and methods: The alanine dosimeter (FWT-50-10, Steris, USA), ionization chamber (TW30013, PTW Freiburge, Germany), and transferring tube were positioned inside the solid phantom (Krieger, T9193, PTW Freiburge, Germany), with the BEBIG Co-60 source located at the center of the phantom. Dwell times were calculated to obtain a radiation dose range of 0.06-1.5 Gy. Following irradiation, the alanine derivative was measured using an ESR spectrometer, and a graph was generated to determine the relationship between radiation dose and ESR signal. The uncertainty and fading of the ESR signal were also evaluated.

Results: The results indicate that there is a linear relationship (R^2 = 0.877) between the radiation dose range of 0.49-1.5 Gy and ESR signal, with a microwave power of 1.5 milliwatt. The uncertainty of the ESR signal was found to be in the range of 0.12% - 3.79%. Signal fading was observed to be in the range of 7.2% - 27.4% over a period of two weeks.

Conclusion: Alanine and ESR technique can be used to measure absorbed dose in brachytherapy. The dose response of alanine was linear for radiation doses above 0.49 Gy. The advantages of alanine dosimetry are that alanine is tissue equivalent, nondestructive, small in size, and has low signal uncertainty.

Introduction

Brachytherapy is a cancer treatment that involves the insertion of a radioactive source enclosed in a catheter into or near a tumor. This treatment is suitable for well-circumscribed cancers, such as cervix, prostate, and breast cancer. The most common radioactive sources used in brachytherapy are Iridium-192 (energy 0.38 MeV), Cobalt-60 (energy 1.25 MeV), and Cesium-137 (energy 0.66 MeV). The beta and gamma radiations emitted from these sources have higher energy than diagnostic X-rays. The effectiveness of radiotherapy lies in delivering high-energy radiation to the tumor while minimizing damage to normal tissue. High-dose and high-energy radiation can increase the likelihood of destroying and controlling

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cancer cells, whereas an insufficient dose may reduce treatment efficacy. Therefore, it is important to ensure the accuracy and precision of the radiation doses delivered to the patient using reliable dosimeters capable of measuring and responding to the range of radiation doses delivered during therapy. The International Commission on Radiological Units and Measurements (ICRU) and the World Health Organization (WHO) have established that an acceptable difference between the calculated dose and the actual dose delivered to a patient is equal to or less than 5%.[1,2]

The alanine/electron spin resonance (ESR) technique is widely used in radiotherapy applications. The advantages of the alanine dosimeter are that it is small and easy to place on the patient's skin, as it is tissue equivalent. The interaction with ionizing radiation produces free radicals proportional to the absorbed dose, and the ESR signal is linearly responsive to the radiation dose. Furthermore, it is energy-independent at energies above 100 keV and is non-destructive after reading or recording the spectrum, making it possible to re-read with low signal fading.[3] However, its limitations include a limited radiation dose response above 1 Gy, sensitivity to temperature and humidity, and an expensive ESR spectrometer requirement.[3,4] Additionally, the ESR technique requires optimal configuration parameters such as microwave power, amplitude, time constant, number of scans, and sweep time.[5] Alanine dosimeters have been used to determine the dose in clinical radiotherapy[4,6,7] and quality assurance.[3,8] Using alanine to measure radiation in the range of 0.6 - 0.8 Gy showed an error of 3%, while thermoluminescent dosimeters (TLDs) have an error of 5%. Other reports found an uncertainty of 1.5 - 3.5% for measuring the dose range of 2-5 Gy.[9]

The aim of this study was to measure the radiation dose of a cobalt-60 brachytherapy machine in a solid phantom using an alanine dosimeter in combination with the electron spin resonance (ESR) technique. Additionally, this work aimed to investigate the relationship between radiation dose and ESR signal and to evaluate the optimal conditions for ESR technique.

Materials and methods

The dwell position accuracy was verified daily as part of quality control, with a tolerance set to within ±1 mm. The position of the dwell was selected at the location where the charge is maximum. A 0.6 cm^3 farmer-type ionization chamber connected to an electrometer was positioned at 0° of a solid phantom to measure the charges. The catheter connected to the Co-60 brachytherapy machine was placed at the center of the solid phantom, and the BEBIG Co-60 source (BEBIG HDR, Germany) was transferred into the catheter. The dwell positions were set at three distances of 0.25 cm, 0.50 cm, and 0.75 cm. The dwell time was set to 70s for each distance. The charges were recorded in nanocoulomb (nC) with an interval time measurement of the 70s. The distance that gives the most charge will be designated as a dwell position for irradiation in the next experiment.

The ionization chamber and an electrometer were calibrated by the Department of Medical Sciences, Thailand Ministry of Public Health. Temperature and humidity were recorded during the measurements. The ionization probe and electrometer certificate data indicate that the reference temperature is 20 °C, the reference air pressure is 1013.25 hPa, and the calibration factor is 54.22 mGy/nC. Other correction factors used in the calculation were based on the research of Azhari H. *et al.*, including air density=1.014, polarity=1.000, saturation=1.000, phantom calibration factor=1.274, K_Q=1.000, K_A=1.027, g_w=0.0028, and $t\frac{en}{w/a}$=0.900.[10] The reference air kerma rate (K_R) was calculated as shown in equation 1, and then the radiation doses (K_R) and dwell time of 22s were calculated to obtain a dose in the range of 0.06-1.5 Gy.[11]

$$k_R\left(\frac{mGy}{h}\right) = \left(\frac{1}{1-g_w}\right) \times \frac{1}{t\frac{en}{w/a}} \times K_{wp} \times K_{zp} \times K_A \times K_p \times k_s \times k_r \times K_Q \times N_w\left(\frac{mGy}{nc}\right) \times M(nC) \quad ....(1)$$

where

g_w: Fraction of energy of the electrons from the source decay liberated by photons in water that is lost to radiative processes (mostly bremsstrahlung) = 0.0028.

$t\frac{en}{w/a}$: Ratio water/air of the mean mass-energy absorption coefficients for Co-60 = 0.900.

K_{wp}: Correction factor accounting for the differences in scatter and distortion of the radiation field between water and PMMA =1.000.

K_{zp}: Correction factor accounting for the differences in scatter and absorption in the PMMA phantom surrounding the measuring probe in comparison to free-in-air condition = 1.276

K_r: Air density correction for differing temperature and air pressure from reference conditions = 1.014

K_A: Correction factor for attenuation and scatter by the applicator = 1.027

K_p: Correction factor for the polarization effect of the ionization chamber =1.000

k_s: Correction factor for recombination losses in the ionization chamber = 1.000

K_Q: Correction factor for the different response of the ionization chamber at the measured radiation quality in comparison to the calibration quality Co-60 = 1.000

N_W: Calibration factor of ionization chamber in terms of absorbed dose to water = 54.22 mGy/nC

M: Reading in nC

Measurement using solid phantom

A solid cylindrical phantom was attached on a tripod at a distance at least 1 m away from the floor and wall in order to avoid scattered radiation. Solid cylindrical phantom has a tissue equivalent. The atomic number H:O ratio is 2:1, density is 0.998 g/cm^3, 20 cm in diameter, 12 cm in height. There is one hole in the middle and 4 around the perimeter at 0°, 90°, 180° and 270°, each hole is 8 cm from the middle hole. The end of the catheter was connected with the high dose rate brachytherapy machine (Multisource, Multi-source HDR), and the other end was inserted at the center hole of the phantom. The 0.6 cm^3 farmer-type ionization chamber with an electrometer was inserted into the 0° hole, and the electrometer was set at a voltage of 300 volts. The irradiation setup was placed in the room for at least one hour to allow the gas in the ionization chamber to reach the same temperature and humidity conditions. The initial temperature and humidity were recorded, and two alanine pellets with a diameter of 0.3 cm from Far West Technology (FWT-50-10, Steris, USA) were inserted into the 180° hole, as shown in Figure 1. The BEBIG cobalt-60 source was then moved through and stopped at the predetermined dwell time was set.

The irradiation was performed with a dwell time specified in the treatment plan to achieve a dose of 0.06 Gy. The charge from the electrometer was recorded, and two irradiated alanine pellets were then stored in a plastic bag to prevent contamination from humidity. The experiment was repeated with two un-irradiated alanine pellets placed in the phantom. The dwell time was adjusted to obtain a dose range of 0.06-1.50 Gy. The ESR signal of the irradiated alanine was then determined using an ESR spectrometer.

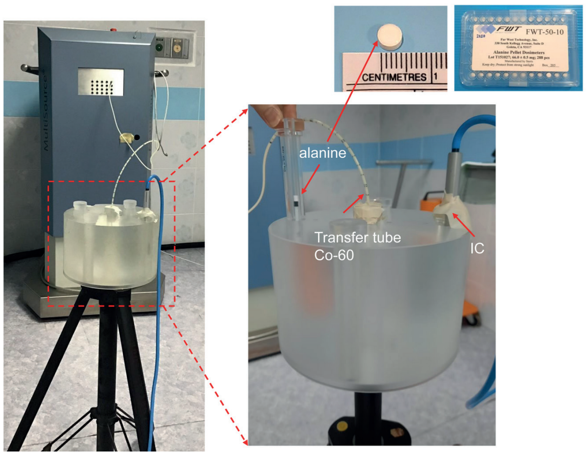

Figure 1 *The irradiation setup using a farmer-type ionization chamber and alanine in the solid cylindrical phantom.*

Electron spin resonance dosimetry with alanine

The ESR signal of alanine was determined using a Bruker A300 ESR spectrometer with a microwave frequency of 9-10 GHz. The alanine was inserted into a sample tube and placed in the center of the ESR spectrometer, also known as the 'resonator', which amplifies the ESR signal of the sample. The ESR signal intensity depends on the positioning of the sample tube within a uniform sensitivity of 1-2 mm from the center. The sample tube was immobilized using a device that does not interfere with the magnetic field and allows for measurements to be taken in the same position (see Figure 2).

The parameters of the ESR spectrometer were adjusted to achieve a high signal-to-noise ratio (SNR) and minimize uncertainties that can occur during ESR signal measurements.[5,9] This was necessary because microwave power can affect the shape of the ESR spectrum, signal intensity, and amplitude. The microwave power modulation was started as low as 0.5 milliwatts (mW) and gradually increased with fine-tuning to achieve a stable ESR signal intensity and avoid saturation effects, which was beneficial for obtaining accurate ESR signals. The parameters of the ESR signals are shown in Table 1. The ESR signal was then recorded under room temperature conditions. The ESR spectrum represents the number of free radicals occurring after alanine was irradiated. The ESR signal curve is expressed as the first derivative of the absorption spectra as a function of the magnetic field. The ESR signals were measured for each dose range, and the relationship between the radiation doses and ESR signals was analyzed.

Results

The results demonstrated that the highest charge reading of 451 pC was obtained at 0.75 cm from the catheter tip. Thus, this distance was selected as the dwell position for alanine irradiation. The corresponding dwell time, charge (nC), and radiation doses are presented in Table 2.

The ESR spectrum and magnetic field intensity were analyzed to determine the relationship between ESR signal intensity and the irradiated dose of alanine. Data analysis showed that the ESR signal had varying signal intensities in each dose range, and alanine had a linear response to radiation doses with the equation $y = 0.0479x+0.0515$. The correlation coefficient (r^2) was 0.8607 (figure 3). The uncertainty of ESR signals from 0.06-1.5 Gy was 0.1231%-3.7870% (Table 2). The signal fading experiment demonstrated that after 2 weeks, the ESR signal reduced by 7.2%-27.4%.

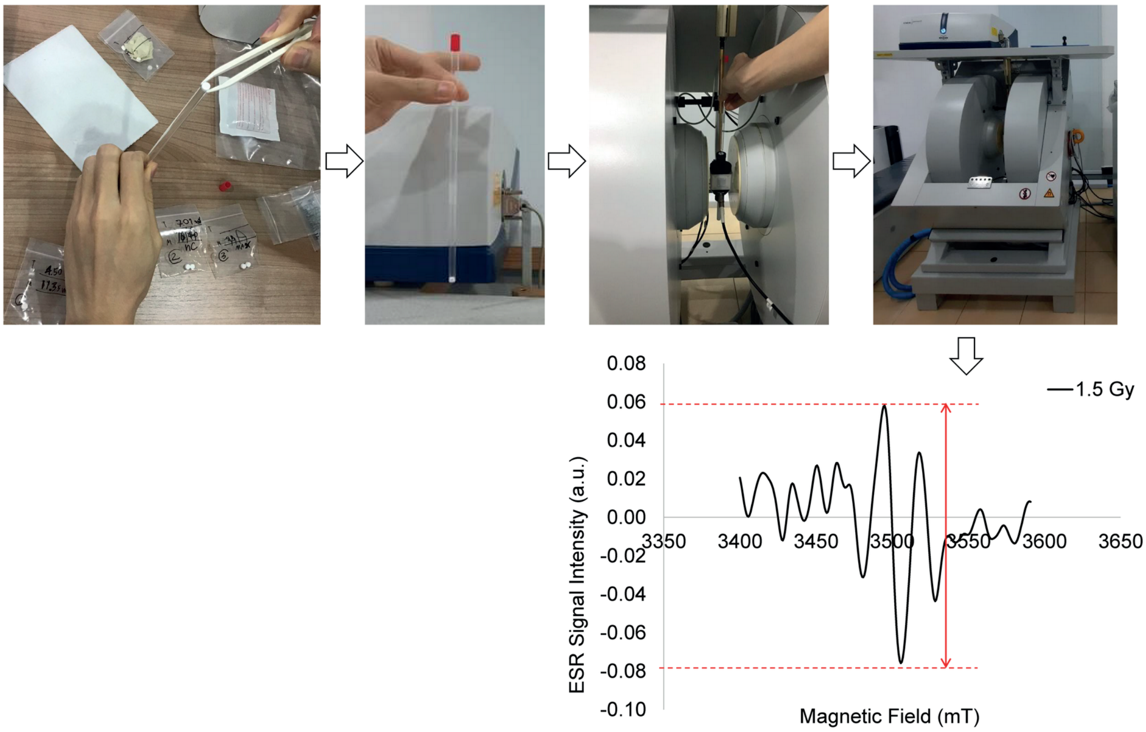

Figure 2 *Illustration of alanine was placed in a sample tube and inserted into the ESR spectrometer. The ESR spectrometer generated a magnetic field and applied microwave power, resulting in a characteristic ESR spectrum of alanine. The signal intensity is quantified by measuring the peak-to-peak height of the spectrum. In the example, the ESR spectrum of irradiated alanine with a 1.5 Gy dose was obtained. The peak-to-peak height was measured, providing ESR signal intensity.*

Table 1 Parameter of ESR spectrometer.

Parameter	Value	Unit
Microwave power	0.5 - 2.5	mW
Modulation amplitude	0.70	mT
Center field	350	mT
Sweep width	2.00	mT
Microwave frequency	9.87	GHz
Time constant	NA	ms
Sweep time	20.02	s
Number of scans	3	time

Table 2 Calculated radiation dose, mean, and uncertainty of ESR signal intensity.

Calculated dwell time (s)	Electrometer reading (nC)	Calculated radiation dose (Gy)	ESR signal Intensity (a.u.)	Standard deviation (SD)	%Uncertainty (%)
113	0.8700	0.0600	0.0692	0.0033	0.3313
226	1.7270	0.1200	0.0571	0.0016	0.1595
339	2.5800	0.1800	0.0625	0.0033	0.3342
452	3.4660	0.2400	0.0580	0.0036	0.3575
564	4.3130	0.3000	0.0604	0.0012	0.1231
677	5.0790	0.3600	0.0625	0.0028	0.2830
790	6.0230	0.4200	0.0749	0.0025	0.2514
903	6.9250	0.4900	0.0707	0.0024	0.2369
1016	7.7600	0.5400	0.0815	0.0019	0.1907
1887	14.6300	1.0000	0.0855	0.0036	0.3583
2831	21.5000	1.5000	0.1342	0.0379	3.7870

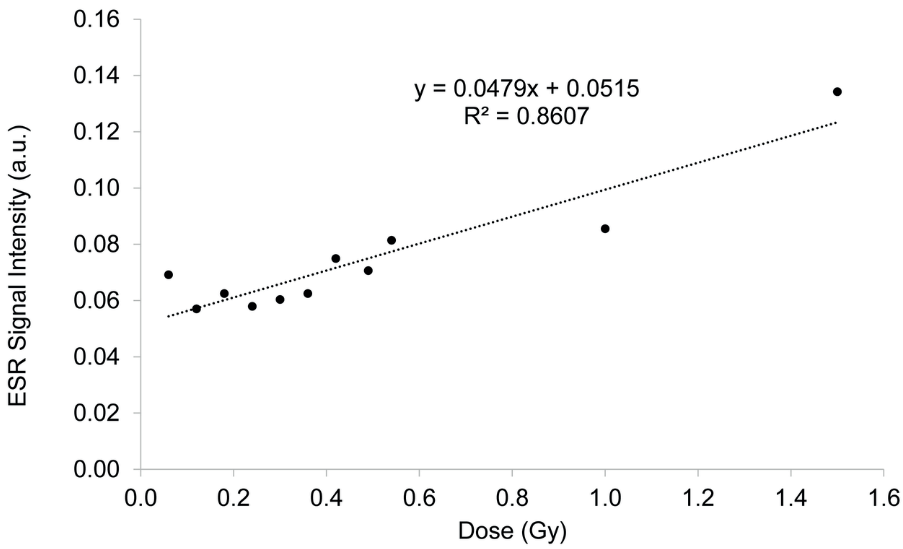

***Figure 3** Relationship between radiation dose and ESR signal intensity.*

Discussion

The accurate measurement of radiation dose using an ionization chamber requires the application of correction factors, including temperature, pressure, ion recombination, beam quality, and a phantom calibration factor of 1.276 as manufactured. The calibration factor $N_{D,w,Q0}$, which was determined by the Department of Medical Sciences, Thailand Ministry of Public Health, is 54.22 mGy/nC. The radiation doses were calculated according to the recommendations of DIN6809-2 and DGMP report 13.[10] Additionally, it is necessary to check the dwell position to determine the distance that gives the maximum dose response.[12]

A phantom study has the advantage of reproducibility in the same position with accuracy and decreases the effect of tissue inhomogeneity. However, the size of the phantom is an important factor that influences the dose distribution around the source.[13] In this study, the alanine dosimeter was placed 8 cm away from the source. In Brachytherapy, the dose decreases rapidly from the source, also known as "rapid fall-off." If the distance is increased, the dose decreases according to the inverse square law. Measuring doses in a large-diameter phantom is difficult and requires a long irradiation time. The result is consistent with Schaeken B. *et al*., who conducted a study to determine the response of alanine in the HDR source. They found that the source-to-detector distance of less than 5 cm significantly affects the dose distribution in brachytherapy.[14]

Alanine, in combination with electron spin resonance, was used to determine the radiation dose by analyzing the peak-to-peak signal amplitude. The results showed that the first alanine derivative in the middle, where the highest signal intensity occurs, is directly proportional to the number of free radicals generated after irradiation. Alanine is suitable for measuring radiation doses in radiotherapy due to its ability to determine doses in the high dose range accurately. The relationship between radiation dose and ESR signal is linearly responsive from 0.1 to 20 Gy, with an R^2 value of 0.9999.[3,12] However, at low doses, the relationship between radiation dose and ESR signal is non-linear due to the limitations of alanine in doses below 1 Gy.[15] This study measured a dose range from 0.49-1.5 Gy (R^2=0.8744) because the ionization chamber can measure charges not exceeding 23 nC, resulting in the measurement of radiation doses up to only 1.5 Gy.

Correcting signal fading is crucial for accurate dose measurements using alanine dosimeters. The signal fading may occur due to various factors, including storage conditions after irradiation, humidity, and dose range. The signal fading can be corrected by applying correction factors to the ESR signal based on the irradiation temperature and time elapsed after irradiation.[5,16] To improve the accuracy and reproducibility of ESR signal measurements, it is recommended to create a calibration curve, increase the number of signal readings, and optimize the measurement parameters, including selecting an appropriate microwave power to reduce saturation effects. Additionally, the ESR signal of irradiated alanine should be read out within 2 hours to avoid significant signal fading.[17] The rectangular cavity has better sensitivity than the circular one and reduces the effects of conditions inside the room that may cause sensitivity changes.[18]

Alanine is a small, tissue-equivalent dosimeter that offers convenient use without wire setup, and the signal endures after reading. However, the electron spin resonance technique used with alanine dosimeters for measuring low radiation doses is relatively time-consuming, and parameters must be determined to improve signal quality and increase the signal-to-noise ratio while taking four minutes per reading. Therefore, it is crucial to consider the time used to increase accuracy.[9] An alternative dosimeter, such as lithium formate, can also be used with the ESR technique.[19] In the future, we suggest using lithium formate instead of alanine, as it provides a better response and has similar properties to human tissue.

Conclusion

In conclusion, the alanine dosimeter with ESR technique proves to be a reliable and valuable method for measuring radiation doses in brachytherapy. The dose-response of alanine demonstrates linearity above 0.49 Gy, rendering it suitable for high-dose range measurements, particularly under specific experimental conditions where the sample tube is accurately positioned in the central region of the ESR spectrometer. It is crucial to optimize the parameters of the ESR spectrometer to ensure precise and accurate readings. This conclusion assumes the ESR signal was recorded at room temperature and that readings should be taken at the appropriate time after irradiation. By adhering to these specified conditions, the accuracy of alanine dosimeters can be significantly enhanced, leading to reliable and precise measurements of radiation doses. The dosimeter offers convenience, exhibits tissue-equivalent properties, and provides a non-destructive measurement process with minimal signal fading. Considering these advantages, alanine can be used in various radiotherapy applications.

References

[1] ICRU REPORT 93: Prescribing, Recording, and Reporting Light Ion Beam Therapy. 4. Dosimetry. Journal of the ICRU. 2016; 16(1-2): 59-70. doi: 10.1093/jicru_ndy 021.

[2] World Health Organization & Institut für Strahlen-hygiene des Bundesgesundheitsamtes (Germany), Federal Republic of. (1988). Quality assurance in radiotherapy: a guide prepared following a workshop held at Schloss Reisensburg, Federal Republic of Germany, 3-7 December 1984 / organized jointly by Institute of Radiation Hygiene, Federal Health Office, Neuherberg, Federal Republic of Germany and World Health Organization, Geneva, Switzerland. World Health Organization. https://apps.who.int/iris/handle/10665/40423.

[3] Alves GG, Kinoshita A, Oliveira HF, Guimarães FS, Amaral LL, Baffa O. Accuracy of dose planning for prostate radiotherapy in the presence of metallic implants evaluated by electron spin resonance dosimetry. Braz J Med Biol Res. 2015; 48(7): 644-9. doi: 10.1590/1414-431X20154367.

[4] Baffa O, Kinoshita A. Clinical applications of alanine/electron spin resonance dosimetry. Radiat Environ Biophys. 2014; 53(2): 233-40. doi: 10.1007/s00411-013-0509-2.

[5] Garcia T, Lin M, Pasquie I, Lourenço V. A methodology for choosing parameters for ESR readout of alanine dosimeters for radiotherapy. Radiat Phys Chem. 2009; 78: 782-90. doi: 10.1016/j.radphyschem.2009.05.020.

[6] Intang A, Oonsiri P, Kingkaew S, Chatchumnan N, Tangboonduangjit P, Stansook N, *et al*. Investigation of alanine dosimeter for output measurement in radiotherapy: Results from multicenter in Thailand. J Assoc Med Sci. 2023; 56(2): 106-16. doi: 10.12982/JAMS.2023.039

[7] Schultka K, Ciesielski B, Serkies K, Sawicki T, Tarnawska Z, Jassem J. EPR/alanine dosimetry in LDR brachytherapy --a feasibility study. Radiat Prot Dosimetry. 2006; 120(1-4): 171-5. doi: 10.1093/rpd/nci528.

[8] Wagner D, Anton M, Vorwerk H, Gsänger T, Christiansen H, Poppe B, *et al*. In vivo alanine/electron spin resonance (ESR) dosimetry in radiotherapy of prostate cancer: a feasibility study. Radiother Oncol. 2008; 88(1): 140-7. doi: 10.1016/j.radonc.2008.03.017.

[9] Safdar MA. Methods of low dose determination using EPR/alanine radiation dosimetry [Dissertation on the Internet]. [Oslo (Norway)]: University of Oslo; 2019. [cited 2022 Jan 28]. Available from: https://www.duo.uio.no/bitstream/handle/10852/74261/1/ADNAN-THESIS.pdf.

[10] Azhari H, Hensley F, Schütte W, Zakaria G. Dosimetric verification of source strength for HDR afterloading units with Ir-192 and Co-60 photon sources: Comparison of three different international protocols. J Med Phys. 2012; 37(4): 183-92. doi: 10.4103/0971-6203.103603.

[11] Chassagne D, Dutreix A, Almond P, Burgers JMV, Busch M, Joslin CA. 3. Recommendations for reporting absorbed doses and volumes in intracavitary therapy. Reports of the International Commission on Radiation Units and Measurements. 1985; os-20(1): 9-14. doi: 10.1093/jicru_os20.1.9.

[12] Oyekunle EO, Akinlade BI, Uwadiae IB, Ajeleti OG, Adedokun AG. Comparative assessment of radioactive source strengths in two high-dose-rate brachytherapy units using three sets of dosimetry equipment. African J Med Phys. 2019; 2(2): 33-8.

[13] Carlsson TA, Carlsson GA. Influence of phantom material and dimensions on experimental 192Ir source. Med Phys. 2009;36:2228-35. doi:10.1118/1.3121508.

[14] Schaeken B, Cuypers R, Goossens J, Weyngaert D, Verellen D. Experimental determination of the energy response of alanine pellets in the high dose rate 192Ir spectrum. Phys Med Biol. 2011; 56: 6625-34. doi: 10.1088/0031-9155/56/20/007.

[15] Ciesielski B, Schultka K, Kobierska A, Nowak R, Peimel-Stuglik Z. In vivo alanine/EPR dosimetry in daily clinical practice: a feasibility study. Int J Radiat Oncol Biol Phys. 2003; 56(3): 899-905. doi: 10.1016/S0360-3016(03)00196-2.

[16] Gago-Arias A, González-Castaño D, 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: T08004. doi: 10.1088/1748-0221/10/08/T08004.

[17] Nasreddine A. Alanine/EPR dosimetry for low to medium energy X-ray radiation processing control [Dissertation on the Internet]. [Strasbourg (France)]: Université de Strasbourg; 2020. [cited 2022 Feb 12]. Available from: https://theses.hal.science/tel-03141195/

[18] Helt-Hansen J, Rosendal F, Kofoed IM, Andersen CE. Medical reference dosimetry using EPR measurements of alanine: development of an improved method for

clinical dose levels. Acta Oncol. 2009; 48(2): 216-22. doi: 10.1080/02841860802279725.

[19] Gustafsson H. Development of sensitive EPR dosimetry methods. [Dissertation on the Internet]. [Linköping, (Sweden)]: Linköping University; 2008. [cited 2022 Feb 12]. Available from: http://www.diva-portal.org/smash/get/diva2:17549/FULLTEXT01.pdf