Continuously Open Research Announcement

soliciting for proposals for

Investigating the Biological Effects of space Radiation

ESA-CORA-IBER

European Space Agency
Agence spatiale européenne

1 INTRODUCTION

ESA's "Science in Space Environment" (SciSpacE) programme – which is part of ESA's overall European Exploration Envelope (E3P) programme – includes scientific activities on research platforms such as ground-based space analogues (e.g. bedrest studies, research on Antarctic stations, radiation facilities, drop tower, sounding rockets, parabolic flights), as well as an ambitious research programme on-board the International Space Station (ISS).

The SciSpacE programme activities cover science in the domains of Human Research, Biology (including Astrobiology) and Physical Sciences, with an emphasis on scientific excellence, space research- and exploration-relevance, innovation and timely delivery. Its research results will advance Europe's knowledge base, support its economy and help prepare future human and robotic space exploration. In addition to gaining fundamental knowledge, the research carried out within ESA's SciSpacE programme is helping to deliver solutions to problems back on Earth, e.g. developing innovative materials to manufacture products, removing pollutants from water, improving engine efficiency, testing new medical techniques and support equipment for the elderly and disabled.

To further enhance and promote ESA's strong non-ISS research programme, ESA's Continuously Open Research Announcement scheme has been expanded to offer dedicated opportunities for research on ESA's non-ISS research platforms.

This document provides an overview on the research opportunity offered within this Continuously Open Research Announcement as well as on the sequence of events starting from submission of the research proposal to selection and implementation of successful proposals.

2 OBJECTIVES OF THE CORA IBER PROGRAMME

Through the Continuously Open Research Announcement Opportunity for IBER (CORA IBER), ESA will provide scientists with an opportunity to conduct research necessary to advance knowledge relevant to the effects of space radiation in the area of Life and Physical Sciences. An overview of key questions to be addressed with this opportunity can be found in Annex 1. Scientists are strongly invited to address one (or more) of the topics outlined in Annex 1 of this document with their proposed experiments.

Proposals shall address these research questions through ground-based experimental studies making use of the facilities listed in Annex 2. The data to be obtained will improve the models, which are necessary for correct radiation risk assessment. In addition to supporting the needs of human space exploration missions the information obtained is relevant to assessment of terrestrial risks due to low dose ionizing radiation exposure and improvement of charged particle therapy in oncology.
In addition to supporting the needs of human space exploration missions the information obtained will be relevant to improve Earth-based technologies and/or medical protocols.

3 FACILITIES PARTICIPATING TO THIS OPPORTUNITY

Together with a group of experts, ESA identified 5 European accelerator facilities (listed in Tables 1 and 2) that that are ideally suited to provide beam-time necessary to conduct experiments addressing the above research questions. Detailed description of the facilities can be found in Annex 2.

Table 1. List of multi-ion facilities

Multi-ion Facilities				
Facility	**Points of Contact Website**	**Energies**	**Infrastructure**	**Estimated costs/hour of beamtime**
GANIL (Caen, FR)	M.H. **Moscatello** (Moscatello@ganil.fr) for beam time requests Y. **Saintigny** (saintigny@ganil.fr) for experiment preparation and coordination http://www.ganil-spiral2.eu/	All ions from C to U are available (full list of available energies: http://pro.ganil-spiral2.eu/users-guide/accelerators)	Several experimental rooms with scanning Biological laboratories (http://cimap.ensicaen.fr/?lang=en) No animal experiments	1.140 €
AGOR KVI-CART (Groningen, NL)	S. **Brandenburg** (s.brandenburg@rug.nl) for contractual matters M.J. **van Goethem** (m.j.van.goethem@rug.nl) for scheduling and practical matters http://www.rug.nl/kvi-cart/research/facilities/agor/	Protons (190 MeV) Heavier ions available ^{20}Ne (75 MeV/u) ^{4}He, 12C, 16O (90 MeV/u) ^{3}He (120 MeV/u) (full list at http://www.rug.nl/kvi-cart/)	One experimental room Biological laboratories available Animal experiments possible	325-720 €
HIT (Heidelberg, DE)	J. **Debus** (Juergen.Debus@med.uni-heidelberg.de) T. **Haberer** (Thomas.Haberer@med.uni-heidelberg.de) https://www.hit-centrum.de	^{12}C: 80-430 MeV/u ^{16}O: 103-430 MeV/u ^{4}He: 50-220 MeV/u Prot.: 50-220 MeV/u	Experimental room with scanning Two biological laboratories Animal experiments possible, but no housing facility on-site	1.300 €

Table 2. List of proton therapy facilities

Proton therapy Facilities				
Facility	**Points of Contact Website**	**Energies**	**Infrastructure**	**Estimated costs/hour of beamtime**
UPTD (Dresden, DE)	W. **Enghardt** (Wolfgang.Enghardt@uniklinikum-dresden.de) S. **Pieck** (Stefan.Pieck@unikliniku m-dresden.de) https://www.unikliniku m-dresden.de/de/das-klinikum/kliniken-polikliniken-institute/universitaets-protonen-therapie-dresden	70 - 230 MeV	Dedicated experimental room (fixed beam, 2nd beam line with scanning from 2018) Biological laboratories nearby the facility Animal facilities available close to UPTD	ca. 560 €
Trento Proton Therapy Center - TIFPA (Trento, IT)	F. **Tommasino** (Francesco.tommasino@tifpa.infn.it) E. **Scifoni** (emanuele.scifoni@tifpa.infn.it) http://www.tifpa.infn.it/	70 – 228 MeV	Dedicated experimental room Biological laboratories and animal facility nearby Advanced dosimetry detectors X-ray machine available	1-2 K€ per experiment

4 APPLICATION PROCESS

4. 1 Who can apply

Scientists from the member states participating to ESA's SciSpace programme may apply to the programme. Participating countries are Austria, Belgium, Canada, Czech Republic, Denmark, France, Germany, Greece, Ireland, Italy, The Netherlands, Norway, Poland, Portugal, Romania, Spain, Sweden, Switzerland and the United Kingdom. Scientists from other ESA member states may participate in proposals as team members.
Scientists who belong to one of the facilities listed in tables 1 and 2 are not allowed to submit proposals using their own facility.

4. 2 Preparing and submitting the proposal

The document "ESA-CORA-IBER submission template" shall be used for submission of the proposal. The proposal shall include a clear description of proposed experiment as well as information on the total funding requested. It is highly recommended to coordinate beforehand

with the facility to be used for the proposed project for suitability, feasibility and availability of the facility, a list of local points of contacts is provided in the tables 1 and 2 and in Annex 2.

The proposals shall be submitted electronically as one single file to:

radbio@esa.int

An acknowledgement of receipt will be sent to the submitting proposer upon receipt and confirmation of completeness of the proposal.

4. 3 Evaluation of proposals

ESA will make use of independent experts for the evaluation of proposals. The proposal coordinator will receive information on the outcome of the review, typically within 2 months.

The evaluation criteria that will be applied for evaluation of the proposals are:

- Significance (30%): Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or technology be advanced? What will be the effect of these studies on the concepts, methods, or products that drive this field?
- Approach (25%): Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does a flight proposal build upon a successful foundation of ground studies? Is the proposed approach likely to yield the desired results? Does the applicant acknowledge potential problem areas and consider alternative tactics?
- Innovation (20%): Does the project employ novel concepts, approaches, or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?
- Personnel (15%): Does the scientific team have the appropriate level of experience, are sufficient & appropriate personnel dedicated to the project. Is there evidence of the science team's satisfactory productivity?
- Environment (10%): Does the scientific environment in which the work will be performed contribute to the probability of success? Do the proposed experiments take advantage of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

5 IMPLEMENTATION OF THE SELECTED PROPOSALS

After positive selection of peer-reviewed proposal, the scientific coordinator of the experiment will be notified and he/she will be required to confirm the availability of resources and of the selected facility.

ESA will support selected proposals with a maximum of 50K€ to cover the access costs to the facility as well as consumables and costs for travel/subsistence for the experimenter(s). Experiment costs exceeding the above-mentioned threshold shall be the responsibility of the Coordinator and his/her partners. Personnel costs will not be covered through this programme.

ESA will place a contract with the proposed facility (i.e. not with individual science teams) to cover the costs of experiment implementation.

Please take note that the acceptance of a proposal is not a guarantee for a flight opportunity. Implementation will be subject to a technical feasibility review carried out by the selected facility after selection.

6 DATA RIGHTS

6.1 The Erasmus Experiment Archive (EEA)

The general data policies of ESA's Directorate for Human and Robotic Exploration Programmes will apply to all data resulting from the experiments in the context of this Continuously Open Research Announcement.
Final results of the study shall be made available by the scientific teams to the scientific community through publication in appropriate journals or other established channels as soon as practicable and consistent with good scientific practice. In the event such reports or publications are copyrighted, ESA shall have a royalty-free right under the copyright to reproduce, distribute, and use such copyrighted work for their purposes.

6.2 The Erasmus Experiment Archive (EEA)

The EEA covers both physical and life sciences, and can be found at the following URL: http://eea.spaceflight.esa.int The EEA is an ESA service to the international scientific community. Abstracts, from all European microgravity experiments performed to date are collected in this database. Experimenters sponsored by ESA have the obligation to provide these abstracts themselves. Special emphasis is placed on the completeness of the list of references of articles where the experiment results can be found.
Scientists in Europe who have performed experiments, be it in orbiting or ground-based facilities are encouraged to either provide an abstract on each of their experiments, or to provide information enabling the updating of their existing abstracts, in particular the list of articles published.

ANNEX 1: SciSpacE Roadmaps

The Science Department of ESA's Human Spaceflight and Exploration Directorate recently undertook an extensive exercise to create a new strategy, focusing on a set of newly defined goals to help to positively shape the future research programme of the Directorate and maximize research potential.

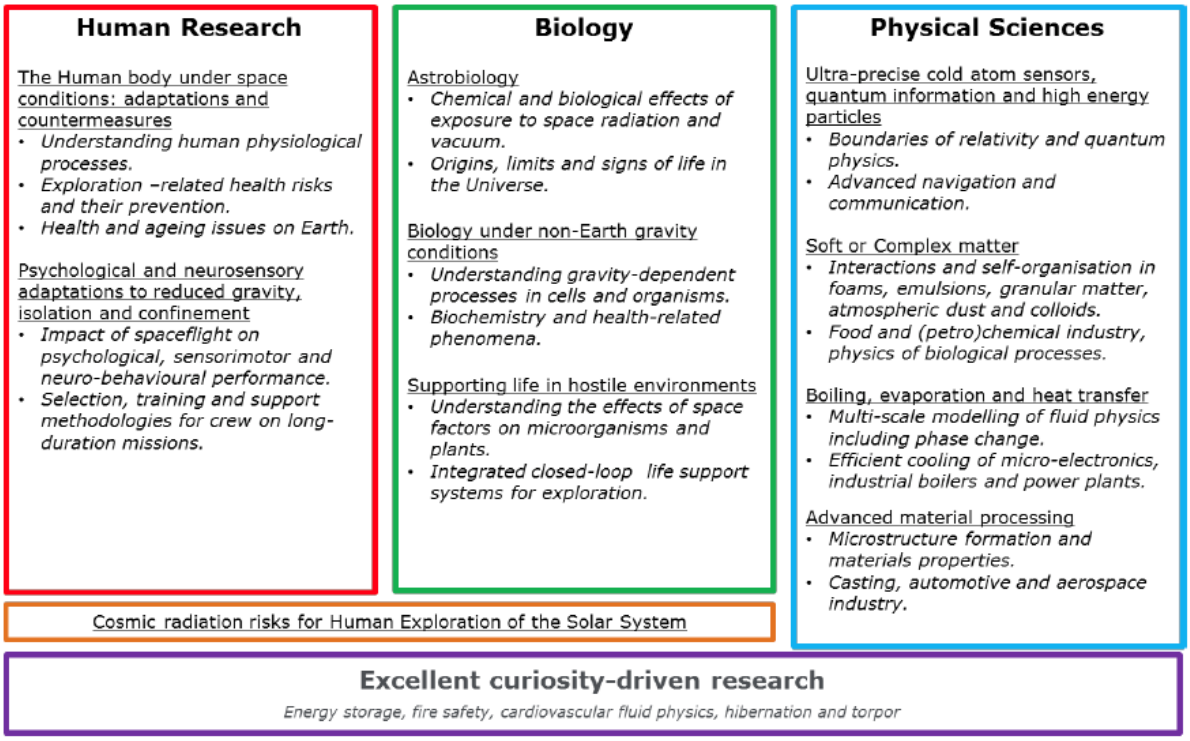

Figure 1. ESA Roadmaps

Figure 1 gives a graphical overview of ESA's Science Roadmap questions, the detailed roadmaps can be found at:
"https://www.esa.int/Our_Activities/Human_Spaceflight/Research/Research_Announcements" on ESA's Research Announcement website.

The topic of radiation crosses over all the scientific research areas within the ESA space research programmes, the priorities identified are:

- To provide quantitative estimates of the dose- and dose-rate dependence of the risk for radiation-induced acute and late morbidity, including cancer and noncancerous effects
- To identify, develop and validate early biomarkers of risk for ensuing radiation-induced health detriment
- To identify, develop and validate biomedical and physical countermeasures, including the potential impact of individual susceptibility.

Figure 2 depicts the objectives of ESA's space radiation goals in more detail:

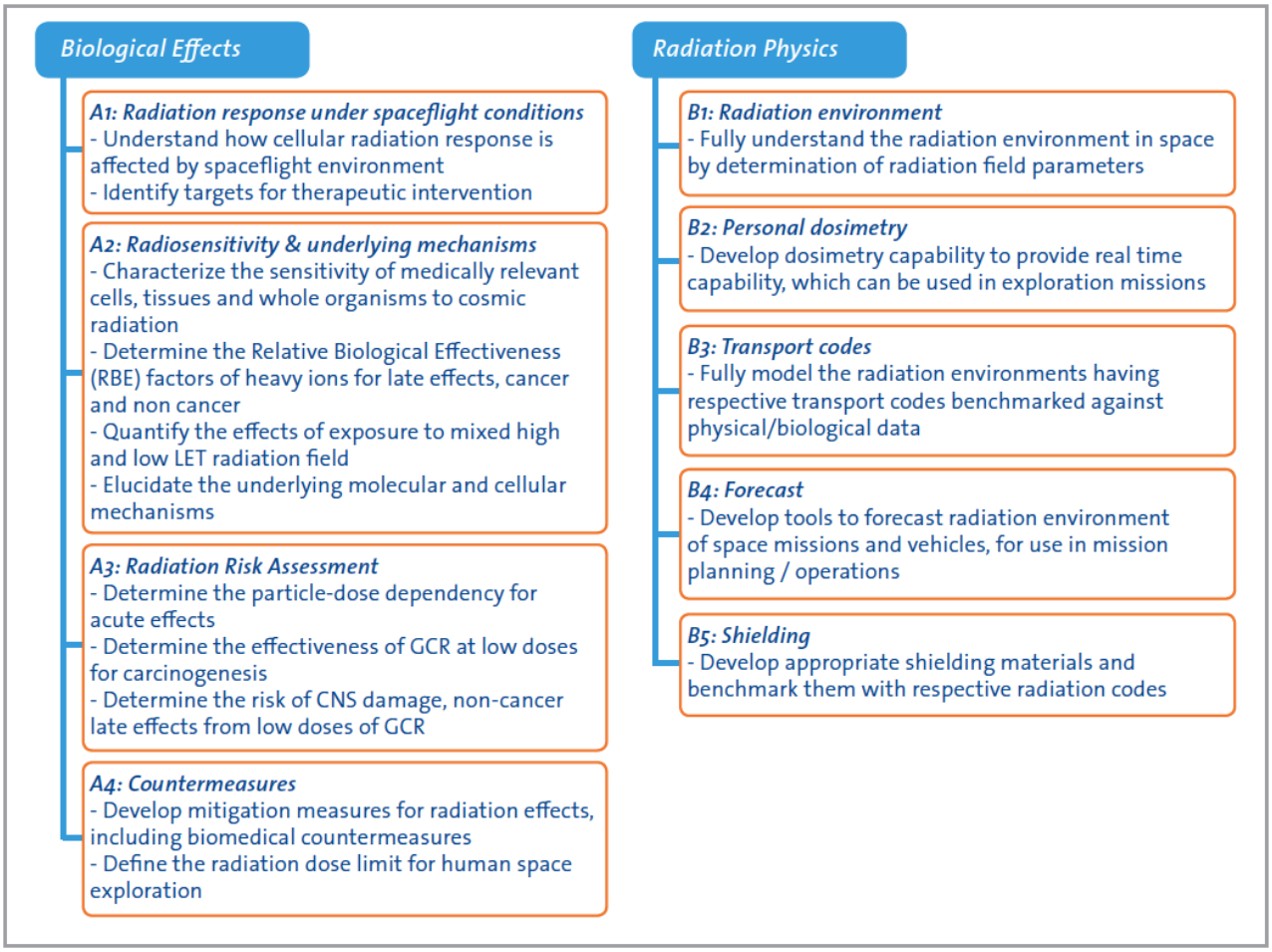

Figure 2. ESA Radiation Roadmap

Scientists are strongly invited to address one (or more) of the topics outlined above with their proposed accelerator-based experiments.

ANNEX 2: DESCRIPTION OF THE FACILITIES

GANIL – Caen, France

For this facility, the number of hours dedicated to ESA users have to be discussed with the facility PoC once the beam scheduling is completed. Due to construction activities, the beam time available for this facility is limited with respect the regular opening schedule (from 5 to 9 months a year).
This facility is dedicated to basic research and industrial applications and has several beam lines. It is also equipped with a radiobiology laboratory (LARIA), where external users are allowed to perform their experiments. Animal irradiations are not permitted. The beam cost for 2017 is 1140 €/hour; it includes experiment preparation and coordination.

Details:

- Machine: 5 cyclotrons (C01, C02, CSS1, CSS2 CIME)
- Beam deliver method: scanned, scattered and pencil beam with active beam energy selection
- Beam size: pencil beam 1 cm2 up to 5x5 cm2 maximum field
- Dose or particle rate: 8*1012 p s-1 (12C), 1.25*1012 p s-1 (56Fe) or 0.5 – Gy/min
- Irradiation rooms: G2 (2 beam lines), G4 (industrial applications), D1 (interdisciplinary research for high-energy beams), IRRSUD (interdisciplinary research for low-energy beams), ARRIBE (interdisciplinary research for very low-energy beams) , and from 2019 NFS (neutron beam line and light ion irradiation station)
- Beam time slots: calendar decided by PAC
- Beam time cost: 1140 €/hour
- Current procedure for beam time approval (PAC or similar): PAC
- Animal irradiation: No
- Additional facilities (animal house, cell labs, etc):
    - radiobiology laboratory LARIA ((http://ircm.cea.fr/drf/ircm/Pages/Equipes/LARIA.aspx) managed by CIMAP (http://cimap.ensicaen.fr/?lang=en)
- Local support (physicists, radiobiologists, engineers): Yes
- Safety protocols: approved and applied
- Local Points of Contact:
    - Marie-Helene MOSCATELLO (Moscatello@ganil.fr) for beam time requests
    - Yannick SAINTIGNY (saintigny@ganil.fr) for experiment preparation and coordination.

AGOR KVI-CART (Center for advanced radiation technology) - Groningen, Netherlands

KVI-CART provides beam time for ESA funded experiments. KVI has a strong collaboration with the Cell biology department University Medical Center Groningen (UMCG), where biology labs are located. KVI is open to the idea of establishing a better equipped annex of the UMCG facilities.

Details:

- Machine: cyclotron
- Ion changes: from minutes to a maximum of 4h depending on the ion species
- Beam deliver method: scanning (under development, available by the end of 2017) and scattering (single and double scatter, depending on ion, energy and field size), active beam energy selection
- Beam size: pencil for all ions. Large fields:
    - protons scattered ≤70 mm diameter with ±3 % homogeneity, 100 x 100 mm^2 with ±10% homogeneity
    - protons scanned: ~100 x 100 mm^2 with ±3 % homogeneity
    - ^4He and ^{12}C: scattered ≤30 mm diameter below ±2 % homogeneity, homogeneity gets worse for larger fields; scanned ~ 50 x 50 mm^2 with ±3 % homogeneity
    - no experimental data for other beams, estimated value for 50 x 50 mm^2 field is ±3 % homogeneity
- Dose or particle rate:
    - Proton: ≥3 x $10^8 cm^{-2} s^{-1}$ for 70*mm* diameter field using double scattering system, higher fluxes can be achieved for smaller fields or lower homogeneity, dose rate at 190 MeV ≥ 14 Gy/min
    - ^4He: (scattering) $3*10^{11}$ for pencil beam and lower for larger field (it also depends on required homogeneity). When scanning is implemented $3*10^8 ions/cm^2$ will be achieved for a ~10x10cm^2 field
    - ^{12}C: dose rate up to ~100 Gy/min in a Spread Out Bragg Peak (SOBP) of 1mm depth and up to ~ 45 Gy/min in an SOBP of 3 mm depth
    - Other ions: flux and dose depend on field size and primary energy. Capability to deliver very low beam intensities (few particles per second), beam monitoring needs to be discussed on a case by case basis
- Irradiation rooms: 1 experimental room. An additional experimental room is under construction (2018)
- Beam time slots: 20-35 weeks per year of operation (it depends on stuffing and users demand). Usual operation hours are from Monday 12:00 to Saturday 06:00 but special user needs can be arranged
- Beam time cost: it depends on beam characteristics (ion species, energy), experiment duration, total annual volume of beam time, amount of support by local staff required, nature of the collaboration with local scientific staff
- Price range indication:
    - For non-scientific use by non-profit organizations (e.g. radiation hardness testing of components) around 720 €/hour
    - For scientific experiments in the framework of EU-supported Transnational Access (involvement of local scientific staff and co-authoring the publications) 325 €/hour
- Current procedure for beam time approval (PAC or similar): PAC (call twice a year)
- Animal irradiation: YES (experiments subject to approval by the Dutch national animal ethics commission)

- Additional facilities (animal house, cell labs, etc): basic cell biology lab facility (flow cabinet and incubator) used for cell culture (and more recently organoid culture) irradiations in collaboration with the Cellbiology department of the University Medical Center Groningen (UMCG). Possibility on a case by case basis to have access at their laboratory facilities (located at about 5 km from KVI-CART). Open to the possibility to establish a better equipped annex of the UMCG facilities at our institute. License to house animals for a restricted period around the experiment, the local animal housing is being refurbished. Possibility to arrange an agreement with the University of Groningen and UMCG to use their large scale animal facility
- Current average number of users groups per year: 40-50
- Local support (physicists, radiobiologists, engineers): experienced technical and scientific staff for experiment design, preparation and execution; support for biology facilities provided by staff of the UMCG Cell biology department has to be arranged prior to the experiment
- Safety protocols: approved and applied
- Local Points of Contact:
    - Prof. Dr. Sytze Brandenburg (s.brandenburg@rug.nl) for contractual issues
    - Dr. M.J. van Goethem (m.j.van.goethem@rug.nl) for scheduling and practical issues

HIT – Heidelberg, Germany

HIT and cooperation partners conduct many biological and physical experiments in the dedicated experimental room (QA room). The QA room is frequently used for experiments (> 200 days per year)

Details:

- Machine: Synchrotron (GSI development)
    - ^{12}C: 80-430 MeV/u
    - ^{16}O: 103-430 MeV/u
    - ^{4}He: 50-220 MeV/u
    - Prot.: 50-220 MeV
- Irradiation rooms:
    - Two medical fixed beam rooms
    - One medical gantry room
    - One dedicated QA/experimental room
- Beam delivery: Scanning, max field size 20 x 20 cm^2, clinical dose rates
- Beam size: pencil beam for all species, energy dependent (4- 30 mm FWHM)
- Beam time slots: Patient treatment has priority. Experiments can normally be scheduled in a night shift 23:00 – 5:00 or on Sundays
- Beam time costs: approx. 1.300 € per hour
- Facilities for biological experiments: In the HIT building are 2 biological labs available
- Animal irradiation: possible, to be coordinate with the PoCs
- Local support (physicists, radiobiologists)

- Safety protocols for experiments (external users): yes
- Local Points of Contact:
    - Prof. Jürgen Debus (Juergen.Debus@med.uni-heidelberg.de)
    - Prof. Thomas Haberer (Thomas.Haberer@med.uni-heidelberg.de)

UPTD – Dresden, Germany

The Dresden proton therapy is embedded in the large university clinic campus and has a good infrastructure for biological and animal experiments. UPTD costs for beam time are approximately 560 € per hour.
Details:

- Machine: Cyclotron (normal conducting, company IBA)
- Protons only
- Irradiation rooms:
    - One medical gantry room
    - One dedicated room for experiments available
- Beam delivery:
    - 1 medical proton gantry for scattering and scanning,
    - 1 fixed beam experimental room
        - 70 – 230 MeV protons, lower energies can be adjusted by range shifter
        - pencil beam, large fields by scatterer, dose rate up to 10 kGy/min (field size and energy dependent)
        - scanning available from 2018, maximum field size 20 x 20 cm^2, dose rate up to 10 Gy/min
- Beam size: pencil beam for protons, energy dependent
- Beam time cost: approx. 560 € per hour.
- Current procedure for beam time approval: contact OncoRay (clinical facility, no fixed procedure for beam time)
- Facilities for biological experiments available : yes
- Facilities for animal irradiation available : yes
- Local support (physicists, radiobiologists)
- Safety protocols for experiments (external users): approved and applied
- Local Points of Contact:
    - Prof. Wolfgang Enghardt, Wolfgang.Enghardt@uniklinikum-dresden.de
    - Stefan Pieck, Stefan.Pieck@uniklinikum-dresden.de
    - Dr. Jörg Pawelke, Joerg.Pawelke@oncoray.de

Trento Protontherapy Center TIFPA – Trento, Italy

The protontherapy center in Trento is run in collaboration between APSS (Trento health care system), which handle the patients' treatment, and the Trento Institute for Fundamental Physics and Applications (TIFPA), which coordinates all activities at the experimental room. The centre is not equipped with a radiobiology lab nor an animal facility but they are planned

to be built in the near future. In the meantime, experiments can be performed in the nearby CIBIO facility, belonging to the University of Trento.

Details:

- Machine: cyclotron (IBA)
- Beam deliver method: scanning (treatment rooms) and scattering (experimental room), active beam energy selection
- Beam size: pencil with ~1.5 cm diameter at the lowest energy or 10x10 cm^2 (experimental room)
- Dose or particle rate: $4*10^6$ per second at 70 MeV and $2*10^8$ per second at 228 MeV with 1 nA beam current at cyclotron exit, can be increased by a factor 10^2 (experimental room) or ~10 Gy/min (gantry)
- Irradiation rooms: 2 treatment rooms (gantry) and 1 experimental room (horizontal beam). The experimental room has no scanning available at the moment and large fields are produced with a scatter
- Beam time slots: 6 h shifts (Saturdays from 8 am to 2 pm) or 3 h shifts (weekdays from 7 pm to 10 pm). Limitation of 4 h/day beam-on-target
- Beam time cost: 1-2 k€ for each experiment independently of the number of hours requested
- Current procedure for beam time approval (PAC or similar): PAC
- Animal irradiation: available soon
- Additional facilities (animal house, cell labs, etc…): The center will be equipped with a basic cell lab and animal housing in the near future. A permanent animal facility and advanced biology labs are available at the CIBIO facility (University of Trento). X-ray machine available at the TIFPA main institute. Advanced dosimetry detectors and beam characterization available
- Current average number of users groups per year: 2
- Local support (physicists, radiobiologists, engineers): experienced scientific and technical staff for physics, biology and engineering experiments
- Safety protocols: approved and applied
- Local Points of Contact:
    - Dr. Francesco Tommasino (Francesco.tommasino@tifpa.infn.it)