INfraStructure in Proton International REsearch

INSPIRE

Outline

1. Project origin
2. Partners
3. Networking
4. Joint Research Activities
5. Trans-National Access

European Commission
Research & Innovation - Participant Portal
Proposal Submission Forms

Horizon 2020

Call: H2020-INFRAIA-2016-2017
(Integrating and opening research infrastructures of European interest)

SECOND STAGE

Topic: INFRAIA-02-2017

Type of action: RIA
(Research and Innovation action)

Proposal number: 730983-2

Proposal acronym: INSPIRE

Deadline Id: H2020-INFRAIA-2017-1-two-stage

Sources of INSPIRE

In the mid of this decade several new PTC in Europe started operation: Prague, Trento, Uppsala, Dresden, Krakow and several was under construction: Manchester, Groningen, Aarhus

Coordinator
Karen Kirkby

Started: March 1st, 2018
End: February 28th, 2022

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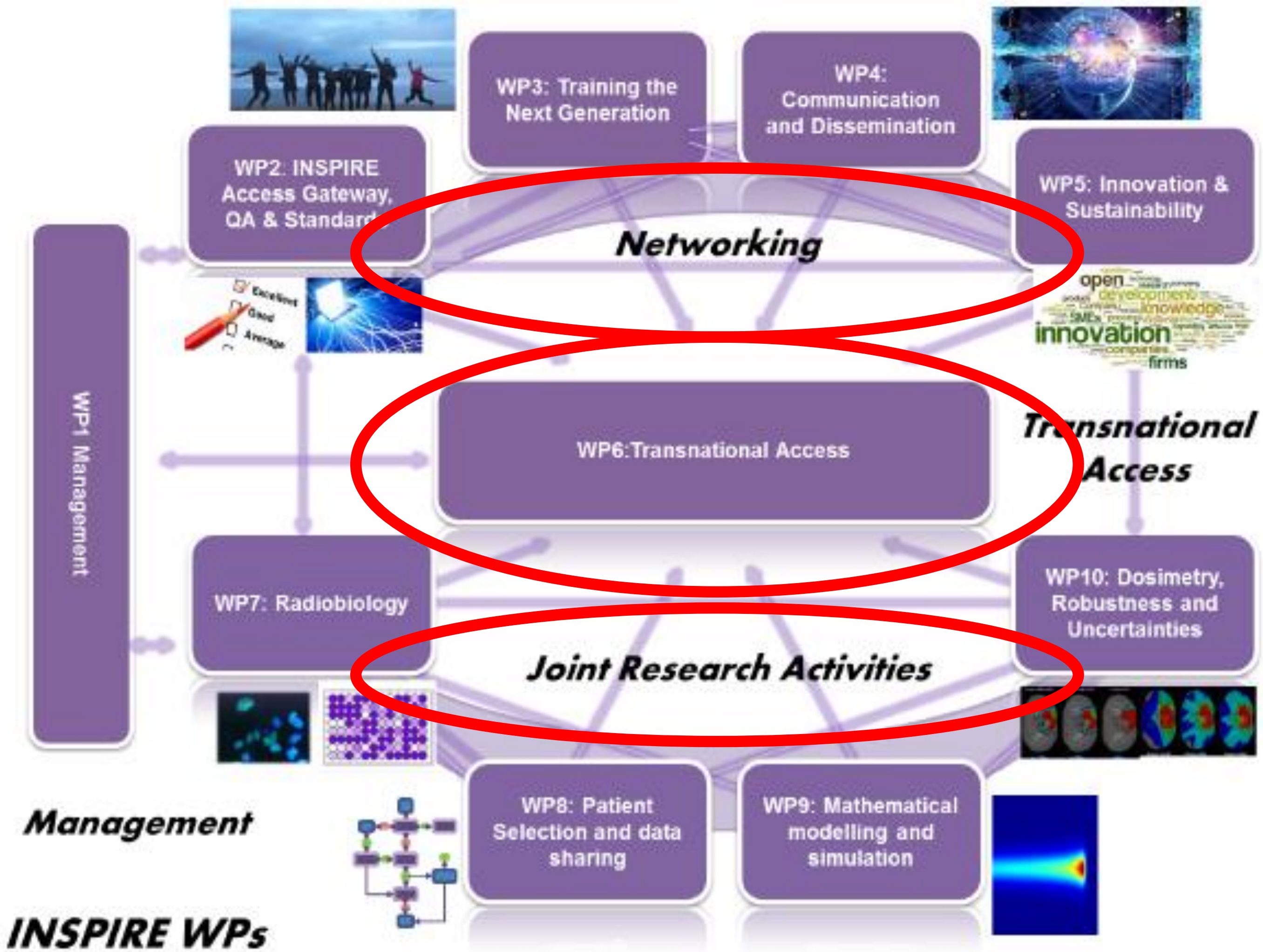
Web page: https://protonsinspire.eu/

INSPIRE Partners

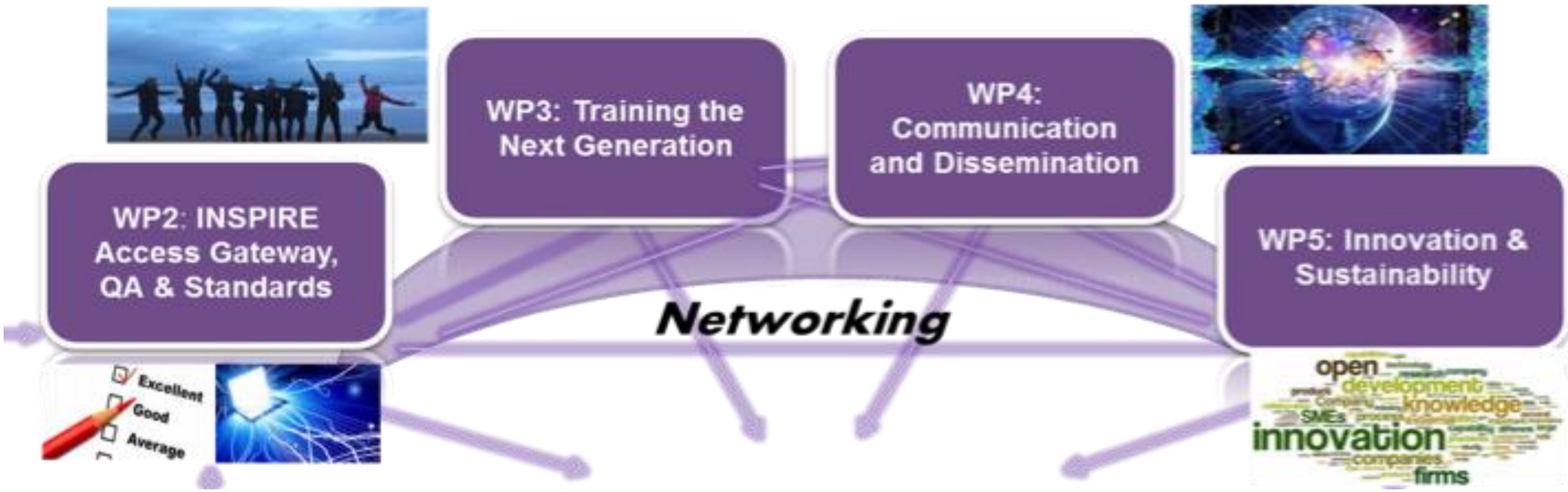
- 1. THE UNIVERSITY OF MANCHESTER (UNIMAN),
- 2. THE CHRISTIE NHS FOUNDATION TRUST (THE CHRISTIE),
- 3. ACADEMISCH ZIEKENHUIS GRONINGEN (UMCG),
- 4. UNIVERSITE DE NAMUR ASBL (UNamur)
- 5. RIJKSUNIVERSITEIT GRONINGEN (RUG),
- 6. INSTITUTE OF NUCLEAR PHYSICS PAN (IFJ PAN),
- 7. VARIAN MEDICAL SYSTEMS PARTICLE THERAPY GMBH (Varian),
- 8. NUCLEAR PHYSICS INSTITUTE OF THE ASCR VVI (NPI-CAS)
- 9. ISTITUTO NAZIONALE DI FISICA NUCLEARE (INFN)
- 10. LIETUVOS SVEIKATOS MOKSLU UNIVERSITETAS (LSMU),
- 11. PAUL SCHERRER INSTITUT (PSI),
- 12. ION BEAM APPLICATIONS SA (IBA),
- 13. AARHUS UNIVERSITET (AU),
- 14. TECHNISCHE UNIVERSITAET DRESDEN (TUD),
- 15. INTERNET-SIMULATION EVALUATION ENVISION SRL (I-SEE),
- 16. INSTITUT CURIE (INSTITUT CURIE),
- 17. KOMMUNALFORBUNDET AVANCERAD STRALBEHANDLING (SKANDION),

Three pillars of INSPIRE

Networking, TransNational Access and Joint Research Activities

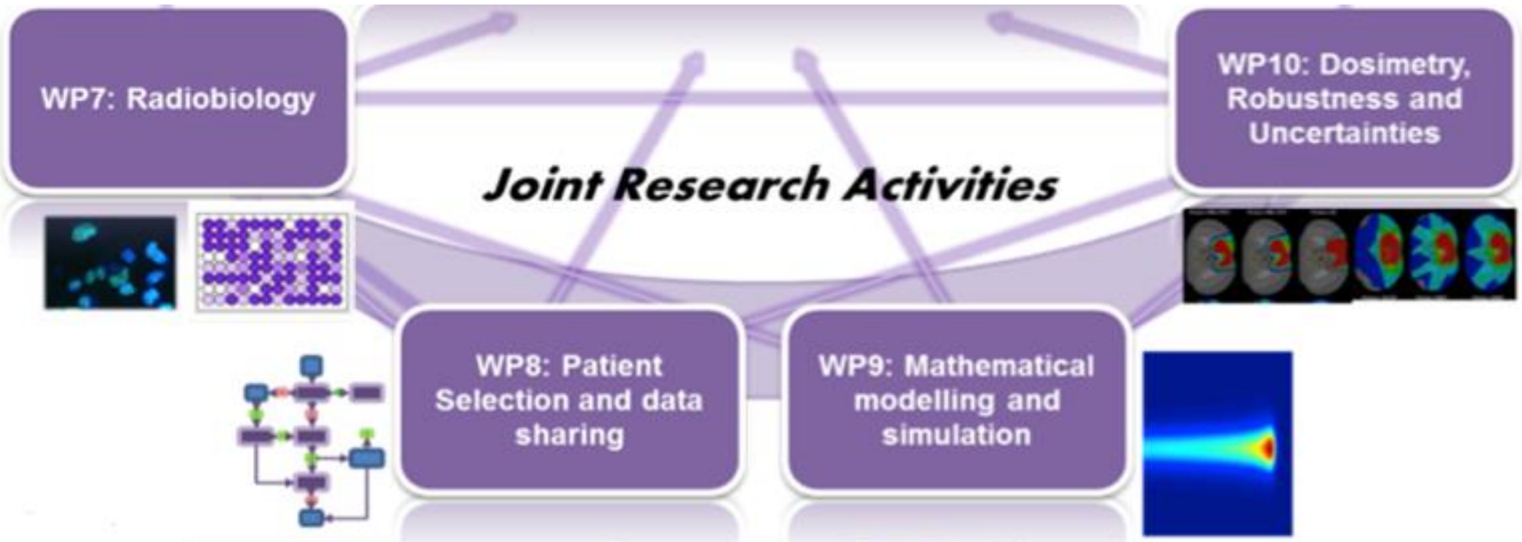


Networking



- WP2 INSPIRE Access Gateway QA & Standards
- WP3 Training the Next Generation
- WP4 Communication & Dissemination
- WP5 Innovation & Sustainability

Joint Research Activities



- WP7 Radiobiology (INFN)
- WP8 Patient Selection & data Sharing (UMCG)
- WP9 Mathematical Modelling & Simulation (TUD)
- WP10 Dosimetry, Robustness & Uncertainties (Unamur)

JRA WP7 Radiobiology
coordinated by INFN

7.1 Equipment and protocols for RBE studies:

- Design the equipment and protocols for depth-dependent radiobiology experiments (2D and 3D cell cultures):
  - RBE-LET dependency for normal and tumor tissues;
  - Effects of fractionation;
  - Oxygen enhancement ratio (OER) (single dose or multiple fractions);
- Produce input for WP9 for functional (survival) and mechanistic (DNA repair) RBE modelling.

7.2 Equipment and protocols to study the effects of radio-sensitisation and radio-resistance:

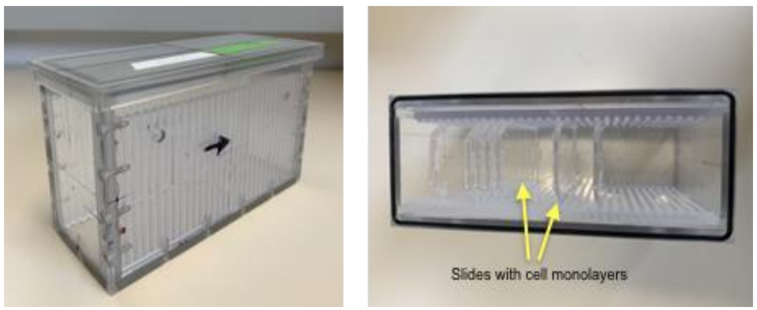
- In vitro: design phantoms to study the effects of radio-sensitising agents in 2D and 3D cell cultures;
- In vivo: develop protocols for testing immunotherapy drugs in combination with proton irradiation;
- Enable preliminary experiments to investigate radio-protective effects of hibernation on small animals.

JRA WP7 Radiobiology
deliverables (D) and milestones (M)

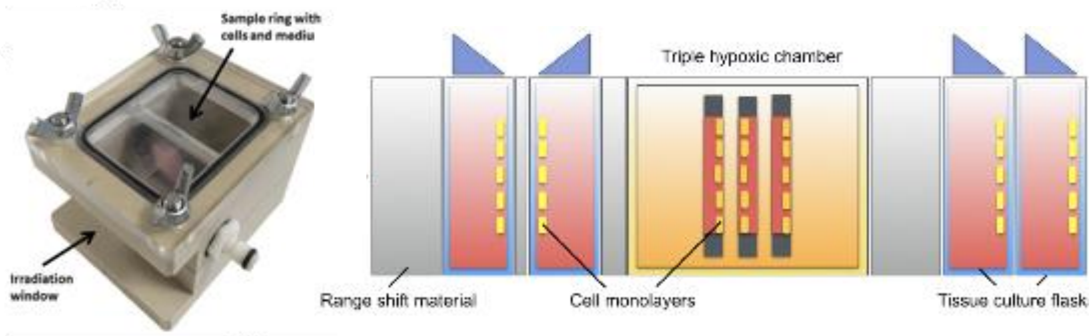
- MS7.1 Phantoms / end stations developed for studying RBE along the Bragg peak (M20).
- D7.1. Development and testing of advanced radiobiological phantoms / end-stations for RBE experiments along the Bragg peak using spot scanning or passive scattering (M36) (INFN)
- D7.2 Benchmark radiobiological models of hypoxia against experimental data; prepare paper for publication (M42). (NPI-CAS)
- D7.3 Protocols for in vitro analysis of dose response of radio sensitising agents with protons; prepare paper for publication (M38). (IFJ-PAN)
- D7.4 Preliminary experiments to investigate radio-protective effects of hibernation on small animals (M40), (INFN)

Phantoms and protocols for 2D and 3D cell cultures

- **2D phantoms** for *in vitro* studies is **already available** for TNA and intercomparison of measurements



1D measurements in normoxic conditions



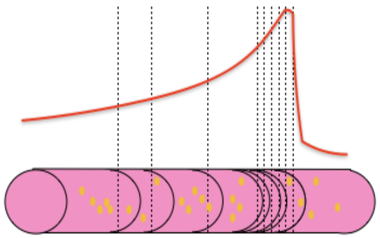
1D measurements in hypoxic conditions

- **3D phantom: under development**

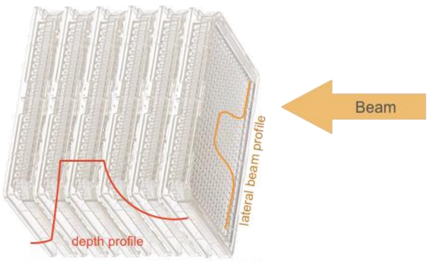
  Details already given by Olga Sokol

  - Protocols for growing cells in Matrigel and alginate established
  - First X-ray and ^{12}C ion irradiations performed with cells in 3D

Alginate-based phantoms



Matrigel-based phantoms



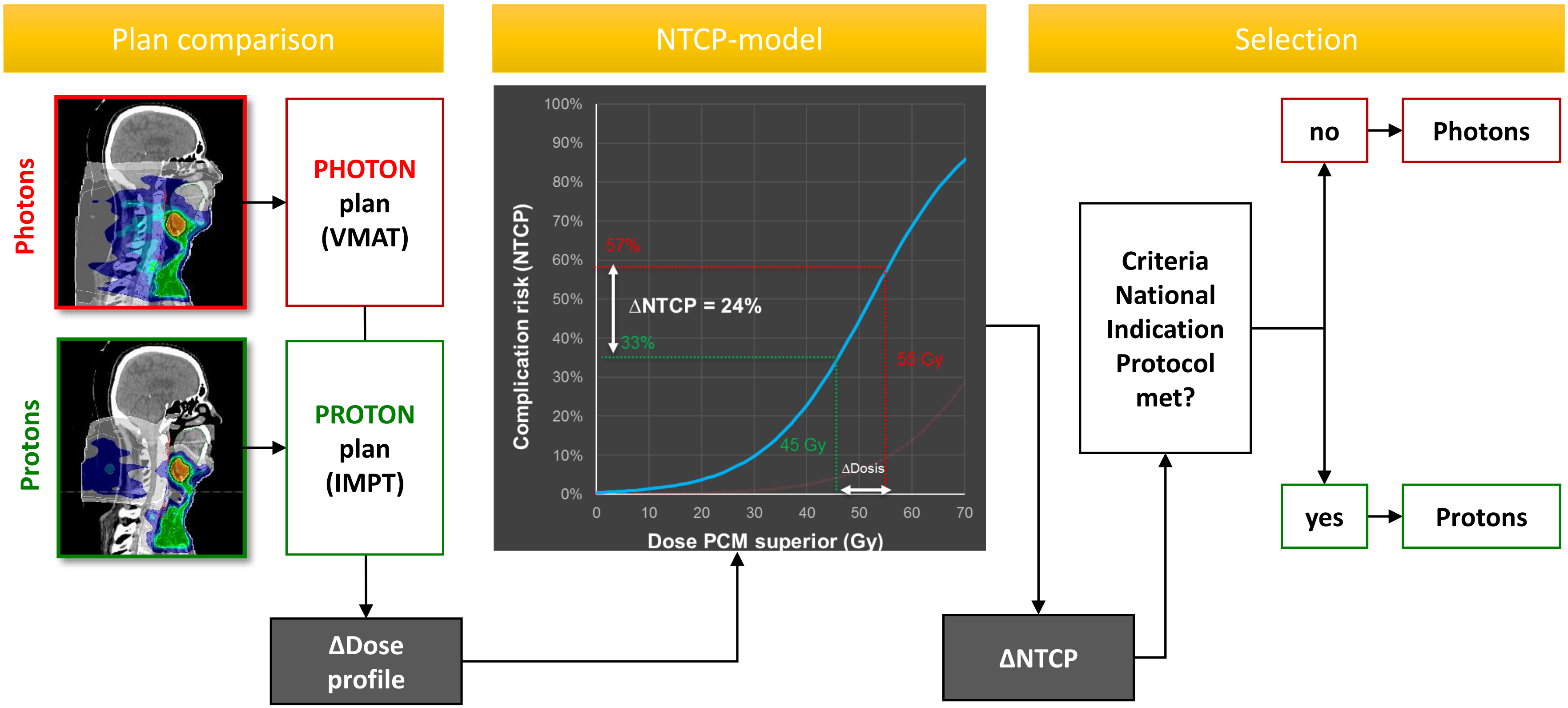
JRA WP8 Patient Selection & data sharing coordinated by UMCG

- Develop the NTCP model of patient selection for a number of tumour sites which are likely to be used in PBT
- Develop the indications list for Malthus so that it can be used for PBT scenario planning and demand modelling and can incorporate NTCP models in to its decision tree modelling.
- Develop automated probabilistic treatment planning taking input from WP7 and WP9.
- Aid in the development of national databases of PBT outcomes

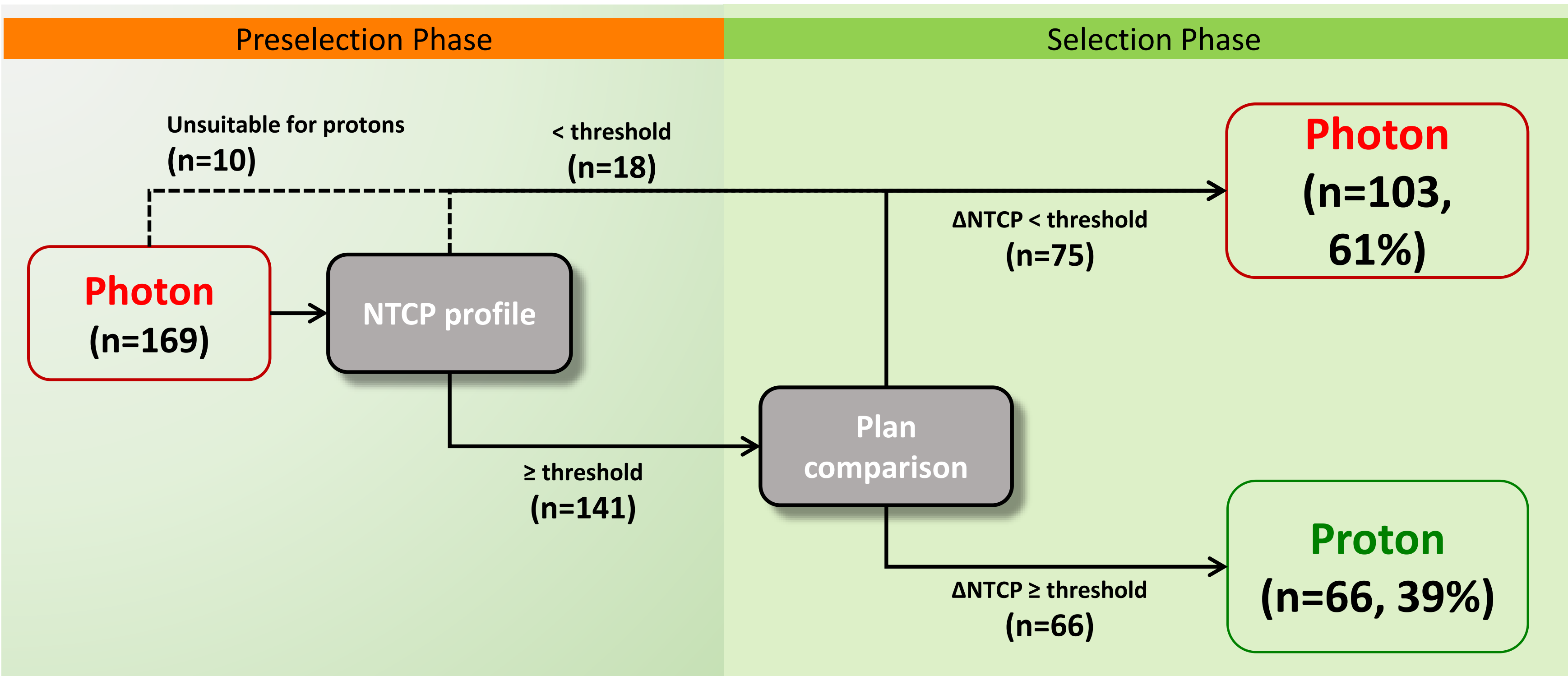
JRA WP8 Patient Selection & data sharing
deliverables and milestones

- D8.1 Definition of key parameters for NTCP based patient selection and tumour sites (M12) (IBA)
- D8.2 Incorporation of PBT indications into Malthus decision trees (M12) (UNIMAN)
- D8.3 Proto-type automated planning tool (42) (PSI)
- MS11 Extension of NTCP models to other tumour sites (M24)
- MS12 Version of Malthus incorporating NTCP models (M36

How does model-based selection work?



% of patients that qualify for proton



JRA WP9 Mathematical Modelling & Simulation
coordinated by TUD

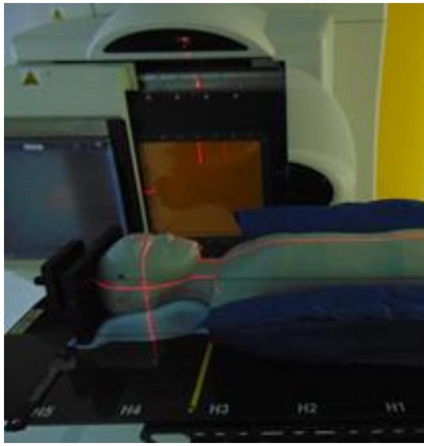
- Integrate HR and OER in to TOPAS nBio and compare with experiments in WP7
- Incorporate RBE into TPs and evaluate its effects
- Study the impact of passive scattering and spot scanning on RBE in TPs and compare with results from WP7
- Evaluate constant vs variable RBE plans wrt anatomical changes and organ motion during treatment
- Incorporate variable RBE into patient selection models (WP8)
- Study the effects of range uncertainties and their impact on TP

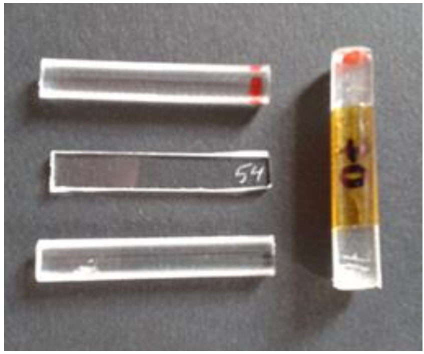
JRA WP9 Mathematical Modelling & Simulation
deliverables (D) and milestones (M)

- D9.1: Report: Recalculation of treatment plans performed assuming a constant RBE=1.1, with two different models for variable RBE, including dependencies on beam quality, dose fractionation, OER and tissue type (M36) (TUD)
- D9.2: Simulator of proton PBS delivery (passive vs spot scanning) and with motion including dose reconstruction (M48) (TUD)
- D9.3 Report on post-treatment assessment of actually delivered dose in patients (M48) (IC).
- MS9.1 Incorporation of variable RBE into TPS; comparison of different models (M18)
- MS9.2 RBE model adaptation to biological data from WP7 completed (M42)
- MS9.3 Analysis of planned dose versus actual dose to patients and RBE considerations (M48)

JRA WP10 Dosimetry, robustness & Uncertainties
coordinated by UNamur

- Develop new detector technology for fast pencil beam scanning including dosimetry for spatially fractionated therapy
- Develop a proton dosimetry standard for pencil beam scanning
- Develop tissue equivalent phantoms for monitoring dosimetry and changes in RBE along the Bragg peak in collaboration with WP7.
- Develop tissue equivalent zoomorphic and anthropomorphic phantoms for evaluating and cross comparing the performance of different detectors
- Carry out round robin experiments to compare dosimetry between TNA providers and inter-comparison of radiobiology using standard experiments
- Evaluate detectors for measuring range uncertainties and evaluate opportunities of using nanoparticles to enhance signals
- Investigate measurement of secondary dose delivered to patients





JRA WP10 Dosimetry, robustness & Uncertainties
deliverables (D) and milestones (M)

- D10.1 Optimized and tested design of position and dose monitor for fast pencil beam scanning with high dose rates (M42) (Varian)
- D10.2 Develop tissue equivalent phantoms for monitoring dosimetry and changes in RBE along the Bragg peak (M24) (NPI-CAS)
- D10.3 Evaluate detectors for measuring range uncertainties and evaluate opportunities of using nanoparticles to enhance signals (M40) (UNamur)
- MS10.1 Decision of best detector technology for pencil beam scanning (M42)
- MS10.2 Determine if nanoparticles enhance prompt gamma signal (M18)

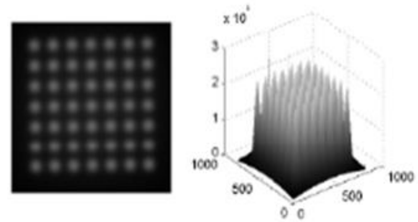
WP10 Dosimetry, Robustness and Uncertainties (IFJ PAN, Kraków)

Dose distribution in proton grid therapy

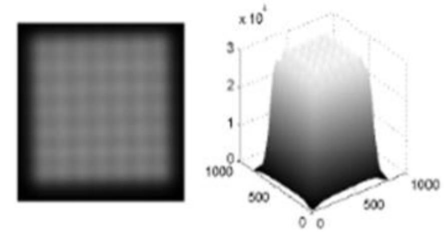
The aim of the work is to determine depth dose distributions and unwanted doses to patients due to scattered radiation in grid therapy with collimators.

The first measurements with 60 MeV protons for small radiation fields (13 mm x 13 mm) and 1 mm mesh collimators demonstrated that the 5% uniformity of lateral dose distribution can be obtained at the depth of Bragg peak maximum.

2-D and 3-D dose distributions



Entrance region



Bragg peak region

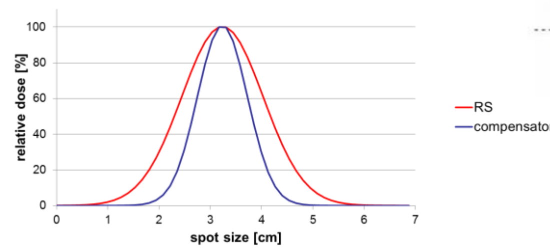
3D technology for printed compensators and phantoms in proton therapy

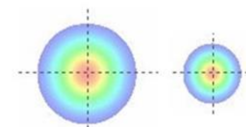
$$WER_{sample} = \frac{R_{pristine} - R_{sample}}{L_{sample}}$$

R – range
L – thickness, 4 cm for PLA sample

WER_{PLA} = 1.167 mm

Water Equivalent Thickness (WET) for different plastic filaments for 3D printers were experimentally determined for their potential use for compensators and dedicated phantoms in proton therapy.



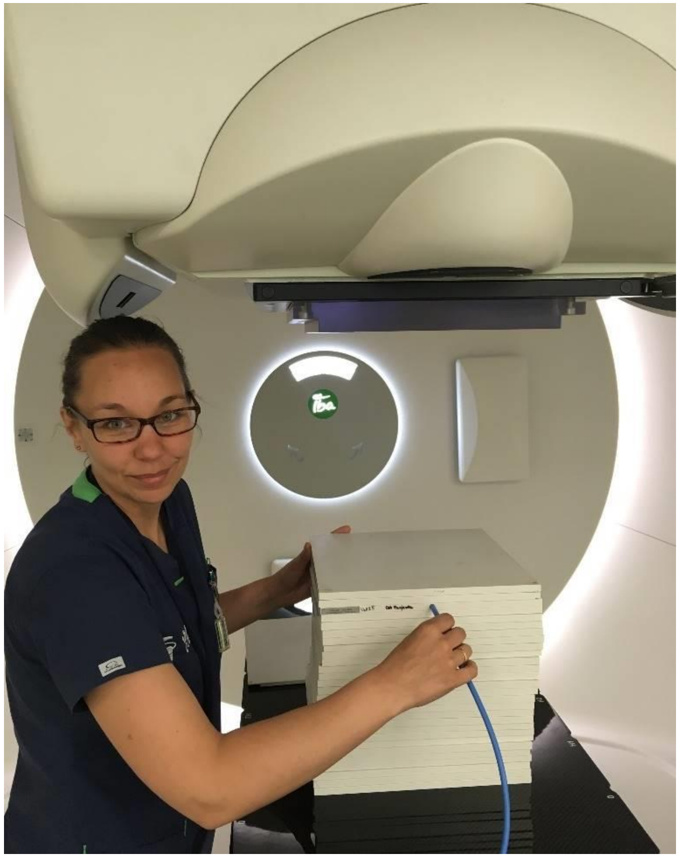


First patient dedicated compensators were printed and tested for their properties of beam formation. The use of compensator reduced the lateral full width at half maximum (FWHM) as compared to Range Shifter by over 60%.

Transnational Access, TNA

What is Trans National Access, TNA?

TNA is ‘free of charge’ provision of access to a Research Infrastructure to selected researchers or research teams



The support of the infrastructure includes:

- free use of the infrastructure facilities
- administrative and logistical support
- technical and scientific support
- specific training for use of the infrastructure

The transnational programme also covers:

- travel,
- subsistence
- local accommodation

Trans-National Access - list of Eligible States

European Community

Austria
Belgium
Bulgaria
Cyprus
Croatia
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Ireland
Italy
Lithuania
Latvia
Luxembourg
Malta
Netherlands
Poland
Portugal
Romania
Slovakia
Slovenia
Spain
Sweden
United Kingdom

Associated States

Albania
Bosnia & Herzegovina
Faroe Islands
Georgia
Iceland
Israel
Moldova
Montenegro
Norway
Serbia
Switzerland
Tunisia
Turkey
Ukraine

- Third country users: up to 20% of the access can be provided to user teams with a majority of users working in third countries
- Users working for SMEs exempted from requirement to disseminate results generated under Trans-national access

INSPIRE Transnational Access Providers

Access Provider	Infrastructure Name	Country Code	Contact
University of Manchester	PBT Research Room	UK	**Karen Kirkby** Karen.kirkby@manchester.ac.uk
The Christie NHS Foundation Trust	PBT Research Room	UK	**Ranald Mackay** Ranald.mackay@christie.nhs.uk
Academisch Ziekenhuis Groningen	Proton Therapy Centre Groningen	NL	**Hans Langendijk** j.a.langendijk@umcg.nl
Universite de Namur ASBL	Walloon Proton Therapy Centre	BE	**Anne-Catherine Heuskin** anne-catherine.heuskin@unamur.be
Rijksuniversiteit Groningen	KVI-CART	NL	**Sytze Brandenburg** brandenburg@kvi.nl
The Henryk Niewodniczanski Institute of Nuclear Physics, Polish Academy of Sciences	Cyclotron Centre Bronowice	PL	**Pawel Olko** Pawel.Olko@ifj.edu.pl
Nuclear Physics Institute of the ASCR VV1	Proton Therapy Czech	CZ	**Marie Davidkova** davidkova@ujf.cas.cz
Nuclear Physics Institute of the ASCR VVI	Nuclear Physics Institute CAS	CZ	**Marie Davidkova** davidkova@ujf.cas.cz
Paul Scherrer Institut	Proton Therapy Centre	CH	**Tony Lomax** tony.lomax@psi.ch
Aarhus Universitet	Danish Centre for Particle Therapy	DK	**Cai Grau** caigrau@dadlnet.dk
Technische Universitaet Dresden	Oncoray Proton Therapy Centre	DE	**Esther Troost** Esther.Troost@uniklinikum-dresden.de
Institut Curie	Centre de Protonthearpie d'Orsay	FR	**Alejandro Mazal** alejandro.mazal@curie.fr
Kommunalforbundet Avancerad Stralbehandling	Skandion Clinic	SE	**Alexandru Dasu** alexandru.dasu@skandion.se

INSPIRE TNA - how to apply?

Just fill the application form and send it by e-mail to Helena.j.kondryn@manchester.ac.uk

Application Form

Please email completed form (2 page maximum) to Helena.j.kondryn@manchester.ac.uk

Name of User Group Leader:
Current role:
Organisation:
Address:
Telephone number:
Email:

Please list all members of the User Team who will be accessing the infrastructure facility	
Name	Organisation (and country)

Title of Project:

Infrastructure facility you wish to access:
Total number of beam time required (hours):
Total number of visits:

Project objectives:

Project description including activities to be undertaken:

Project outcomes:

Impact and use of results:

Estimate of total costs (in €)			
Air Fare	Train fares/Additional transport	Accommodation	Living Costs

INSPIRE TNA - how to apply?

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Project objectives:

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Estimate of total costs (in €)			
Air Fare	**Train fares/Additional transport**	**Accommodation**	**Living Costs**

Please submit your proposal for INSPIRE TNA

Several hundreds of beam hours are available until February 2022

Priorities are for groups from countries without Proton Therapy infrastructure

Web page: https://protonsinspire.eu/