

Microdosimetry of kidney cells exposed to ^{243}Am and X-ray irradiation

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Abstract—*In vitro* experiments with rat kidney cells exposed to ^{243}Am in cell culture medium show a decreasing cell viability with increasing americium concentration. Both the chemical cytotoxicity of americium and the dose caused by ionizing radiation have to be considered as possible causes. To determine the dose rate, a model which was reduced to the dosimetric relevant circumstances was set up. Since the size of the cells is in the micrometer range α -radiation makes the biggest contribution to the dose rate. Using the characteristic behaviour of α -particles the dose rate can be calculated from fluence and stopping power. Biological aspects like uptake of Americium into the cells as well as inaccuracies arising from inhomogeneity and dynamic behaviour in biological systems were taken into account. The dose rate was considered pointwise in the cell center and averaged over the whole cell. Calculations show that dose rates up to the Gy/h range were achieved at the highest americium concentrations of $8 \cdot 10^{-4}$ M. For an experimental comparison of the effect in dependence of the dose reference samples of untreated kidney cells were exposed to analog doses in an X-ray field. Taking relative biological effectiveness into account the cell viability curves depending on the dose show good agreement.

Keywords —Microdosimetry, Relative Biological Effectiveness

I. INTRODUCTION

In the fuel cycle of nuclear power plants various heavy nuclides are produced and can be released into the environment. Therefore the impact on living systems is of particular interest for research. This work focuses on experiments with rat kidney cells exposed to ^{243}Am . With increasing ^{243}Am concentration the cells show, among others, decreasing viability [1]. Since ^{243}Am is radioactive, the following analysis examines if dose caused by ionizing radiation has to be considered as an influencing parameter on the cell viability.

^{243}Am decays by emitting α -particles with a range of 40 μm in water. The size of the cells is also in the μm range, therefore α -particles deposit a significant amount of their energy in the cells. α -decay transfers about 5 MeV to the α -particles, which is considerably more than usually emitted by γ - and β -conversion. Furthermore the range of beta- and low energy gamma-radiation is in the range of millimeters, which means the transferred proportion of the total energy to the cells is much lower than for α -particles.

Therefore it is expected, that the dose caused by β -, and γ -radiation is negligible compared to the dose caused by α -

particles. But the dose caused by α -particles may have impact on the cell viability. In the following the dose caused by a ^{243}Am solution covering the cells will be determined analytically.

II. METHODS

A. Contribution from α -particles

Kidney cells from rats (NRK-52E) were covered with a solution of ^{243}Am for 24 h (see Fig. 1). Therefore, the activity is distributed homogeneously in the volume above the cells. The experiments were carried out with different concentrations of ^{243}Am ($10^{-6} - 8 \cdot 10^{-4}$ M). Calculations were done with the highest used concentration of $8 \cdot 10^{-4}$ M.

Additionally the cells internalize some amount of ^{243}Am . Inside the cells, the concentration of ^{243}Am and consequently the activity per volume amounts 0.5 % to 1 % of the applied concentration respectively the activity outside the cells. The percentage of the uptake depends on the concentration of ^{243}Am outside the cells. [1]

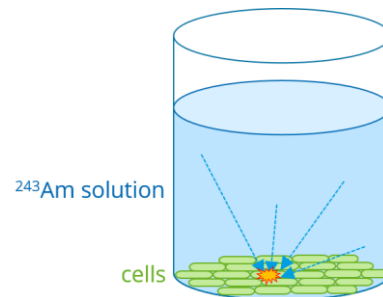


Fig. 1. Experimental setup.

^{243}Am decays to ^{239}Np by emitting α -particles with energies between 5.2 MeV and 5.3 MeV. Since α -particles move nearly in a straight line and every point of their path is clearly assigned to a stopping power value, the mean imparted energy per mass (dose) can be calculated for a certain point in the cells. For this purpose, a model was created taking only the dosimetric relevant aspects into account. A two-dimensional view of this model is given in Fig. 2.

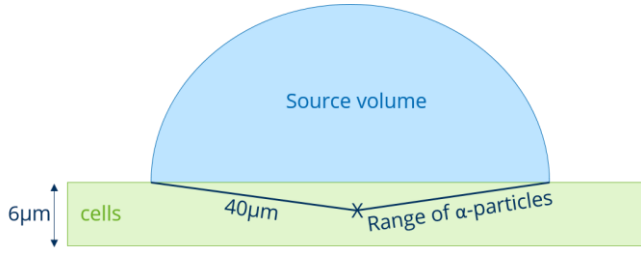


Fig. 2. Microdosimetric model for in vitro experiments.

In the experiment, the cells form a monolayer (see Fig. 4a). Because of that, from the dosimetric point of view, they are a continuous layer and the width of the cells is not relevant. ^{243}Am and, thus, also the activity is homogeneously distributed in a solution above the cells. Since the dose is considered for one point inside the cells and α -particles have a clearly defined range, only those α -particles which originate within a fixed radius around this point are relevant. Consequently, a hemisphere above the point of interest is considered. The dose caused by α -particles can be calculated by the following formula:

$$D(r) = \frac{1}{V_{\text{source}}} \int \Phi(r) \cdot \frac{S}{\rho}(E(r)) dV_{\text{source}}$$

with dose D , particlefluence Φ , mass collision stopping power $\frac{S}{\rho}$ and source volume V_{source} . Dose is the mean energy dE imparted by ionizing radiation to matter of mass dm :

$$D = \frac{dE}{dm}$$

Fluence is the number of particles dN incident on a sphere of cross-sectional area dA :

$$\Phi = \frac{dN}{dA}$$

Collision stopping power describes the average energy loss dE of charged particles due to inelastic collisions per path length dx :

$$\frac{S}{\rho} = \frac{1}{\rho} \frac{dE}{dx}$$

Fluence can be calculated from the concentration of ^{243}Am in the solution and its half-life.

Stopping power in dependence on the distance of the particles from the origin were taken from the NIST astar database [2]. It is assumed that the stopping power in the cells is equal to the stopping power in water. This approximation is very close to reality and simplifies the model considerably.

The α -particles originate both from the cell culture medium above the cells (extracellular) and from the uptake of ^{243}Am inside the cells (intracellular).

In the following, the calculation of the dose will be described starting with the dose from extracellular α -radiation.

Since the activity is homogeneously distributed along the radius of the source volume, the stopping power is integrated over the path of the α -particles. The lower integration limit corresponds to the inner border of the extracellular source volume.

Consequently, the lower integration limit depends on the polar angle. The maximum range of the α -particles defines the upper integration limit.

Next, integration is carried out over the polar angle. The integration limits depend on the height of the cells.

To cover all dimensions of the source volume, integration has to be carried out over the azimuthal angle from 0 to 2π as well. Expressed in spheric coordinates and with integration limits the formula is:

$$\dot{D} = \frac{1}{V_{\text{source}}} \int_0^{2\pi} \int_0^{\theta} \int_{R_0(\theta)}^R \frac{Af_{\alpha} S}{4\pi r^2 \rho}(E(r)) r^2 \sin \theta dr d\theta d\varphi$$

The calculation of the intracellular dose is analog to the calculation of the extracellular dose. However the integration limits in the radial dimension have to be changed.

The upper integration limit corresponds to the lower integration limit from the extracellular calculation and the lower integration limit is set to 0.

Moreover, for the dose from intracellular α -radiation, the particles which originate from the sides of the point under consideration, must be taken into account. In this area, the stopping power is integrated radially over the entire range of the α -particles, because they can originate from every point within the maximum range.

B. Contribution from photons and electrons

Due to the small scale of the model (3 mm filling height of the cell culture well), γ -radiation (44 keV - 334 keV) is not expected to make a single interaction, because the mean free path is between 4 cm and 8 cm.

X-rays are emitted with 12 keV – 23 keV in this decay chain. Their mean free path amounts 3 mm to 1.7 cm. Consequently an interaction with the cells can happen. Nevertheless the kinetic energy of the X-rays is less than 0.5 % of the α -energies. Electrons are emitted by the daughter nucleus ^{239}Np with 341 keV respectively 438 keV maximum β -energy. The corresponding maximum range is 1.4 mm in water. Therefore the stopping power of electrons is much lower than the stopping power of α -particles.

For these reasons β - and γ -radiation is neglected in this consideration.

III. RESULTS

A. Dose rate

The results of the calculations are given in Tab. 1.

Tab. 1: Radiation contributions to the dose rate at the cell center

Origin of radiation	Dose rate in Gy/h
extracellular α -radiation ($8 \cdot 10^{-4} \text{ M } ^{243}\text{Am}$)	1.70
intracellular α -radiation (estimated uptake: $3.5 \cdot 10^{-6} \text{ M } ^{243}\text{Am}$)	0.003

Values were not only calculated for the center of the cells (results in Tab. 1), but also for different points distributed over the cell thickness. The average of them is 1.75 Gy/h at the highest ^{243}Am concentration of $8 \cdot 10^{-4} \text{ M}$.

The contribution of intracellular α -radiation to the total dose is very small compared to extracellular α -radiation. On the one hand only 0.5 % to 1 % of the ^{243}Am applied is accumulated inside the cells. On the other hand, within the range of the α -particles, the volume inside the cells is very small compared to the hemispheric volume above the cells.

B. Inaccuracy from varying size of the cells

A crucial parameter for the dose rate at the center of the cells is the height of the cells. Fig. 3 shows the dependence of the dose rate to the height of the cells. With increasing height of the cells the extracellular contribution decreases while the intracellular contribution increases. That is because with increasing cell volume there is less extracellular volume from where α -particles can reach the cells. But concurrently, there is more intracellular volume from where α -particles can originate. Before irradiation, the cells have a height of $6\ \mu\text{m}$. Because of the cells being stressed upon exposure to ^{243}Am , they swell to approximately twice their size (see Fig.4). In consequence the total dose rate decreases during exposure. Since the exact time course of the swelling is not known, inaccuracies arise in the analysis. To estimate the impact of swelling on the dose rate, it was assumed, that the height of the cells increases linear with time. Under this assumption the mean dose rate of 24 h exposure time is $1.54\ \text{Gy/h}$ at the highest ^{243}Am concentration of $8 \cdot 10^{-4}\ \text{M}$.

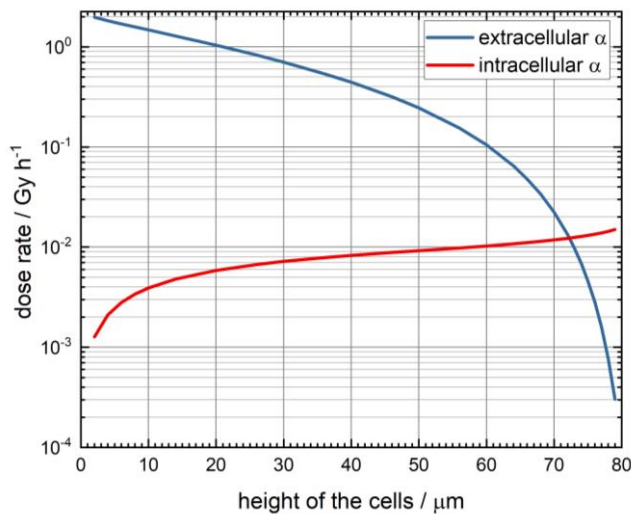


Fig. 3. Influence of the cell height on the dose rate.

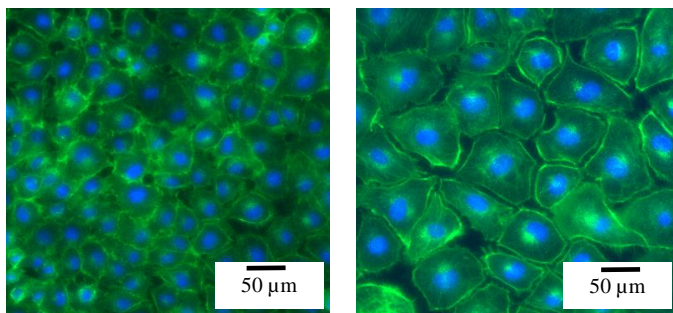


Fig. 4. Untreated cells (a) and cells treated with $300\ \mu\text{M}\ ^{243}\text{Am}$ (b).

C. Reference irradiations with X-ray

To compare if the effect fits to the determined dose, reference samples of untreated kidney cells were exposed to analog doses in an X-ray operated with 50 kV and 50 mA. Dose in the X-ray field was measured by tissue equivalent dosimeters, which use optical stimulated luminescence of Berylliumoxide.

For the comparison of damage caused by different kinds of radiation Relative Biological Effectiveness (RBE) has to be taken into account. The RBE model says that different kinds of radiation need a different amount of dose to cause the same effect. The difference is described by the RBE-factor.

$$D_{\text{X-ray}} = D_{\alpha} \cdot \text{RBE} \rightarrow \text{same effect}$$

Fig. 5 shows the results of the irradiation experiments. For both treatments cell viability decreases with increasing dose. By applying two x-axis, one for each kind of radiation, the data points can be moved to the same effect to read out the RBE factor.

The viability measurements of the cells treated with α -radiation are shown in red, as well as the corresponding x-axis (dose) at the top of the diagram. In blue, the results and the corresponding x-axis of the cells treated with X-rays are shown. Within the uncertainties the measurement points show the same effect at a RBE-factor of about 2.3.

The RBE depends on various parameters like the endpoint of the measurement, the cell line or the Linear Energy Transfer. Consequently, experiments with mixed α -energies, like in this case, are not comparable to experiments in a helium beam.

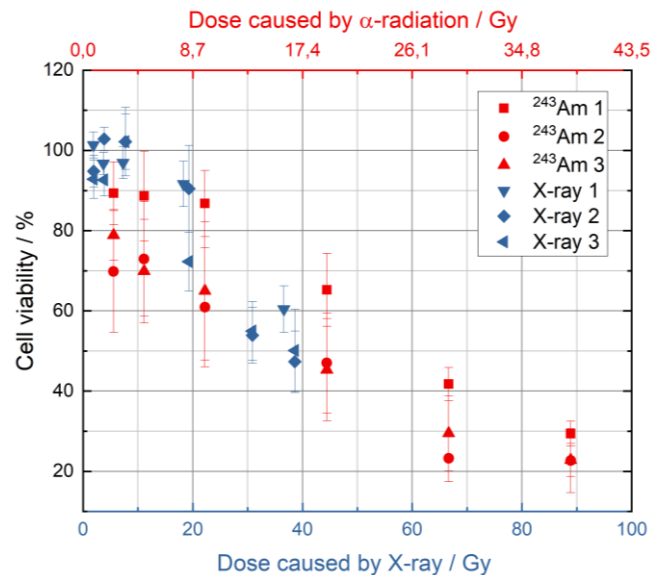


Fig. 5. Viability of cells treated with α -radiation (red) and X-rays (blue) in dependence of the applied dose.

IV. CONCLUSIONS

The complex system of cells in a radioactive solution was simplified to the dosimetrically relevant circumstances.

Using this model, it is possible to calculate the dose rate caused by α -particles at certain points by looking at fluence and stopping power. This analytical method is faster and easier to handle compared to a detailed simulation.

The result of the analysis is 1.70 Gy/h in the center of the cell. Alpha-radiation from inside the cells contribute 0.003 Gy/h. Averaged over the whole cell the dose rate amounts 1.75 Gy/h. The only dosimetric relevant parameter with a non-negligible inaccuracy is the height of the cells. Since the cells are swelling to approximately twice their size while irradiation, the average dose rate is about 1.5 Gy/h.

After 24 h exposure time, dose rates in the Gy/h range are likely to cause a decrease in cell viability, as it was observed in the experiments.

To compare the calculation to an experiment with known dose rate, the cells were irradiated with X-ray. In comparison to the irradiation with ^{243}Am , the results are in good agreement with the RBE model. With X-rays, about 2.3 times the dose was necessary to cause the same effect as with the ^{243}Am -solution. It has to be mentioned that RBE values are difficult to compare because they depend on many different parameters in the experiment. Furthermore, the inaccuracy of the viability measurements influence the accuracy of the determined RBE value.

The measurements with X-rays demonstrated that the calculated dose rate is in the right order of magnitude. To proof the accuracy of the calculation, further experiments with exact known dose rates under the same circumstances as in the corresponding model would be necessary. The calculation would also be applicable to other orders of magnitude.

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