ANEXA 1.A

Call: ELI-RO/RDI/2024 **Project acronym: DRAM**

ELI-NP Thematic:
LDE/IV.4 Radiation detector and instrumentation developments for ELI-NP laser experiments
LDE/III.6 Biological Systems under Irradiation

Annual Summary Document*

Year: 2025

Months: 1 - 12

Project Title: Dose RAte Measurement and identification of biological effects in a Laser-Plasma Accelerator at ELI-NP

Project Work Plan (according to the contract)

Stage: II. 2025

Activities:

II.1 „Water Phantom design, construction and implementation" – WP1

II.1.2 Design and implementation of the detector system through the PMMA plates

II.1.3 Monte Carlo simulations for dosimetry quantities

II.2 „Laser-plasma accelerated VHEE bunch duration measurement" – WP2

II.2.1 Design and construction of the set-up

II.2.2 Pre-alignment and tests

II.3 „Laser-plasma accelerated VHEE bunch duration measurement" – WP3

II.3.1 Set-up preparation for electron acceleration experiment with 100 TW laser in E4

II.3.2 LPA VHEE dosimetry

II.3.3 Dose measurement cross-check by MC simulations for ultra-short electron bunches accelerated at E4

II.3.4 Cell irradiation

II.3.5 Biological analysis of cell irradiation effects

* Please fill in all the required items and do not alter the template

Allocated budget: 2,000,000.00

Realized budget: 2,000,000.00

1. Cover Page (1 page):
   - Group list (physicists, staff, postdocs, students);
   - Specific scientific focus of group (state physics of subfield of focus and group's role);
   - Summary of accomplishments during the reporting period.

2. Scientific accomplishments (max. 3 pages) – Results obtained during the reporting period.

3. Group members (table):
   - List each member, his/her role in project and the Full Time Equivalent (FTE) time in project. The FTE formula to be used is: FTE = Total number of worked hours /Total number of hours per reporting period[†];
   - List PhD/Master students and current position/job in the institution.

4. Deliverables in the last year related to the project:
   - List of papers (journal or conference proceeding);
   - List of talks of group members (title, conference or meeting, date);
   - Other deliverables (patents, books etc.).

5. Further group activities (max. 1 page):
   - Collaborations, education, outreach.
   - ……

6. Financial Report (budget usage) for the reporting period (see the Annex).

7. Research plan and goals for the next year (max. 1 page).

[†] Total number of hours (for a certain period) = 170 average monthly hours x number of months (e.g., for a full year: 170 hours/month x 12 months = 2040 hours)

1. Cover Page (1 page):

- Group list (physicists, staff, postdocs, students);
- Specific scientific focus of group (state physics of subfield of focus and group's role);

The activities of the project were performed by two teams and three groups, organized as follows:
Team 1 – IFIN-HH (ELI-NP subunit)
Group „Experiments”: physicists Georgiana Giubega, Yoshihide Nakamiya, Gabriel Cojocaru, Liviu Neagu, Madalin Rosu, Andrei Berceanu, Vanessa Phung, Ionut Slabu, Iani Mitu, PhD student Mara Popovici, Engineers Antonia Toma, Saidbek Norbaev and Catalin Chiochiu, and Technician Stefan Tazlauanu
Group „Biophysics and biomedical applications”: researchers Paul Vasos, Aude Sadet, and PhD students Ioana Fidel and Silvana Vasilca
Team 2 – University of Bucharest
Group „Biology studies”: Researchers Alexandru Babes, Tudor Selescu and Violeta Caragea, and PhD students Dan Domocos and George Oprita.

- Summary of accomplishments during the reporting period.

The project team has obtained beamtime at the 100TW beamline in E4 for autumn (Nov-Dec) 2025, based on the application submitted in the autumn 2024 call for proposals. Taking advantage of the possibility appeared during 2025 to reschedule the beamtime sooner, and at the 1PW E7 area, we have performed the experiment in Sept-Oct 2025 at E7 (in order to allow us more time for data analysis during the project period).

In preparation of the scheduled beamtime, the water phantom construction has been completed (based on the updated design resulting from Monte Carlo numerical simulations), the DAQ system based on CMOS cameras implemented and tested.

We have also performed a preparatory experiment at a medical electron accelerator in Bucharest, with a prototype phantom segment, for dose calibration purposes and equipment commissioning.

During the beamtime, laser pulses at power level of 200-300TW (energy per pulse of 9-12J) were delivered on a gas jet target, with a supersonic nozzle of 2.5mm diameter, and conditions were optimized for the generation of collimated, intense bunches of accelerated electrons. Irradiation of EBT screens and DRZ scintillator screens at the same time was performed in order to compare the results. Moreover, an ICT (integrated current transformer) was employed for a supplemental reading of the total charge of the accelerated electron bunches. The distribution of radiation was recorded on the screens placed in between the segments of the water phantom. Also, several batches of cells were irradiated with significant total doses and high dose rate. These were then analyzed in the ELI-NP Biophysics laboratory and at the collaborators at the Faculty of Biology, partner institution University of Bucharest.

After the beamtime, we have also taken steps for a calibration of the optical system relaying the light emitted by the scintillator screens to the camera sensor.

We have published partial results related to the electron acceleration in two papers, while two other ones are in preparation, focusing on the numerical simulations (advanced draft) and experiment, respectively.

2. Scientific accomplishments (max. 3 pages) – Results obtained during the reporting period.

The project team members have continued the activities of Monte Carlo numerical simulations, detailing the implementation in FLUKA of the segmented water phantom, including the scintillator screens (see Fig.1). Tests were done with the CMOS cameras and various objective lenses in order to set the optimal configuration for the water phantom readout system.

Several batches of simulations were performed in FLUKA (on the high-performance workstations procured during the previous phase of the project), at different energies of the accelerated electrons (monoenergetic spectra at 50, 100, 150, 200 and 250 MeV, and two spectra obtained in experiments, with peaks at 120 and 160MeV, respectively).

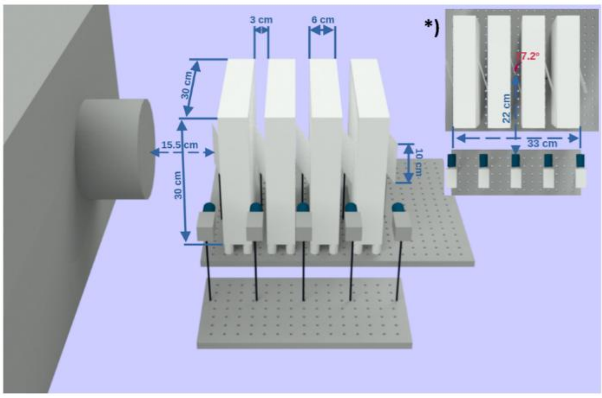

Fig. 1 *Detailed sketch of the segmented water phantom geometry: the entire set-up is placed at 155 mm far from a Mylar exit window, where a first DRZ screen is installed. The screens are monitored with cMOS cameras placed at 220 mm from the center of the screens.*

The results in terms of simulated absorbed dose are presented in Fig. 2, for various electron energies in our range of interest (VHEE) – both monochromatic spectra and two experimentally – recovered spectra (with peaks at 120 and 160MeV, respectively).

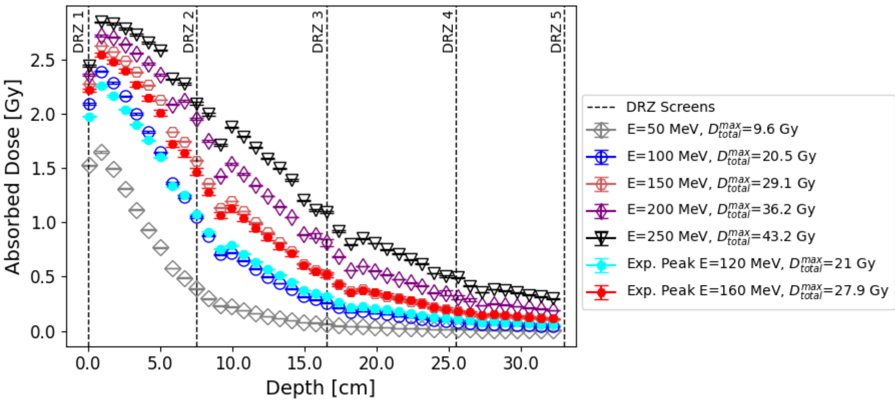

Fig. 2 *Depth-dose distributions along the entire segmented water phantom. Theoretical electron beams are represented by open symbols and experimental beams with full ones.*

A comparison of the total dose absorbed in the phantom volume, between the segmented phantom and a full (contiguous) cubic (300mm edge) water phantom, was also performed, and the results are presented in Table 1 below.

Table 1 Maximum total dose D_{total}^{max} in the entire phantom system at different incident energies

Beam energy [MeV]	D_{total}^{max} **for segmented phantom [Gy]**	D_{total}^{max} **for one-piece phantom [Gy]**
50	9.6	11.5
100	20.5	22.3
150	29.1	30.6
200	36.2	37.7
250	43.2	43.7
exp 120	21	22.6
exp 160	27.9	26.9

In order to validate the simulation results, a smaller, prototype PMMA phantom was tested under 12 MeV electron irradiation at the Coltea Hospital in Bucharest. The phantom consisted in 10 mm thick PMMA walls of surface of (100 x 100) mm^2 and height 60 mm. It was placed at 50 mm distance from a circular 50 mm diameter applicator like in **Fig. 3**. Along the propagation axis, the beam interacts with the following components, in this order: a first *DRZ High*-type screen, a layer of 10 mm thick PMMA, 40 mm air gap (or water), another 10 mm thick PMAA layer and a DRZ screen at the exit from the phantom.

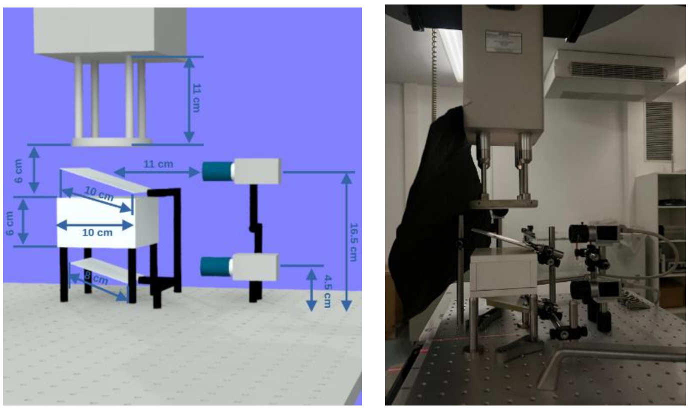

Fig. 3 Set-up for a (100x100) mm^2 and 60 mm height prototype phantom irradiation under 12 MeV electron beam at a Siemens MEVATRON Primus clinical accelerator at “Coltea” Clinical Hospital in Bucharest: sketch (left) and image (right) of the real set-up.

We took advantage of this test experiment in order to calibrate for dose the DRZ (Mitsubishi scintillator screens), in comparison to radiochromic films (Gafchromic EBT3). The irradiation was performed at several incident electron energies, *i.e.* 5, 7, 8, 10 12 MeV, and for each energy several irradiation times corresponding to different doses/MU (monitor unit).

The application for beamtime submitted in autumn 2024 in the joint ELI-NP/ELI-ERIC open call for users was approved and a session of beamtime was allocated for DRAM in September-October 2025 at the E7 experimental area.

The full 4-segment water phantom was constructed for the beamtime, and the data acquisition system was optimized to run all CMOS cameras in parallel. The output window for the accelerated electrons was designed and assembled, featuring a 150μm thick Kapton foil protected by an outer thin layer of carbon fiber.

During the beamtime, we have used a laser energy per pulse of 9-12J (with respect to the maximum of 30J possible on the 1PW beamline) with a pulse duration of 25 fs and a spot dimension at full width half maximum (FWHM) of 18 μm (laser intensity: 7-9x10^{19} W/cm^2), this resulting to be optimal in combination with the 2.5mm diameter supersonic nozzle employed in the experiment. More than 2600 shots were delivered during the experiment, used for the optimization of electron acceleration (obtaining a very good collimation, stability and high charge of the electron bunches), for the timing scan of the electro-optical crystal and for the irradiation of bio cells.

The electro-optical thin crystal (ZnTe, 0.5mm and 0.1mm thickness used in the experiment) was placed perpendicularly on the direction of propagation of the laser beam, few millimeters (variable) downstream with respect to the gas jet and few millimeters off-axis, so that the electron bunch and the laser light do not directly hit the crystal. Birefringence effects are expected due to the THz radiation produced by the relativistic moving charges (accelerated electron bunches). Using a synchronized laser probe beam and cross-polarizers, one can reach a “dark state” in with the visible (light) signal. When the THz-induced birefringence occurs on the EO crystal, this would change the polarization of the probe beam and allow it to “pass” through the analyzer. By varying the delay of the probe beam with very small steps, snapshots as those presented in Fig. 4 can be obtained (from left to right, delays are 0, 20ps, 200ps). (here t = 0 is defined as the first signal visible on the EO crystal due to the birefringence effect on the crystal)

One can see various structures on the EO crystal, such as the thin horizontal line aligned with the laser beam axis, or the three circularly-shaped lines. The project team started analyzing the data, debating the sources for the signals identified on the crystal. The amount of data acquired is large, since we have aimed to characterize the response of the EO crystal depending on several variables, such as the laser pulse energy, the GDD, thickness, timing.

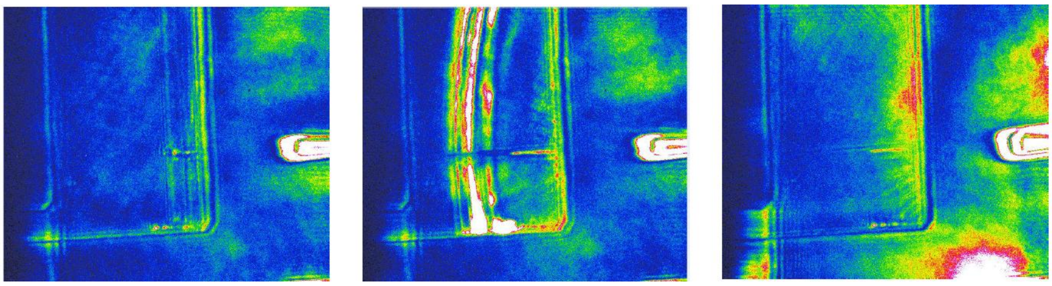

Fig. 4 Images obtained on the EO crystal at t = [0, 20ps, 200ps] (from left to right), where several structures can be identified, such as the plasma channel in the gas target (right side of images), curved THz signals (3 lines), scattering light on the gas nozzle and edge of crystal (especially in the image on the right).

Since the beamtime was allocated in autumn 2025 and ELI-NP did not open for more allocations in spring 2025, the application for a second beamtime during the timeframe of the project was not possible, therefore the team has tackled the irradiation of bio cells, to the maximum extent possible, during the beamtime in September-October.

During this experimental campaign, BV-2 Microglia cells (healthy cells, part of the immune system from the brain) were used as a model to study the biomolecular effects of radiation in cells. The samples were irradiated with electrons and were placed in different positions before, after and between the 4 water phantoms

The cells were maintained in Dulbecco`s Modified Eagle Medium (DMEM) supplemented with 10% Fetal Bovine Serum (FBS) and 0.1% Penicillin-Streptomycin at 37 grade C in a 5% CO2 atmosphere and sub-cultured as often as was necessary. The cells were grown in the Biophysics and Biomedical Application Laboratory (LP47).

Microglia cells grow in an attach layer on the bottom of the Flask. For this experiment, the cells were irradiated in suspension, in cryotubes. Samples preparation implied the removal of cell culture media in which cells grew, after that the cell layer was washed with cold PBS (phosphate buffer saline). To detach them, 1% trypsin in PBS was used, and the flasks were let at room temperature for a few minutes in order for the trypsin to action. The flasks were mechanical actioned and a double quantity of medium was added to stop the trypsin activity. All the cells were collected and they were counted with a Hemocytometer. Each sample was composed from 2xT75 flasks. The cells were centrifuged for 5 min to adjust the cellular media. In the end, the cell pellet was resuspended in 1 mL of fresh DMEM.

During the irradiation 10 samples were placed in the setup in different positions, on two rows along the electron beam. Two controls were placed in the experimental area and two in the Biophysics and Biomedical Application Laboratory.

There were 3 days of irradiation, the samples were irradiated for 30 min each day. In the first day 52 laser pulses reached the samples, on the second day 68 and in the last day 80 pulses. 2 cryotubes with fresh cell culture media were irradiated using 97 pulses in order to check if there are changes between the irradiated media and the one that wasn`t irradiated.

After the irradiation the cells were split in 3 – 4 different samples to check the effects in time after irradiation. The times were 2h, 4h, 8h and 24 h and the cells stayed in Eppendorf tubes in suspension in the incubator until other measurements.

For each time point a specific protocol was applied: an amount of cells were kept for different assays (clonogenic – too see if they will proliferate or not after the irradiation treatment, others for the analysis that was performed by our colleagues from the Faculty of Biology). The other part of the sample was centrifugated, the medium was removed and the cells were washed for 2 times with PBS. The cells were pelleted and frozen at –80 degrees Celsius for further processing.

In the day of the NMR measurements the pellets will be suspended in ice cold acetonitrile: deionized water at 1:1 ratio and homogenized using an ultrasound probe. Lysates will be centrifuged at 4 degrees. The supernatant will be collected and the acetonitrile will be evaporated at 37 degrees. The residue will be resuspended with D2O containing 1 M phosphate buffer with pH=7.

For each sample cell culture media that was used during the irradiation was kept and stored at –80 degrees to perform an metabolomic analysis at the compounds that were realized by the cells in the media during the irradiation.

The UB group was able to quantify the consequences of the irradiation on the BV-2 microglial cell line. This aforementioned cell line is commonly used for the *in vitro* study of microglial properties, mainly regarding their involvement in central nervous system inflammatory processes and neuronal-glial interactions. The cultured cells were treated with various amounts of beamtime with various degrees of intensity. The effects of this treatment were later assessed with calcium microfluorimetry, a technique which allows the measurement of the intracellular calcium alterations in cells. The synthetic fluorophore used was Calcium Green 1-AM, a compound which can absorb light at approximately 500 nm wavelength and emit at 536 nm wavelength. The amount of intracellular calcium in a recorded cell is proportional to the emission intensity, thus making possible the quantification of variations of this ion in different conditions. As ATP can act as an inflammatory intermediary, the microglial cells express various ion channels that can be activated by the molecule, namely P2X4 and P2X7. Our experiments centered around the ATP induced calcium influx and chemically induced calcium release from internal stores (with Tapsigargin - TAP) in BV-2 cells which were pretreated with various amounts of beamtime. Moreover, after the irradiation protocols, cells were kept in normal culture conditions for various amounts of time, namely 24, 120 or 168 hours (see Fig. 5).

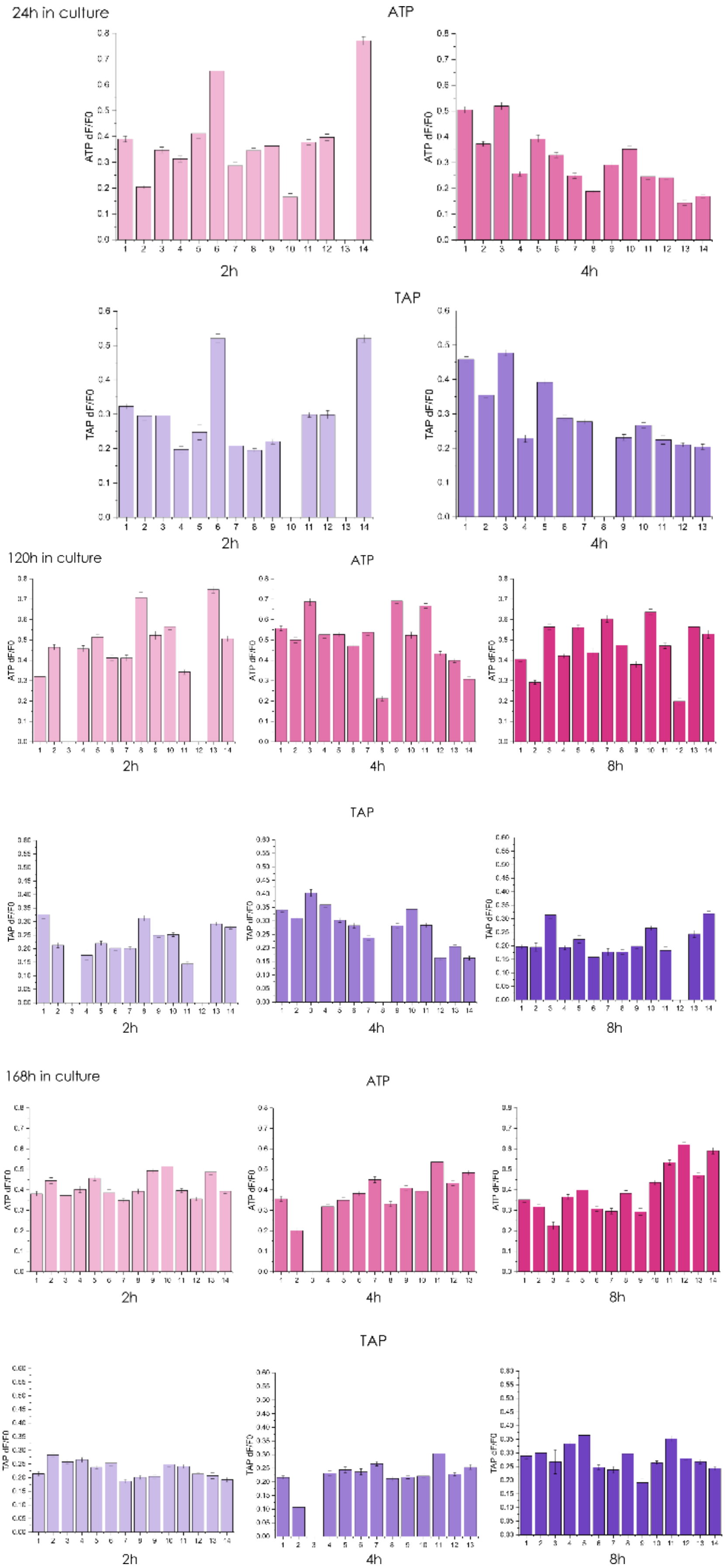

Fig 5: Fluorescence signals generated by the ATP and TAP chemical challenges quantified from BV-2 cells. The X axis represent the amount of irradiation and its duration, while the Y axis reveals the amplitude of the calcium signals

generated by the chemical agonists. After the irradiation protocol, cells were kept in normal culture conditions for 24h (top left), 120h (top right) or 168h (bottom).

Water diffusion measurements based on proton NMR have been recorded on irradiated cells in a magnetic field of 11.4 T or 500 MHz proton Larmor frequency and water signals have been observed to decay with increasing field gradients. Therefore, this constitutes a basis for follow-up measurements comparing metabolite and water diffusion in irradiated and non-irradiated cells.

The data analysis following the experiment is currently ongoing.

3. Group members (table):

- List each member, his/her role in project and the Full Time Equivalent (FTE) time in project. The FTE formula to be used is: FTE = Total number of worked hours /Total number of hours per reporting period[‡];

Name	**Role**	**Total 2025**	
		Hours	**% FTE**
IFIN-HH			
Berceanu Andrei Ciprian	TM / ME	620	0.313
Chiochiu Catalin	TM / ME	541	0.273
Cojocaru Gabriel	TM / ME	526	0.265
Fidel Ioana Ileana	TM / ME	580	0.292
Giubega Larisa Georgiana	TM / ME	662	0.334
Manjakotya Vighnaraj	TM / ME	1036	0.522
Mitu Iani-Octavian	TM / ME	306	0.154
Nakamiya Yoshihide	TM / ME	550	0.277
Neagu Liviu	TM / ME	417	0.21
Norbaev Saidbek	TM / ME	440	0.222
Phung Vanessa Ling Jen	TM / ME	378	0.191
Popovici Mara-Georgiana	TM / ME	375	0.189
Rosu Madalin Mihai	TM / ME	619	0.312
Sadet Aude Michele Olga	TM / ME	400	0.202
Slabu Ionut	TM / ME	490	0.247
Tazlauanu Stefan Victor	TM / ME	461	0.232
Tesileanu Ovidiu	PD / DP	585	0.295
Toma Antonia	TM / ME	388	0.196
Vasilca Silvana	TM / ME	155	0.078
Vasos Paul Romeo	TM / ME	265	0.134
UB			
Babes Alexandru	PRP / RPP	480	0.242
Caragea Violeta-Maria	TM / ME	1984	1
Domocos Dan Tudor	TM / ME	1091	0.55

[‡] Total number of hours (for a certain period) = 170 average monthly hours x number of months (e.g., for a full year: 170 hours/month x 12 months = 2040 hours)

Oprita George	TM / ME	480	0.242
Selescu Tudor Richard	TM / ME	480	0.242

- List PhD/Master students and current position/job in the institution.

PhD students: Ioana Fidel – current position PhD student
Mara Popovici – current position PhD student
Ionuț Slabu – started PhD in Oct 2025 – current position Physicist
George Oprita – current position research assistant (ACS)
Master students: Ionut Slabu – completed MSc in July 2025

4. Deliverables in the last year related to the project:

- List of papers (journal or conference proceeding);

- G. Giubega et al., „High-power laser-driven gamma irradiation station for industrial imaging: concept, setup and experimental benchmarking", accepted for publication in Romanian Reports in Physics
- O. Tesileanu et al., „Preliminary studies on laser-driven production of nuclear isomeric states for fundamental and applied research at ELI-NP", Proc. of SPIE Vol. 13535 1353507-1, doi: 10.1117/12.3062176

- List of talks of group members (title, conference or meeting, date);

1. Georgiana Giubega, Ionut Slabu, Ovidiu Tesileanu, "A scintillator screen-based water phantom for real-time measurements of LPA VHEE dose distributions", ELI-User Meeting, Szeged, Hungary, 18-20 June 2025
2. I. Slabu et al., *ELI Summer School 2025,* Prague, "Monte Carlo Simulations of Laser Driven Electron Dose Distributions in a Water Phantom" - poster
3. O. Tesileanu et al. – talk at the *SPIE Optics and Optoelectronics 2025 – Research Using Extreme Light Infrastructures: New Frontiers with Petawatt-Level Lasers VI*, Prague, April 7-9, 2025
4. I.I. Fidel et al., *ELI Summer School 2025*, Prague, „High dose-rate radiation effects on biological targets and timely metabolic detection by NMR at ELI-NP" - poster
5. I.I. Fidel et al., *ELI User Meeting 2025,* Szeged - „High dose-rate radiation effects on biological targets and timely metabolic detection by NMR at ELI-NP" - poster
6. P. R. Vasos et al., *FRPT*, Prague - „Magnetic resonance biomarkers of redox metabolism: towards image-guided FLASH therapy – oral presentation

5. Further group activities (max. 1 page):

Outreach activities performed in relation to the project:

- *Noaptea Cercetătorului, 26-27 septembrie 2025*
- *Facility Visits (groups from schools and highschools, universities) where the activity of the project was presented*

6. Financial Report (budget usage) for the reporting period (see the Annex).

7. Research plan and goals for the next year (max. 1 page).

Currently, the data analysis following the experiment in E7 is ongoing, with a draft for a publication in preparation. We will continue this in 2026 until the end of the project, and submit as soon as possible the two papers for publication.

The next activities of data analysis will go deeper in the analysis of total charge of the accelerated electron bunch and its propagation direction, correlating this with the dose distribution. Also, we will compare the results from scanning the EBT films with the results from the DRZ scintillator screens, to reach a common calibration in dose. One important point is the continuation of the analysis of the data from the electro-optical crystal – the interpretation of the signal's complex structure proved challenging, with several lined likely originating from various processes and locations.

The next (and final) phase of the DRAM project, extending to mid-2026, will consist of finalizing the data analysis (and drawing the conclusions) and final reporting of the project, and submission of papers for publication.

Annex

Financial Report – IFIN-HH

according to the regulations from H.G. 134/2011

			lei
Type of expenditures		**Year 2025**	
		Value	
		Planned	**Realized**
1	**PERSONNEL EXPENDITURES**, from which:	1037410,00	1041874,00
	1.1. wages and similar income, according to the law	1014582,00	1018948,00
	1.2. contributions related to wages and assimilated incomes	22828,00	22926,00
2	**LOGISTICS EXPENDITURES**, from which:	73553,00	81006,36
	2.1. capital expenditures	30000,00	0
	2.2. stocks expenditures	33553,00	80038,36
	2.3. expenditures on services performed by third parties, including:	10000,00	968,00
	....		
3	**TRAVEL EXPENDITURES**	50000,00	30299,21
4	**INDIRECT EXPENDITURES – (OVERHEADS) *** **35% of direct costs excluding capital expenditures**	395837,00	403620,43
TOTAL EXPENDITURES *(1+2+3+4)*		1556800,00	1556800,00

* Specify the rate (%) and key of distribution (excluding capital expenditures).

Annex

Financial Report – UB

according to the regulations from H.G. 134/2011

			lei
Type of expenditures		**Year 2025**	
		Value	
		Planned	**Realized**
1	**PERSONNEL EXPENDITURES**, from which:	336075,00	336075,00
	1.1. wages and similar income, according to the law	328680,00	328680,00
	1.2. contributions related to wages and assimilated incomes	7395,00	7395,00
2	**LOGISTICS EXPENDITURES**, from which:	8485,00	18485,00
	2.1. capital expenditures	0	0
	2.2. stocks expenditures	7485,00	18485,00
	2.3. expenditures on services performed by third parties, including:	1000,00	0
	....		
3	**TRAVEL EXPENDITURES**	10000,00	0
4	**INDIRECT EXPENDITURES – (OVERHEADS) *** **25% of direct costs excluding capital expenditures**	88640,00	88640,00
TOTAL EXPENDITURES *(1+2+3+4)*		443200,00	443200,00

* Specify the rate (%) and key of distribution (excluding capital expenditures).

Annex

Financial Report – TOTAL DRAM project

according to the regulations from H.G. 134/2011

			lei
	Type of expenditures	**Year 2025**	
		Value	
		Planned	**Realized**
1	**PERSONNEL EXPENDITURES**, from which:	1373485,00	1377949,00
	1.1. wages and similar income, according to the law	1343262,00	1347628,00
	1.2. contributions related to wages and assimilated incomes	30233,00	30321,00
2	**LOGISTICS EXPENDITURES**, from which:	82038,00	99491,36
	2.1. capital expenditures	30000,00	0
	2.2. stocks expenditures	41038,00	98523,36
	2.3. expenditures on services performed by third parties, including:	11000,00	968,00
	....		
3	**TRAVEL EXPENDITURES**	60000,00	30299,21
4	**INDIRECT EXPENDITURES – (OVERHEADS) ***	484477,00	492260,43
	TOTAL EXPENDITURES *(1+2+3+4)*	2000000,00	2000000,00

* Specify the rate (%) and key of distribution (excluding capital expenditures).