Towards radiobiological experiments at ELI-NP facility: the first trials at 100 TW and 1 PW

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Team

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- **Department of Life and Environmental Sciences:** R. Popescu
- **IRASM :** D. Neguț

3. AccentPro 2000 S.R.L.

- M. Iovea, E. Hermann, M. Mirea, M. Neagu, L. Niță

Fig. 1 A snapshot before the last LASER shots in the 100 TW experimental area, February 14, 2023 [*Courtesy G. Bleotu*]

Context for conducting radiobiology experiments at ELI-NP

100 TW experimental area - UPM28 beamtime

„LASER-driven Gamma Imaging studies and experiments for applications development"

PI - Mihai IOVEA - AccentPro 2000 S.R.L.
CoPI - Ovidiu TESILEANU, Liviu NEAGU - ELI-NP

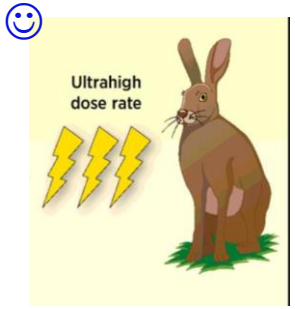
1 PW experimental area - Nucleu Phase 1 beamtime

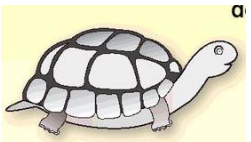
„Improvement of the characteristics of the Bremsstrahlung gamma sources based on laser-accelerated electrons for biomedical and imaging applications"

PI - Ovidiu TESILEANU

Early prediction of radiation effects

FLASH radiation ☺





LATE assessment of effects ☹

Radiotherapy AIM: EFFICIENCY: cancer cells destroying & LACK OF TOXICITY: while sparing the healthy cells.

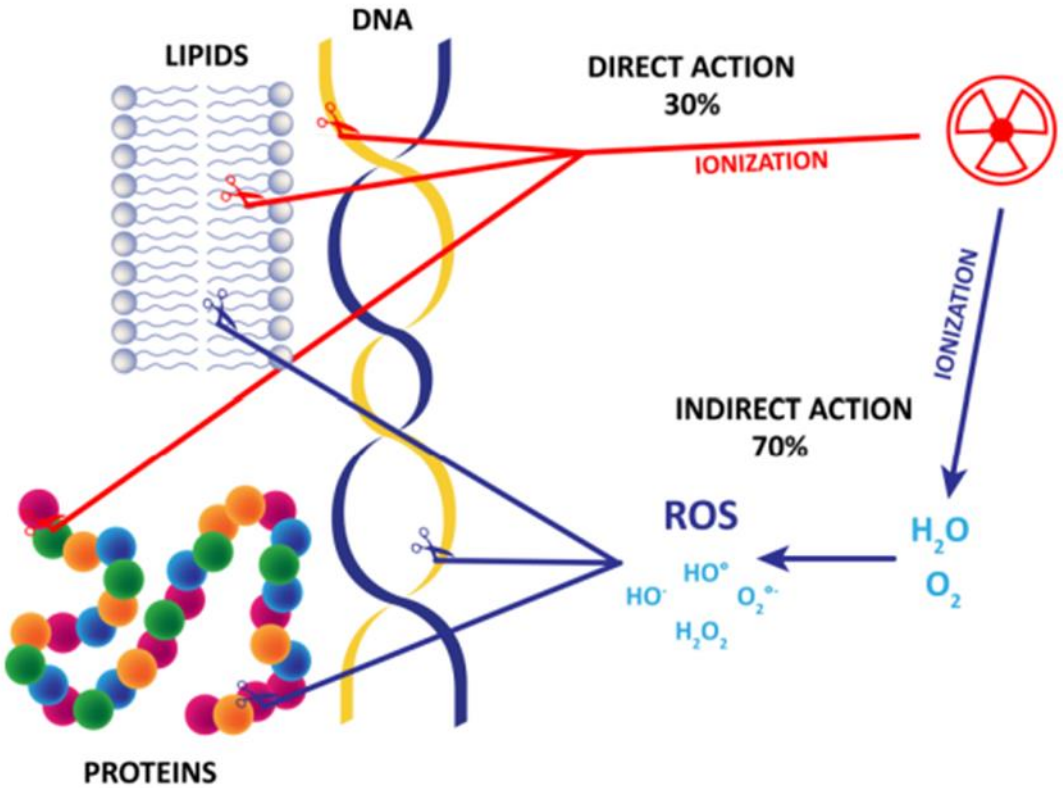


Fig. 2 Interaction between ionizing radiation and cellular systems (ROS – Reactive Oxygen Species)
[*P. Montay-Gruel 2018*]

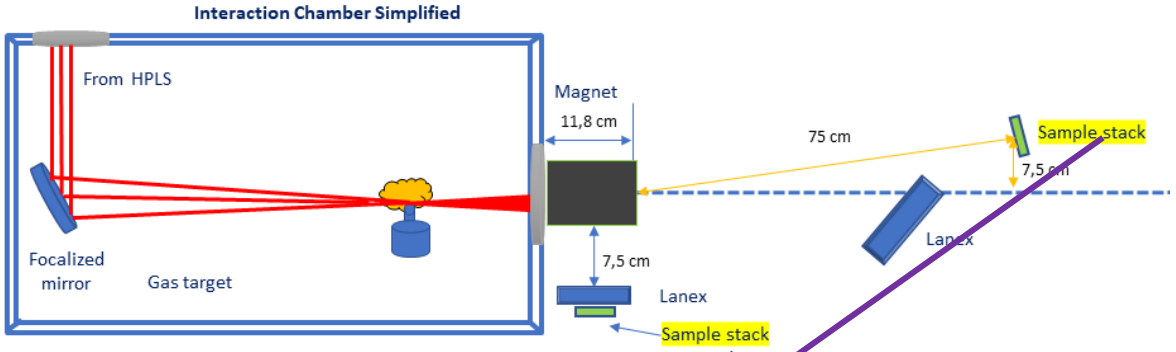
Fig. 3 The steps of cellular degradation at the interaction with ionizing radiation (OH – hydroxyl radical, GSH – Glutathione, Cho – Choline, Lac – Lactate)
[*Fidel I. et al, paper submmited, Asavei T. et al., Med. Phys. 2019*]

E4 - 100 TW Experimental Setup E5 area - 1 PW

3 configurations for sample placing. Samples - outside the focus. 3 types of cells.

Samples were in the focus. Only Microglia was used.

Fig. 4 Experimental setup for E4 irradiation



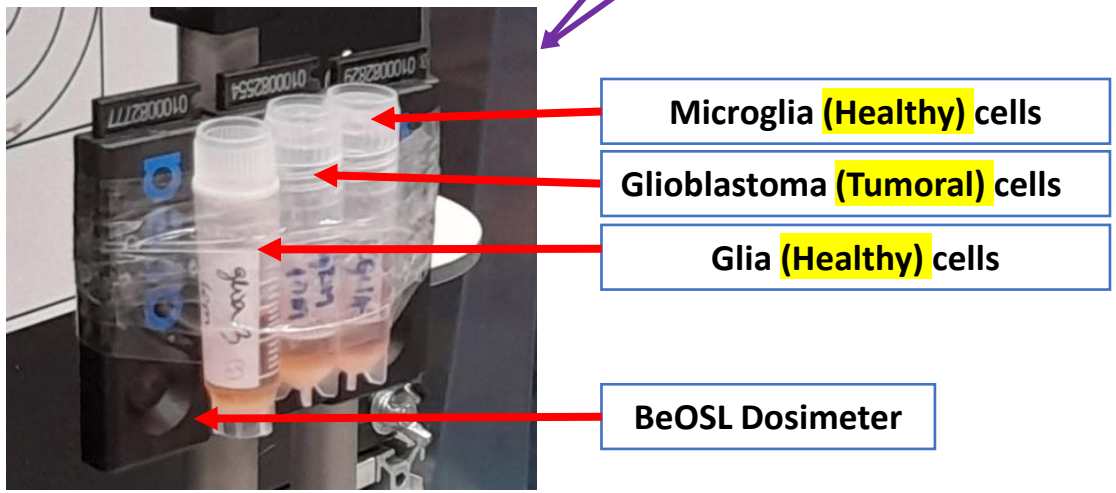
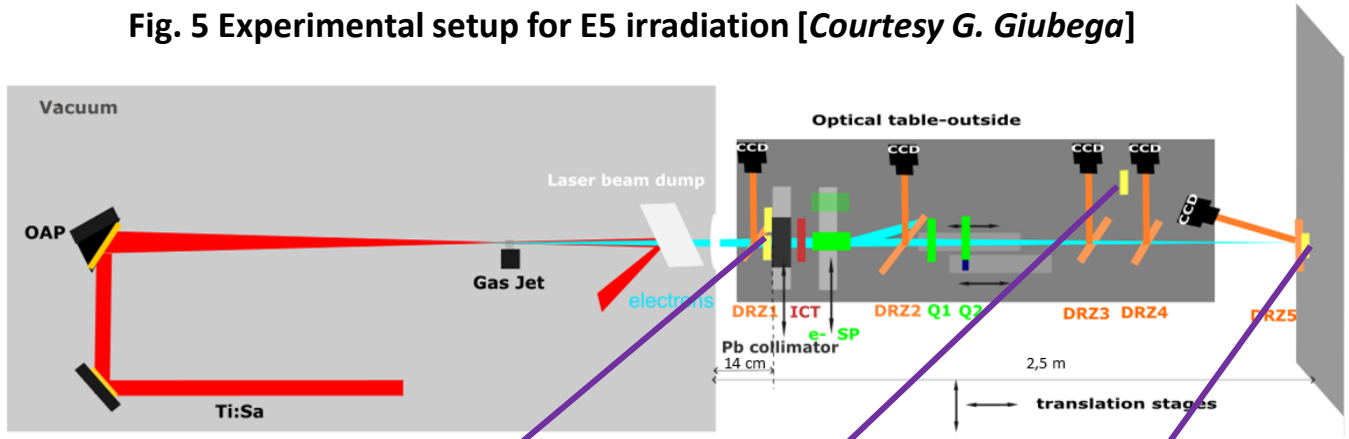


Fig. 6 Biological samples in E4

Fig. 5 Experimental setup for E5 irradiation [*Courtesy G. Giubega*]



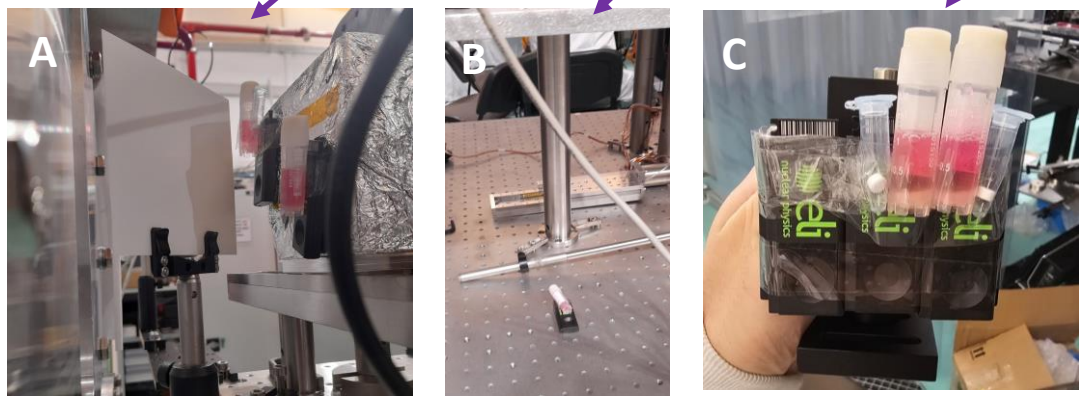


Fig. 7 Biological samples in E5: A) Samples placed on the collimator B) Sample placed on the optical table C) Samples from the beam dump [*Courtesy G. Bleotu*]

Dosimetry results

E4 - 100 TW

Table 1. Results for the E4 experimental area cells irradiation							
Type	**Irrad Time [min]**	**No. Pulses**	**Avg laser pulse energy [J]**	**Dose [mGy] - Glia**	**Dose [mGy] - Glioblastoma**	**Dose [mGy] - Microglia**	**Gas species**
Electrons 1- High Energy	38	16	1,76	0,1	45	-	98% He - 2% N
Electrons 2 - High Energy	62	37	1,76	17	17	32	Ar
Electrons 3 - Low Energy	116	59	1,86	19	14	17	Ar
Gamma	33	22	2,03	37	0,5	0,7	Ar

Shot on demand = different times between the pulses

E4 – 1x10^7 cells / 1 mL of cell culture media

E5 – 2x10^7 cells / 1 mL of cell culture media

E5 area - 1 PW

- Only **Microglia** was irradiated.

Table 2. Results for the E5 experimental area cells irradiation									
Type	**Irrad Time [min]**	**No. Pulses**	**Avg laser pulse energy [J]**	**Sample 1 - near the exit flange**	**Sample 2 - near the exit flange**	**Sample 3 - in the beam dump**	**Sample 4 - in the beam dump**	**Sample 5 - On the optical table**	**Gas species**
Electrons	17	30	30.1	2 Gy	2.5 Gy	9.5 mGy	11.8 mGy	2.3 mGy	98% He - 2% N

BeOSL dosimeter give the - Ambiental equivalent dose – Sv. 13% uncertainty calculated up to 1 Sv. These have not been tested for electrons.

1H NMR spectra assignment

A series of 25 metabolites was identified based on literature and online-available databases (HMDB, BMRB).

Tumoral cells

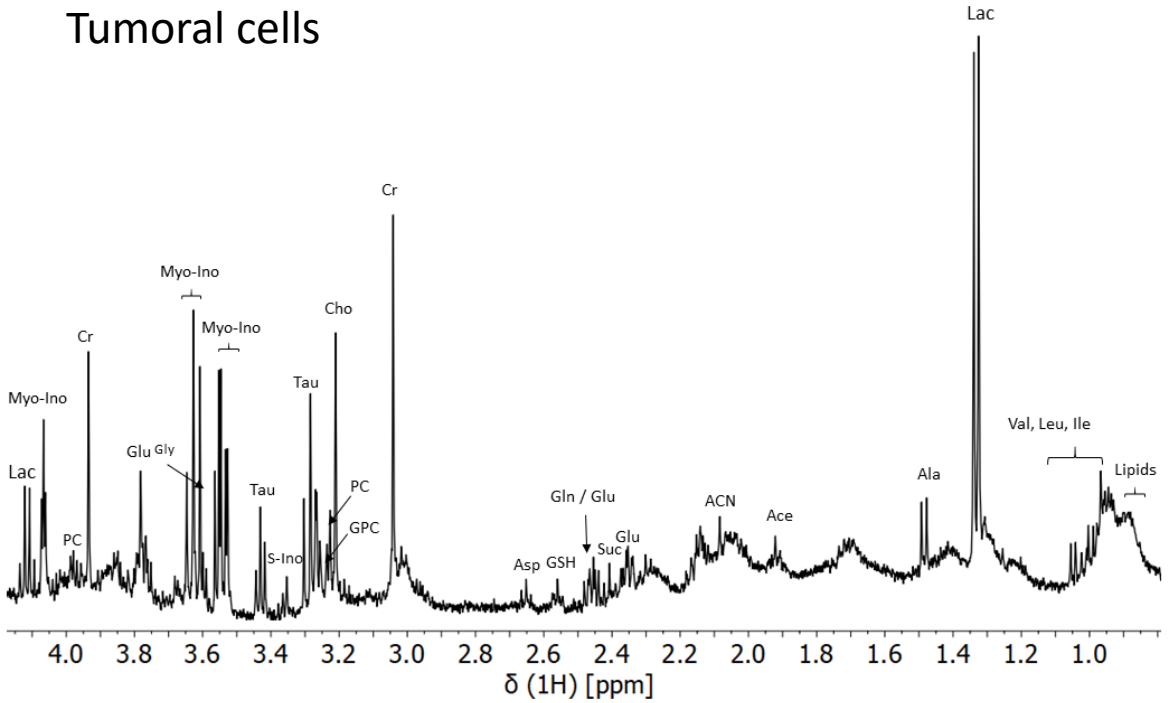


Fig. 8 1 H NMR spectrum for non-irradiated U251 Glioblastoma cell line

Healthy cells

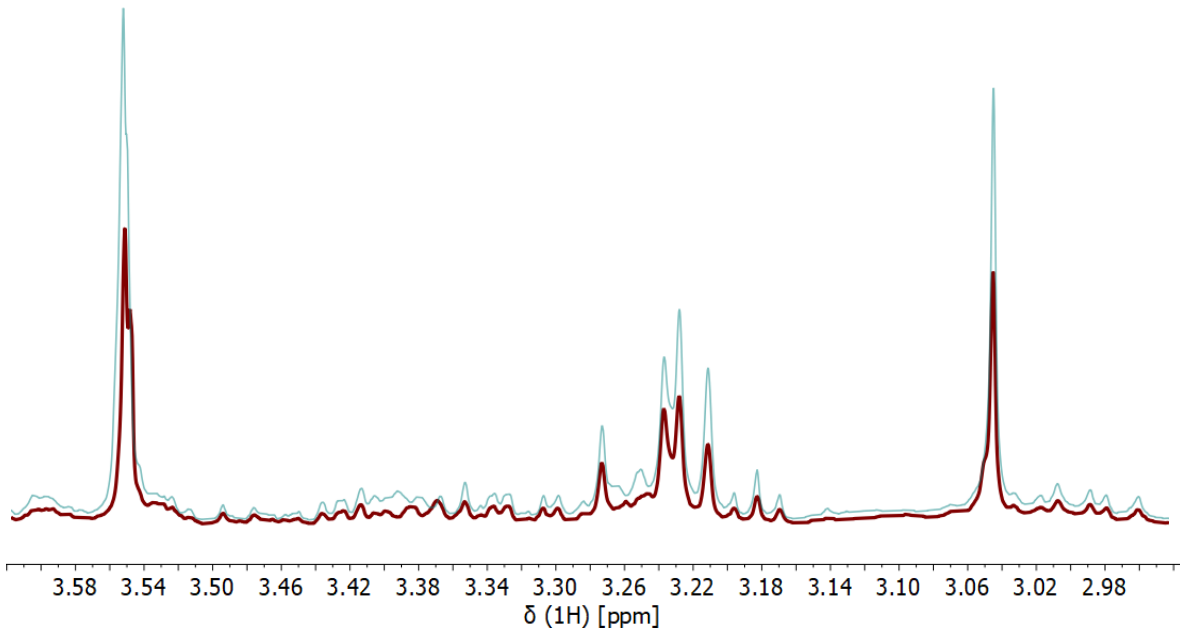
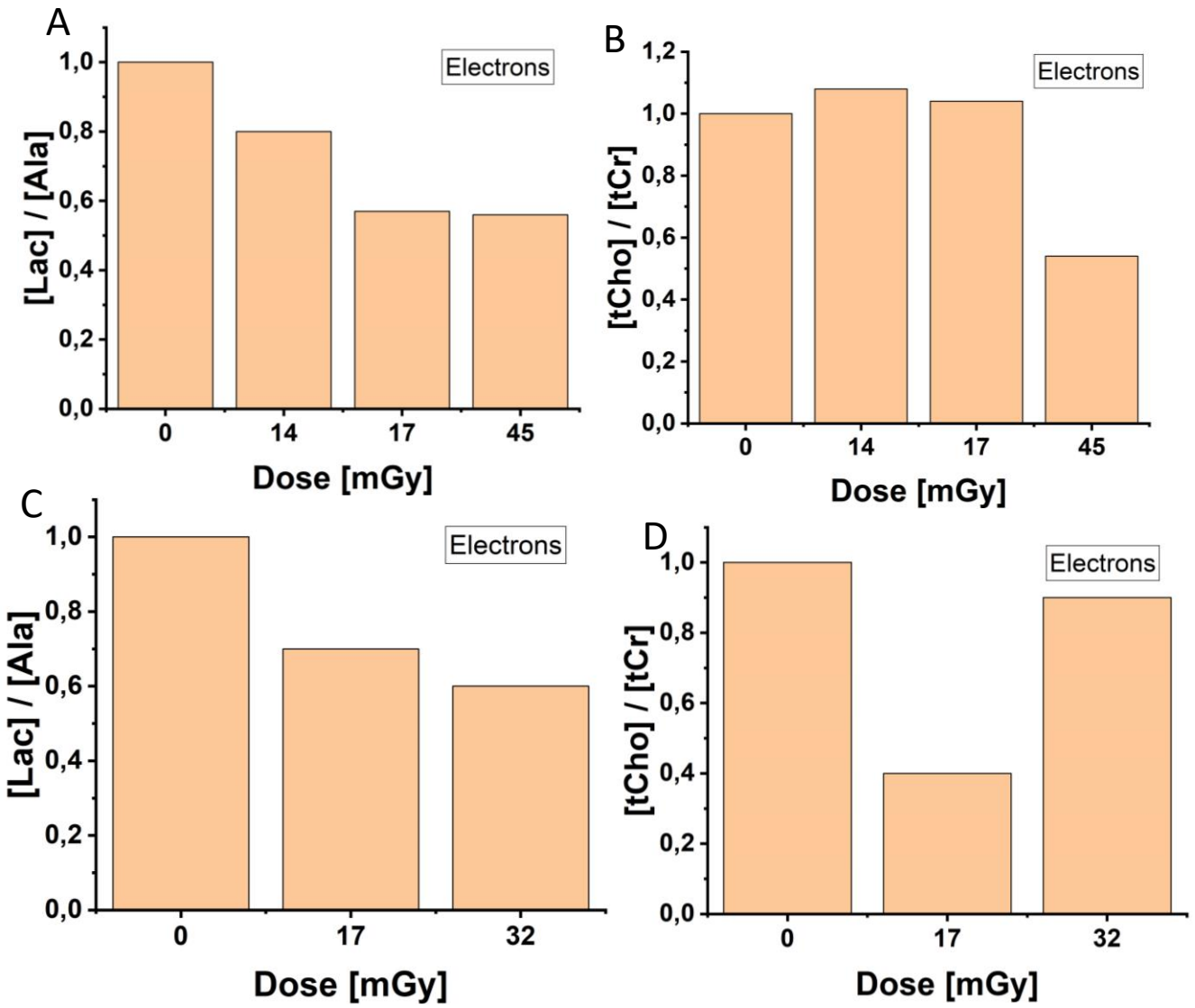


Fig.9 Comparison between non-irradiated (blue) and irradiated (red) with 2.5 Gy for the BV2 Microglia cell line

Ace (Acetate), **Ala** (Alanine), **Asp** (Aspartate), **β-Ala** (Beta-Alanine) **Cho** (Choline), **Cr** (Creatine), **Dmg** (Dimethylglycine), **GSH** (Glutathione), **Gln** (Glutamine), **Glu** (Glutamic acid), **Gly** (Glycine), **GPC** (Glycerophosphocholine) **Ile** (Isoleucine), **Lac** (Lactate), **Leu** (Leucine), **Myo-Ino** (Myo-Inositol), **PC** (Phosphocholine), **PCr** (Phosphocreatine), **PdCho** (Phosphathydylcholine), **Pro** (Proline), **Ser** (Serine), **S-Ino** (Scyllo-Inositol), **Suc** (Succinate), **Tau** (Taurine), **Val** (Valine).

ACN (Acetonitrile) - this appear due to the buffer that we use for preparing the NMR samples.

Effects of radiation as detected by biomarkers - E4 beamtime



- **No samples replicates = no error estimation**

→ Glioblastoma cells (Tumoral)

- Too much time between the laser pulses = time for free radicals to recombine and recovery processes to take place.

→ Microglia cells (Healthy)

- More samples are needed in order to have a conclusion.

Fig. 10 Total Choline to total Creatine ratios and Lactate to Alanine ratio for electron irradiation for Glioblatoma cells (A, B) and Microglia cells (C, D)

Effects of radiation as detected by biomarkers - E5 beamtime

Even though the metabolic ratios were obtained, in order to have a proper evaluation of irradiation effects more samples are needed.

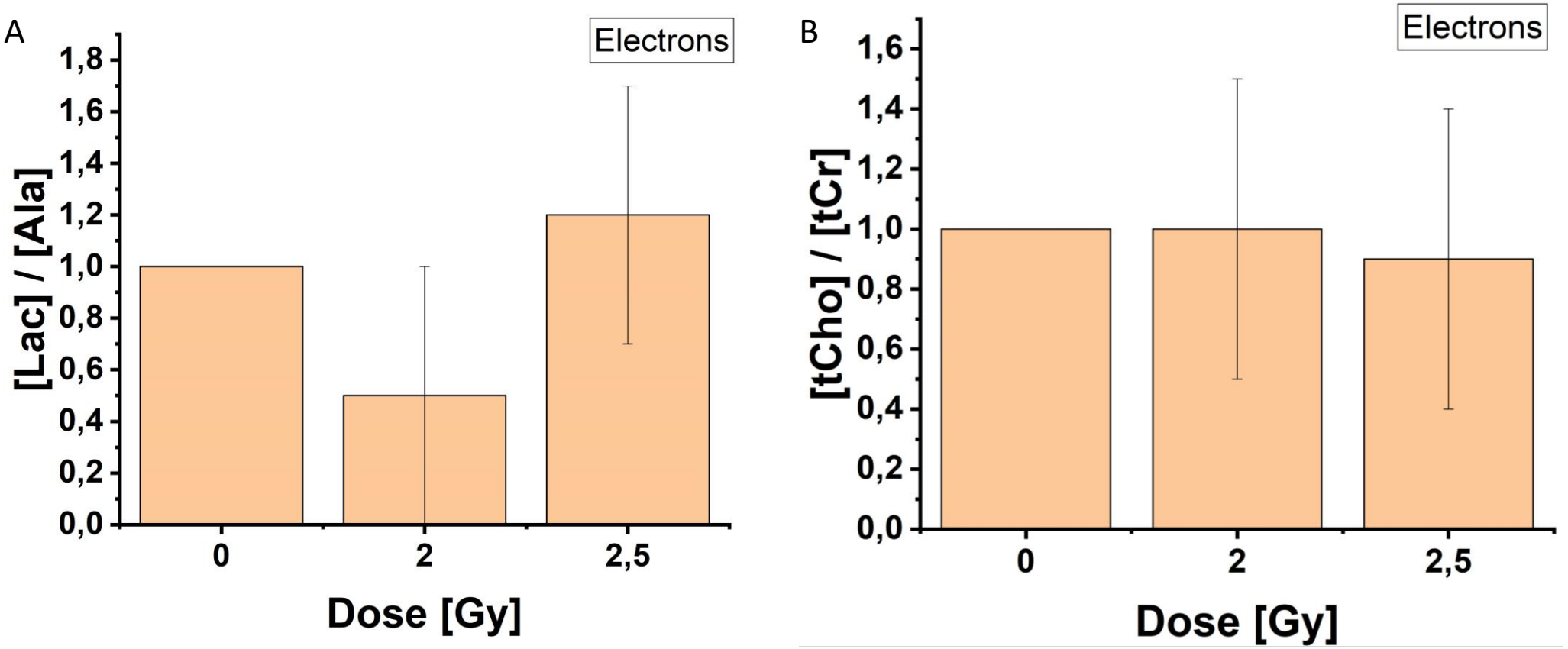


Fig. 11 Lactate to Alanine ratio (A) and total Choline to total Creatine ratios (B) for electron irradiation for Microglia cells

Conclusions

- ✓ **We have established an irradiation setup using secondary radiation (electrons) stemming from the interaction chamber of a 100 TW and 1 PW laser operating in pulses delivered onto a gas target.**
- ✓ There are no replicates, that means we can not have a relevant conclusion about the effects of these irradiations.
- ✓ There are to many parameters that were during these experiments.

What have we learned and how can we improve?

- ➢ **Sample replicates are mandatory.**
- ➢ **Samples should be as near as possible to the exit flange** or put them into **a water phantom** to increase the dose due to the low energy electrons.
- ➢ **Dosimetry improvement:** proper precalibration of the dosimetry systems, the addition of other dosimetry for cross check the measurements;
- ➢ **Viability tests are necessary.**

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Thank you for your attention!