Fourth Semester Report (2019/2020 spring)

By Tariq Hailat (hailat@caesar.elte.hu)

Doctoral School of Physics-ELTE

Supervisor: Balázs Madas, Radiation Biophysics Group, MTA Centre for Energy Research, Budapest, Hungary.

Ph.D Thesis topic: Characterization of radiation exposure and its biological effects at different spatial scales

Place of research: MTA Centre for Energy Research, Budapest, Hungary

Introduction

Ionizing radiation is a health hazard to humans, but is exploited at the same time in various applications, in particular in diagnostic and therapeutic medicine. A profound understanding of the underlying processes, starting from the physical energy deposit up to the biological radiation response, is the basis for a reliable prediction of radiation effects. The subject of this work is the formulation of predictive dose response models.

The purposes of the work presented here were: (1) to study some tasks related to the effect of Radium-223 and its progeny on the cells using Monte Carlo simulation. (2) to evaluate important key aspects of SSA-Ferrous-PVA-GTA hydrogel dosimeter such as radiation energy dependence, dose rate dependence, temperature dependence, and overall uncertainty of the estimated doses which were not previously studied using UV-Vis spectrophotometer; and (3) to introduce a new evaluating performance of SSA-Ferrous-PVA-GTA hydrogel dosimeter using the nuclear magnetic resonance (NMR) technique.

Summary of research work in the previous semesters

The research started by calculating the average of alpha particles that hitting blood cell with known radius and a certain distance from a radioactive source such as radium 223 which has a known radioactivity. This task of research was carried out in two ways:

The first way was analytical in that it used mathematical formulas and illustrative figures to calculate the hits average and probability.

The second way was based on creating a Monte Carlo simulation using Python program. Therefore, the quadratic equation representing the relationship between the equation of spherical blood cells and the directions of nuclei that decayed from a radioactive source has been solved.

The Monte Carlo simulation using Python program includes

- Checking if alpha particles hit cell
- Knowing the average of alpha particles hit cell
- Calculating the probability of alpha particles hit cell

After that, the python script was improved to include many of cells that put in a plastic holder at a certain distance above the point source of alpha particles. In addition to that, another python script was written based on open source of alpha particles. Through these two scripts of the snake, many results were achieved such as:

- Checking if the alpha particles reach the plastic holder and knowing the number of alpha particles that reached.
- Knowing the number of alpha particles that penetrate the plastic holder.
- Solving the quadratic equation that represents the relationship between the equation of spherical blood cells and the directions of nuclei that degrade from a radioactive source
- Knowing the total number of alpha particles hit cells
- Knowing the number of cells that were hit by alpha particles
- Plotting the locations of cells that were hit and non-hit
- Determining the number of alpha particles hit each cell
- Determining the number of cells have 0,1,2,…. Hits
- Calculating the energy absorbed for each hit cell
- Calculating the total dose for each hit cell

In addition to the Monte Carlo simulations, experimental techniques were performed using CR-39 detectors in order to quantify absorbed doses and the number of interactions between alpha-particles and cell nuclei (hits). CR-39 detectors were placed to the location of the cells (the upper well of the Transwell® system) (see figure1). After exposure time, the detectors were collected and washed in distilled water and chemically etched. Then an optical microscope was used to count the number of alpha particles tracks on each CR-39 detector surface.

Figure 1. Detectors exposed to a Ra-223 activity of 10 kBq

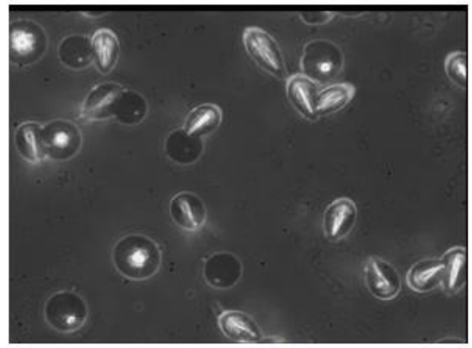

Figure 2. Tracks view of alpha particles from the surface of detector.

The tracks were counted in 10 fields of each detector. The results can be seen in Figure 3.

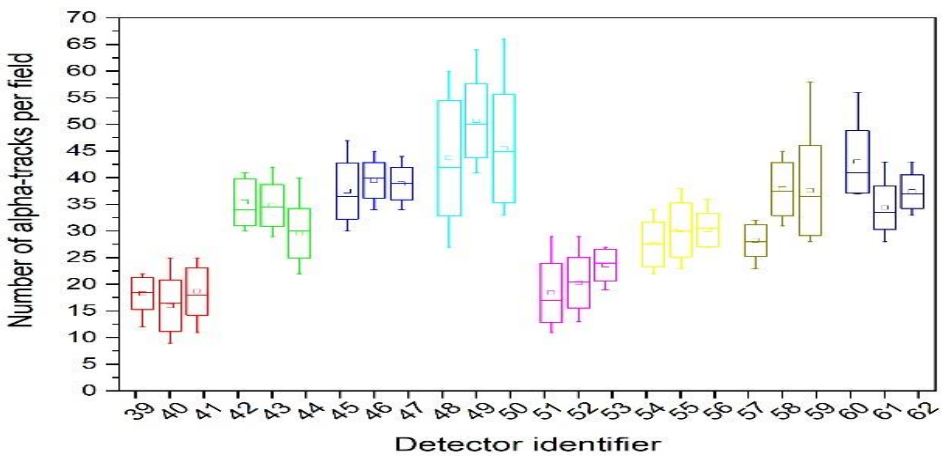

Figure 3: Distribution of alpha-particle tracks over of the surface of the detectors irradiated at the top of the inserts of the 24-well systems. Squares show the average where the box is +/- standard deviation. Whiskers show the minimum and maximum, while the median is the horizontal line within the box.

The measurement of alpha-particle track density for 24 CR-39 detectors showed that the activity distribution in the in vitro experiments with Ra-223 is highly inhomogeneous. But in future experiments, it is desired to ensure homogeneous activity distribution. If the track density is homogeneous, then reliable mathematical modelling of cell survival will also become possible in order to estimate the efficacy of Xophigo® or other alpha-emitting radionuclide in in vitro experiments. In addition, if the activity distribution is known, then the therapeutic efficacy can be estimated much more precisely in in vivo experiments by applying computational dosimetry along with mathematical modelling of cell survival.

I did another task related to studying the effect of alpha particles on gel dosimetry. So, I prepared some chemical samples in Hashemite University, Al-Zarqa, Jordan. These samples are used for medical purposes and they include 4 wt% Gelatin (300 Bloom porcine skin gelatin), 1 mM Ferrous Ammonium Sulfate (FAS), 25 mM Sulfuric Acid (SA) and 0.1mM Methylthymol

Blue Sodium Salts (MTB). The three stock solutions of SA, FAS and MTB were prepared and mixed separately and slowly in 500 g volumetric flasks of distilled water, kept at room temperature, meanwhile, 8% (w/v) gelatin was dissolved in 100 mL distilled water at room temperature and was left to hydrate for 10 min, and then the solution of gelatin-water was stirred and heated to 50 °C for 2 h under normal atmospheric pressure using a hot plate stirrer. After cooling the gelatin-water solution to approximately 30 °C, 100 mL stock solutions were added separately to the 100 mL gelatin hydrogel and mixing slowly for another 10 min. Finally, the solution was poured into 3 mL cuvette (see **Figure 4**), and sealed using suitable covers and parafilm. The cuvette was stored in a refrigerator (10 °C) prior to irradiation.

Figure 4: A photograph of the unirradiated sample (Cuvette) of 0.1 mM Fricke-MTB gelatin dosimeter system.

Figure 5: A photograph of the irradiated sample (Cuvette) of 0.1 mM Fricke-MTB gelatin dosimeter system by Am-243.

After that the MTB gel sample was injected by using a tracer (spike) 0.14 g of Am-243 that has activity 1.054 kBq/g. The color of MTB gel sample changed to become blue (see **Figure 5**) after injected by Am-243, this means that the MTB gel sample took a certain radiation dose. Then the MTB gel samples were investigated using Spectrophotometer.

The Fricke-MTB dosimeter shows a high sensitivity of the absorbance at 620 nm, which can be imaged with a red-light source (See **Figure 6**).

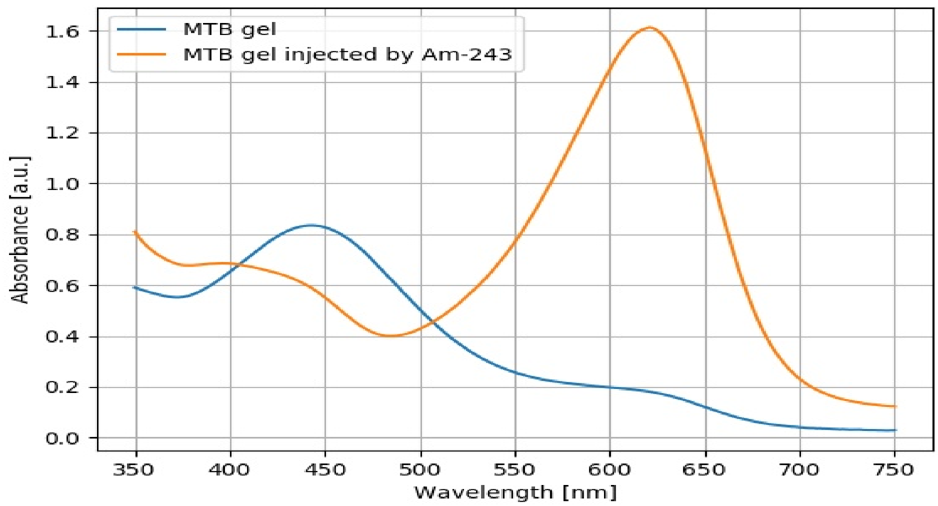

Figure 6: The absorbance change of 0.1 mM MTB-Fricke dosimeter as a function of wavelength for different absorbed doses.

Description of research in the current semester

I submitted paper related to evaluate of sulfosalicylic acid-ferrous-polyvinyl alcohol-glutaraldehyde hydrogel dosimeters using nuclear magnetic resonance and optical technique. Also, I completed some tasks related to the effect of Radium-223 and its progeny on the cells using Monte Carlo simulation.

Firstly, In order to study the effect of alpha particles that decaying from Ra-223 and its progeny on the cells, the Bateman equation was expanded to find the number of atoms for each isotope (N_n).

$$^{223}Ra \xrightarrow{\alpha} {}^{219}Rn \xrightarrow{\alpha} {}^{215}Po \xrightarrow{\alpha} {}^{211}Pb \xrightarrow{\beta} {}^{211}Bi \xrightarrow{\alpha} {}^{207}Ti$$

$$N_1 \longrightarrow N_2 \longrightarrow N_3 \longrightarrow N_4 \longrightarrow N_5 \longrightarrow N_6$$

$$N_n(t) = \sum_{i=1}^{n}\left[N_i(0) \times \left(\prod_{j=1}^{n-1}\lambda_j\right) \times \left(\sum_{j=i}^{n}\left(\frac{e^{-\lambda_j t}}{\prod_{p=i,p\neq j}^{n}(\lambda_p - \lambda_j)}\right)\right)\right]$$

$\lambda_i = \frac{\ln(2)}{t_{1/2}}$, $N_i(0) = \frac{A_i}{\lambda_i}$

$t_{\frac{1}{2}i}: Half\ life\ of\ isotope\ i.$ $A_i: Activity\ of\ isotope\ i$

$\lambda_i: Decay\ constant\ of\ radioactive\ source\ i.$
$N_i(0): Initial\ number\ of\ atoms\ for\ radioavtive\ source\ i$ *at t=0*

$N_n: Number\ of\ atoms\ for\ radioavtive\ source\ n.$

After that, the number of alpha particles was calculated by taking the integral from (0) to certain time (t).

$\#\ of\ \alpha - particles$ decaying from radioactive source $n = \int_0^t \lambda_n N_n dt$

These equations related to the number of alpha particles from radioactive source were added to python code. Then, the effect of alpha particles of the cells were studied with increased the distance between the source and cell sample, increased the radioactivity of the source and increased exposure time of the cells sample.

The results illustrate that the number of hits decreases with the increase in the distance between the source and the cell sample (see **Figure 7**)while the number of hits increases with the increase in radioactivity of the source or in exposure time of the cells sample (see **Figure 8** and **Figure 9**).

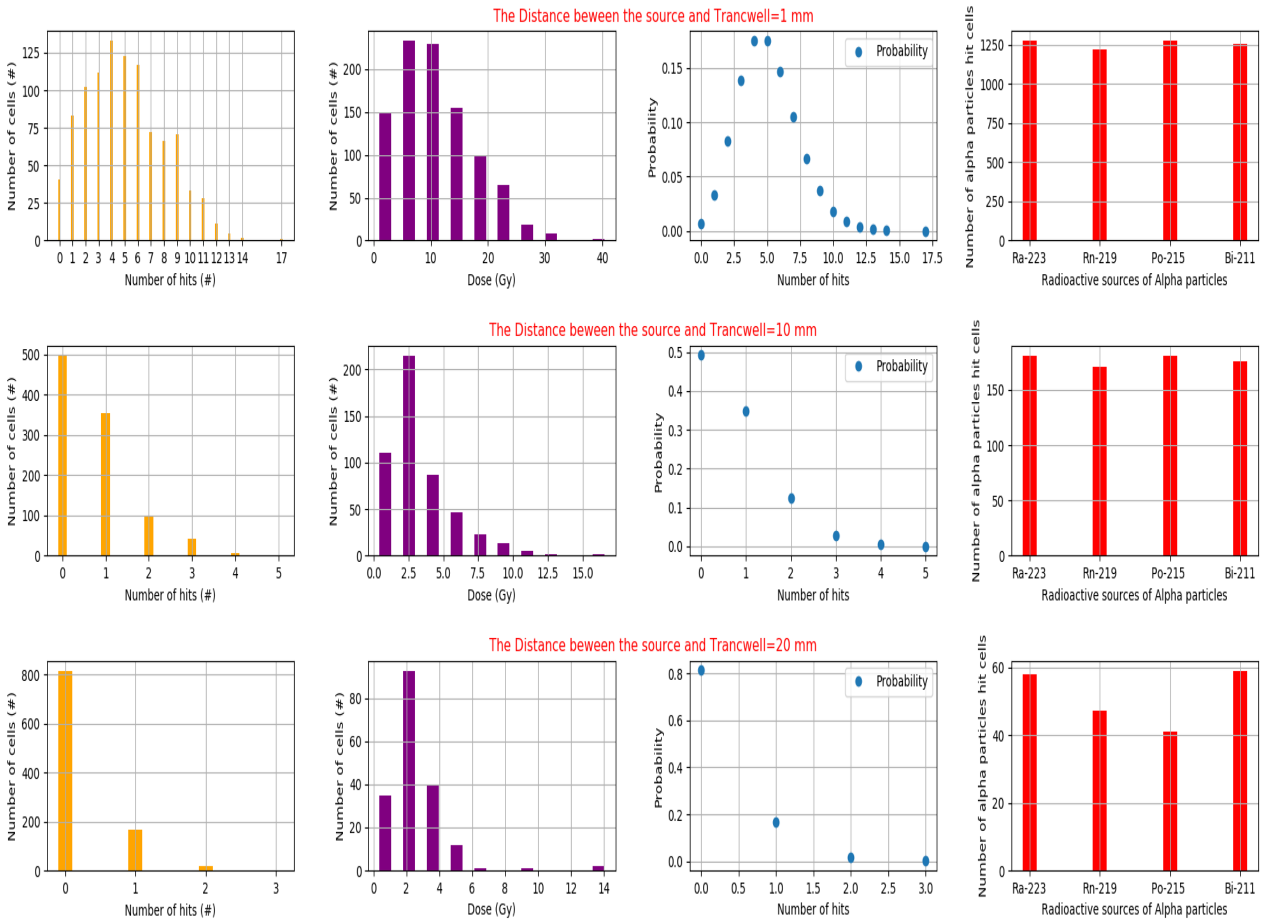

Figure 7: The effect of alpha particles on cells with increased distance (1, 10 and 20 mm) between the radioactive source and Trancwell. The activity of the radioactive source 5000 Bq and the exposure time 15 minutes.

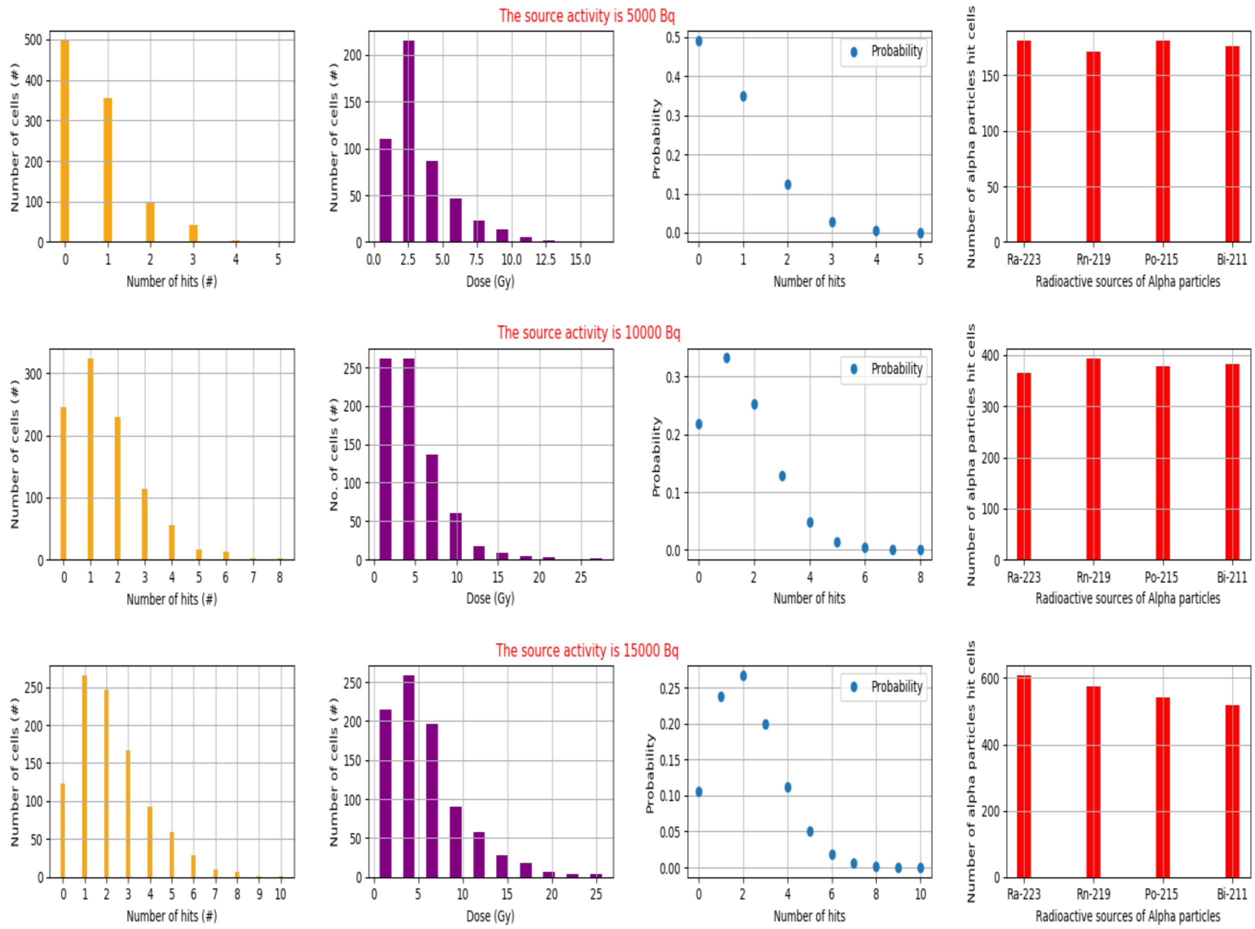

Figure 8: The effect of alpha particles on cells with increased activity of the radioactive source (5000, 1000 and 15000 Bq). The distance between the source and Trancwell 10 mm and the exposure time 15 minutes.

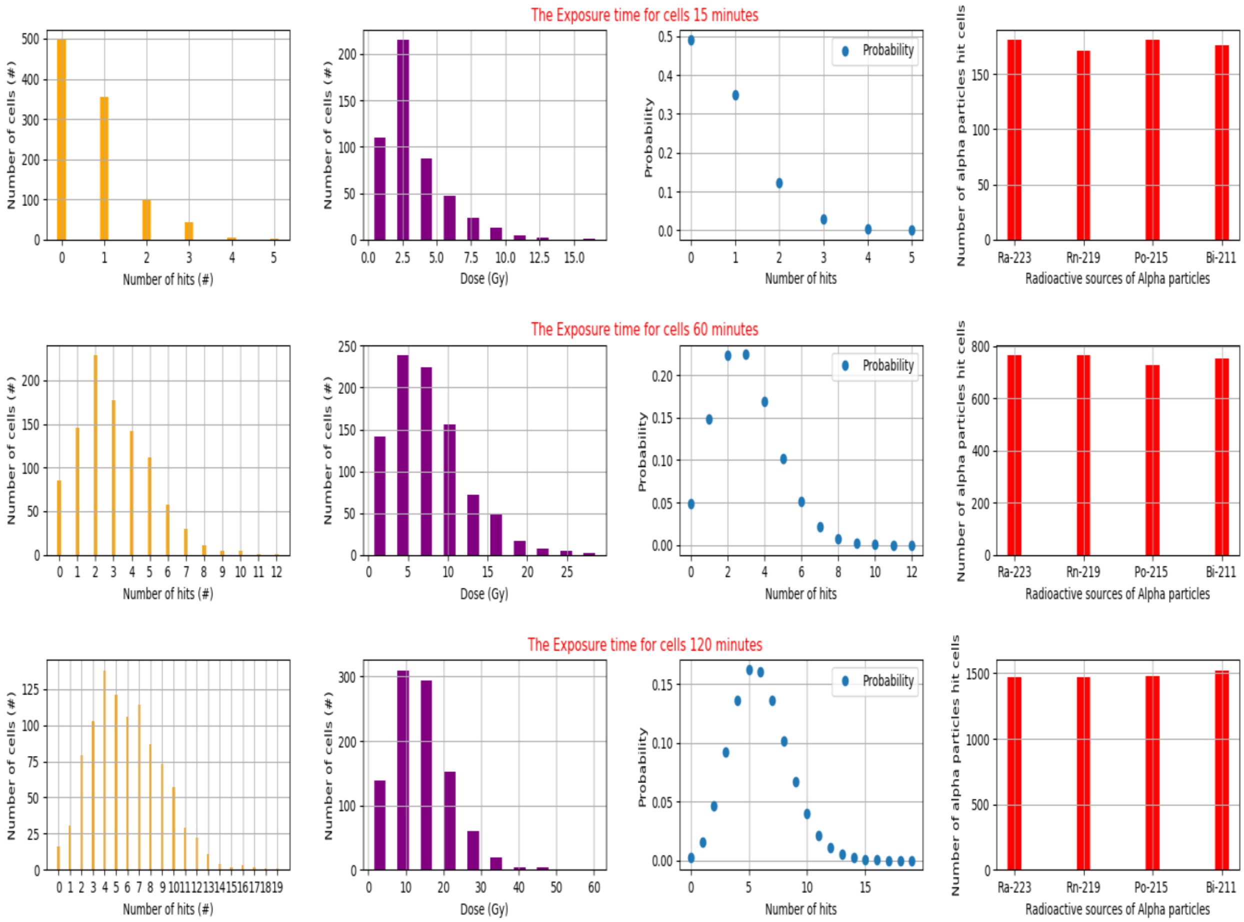

Figure 9: The effect of alpha particles on cells with increased exposure times of the cells sample (15, 60 and 120 minutes. The activity of the radioactive source 5000 Bq and the distance between the source and Trancwell 10 mm

In the experimental techniques, Fricke dosimeter containing SSA was prepared for radiotherapy applications. The PVA solution was cross-linked by glutaraldehyde to make a gelatinous media for ferrous-SSA. Five recipes of SSA-Ferrous-PVA-GTA containing different concentrations of ferrous ions and SSA(see **Table1**) were irradiated using a medical linear accelerator to doses up to 40 Gy (see **Figure 10**) and characterized by optical and NMR techniques. The absorption peaks centered at 502 nm, and increase significantly with increased absorbed dose (see **Figure 11**). Linear dose-response relationships were noticed in the range of 0-40 Gy for all recipes, and the highest dose-response was obtained at 40 mM SSA and 4 mM Fe^{2+} concentration for both readout techniques (see **Figure 12** and **Figure 13**). A small increase in absorbance and R_2 values was observed up to 8 hours after irradiation. After 8 hours of irradiation, it was almost stable up to 60 hours (see **Figure 14**). The absorbance measurement was almost constant with different scanning temperatures (see **Figure 15**). The hydrogel dosimeter performance was found to be independent of dose rate and radiation beam energy (see **Figure 16** and **Figure 17**). On the other hand, the NMR measurement showed an obvious increase in R_2 with decreasing scanning temperature.

Table 1: Concentrations of ingredients used in the SSA-Ferrous-PVA-GTA dosimeters preparation

Gel dosimeter	Distilled Water (mL)	polyvinyl alcohol PVA (%) (w/v)	Ferrous ammonium sulfate FAS (mM)	5-sulfosalicylic acid SSA (mM)	GlutaraldehydeGTA (mM)
Gel 1	95	5	4	20	26.6
Gel 2	95	5	4	40	26.6
Gel 3	95	5	4	60	26.6
Gel 4	95	5	1	40	26.6
Gel 5	95	5	8	40	26.6

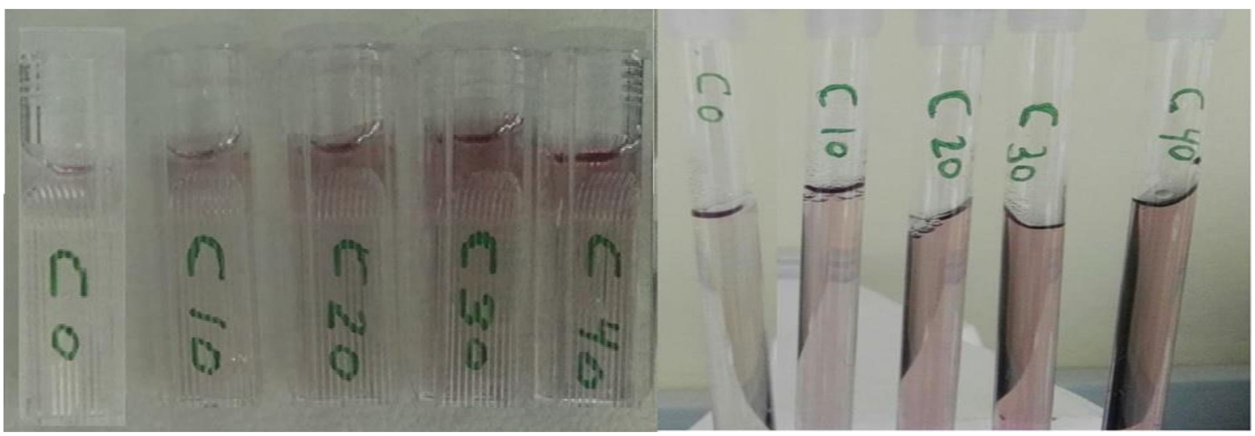

Figure 10: A photograph of the unirradiated and irradiated samples (Cuvettes and NMR Tubes) of the SSA-Ferrous-PVA-GTA dosimeter system (gel 2).

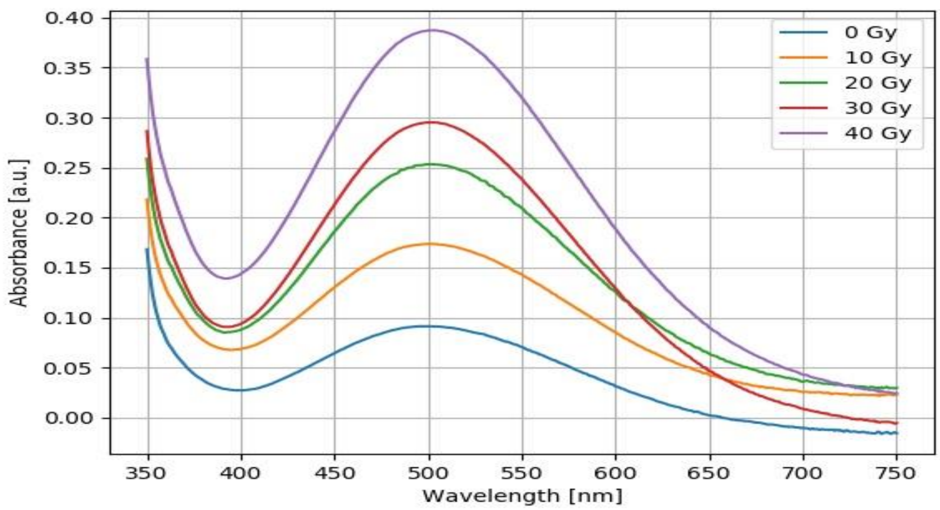

Figure 11: The absorbance change of SSA-Ferrous-PVA-GTA dosimeter as a function of wavelength at different absorbed doses.

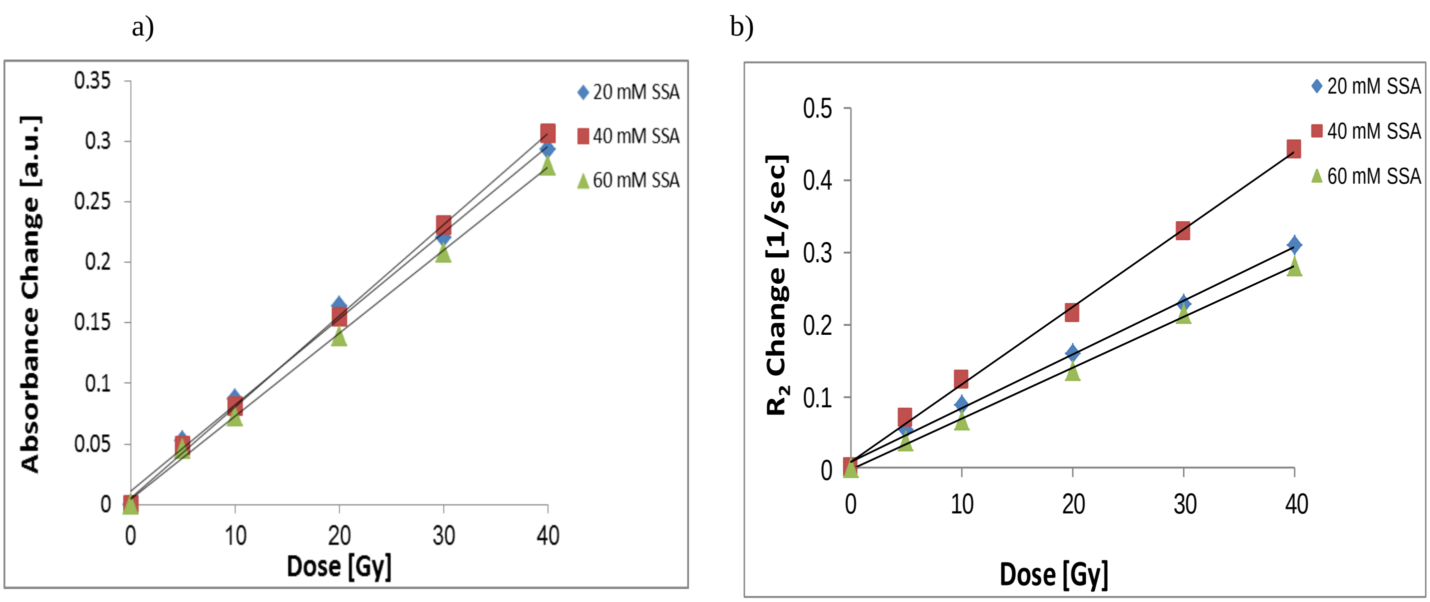

Figure 12: Dose-response curves of SSA-Ferrous-PVA-GTA gel dosimeters at different concentrations of SSA in terms of a) absorbance at 502 nm, and b) proton relaxation rate (R_2).

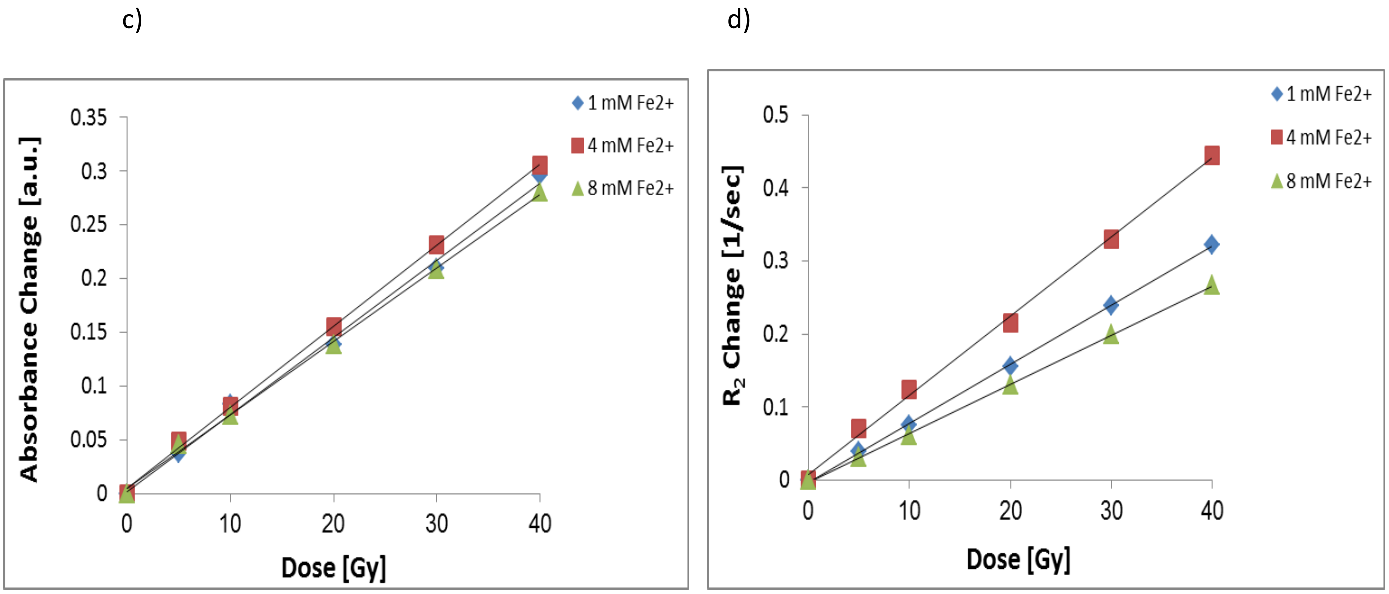

Figure 13: Dose-response curves of SSA-Ferrous-PVA-GTA gel dosimeters at different concentrations of ferrous ammonium sulfate in terms of c) absorbance at 502 nm, and d) proton relaxation rate (R_2).

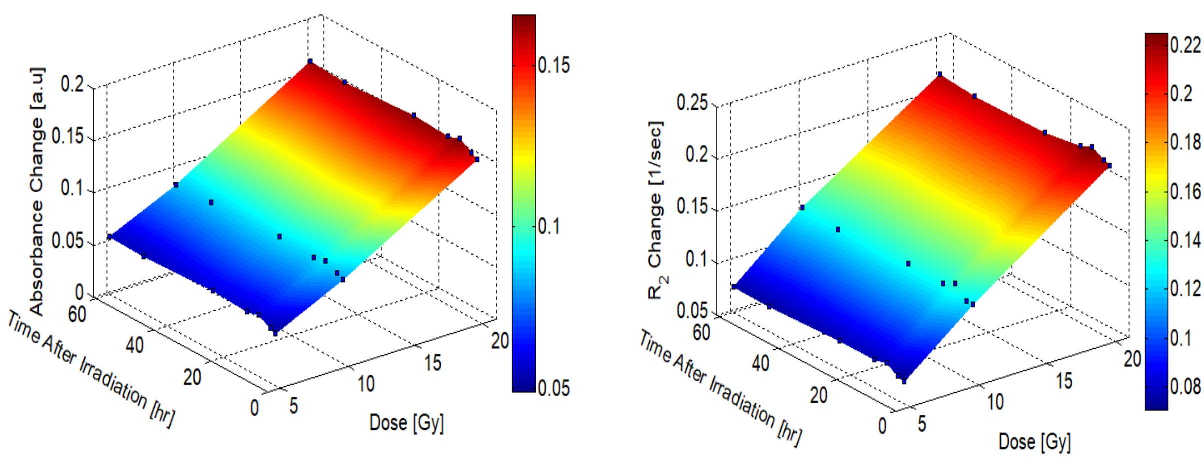

Figure 14: The effect versus time up to 60 hours for irradiated samples of SSA-Ferrous-PVA-GTA gel dosimeter system (gel 2) irradiated with 5, 10, and 20 Gy in terms of a) Absorbance at 502 nm, and b) R_2 measurements.

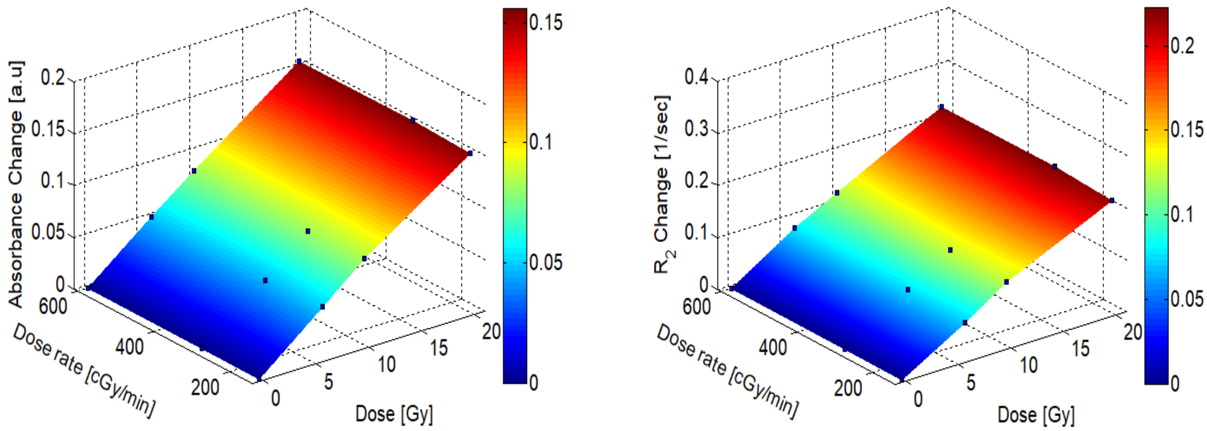

Figure 15: The effect of scanning temperature on SSA-Ferrous-PVA-GTA dosimeter (gel 2) after irradiation to 5, 10, and 20 Gy in terms of a) absorbance at 502 nm, and b) R_2 measurements.

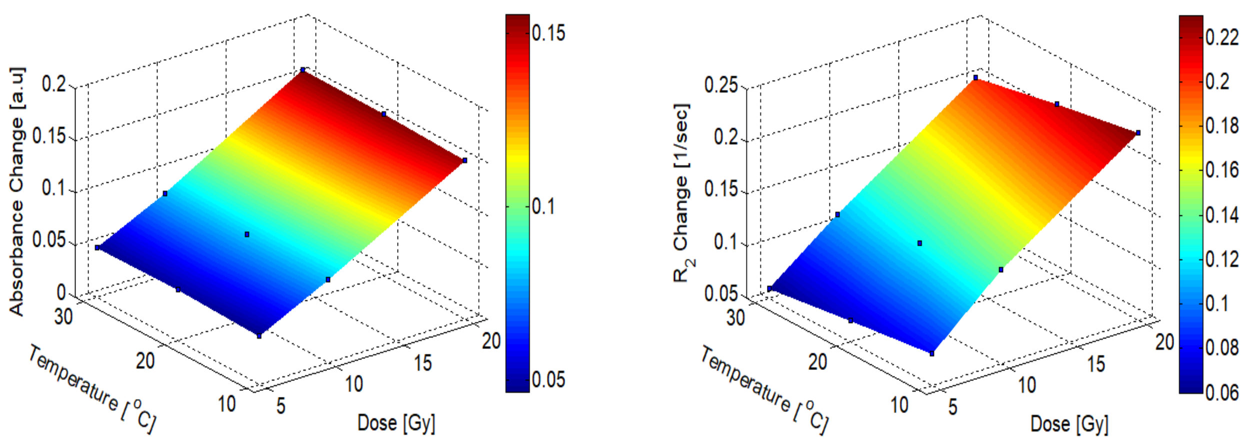

Figure 16: The effect of dose rate on SSA-Ferrous-PVA-GTA dosimeter (gel 2) response after irradiation in terms of a) absorbance at 502 nm, and b) R_2 measurements.

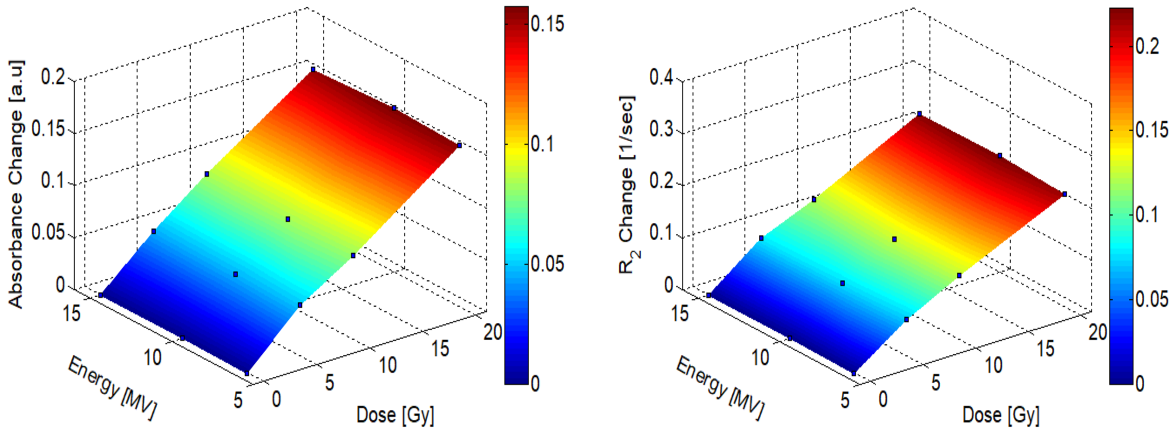

Figure 17: The effect of photon energy on SSA-Ferrous-PVA-GTA dosimeter (gel 2) response after irradiation in terms of a) absorbance change at 502 nm, and b) R_2 measurements.

Publications

- EYADEH, M. M., RABAEH, K. A., **HAILAT, T. F**., AL-SHORMAN, M. Y., ALDWERI, F. M., KANAN, H. M. & AWAD, S. I. 2018a. Investigation of a novel chemically cross-linked fricke-Methylthymol blue-synthetic polymer gel dosimeter with glutaraldehyde cross-linker. *Radiation Measurements*, 118, 77-85.

- EYADEH, M. M., RABAEH, K. A., ALDWERI, F. M., AL-SHORMAN, M. Y., ALHEET, S. M., AWAD, S. I. & **HAILAT, T. F.** 2019. Nuclear magnetic resonance analysis of a chemically cross-linked ferrous–methylthymol blue–polyvinyl alcohol radiochromic gel dosimeter. *Applied Radiation and Isotopes*, 153**,** 108812.

- RABAEH, K. A., **HAILAT, T. F**., EYADEH, M. M., AL-SHORMAN, M. Y., ALDWERI, F. M., ALHEET, S. M., Madas B. G., AWAD, S. I. Magnetic and optical properties of Sulfosalicylic acid-Ferrous-Polyvinyl alcohol- glutaraldehyde hydrogel dosimeters. *Radiation Physics and Chemistry* **(Submitted)**

- characterization of ferrous Dimethyl sulfoxide (DMSO) gel dosimeters using NMR and UV-Vis spectroscopy techniques **(unpublished)**

Studies in current semester

- Systems biology: quantitative analysis of intracellular signal transduction networks (FIZ/3/055E) – Dr. Czirók András
- Nuclear Environmental Protection (KÖR-2/2, 3/20) – Dr. Homonnay Zoltán
- Guided research work (FIZ/KUT-S4)

Conference participations during the doctoral studies

1- I contributed in **Two Oral Presentations** at the Seventh International Conference on Radiation in Various Fields of Research (RAD 2019) about radiation measurements at the Hunguest Hotel Sun Resort, Herceg Novi, Montenegro in the period from June10 to June 14, 2019.
   - The first abstract entitled: "Computational cell dosimetry for alpha-particle exposure by Monte-Carlo methods". **Tariq F. Hailat**, Emese Drozsdik, Balázs G. Madas.
   - The second abstract entitled: "Dosimetric characterization Methylthymol blue Fricke gel dosimeters using nuclear magnetic resonance and optical techniques". **Tariq F. Hailat**, Molham M. Eyadeh, Khalid A. Rabaeh, Balázs G. Madas, Feras M. Aldweri.

2- Hailat TF, Al-Bataina B, Madas BG *Measurement of radon and thoron concentration levels in Disi soil (in Jordan) using CR-39 detector* International Conference on Radiation Applications. 16-19 September, 2019 Belgrade, Serbia, p. 35. (**Oral presentation**)

Activities

- *Workshop(s):*

  1- On Thursday, September 27. I attended some events were held by the European Radiation Dosimetry Group (EURADOS) in MTA EK – Budapest.
   - PROCORAD – The Association for the Promotion of Quality Control in Radiotoxicological Analysis which was introduced by C. Guichet (CEA, France)
   - Internal Microdosimetry which was introduced by W. Hofmann (Univ. Salzburg, Austria) and W.Li (HMGU. Germany).

- *School(s):*
   - I attended **the XVI Seminar on Software for Nuclear, Sub nuclear and Applied Physics** in Hotel Porto Conte, Alghero, Italy, in the period from May 26 to May 31, 2019. This seminar was very useful and interesting as it contained and included the following full subjects: introduction to Python, Introduction to Machine Learning, introduction to Geant4 and Monte Carlo methods and practical exercises about geant4 and practical Sessions on Kernel.

- *Grant(s):*
   - I got a grant to attend **"XVI Seminar on Software for Nuclear, Subnuclear and Applied Physics"** in Hotel Porto Conte, Alghero, Italy, in the period from May 26 to May 31, 2019. This grant included the registration fee of the seminar.