Direct Determination of Radiation Dose in Human Blood

A. Güneş Tanır*, Özge Güleç*, Eren Şahiner†, Mustafa H. Bölükdemir*, Kemal Koç‡, Niyazi Meriç†, Şule K. Keleş†

ABSTRACT

In this work, it has been shown that it is possible to determine the radiation doses in human blood exposed to internal or external ionizing radiation treatment, both directly and retrospectively. OSL counts from the waste blood of a patient injected with a radiopharmaceutical for diagnostic or treatment purposes and from a blood sample having a laboratory-injected radiation dose were both used for measurements. The dose values obtained the bloods were found as ~0.46 Gy for the 1-5Gy dose range and as ~0.51 Gy for the 0.143-0.858 Gy dose range using the optically stimulated luminescence technique. The blood aliquots from a healthy person were exposed to different external laboratory doses. The dose values corresponding to a 10Gy laboratory dose from the aliquots exposed to external radiation were found as 10.94 ± 3.30 Gy for Disc 3 and 10.79 ± 3.28 Gy for Disc 1. This study shows that the dose received by a person can be measured simply and retrospectively, using only a very small amount of blood. The results may have important ramifications for the medicine and healthcare fields in particular.

Key Words: ionizing radiation, human blood, optically stimulated luminescence, retrospective dosimetry

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Introduction

It is common knowledge that ionizing radiation is being used more and more in the field of medicine. Patients are exposed to internal radiation doses in various ways, such as ingestion or injection for the diagnosis or cancer treatment. Martin states, "an internal radiation dose can occur due to inhalation or ingestion of radionuclide, a direct injection for diagnosis or treatment of disease, a puncture wound, or skin absorption. Internal radiation doses cannot be measured; they must be calculated based on an estimated / measured intake, an estimated / measured quantity in an organ or an amount eliminated from the body" (Martin, 2011).

It is well known that the dose is defined as the deposited energy per unit mass of the target. The calculations of internal doses are based on certain assumptions, such as the homogeneously distributed activity on the target organ or the target organ being treated as the source organ. In medical applications, cumulative activity is defined using the values for the activity and time, and the absorbed dose is given as: $D=AxS$ (Target←Source). Here, A is the cumulative activity, S(Target←Source) represents the combination of the energy deposit parameters with the transformation constants; the S-value is fixed for a given radionuclide (Martin, 2011). These processes do not provide a direct measurement to determine the internal radiation

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doses received by a person. The knowledge of the dose that will be given to the target volume is the most important factor affecting the success of therapy when using ionizing radiation for diagnosis and/or treatment.

In the field of radiation therapy, the dose that will be given to a patient is planned using a treatment planning system. However, how much dose had a patient already received? It has not been possible to answer this question accurately. The retrospective dosimeter method is needed to determine the dose already received by a patient.

The optically stimulated luminescence (OSL) technique has been used in radiation dose measurements (Tanır *et al.,* 2012; Pradhan *et al.,* 2008). Some studies showed that the luminescence signal from halides, such as NaCl and KCl, that exist in crystallized blood are very bright (Tanır *et al.,* 2007; Tanır and Bölükdemir, 2007; Polymeris *et al.,* 2011). The OSL technique has been suggested for inorganic material, with studies on the OSL of organic materials such as bone, coral skeleton and shell (Barnes *et al.,* 2003; Meriç *et al.,* 2008). However, no work has been reported on the direct measurement of internal radiation doses using a blood sample. In this study, the OSL dosimetry technique, which is becoming increasingly important in the field of radiation physics, was used to determine the dose given to blood samples.

Basics of the OSL technique

The OSL technique was first introduced by Huntley et al. for dosimeter (Huntley *et al.,* 1985). This technique is based on measuring the luminescence signal from a sample that has been exposed to ionizing radiation. The optical luminescence concept has been described as using an energy band model of solids, applied to retrospective dosimetry (Aitken, 1998; Botter-Jensen *et al.,* 2003). The ionizing radiation produces electron-hole pairs in the crystallized structure, and thus they are trapped. When the crystal structure is stimulated by light, the electrons can be removed from traps and can go into the conduction band. From the conduction band, they may recombine with holes trapped in hole-traps, and then luminescence signals are emitted. The luminescence intensity is proportional to the number of trapped electrons, and the number of trapped electrons is proportional to the dose of ionizing radiation absorbed by the material. The basic representation of radiation induced luminescence is shown in Figure 1. It is known that radiation-induced luminescence is different from other luminescence phenomena, such as photoluminescence and phosphorescence, which are not dose dependent, and thus not relevant to dosimetry.

OSL measurements were performed using constant stimulation intensity, which is called continuous-wave OSL (CW-OSL). CW-OSL is the simplest and the most straightforward process. In CW-OSL, the excitation is continuous and the emitted signals are detected during stimulation. In this process, the filters to discriminate between the stimulation light and the emitted light were used (Botter-Jensen *et al.,* 2003). The reduction of OSL signals is observed up to a low level as the trapped charge is depleted (decay curve).

The blood samples used in this study were dried, and thus were crystallized. Regarding the atomic components of the blood, it can be seen that the crystallization of NaCl and KCl will be much more than that of other halides. Furthermore, it is known from previous studies, that more luminescence signals are obtained from NaCl and KCl, in solid form or recrystallized, than from other halides.

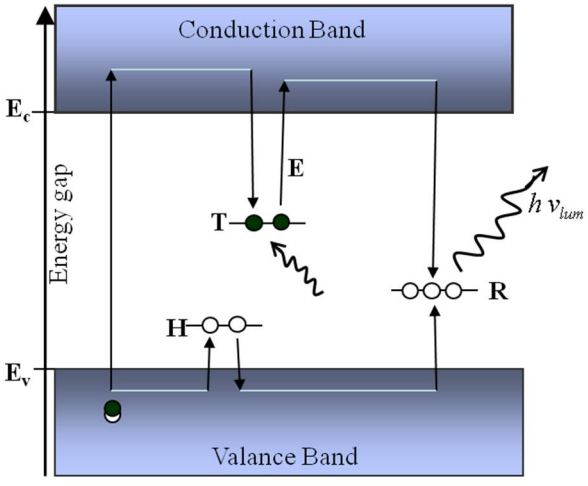

Figure 1. Luminescence arises from the optical stimulation of crystal exposed to ionizing radiation. During exposure, radiation energy is stored in crystal lattice, such as halides; T: electron traps; H: holes; and R: recombination center.

The blood samples used in this study were crystallized by drying. If one looks at the atomic structure of blood, it can be seen that the amount of NaCl and KCl crystals is greater than that of

others. Therefore, as seen from some studies (Tanir *et al.,* 2012; Tanir *et al.,* 2007; Spooner *et al.,* 2012), the cause of luminescence signals from blood samples must be due to its crystallized structure.

Materials and methods

The luminescence signal from blood samples was read using the ELSEC 9010 OSL system (Spooner *et al.,* 1990) as well as the Risø TL/OSL-DA-20 automatic system (Nutech, Technical University of Denmark). The photomultiplier (PM) tube used in the experiments were bialkali EMI 9235QA for ELSEC 9010 and EMI 9235QB15 for Risø TL/OSL systems. The total power from the LEDs (blue, 470 nm) in the Risø TL/OSL-DA-20 system was approximately 80 mW/cm^2 at the sample position. A Hoya U-340 filter was incorporated to minimize the amount of directly scattered blue light reaching the detector system.

Blue-green light LEDs (420–550 nm) from Osram were installed in the ELSEC 9010 OSL system by the Nuclear Sciences Institute of Ankara University, which have a power output of about 6 cd at 39 mA. A long-pass Schott UG11 filter was fitted in front of the blue LEDs to minimize the amount of directly scattered blue light reaching the PM photocathode. In 24 LEDs, the total power delivered to the sample was measured as 24 mW/cm^2 at a distance of 16 mm. The irradiator was a ^{90}Sr/^{90}Y beta source with a 1.48-GBq activity. The dose rate at the sample position was approximately 0.143Gy/s for both systems.

All of the samples were settled onto 1cm diameter Al discs using paraffin oil and protected from light between the irradiation and OSL measurements. All of the blood aliquots prepared were ~3 mg. The blood aliquots were left at room temperature (RT) at our institution for 72 h. All of the signals were measured at RT and under red light. None of the aliquots were preheated. The background counts of the OSL systems were measured as 20–30 counts/s.

Experiment 1

The waste blood sample of a patient undergoing radioisotope treatment was taken from the Nuclear Medicine Center of Ankara University. For dose calculation, the natural luminescence counts (from aliquots not given doses in the OSL laboratory) were measured. The background counts were subtracted from the total luminescence counts. Natural luminescence measurements were repeated using different aliquots. One of the aliquots was exposed to four different laboratory radiation doses, ranging from 1 Gy to 5 Gy, using a ^{90}Sr–^{90}Y beta source. The other aliquot was given five different laboratory radiation doses in the 0.143–0.858 Gy range. The algorithm for the measurements was as follows: the natural luminescence counts were measured for 50 s; the bleached aliquot was exposed to a dose and its luminescence counts were measured for 50 s. That is, the time gap between the irradiation and readout was ~50 s.

Experiment 2

The blood serum that was not subjected to radioisotope treatment was put into a tube that was 1 cm in diameter and 3.5 cm in length. As the next step, 1.530 ± 0.103 mCi of ^{99m}Tc was injected into the tube. The mixture was left at RT for 72 h in a dark room. The serum with ^{99m}Tc was dropped onto the Al discs as follows: one drop on one of the discs, two drops on another disc, and three and five drops on the others. These aliquots were dried at RT and shielded from sunlight. The activity of one drop was calculated assuming uniform distribution. The activities of the aliquots were 17 µCi, 34µCi, 51µCi, and 85µCi. The integrated luminescence counts were measured for 50 s.

Experiment 3

The aliquots from the healthy blood sample were prepared by dropping onto 1 cm diameter Al discs. Four aliquots from the blood sample were prepared carefully, as identically as possible. They were left at RT for 72 h and shielded from sunlight. The signals from the aliquots were measured before laboratory irradiation (for 0 Gy). Next, 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, 100, and 200 Gy laboratory beta doses were given to each aliquot, and the luminescence counts were measured. The algorithm for the measurements was same that as in Experiment 1.

Results and discussion

First, blood that was not subjected to radiation exposure was tested to determine whether a OSL signal exited or not. The blood was found to have no luminescence signal (Figure 2). In this study, three different experiments were carried out, and

although the sample preparation was similar for all of them, the algorithms for dosing were different.

Waste blood sample from a patient

The natural OSL decay curves from two different aliquots prepared from the waste blood sample of a patient are shown in Figure 3. It is indicated that the blood aliquots include the given ionizing radiation, and that it is possible to measure the luminescence signal from the blood sample that received a radiopharmaceutical. If such a curve could not have been obtained, then one would not be able to use the OSL technique to measure the dose received by the sample. The decay curves from the aliquots irradiated by 1–5 Gy and 0.143–0.858 Gy laboratory doses are shown in Figure 4 and Figure 5, respectively. The bleaching time was considered as about 3 s from these decay curves.

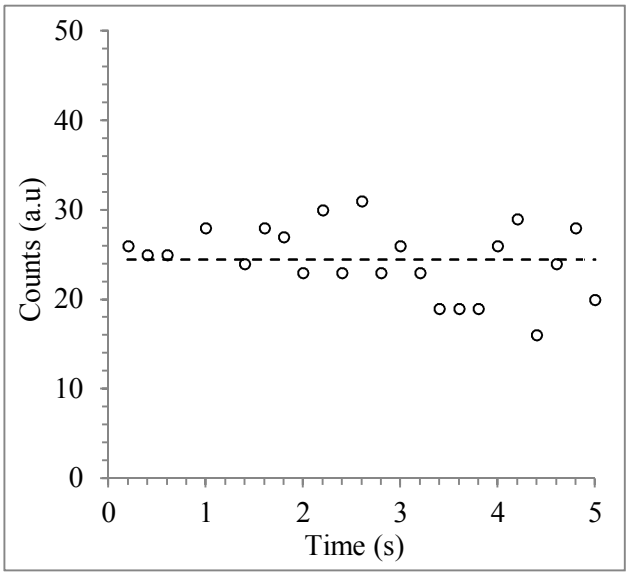

Figure 2. Signals from the blood sample that was not subjected to radiation did not contain luminescence signals. As seen, they were only background level.

The graphs in Figure 3, 4, and 5 are sufficient to prove that it is possible to determine the paleodose using a blood sample given radioisotope treatment. That is, these graphs show that the luminescence counts increase with an increasing laboratory dose and the internal radiation dose can directly be determined using the OSL technique.

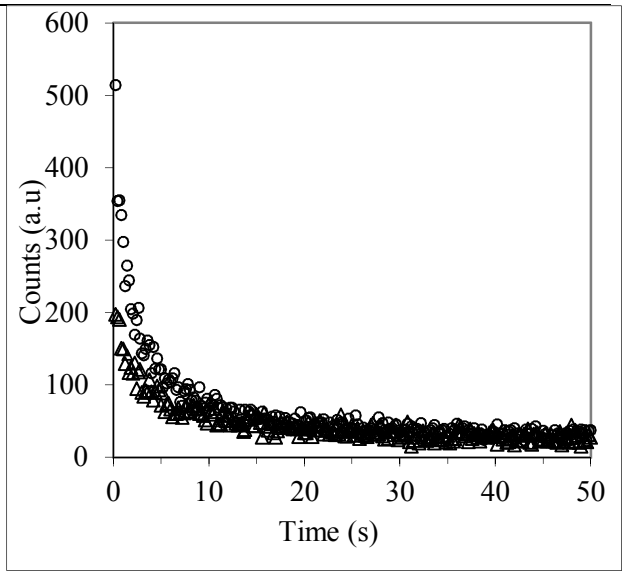

Figure 3. OSL decay curves (natural counts) from two different blood aliquots injected with a radiopharmaceutical in the nuclear medicine center.

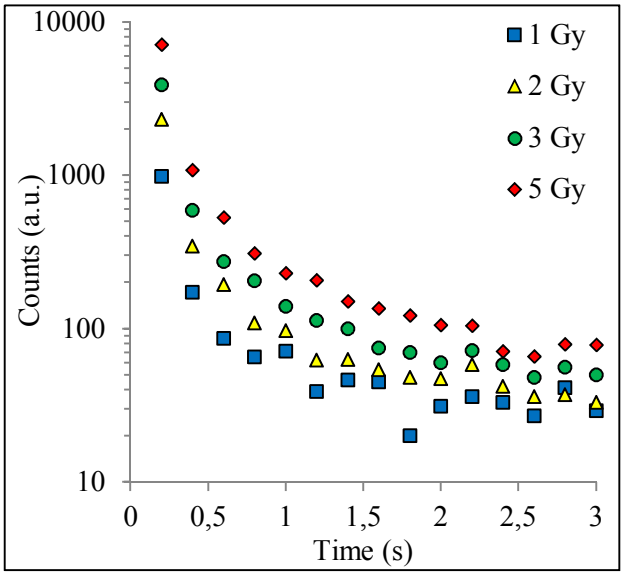

Figure 4. Decay curves from the blood aliquot received radioisotope treatment for laboratory doses of 1, 2, 3, and 5 Gy.

The dose-response graphs corresponding to the decay curves in Figure 4 and Figure 5 are seen in Figure 6 and Figure 7. The dose-response graph obtained using the maximum luminescence counts (for 0.2 s) was found to be linear ($y = 1545x - 676.17$; $R^2 = 0.9985$ for Figure 6). When the dose-response graph was plotted using the integrated counts (for 3 s), the equation obtained was $y = 2189.2x - 659.8$; $R^2 = 0.9978$ for Figure 6. The internal dose from a blood sample can be determined using the dose-response equation by interpolating the natural luminescence count on the dose-response graph. The natural

luminescence count was measured as 33 for 0.2 s and 347 for 3 s. Using these values, the internal doses from Figure 6 were found as 0.4590 Gy and 0.4598 Gy, respectively. The natural luminescence count was measured as 515 for 0.2 s and 2068 for 3 s from the other aliquot. When the same calculations were made by making use of Figure 7, the internal doses were found as 0.22 Gy for the maximum counts and 0.51 Gy for the integrated counts. Figure 6 and Figure 7 show that the internal dose can be determined by considering either the integrated counts or the maximum counts. The dose response curves for each decay curve were found to be linear for the blood aliquots. The difference between the slopes of the dose response curves for different doses was attributed to the difference in the blood aliquots.

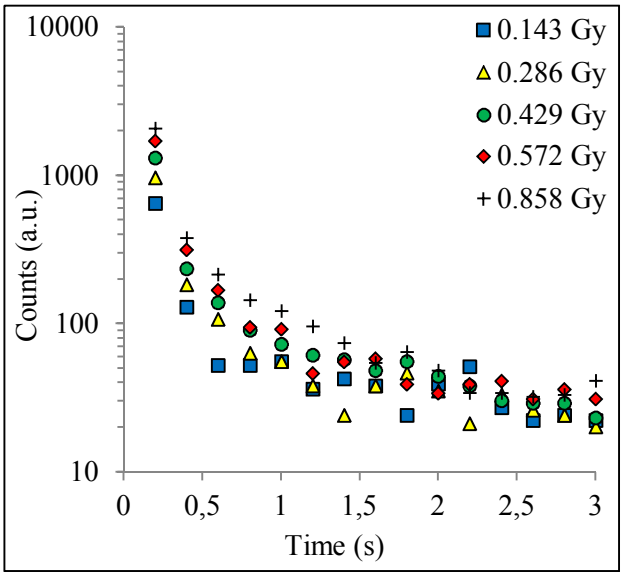

Figure 5. Decay curves from the blood aliquot taken radioisotope treatment for laboratory doses in the 0.143–0.858 Gy range.

The blood serum

The decay curves from the blood serum aliquots are shown in Figure 8. The integrated luminescence signals were corrected by applying the mass normalization. Since four different aliquots were used, the activities given to each was different. The activity-response curve corresponding to the decay-curves is shown in Figure9. The linearity of Figure 9 was realized by making mass normalization. It is seen from Figure 8 that the luminescence counts from the blood serum are higher than those from the whole blood (see Figure3), since the halides (especially NaCl, KCl, $CaCl_2$, etc.) are more concentrated in blood serum than in whole blood, as expected. Thus, it is recommended to use blood serum rather than whole blood for internal dose determination rather than to use whole blood.

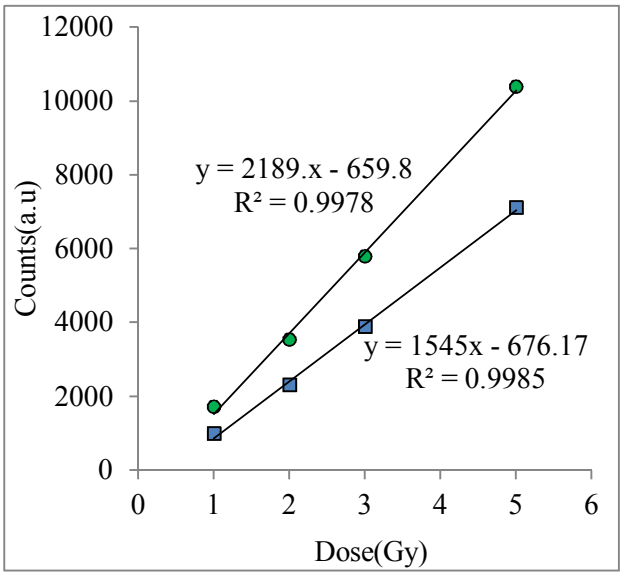

Figure 6. Dose-response curves using integrated counts (circle) and maximum counts (square) for the 1–5 Gy range.

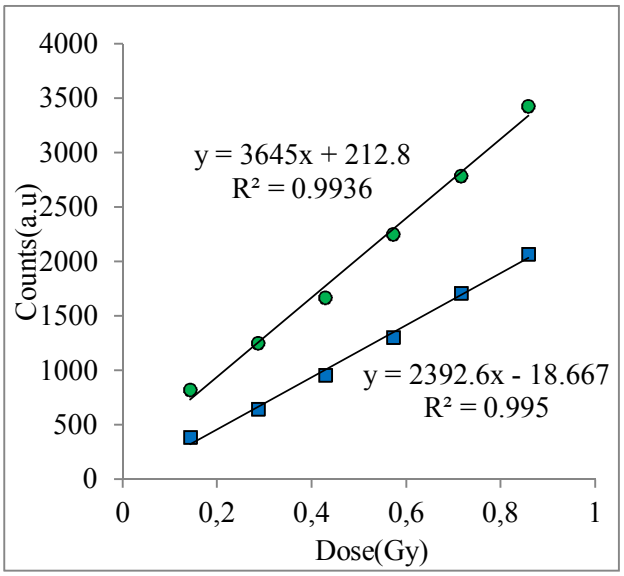

Figure 7. Dose-response curves using integrated counts (circle) and maximum counts (square) for the 0.143–0.858 Gy range.

Blood sample exposed to external radiation beam

In Figure 10, the luminescence signals from the blood aliquot that was not exposed to a laboratory dose and the decay curve for the same aliquot given a 50-Gy laboratory dose are seen. Healthy blood has no luminescence signal (Figure 10a). Figure 10b shows that it is possible to measure the luminescence counts from blood exposed to

external radiation. The signals were integrated in 5 s.

Next, the decay curves from two aliquots (Disc 1 and Disc 3) for different radiation doses were obtained and shown in Figure 11 and Figure 12. Because the luminescence counts were relatively weak up to 10 Gy, the decay curves were plotted for doses higher than 10 Gy. The maximum luminescence counts were 26, 38, 52, 85, 100, and 113, corresponding to 0, 1, 2, 3, 4, and 5 Gy doses, respectively.

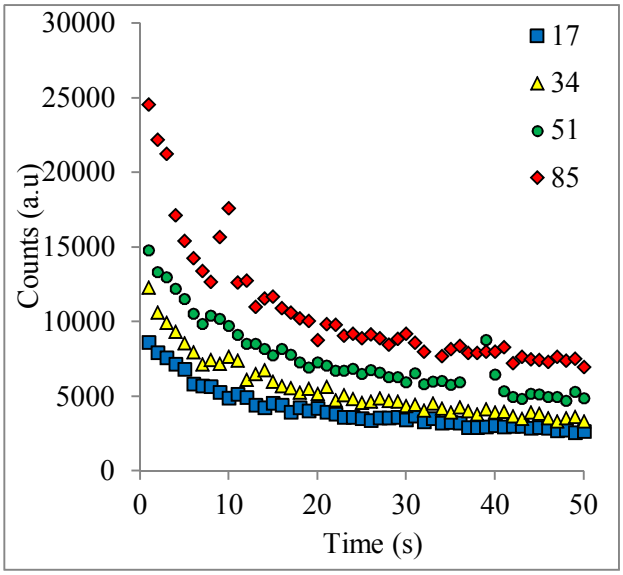

Figure 8. Decay curves from aliquots injected to 17 µCi, 34 µCi, 51 µCi, and 85 µCi.

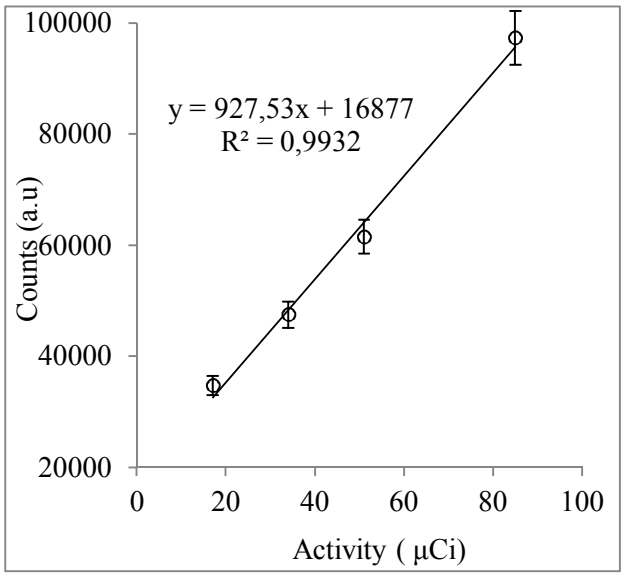

Figure 9. Activity-response curve using the data in Figure 8.

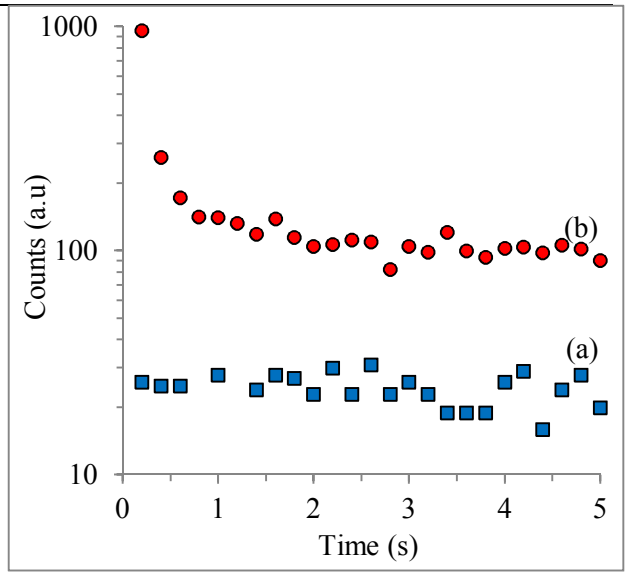

Figure 10. (a) Background level signals from the blood aliquot not exposed to external radiation dose **(b)** Luminescence decay curve from the blood aliquot exposed to a 50-Gy external radiation dose.

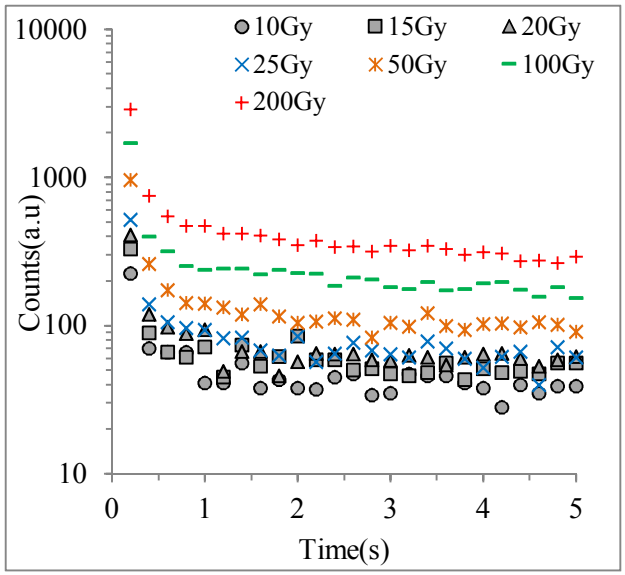

Figure 11. Decay curves from the blood aliquot (Disc 1) for different doses.

The dose-response curves obtained using signals from the two aliquots are plotted in Figure 13 and Figure 14. The luminescence counts from Disc 1 were measured as 467 counts/5 s when a 10-Gy dose was given. By inserting this value into the Equation in Figure 13, the dose was calculated as 8.54 ± 2.92 Gy. The luminescence count from Disc 3 was measured as 459 counts/5 s and then inserted into the Equation in Figure 14. The dose was calculated as 8.01 ± 2.83 Gy.

Figure 15 and Figure 16 were also plotted for the 1–5 Gy dose range for Disc 3 and Disc 1,

respectively, since the dose-response graph was expected to be linear for low doses. The dose value was calculated as 11.02 ± 3.30 Gy for Disc 3 from y = 36.8x + 53.4, by inserting 459 counts/5 s corresponding to 10 Gy. The dose value was calculated as 10.79 ± 3.28 Gy for Disc 1 from y = 18.68x + 22.286, by inserting 224 counts/0.2 s corresponding to 10 Gy.

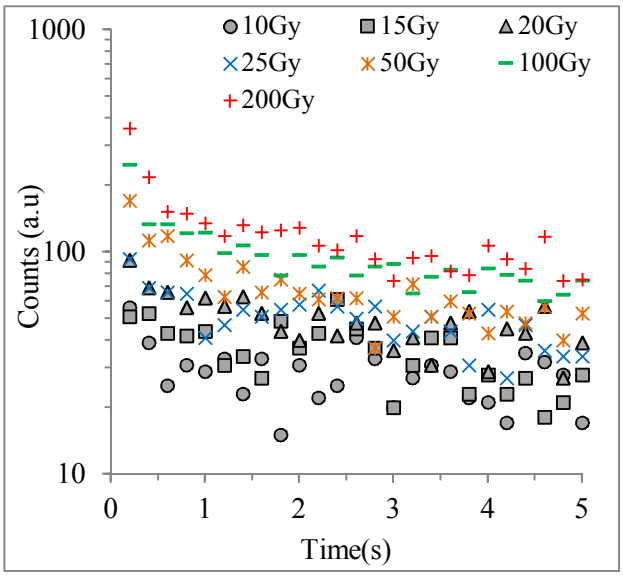

Figure 12. Decay curves from the blood aliquot (Disc 3) for different doses.

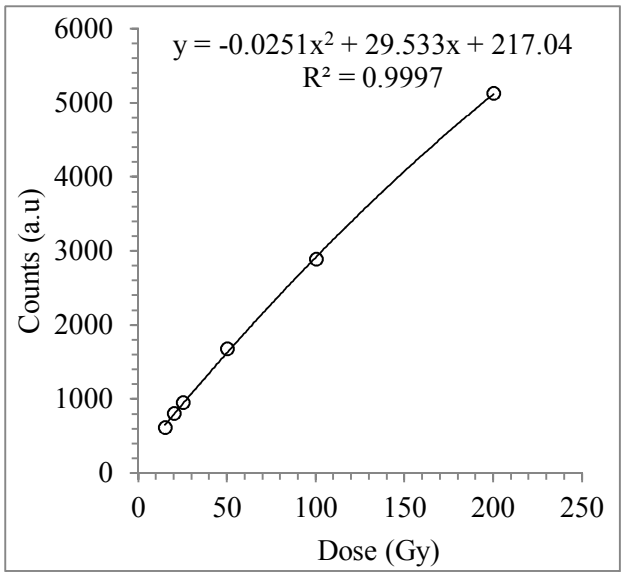

Figure 13. Dose-response curve for Disc 1. The count for 10 Gy was not included in the curve.

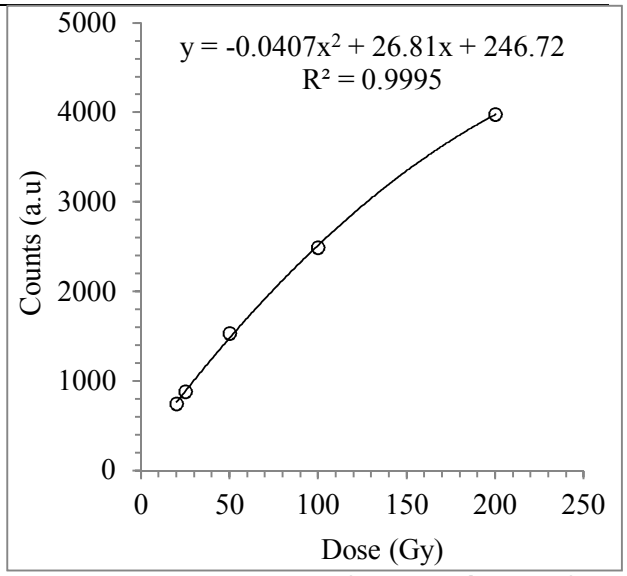

Figure 14. Dose-response curve for Disc 3. The count for 10 Gy was not included in the curve.

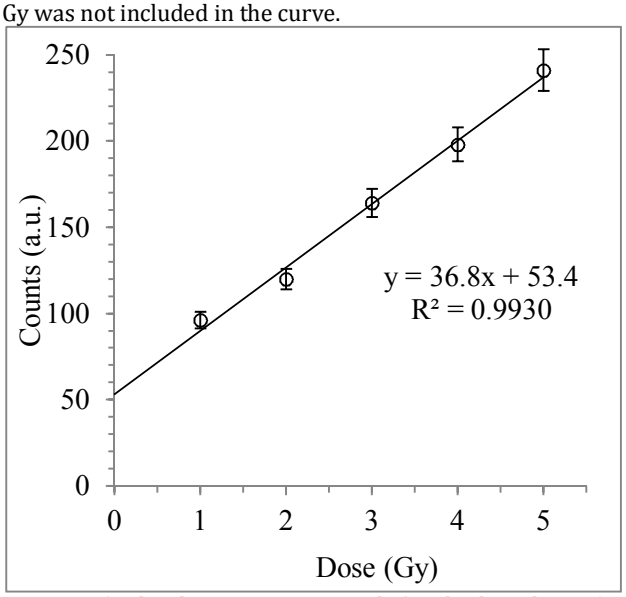

Figure 15. The dose-response graph for the low doses (1–5Gy) for Disc 3.

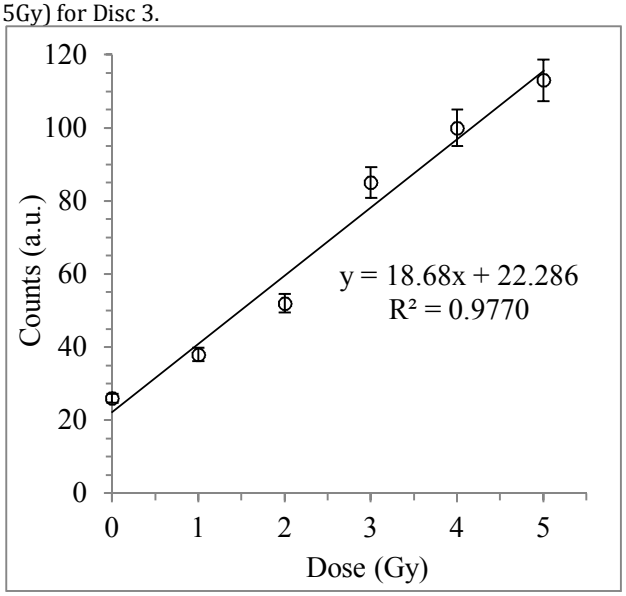

Figure 16. Dose-response graph for the low doses (1–5 Gy) for Disc 1.

Conclusion

This study shows that the ionizing radiation received by a person can be measured directly and retrospectively using only a very small amount of blood with the OSL technique. This process should be applied before the biological life of radioisotopes and/or immediately after external irradiation. This application of OSL is important because it can prevent patients from being given the wrong dose when undergoing treatment. Moreover, the dose thought to be the cause of frequent cancer cases in certain regions can be determined, and necessary precautions can then be taken. It can be concluded that this application of OSL will be very illuminating in such fields as health care, medicine, and radiation protection.

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