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Sub-cellular imaging and irradiation using accelerator-based techniques | IAEA

IAEA
International Atomic Energy Agency
Atoms for Peace and Development

IAEA Coordinated Research Project on
"Sub-cellular imaging and irradiation using accelerator-based techniques"
(SCIMIRAC) CRP F11024
Call for proposals

Summary

Accelerator techniques play an important role in the study of radiation effects in biological cells and, provide important information on DNA damage and response that can potentially be translated to clinical trials and improved health outcomes for radiotherapy. With recent developments in high resolution ion beam and synchrotron-based X-ray microscopy imaging and sub-cellular targeting techniques, there is an opportunity to further develop, disseminate and promote the use of these techniques to better understand fundamental problems in radiobiology and cancer treatment. The areas of investigation include the study of cell response to targeted sub cellular irradiation, uptake of nanoparticles for radio sensitization aided by high resolution imaging and irradiation, development of sample preparation protocols for live and fixed cell samples and the development of data acquisition systems, novel radiation detection systems based on quantum sensing, electronics and software tools for imaging and irradiation analysis at accelerator beamlines.

Background

Many of the structures that lie within cells are of the order on 1 micron or below. An understanding of the cell function can be facilitated by imaging techniques with spatial resolution below the diffraction limit of traditional optical/confocal microscopy. Accelerator techniques such as STIM, PIF and XRF have been used in cell imaging applications and have demonstrated their ability to achieve sub-100 nm resolution. High resolution imaging techniques can be coupled to high resolution cell targeting techniques to aid in understanding the radiobiology of radiotherapy.

Besides imaging at sub-100 nm resolution, ion microbeam techniques provide a way to quantify the elemental concentration at the cellular scale with a sensitivity of the order of 10 ppm. This feature is particularly relevant for studies of the cell response when exposed to exogenous compounds (metals, nanoparticles…).

Living organisms are constantly exposed to ionizing radiation either from natural sources (telluric radioactivity, cosmic rays) or from industrial / medical sources. Although they have been studied for decades, there is still an interest to improve our understanding of the radiation-induced biological responses. There is still a strong need to decipher the molecular mechanisms

involved in the radiation response to better understand the effect of low dose exposures and to improve the use of ionizing radiation in radiotherapy.

Radiation therapy is used to treat roughly 50% of all cancers. In recent times, there have been many new developments in the field of radiotherapy. These include the use of protons and carbon to target tumors, and the use of pulsed (FLASH) and pencil beams (Focused arrays) in both particle and photon-based therapies. However, particle therapy can be a novel option to improve sensitivity of cancer to radiotherapy, several biological and molecular rationales are not yet fully explored.

This coordinated research project addresses gaps to better understand how biological cells respond to radiation. Such information can support more efficient and tailored particle therapy. However, this still requires significant research and development from the accelerator technology point of view, as well.

The following problems are to be addressed within the CRP:

Work package A – Accelerators for Radiobiology of single cells

This work package will focus on the study of how cells respond to various forms of radiation including particles such as protons, alpha and carbon, and energetic photons such as x-rays and gamma rays. How the radiation is delivered to the cell both spatially and temporally will be studied in detail. Emerging radiotherapy techniques such as FLASH irradiation utilize very high doses of radiation delivered rapidly in pulsed beams. This will be compared to radiation delivered in a more conventional continuous manner. Time studies on the effects of radiation in cell populations will be studied with advanced imaging techniques. The effect of how cells respond to radiation when certain sub-cellular structures (e.g. organelles) are targeted with single ions or photons, will be important for studies including the bystander effect and radio-sensitization by nano particles. The use of state-of-the-art high resolution ion beam and x-ray facilities will enable unprecedented control over where and how radiation is delivered to cells in a quantitative manner.

Work package B – High resolution imaging of single cells using particle and photon beams

This work package will focus on high resolution imaging techniques that are available at accelerator/microbeam facilities world-wide. The high-resolution single ion beam imaging techniques and complementary techniques that are being developed at synchrotron facilities can be used to study the effects of irradiation at the cellular and sub-cellular level. The focus of this work package will be to further develop these techniques and the protocols that are involved in preparing irradiated samples for imaging. The results will be used to inform experiments performed in WPA and to complement other technologies such as Omics technologies etc. The imaging studies will involve imaging the uptake of nanoparticles in cells for applications in radio-sensitization and drug delivery. It will also include studies that quantify DNA damage in cells. The use of complementary super-resolution optical and beam techniques (HIM and electron) can be used for correlative experiments.

Work package C – Detectors and novel technologies for quantification of radiation and imaging

This work package will focus on the development of technologies, both software and hardware, that will enable WPA and WPB. It will include the development of data acquisition systems, novel radiation detection systems, electronics and software tools for imaging and irradiation analysis. The use of new and emerging quantum sensors will also be explored to provide information on radiation effects in cells. These can include the use of spin defects in semiconductors (e.g. NV centres in diamond) for measuring electric and magnetic properties, and temperature in biological systems. Accelerator techniques (e.g. IBIC) will also be used to characterize the new semiconductor detectors (e.g. diamond). In addition, irradiation facilities can be used to generate defects in new materials for the development of quantum bio sensors.

Overall Objective

To develop novel accelerator-based techniques for sub-cellular imaging and biological cell irradiation techniques in order to advance knowledge and capabilities in understanding how biological cells respond to radiation towards more efficient and tailored particle therapy.

Specific Research Objectives

- Compare the effectiveness of particle and photon-based irradiation techniques for cancer therapy through a detailed quantitative study of cell survival and other techniques;
- Utilize advanced accelerator-based imaging techniques to enhance our understanding of fundamental processes that occur during and post irradiation under a wide variety of conditions such as beam, energy and dose;
- Study the effectiveness and uptake of various types of nano particles used for radio-sensitization with high resolution imaging and irradiation using various particle and photon beams;
- Develop new hardware and software for irradiation and imaging beamlines and to develop standard techniques that will be applied across partner laboratories;
- Develop new and novel detector platforms for quantification of radiation and imaging for a variety of beam types and energies.

Expected Research Outcomes

- Benchmarking proton/heavy ion with photon irradiation across cancer cell lines that are of interest in various regions to inform clinicians on optimum treatment planning and hardware for radiotherapy.

Expected Research Outputs

- Establishment of new collaboration between partner countries to enhance experimental capabilities and to share beamline hardware and software design for imaging and targeted irradiation;
- Development and exchange of best practices in cell sample preparation for live and fixed cell experiments such as cell targeting for radiobiology experiments and high-resolution cell imaging;
- Development of radiation dosimetry techniques/detectors and the associated best practices for quantifying radiation dose in single ion and large area radiobiology experiments;
- Exchanging experimental results that have been obtained from complementary techniques in partner countries;
- Joint publications between partner facilities on imaging and radiobiology.

Project duration

4 years

Eligibility for participation

- Proven record of active scientific research in the application **of ion beam accelerators and/or synchrotron light sources** with focused or collimated ion or photon beams by complying with any or multiple requirements for radiobiology studies of cells as stated below:
    - Capable of targeting single cells with ions or x-ray photons;
    - Capable of conducting sub-cellular imaging;
    - Detector technology development for radiobiology dosimetry.
- Accelerator facility providing highly focused ion or photon beams with access to Biosafety level 2 laboratory and facilities for pre- and post-irradiation, cell preparation and/or processing.

Primarily this CRP is formulated for accelerator facilities; however, clinicians, scientists from ion therapy centers, can also apply if they have regular access to relevant accelerator facilities for cell studies.

Laboratories are encouraged to form an interdisciplinary project team including expertise from accelerator- and biomedical sciences at national level.

Groups capable of contributing to multiple work packages are preferred.

How to participate

The CRP proposal forms with additional information on the IAEA CRP programme can be found on this website" How to participate | IAEA. The IAEA Technical Cooperation programme recipient countries (please check the participating countries in the regional pages: How to participate | IAEA) are eligible to apply for research contract, and anybody can apply for research agreement. Please extend the proposal form with additional, F11024 CRP specific info in Annex and attach it to the proposal form. Annex can include also graphs, figures, photos etc.

Please tailor your proposal according to the key elements of the F11024 CRP as objectives, work packages, outputs, and outcomes. Please strongly link the proposed work to them and explain in detail how you would contribute to them.

Please provide a detailed description of the

- Proposed scientific project;
- Scientific excellence of the CSI and project team (expertise, role, track record, young scientists);
- Available facilities and how they are to be utilized in the proposed project;
- National or international collaborations, networks that the proposed research work is linked to;
- Resources available for sustainable research for the duration of the CRP;
- Involvement/collaboration with end-users like bio-medical experts/ clinicians, etc.;

Please submit the proposal to the IAEA according to the instructions given in the proposal form and copy the Project Officer to the submission email.

Please kindly send in a separate email the project proposal in word format to the Project Officer.

Qualified female scientists and young scientists are encouraged to submit a proposal.

Proposal submission deadline: 15 February 2023

Should you have any questions, please do not hesitate contacting the Project Officer:

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