Report on the 6th European Particle Therapy Network workshop

The 6th European Particle Therapy Network (EPTN) workshop took place in a virtual setting on 23 October 2020. The workshop was attended by 55 participants.

New centres joining the EPTN
The workshop started with the announcement of the new centres that had opened since the last annual meeting: the Zuid-Oost Nederland Protonen Therapie Centrum (ZON-PTC, the South-East Netherlands Proton Therapy Centre), in Maastricht, The Netherlands; the Particle Therapy Interuniversity Centre Leuven (ParticLE), Belgium; and a new Rutherford Cancer Centre, UK.

Involvement of radiotherapists in the EPTN
The Radiotherapists Committee of the European SocieTy for Radiotherapy and Oncology (ESTRO) had reached out to the EPTN with a request to involve the radiation therapists (RTTs) in the EPTN network. This request was initially presented to the ESTRO Scientific Council where it was approved. A meeting between the EPTN coordinators and key members of the RTT Committee took place in June. At that meeting the areas of interest for RTTs were discussed.
The EPTN network was consulted during the workshop on the involvement of RTTs, and this involvement was approved. RTTs and coordinators of the EPTN working parties (WPs) will discuss how to optimise this collaboration.

Report from European Commission DG Santé / EIB
The sub-group on proton therapy of the European Commission (EC) steering group on health promotion, disease prevention and management of non-communicable diseases, which is co-chaired by the directorate-general on health and food safety (DG SANTE) and the European Investment Bank (EIB), was created in 2018. A first physical meeting of the subgroup took place in Luxembourg approximately two years ago.
The mandate of the sub-group is to examine the current state of play of availability and use of proton therapy centres across the European Union (EU) and to identify options through which willing member states can cooperate sustainably to improve information exchange and avoid duplication of effort.
In this respect, the EC supports the formation of a European network and it is evident that EPTN has a role to play in this arena.

On 21 October, the sub-group on proton therapy met virtually. Representatives of member states' health authorities, the EPTN, the EIB and the DG SANTE / directorate-general of research and innovation were present. The meeting was attended by approx. 40 participants.

A flash report by the DG SANTE is available here:
https://ec.europa.eu/health/sites/health/files/non_communicable_diseases/docs/ev_20201021_flash_en.pdf

Patterns of practice for adaptive and real-time radiation therapy (POP ART RT)
POP-ART RT was a project that originated from the 2nd ESTRO Physics Workshop, which was held in 2018. A POP-ART RT survey was conducted, and the results of the survey have been published in *Radiotherapy & Oncology:* https://doi.org/10.1016/j.radonc.2020.06.018.
POP-ART PT is a spin-off project that is intended for the particle therapy community. A survey is being distributed that aims: to determine the status of real-time and adaptive particle therapy; to discover the demand for its implementation; and to understand the barriers to future implementation.

The survey addresses two concerns regarding anatomical changes that occur due to respiration: those that occur intra-fraction and those that occur inter-fraction. The questions that are asked in each part of the survey link to delivery type, sites treated, strategies implemented, and imaging and monitoring tools used.
The survey links to the work of EPTN WPs 4 and 5 but it focuses only on workflow. Twenty responses to the survey have been received to date. The EPTN has been approached regarding distribution of this survey in November 2020.
The analysis and dissemination of results is expected by the end of 2021. In terms of dissemination, the authors intend to submit abstracts for preliminary presentation of the results at 2021/2022 meetings of the Particle Therapy Co-Operative Group (PTCOG) or ESTRO, and to publish the results in two papers, one to address intra-fractional changes and the other inter-fractional changes, in peer-reviewed journals.
The survey can be completed online at https://www.surveymonkey.com/r/FR9KZCG.

WP8 and INfraStructure in Proton International Research (INSPIRE)
WP8 concentrates on selection procedures of patients for proton therapy by addressing different components of the selection, such as: how the patients are selected for proton therapy; what are the indications; patient selection methods and criteria etc.
A questionnaire was created and sent out. Two EPTN centres have responded to date. EPTN network centres are encouraged to fill out the questionnaire.
The questionnaire looks at different criteria for different tumour sites. It is estimated that completion of each part of the survey that considers one site will take approx. 10 minutes.
You can fill in the questionnaire online via the links below:

- Head and neck cancers: https://forms.gle/eUbJfyXbLYFikrYr5
- Lung cancer: https://forms.gle/oB7RHY6t6pNBJ9aeA
- Breast cancer: https://forms.gle/RLXpWe4o9aQxBjSi8
- Prostate cancer: https://forms.gle/wQ55xvRooFv2Lutb9
- Lymphoma: https://forms.gle/Mf376KTFj9pVFmfz6
- Central nervous system tumours: https://forms.gle/HqUKr5So34KVJvsz7
- Gastrointestinal cancers: https://forms.gle/Df9rugyMFnUmQ3XE8
- Gynaecological cancers: https://forms.gle/YhwLuh63S8YqDhb79

Involvement of vendors in clinical research
Major vendors in proton therapy have declared their recognition of the importance of generating high-quality data and have stated their willingness to support data collection through research studies. The preoperative chemoradiation (paclitaxel-carboplatin or folfox) for resectable oesophageal and junctional cancer (PROTECT) trial sees the financial involvement of two vendors.

Covid-19 survey
A survey on SARS-CoV-2 protocols for particle therapy was launched at the start of the outbreak in March to address the consequences of the outbreak on workflow, staffing, patient selection etc. and to consider whether fractionation schedules would be altered in proton therapy.
Two rounds of questionnaires were circulated in March and May; 12 centres answered.
It was found that all sites accepted patients from outside their regions; 73% had discontinued follow-up visits in person; 82% had limited access for adult patients; and all sites had limited access for parents / caregivers of paediatric patients.
It was found that 70% of sites had treated asymptomatic SARS-CoV-2-positive cancer patients while 50% of sites had treated symptomatic SARS-CoV-2-positive cancer patients.
Regarding the use of hypofractionated schedules, for both photon therapy and particle therapy, in palliative and curative settings, 100% of the centres responded that they used

hypofractionated schedules in treatment with photons in curative settings whereas 80% did in palliative settings. In particle therapy, the percentages were respectively 60% and 30%. Hypofractionated schedules were mainly used in prostate and breast cancer. For gastrointestinal neuro-oncology, the schedules mainly stayed the same, but e.g. for glioblastoma it was noted that centres changed indication and focus from glioblastoma to grade 2/3 glioma.
The next rounds of the survey are taking place in November 2020 and planned for early 2021 with the aim of publishing a white paper on the findings shortly thereafter.
Moreover, a new survey on the effect of delay in patient referrals and on the multidisciplinary approach that has been applied during the pandemic is planned to be launched in 2021.

In the report below, you can read about our progress across our seven working parties.

Damien Weber, Cai Grau & Dietmar Georg
Co-chairs, EPTN task force


Damien Weber


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WP1: Clinical

The first objective of WP1 was the assessment of the content of the prospective data registration programmes for the most important indications for proton therapy. The current status is that this has been completed for cancers of the central nervous system, head and neck, breast, oesophagus, lung and prostate. For paediatric patients, it was decided to link to the ongoing US Registry. As this registry is very extensive, the content for the European registry will be determined in the EU project that is entitled health effects of cardiac fluoroscopy and modern radiotherapy in paediatrics (HARMONIC). The EPTN will eventually follow the recommendations of the HARMONIC project.

A recent survey among EPTN members showed that there was a broad commitment of the members to collect data that were integrated in the E2Radiate project (ParticleCare), which is coordinated by the European Organisation for the Research and Treatment of Cancer (EORTC). This commitment was on condition that the transfer of existing centre-based or nationwide bulk data should be possible to prevent redundant data entry by the participating centres. EORTC is willing to facilitate this.

WP2: Dose assessment, quality assurance, dummy runs, technology inventory

As of October 2020, 28 centres in 12 different countries were contributing to WP2. This comprised a total of 38 participants and represented a significant increase compared with the 22 centres, 10 countries and 30 participants that were reported in 2019.

At the 3rd EPTN WP2 workshop in 2019, representatives of several proton centres across Europe came to the conclusion that it would be extremely beneficial if a dedicated quality assurance (QA) workshop was organised, in which centres could get together to share their QA experiences. We were pleased that such a workshop could take place in autumn 2019. The event was hosted by the Holland Particle Therapy Center (HollandPTC) in Delft, The Netherlands. It was a two-day gathering (23 – 24 October) with the scope to share and compare experiences of QA procedures as currently carried out at different European centres. Each facility had the opportunity to give a presentation on its QA procedures, QA tools/devices and workflows. Dedicated sessions and group activities to discuss the results of the QA survey and to discuss critical QA tests such as patient-specific verifications were also part of the programme. The two-day event was a success. The discussions and interactions were excellent. It was great for networking and for learning from each other's experiences. The participants were very much in favour of repeating the experience in 2020.

In the framework of WP2 activities, in the following we present two projects that were submitted in 2019 to INSPIRE for support through the transnational access (TNA) infrastructure. Both projects have been approved.

i) ***Absolute/reference dosimetry project:***

The National Physical Laboratory (NPL) in Teddington, UK, proposed a project, the aim of which was to perform an international dosimetry comparison between facilities that used scanned proton therapy beams. The project would use the NPL primary-standard calorimeter and several types of ionisation chamber that were used as reference instruments in the clinics. Two access providers were included in the project: the Paul Scherrer Institute (Villigen, Switzerland) and the Danish Centre for Particle Therapy (Aarhus, Denmark). The measurements at PSI took place in 2019 in two separate sessions. In order to determine experimentally the $k_{Q,Q0}$ factors, 30 ionisation chambers of seven different types for seven beam qualities were investigated. The data analysis is ongoing and Monte Carlo simulations are running to determine beam-dependent corrections for the calorimeter analysis. The

measurements in Aarhus have not yet taken place since NPL off-site measurements had to be postponed due to the Covid-19 pandemic.

ii) ***Dosimetry audits:***
In the following we present the aims of the projects as described by MedAustron, an Austrian centre for cancer treatment and research, in the original proposal: the lack of international and national dosimetry standards for proton beams demands other effective methodologies to confirm the integrity of the dosimetry techniques that are used at different proton facilities, such as dosimetry intercomparisons or external dosimetry audits. Such studies are extremely useful, especially for new facilities with pencil beam scanning (PBS) dose delivery, to detect and eliminate any possible systematic errors that occur in the dosimetry process. Comparison studies and audits are also important for interchange of clinical experience and treatment protocols between facilities, and if the institutions plan to participate in clinical trials, then such dosimetry studies are mandatory and may serve as a procedure to prove credentials. The objective, therefore, is to test and establish such a dosimetry audit based on a dosimetric end-to-end test, which has been developed at MedAustron in collaboration with the NPL. Several centres are listed as access providers. The project was approved at the end of 2019 but, due to the pandemic, visits to the participating centres had to be postponed.

Furthermore, we have previously reported on the update of international recommendations, i.e. the newly issued standard 93 entitled *Prescribing, Reporting and Recording Light Ion Beam Therapy* from the International Commission on Radiation Units and Measurements (ICRU) and the update of the dosimetry code of practice, TRS-398, by the International Atomic Energy Agency (IAEA). The update of TRS-398 has direct impact on reference dosimetry procedures, especially now as it includes recommendations for scanned beams. ICRU 93 intrinsically also gives recommendations on the use of dose and dose reporting that is weighted according to relative biological effectiveness (RBE), which are relevant also for proton therapy.

Finally, the 4th WP2 general workshop has been postponed to December 2020 and will be held online. Unfortunately, the experience with the QA event of 2019 could not be repeated in 2020; however, an attempt to organise a similar event by spring 2021 is being pursued.

WP3: Education
In order to meet the increasing need for education and training in the field of particle therapy, the working group decided to develop a new initiative, i.e. site-specific workshops.
These will be two-day events that will be hosted by institutions that have solid clinical experience of treating a specific disease site with protons. They will be open to a small number of participants (30 people maximum). The workshops will be aimed at medical doctors, physicists and RTTs who are already involved in particle therapy, so that it will be possible both to address detailed aspects, and to get as close as possible to a “hands-on” experience, e.g. by discussing how to contour, plan and treat specific cases.
As such, the workshops are definitely not meant to replace, but rather to complement, the ESTRO school course on clinical particle therapy, which remains the main educational ESTRO event on particle therapy and which represents an excellent starting point for those who are approaching the field of particle therapy and may then be interested in more specific events such as the workshops.

The first workshop will be on brain and skull-base tumours and will be hosted by the Paul Scherrer Institute (PSI). During the workshop we will discuss topics such as:

how to select the ideal brain tumour patients for proton therapy;
the EPTN contouring atlas and dose volume constraints in the brain;
principles of immobilisation and imaging, management of metal implants;
uncertainties in treatment planning and how to handle them;
robustness in planning and plan evaluation in clinical practice;
whether morbidity and imaging changes in the brain are different with protons;
distal edge effects: physics and biology;
FLASH to spare the brain; and
should all skull-base tumours be referred for proton therapy?

We initially set a date for spring 2021, but due to the pandemic situation we have had to postpone. We think that the workshop is not well suited for transformation into an online event, so we are now aiming at October 2021 as the new date.

If the first "experiments" with workshops are successful, we will plan a similar event for other disease sites, aiming at one to two workshops per year.

WP4: Image guidance in particle therapy
Image guidance in particle therapy (IGPT) is critical to achieve high-precision therapy. However, imaging equipment, procedures and clinical workflows vary substantially between particle therapy centres. Currently, there is a lack of standardisation for IGPT.

The aim of this working party is to gain insight into the current practice parameters of IGPT and to drive harmonisation through the establishment of body-site specific consensus guidelines.

As a first step, the current standard of practice from the EU particle centres has been investigated, and we have reached out to the centres with detailed surveys that were specific to each body site.

For the body sites that we have classified as prostate, abdomen, extremities and Cranio-Spinal (CSI) the data collections through the surveys have been completed and the next planned step is to analyse the responses carefully, in order to identify common procedures and standards.
During the preparation of the surveys, the sub-working group coordinators identified a need for a general consensus on guidelines for IGPT for Cranio-Spinal (CSI) irradiation. CSI is a widely adopted standard indication for particle therapy that heavily relies on time-consuming image guidance procedures and consensus guidelines are missing.

The surveys for brain and breast were sent out to the particle centres in September and data collection is on-going. The final survey, on thorax, is in the pre-testing phase, and it will be ready soon for distribution to the centres.

The fourth annual workshop of the EPTN-WP4, which was supposed to take place at MedAustron on 5-6 March, had to be cancelled due to the Covid-19 pandemic. This meeting was replaced by an on-line session that was organised with the coordinators of the different body-site-specific sub-working groups. The main topic of this meeting, which took place on 26 June, was IGPT projects that could be investigated under EPTN-WP4 coordination and with a potential significant impact for the particle therapy community.

Four projects were presented and evaluated:

1. Advantages and disadvantages of external and in-room positioning (M. Stock)

2. Motion confirmation: online imaging confirmation (fluoroscopy) vs. prior 4D-computer tomography (CT) - information (A. Knopf)
3. Comprehensive overview of accuracy of inter- and intrafraction uncertainties of immobilisation tools for brain and head-and-neck treatments (D. Amelio)
4. Wish list for vendors for image-guided proton therapy (L. Placidi)

The evaluation of these projects was based on key performance indicators (KPIs) that were focused on five metrics: i) fits into the EPTN-WP4 scope; ii) brings value for the EPTN community; iii) probability of success; iv) significant impact on clinical practice; v) resources required are available.

The KPI evaluation identified the project that was entitled "Comprehensive overview of accuracy of inter- and intrafraction uncertainties of immobilisation tools for brain and head-and-neck treatments" as the one to pursue with first priority.

The next steps for EPTN-WP4 will mainly focus on the completion of data collection from the missing surveys and the analysis of the already collected data. The newly acquired data, combined with already published data, will be used to draft body-site-specific IGPT consensus guidelines. Furthermore, the project on accuracy of immobilisation tools for brain and head-and-neck treatments will be organised and structured among the participating centres.

WP5: Treatment planning systems in particle therapy

Treatment planning systems (TPSs) are essential for accurate and effective particle therapy, and are an important part of the particle therapy workflow. In this working group, our aim is to review and to provide recommendations on numerous aspects of the treatment-planning process.

The work was initially divided into six main tasks:

- Collective TPS specifications
- Planning standards and case solutions (together with the Italy, Poland, Austria, Czech Republic and Sweden group (IPACS))
- TPS commissioning and validation
- Alternatives to patient-specific verifications
- CT/ Hounsfield units (HU) calibration
- Robustness analysis.

Two new ones have recently been added:

- The role of linear energy transfer (LET)
- 4D planning.

Collective TPS specifications

These have been defined and have been published on the ESTRO website. In addition, a dialogue with TPS vendors has been initiated and four have responded to a questionnaire that was sent out by this task group. A follow-up round is planned to assess the overlap between the interests of WP5 members and the development strategies and road maps of the vendors.

Planning standards and case solutions

This task is running in collaboration with the IPACS group, with most of the work already having been done by this group. Planning comparisons for a head-and-neck case have been performed within the IPACS group, and a publication on this is in the pipeline. Next cases to be studied are the skull-base and breast. It is also planned to address planning issues due to metallic implants.

The ultimate goal of the task group is to define guidelines for planning standards in different indications.

TPS commissioning and validation
This task is still very much a work in progress, but aims to define a minimum set of commissioning and validation tools for the commissioning of TP systems, which can be used as a starting point for new centres.

Alternatives to patient-specific verifications
In order to obtain a 'snap-shot' of current patient-specific verification (PSV) protocols within the European particle therapy community, a workshop was organised at PSI in September 2019. This attracted 25 participants from 12 different facilities. Each of these participants presented their protocols and workflows for PSVs. Every centre currently performs experiment-based verifications on a field-by-field basis, with widely varying times reported per verification. There is a general consensus, however, that PSV could be made more efficient through the use of delivery log-files. A follow-up workshop is planned for 2021.

CT/HU calibration
This has been a very active task group, which has recently completed an important inter-centre comparison of CT calibration procedures. For this, a standardised phantom was shipped between all centres for which the calibration procedures of each centre could be compared. When converted into range deviations for typical beam paths, inter-centre variations in range reached 2.9%; the range deviation exceeded 2% in four of 17 centres. Empirical calibration curves showed the largest deviations, whereas deviations were lowest for the stoichiometric or tissue-based methods.

Robustness analysis
Robustness analysis is an area of ever growing interest in the particle therapy community. This task group aims to produce a 'white-paper' that will review the use of robustness analysis and will define a common nomenclature. This group has published two papers that have partially resulted from the work that has been performed in this area as part of WP5. As a next step, the group plans to perform an international cross-centre comparison of plan robustness.

The role of LET
This is a new task group, which aims to assess whether, in current proton therapy clinical practice, there is a need to incorporate LET-based optimisation and evaluation into treatment planning. The group plans to review open-source Monte Carlo calculation engines and clinical treatment planning algorithms for LET calculation and to make technical recommendations towards clinical implementation, as well as to identify gaps in current knowledge that may hinder clinical translation of LET/RBE into treatment planning. A group of interested participants has been formed, and more will be reported on this at the next EPTN meeting.

4D planning
This is the second new task group to be formed in WP5, and aims to make recommendations about motion management and 4D-planning in particle therapy. There are currently 11 participants in the group, who aim to work on 4D treatment-planning guidelines (delineation, optimisation, motion mitigation strategies etc.), 4D plan evaluation guidelines and 4D imaging standards.

Next steps for WP5

Although much has been done, progress in some areas has been unfortunately but understandably slow due to the current situation. A meeting of the different task-group coordinators in WP5 is currently being organised to take place in December 2020 (remotely) in order to review progress, but also to discuss new directions in which the group may go.

WP6: Radiobiology and relative biological effectiveness

Protons and heavier particles have a different effect on human biology compared with photon irradiation. Part of this is accounted for in the concept of relative biological effectiveness (RBE). The current clinical use of an RBE of 1.1 for proton irradiation is under debate, as a fixed RBE of 1.1 is a simplification of the actual biological response to proton irradiation. The RBE is known to be affected by tissue type, biological endpoint, dose and dose fractionation as well as by the LET. In a proton treatment field, the LET increases moderately through the spread-out Bragg peak, SOBP, but increases considerably in the very distal edge of the SOBP. This has been demonstrated in vitro to translate into an increased distal-edge RBE. This is a critical issue, as the distal edge of an SOBP in a patient treatment plan may be located in a tumour that surrounds normal tissue. This increase in RBE has been a subject of discussion, as the clinical impact in proton therapy is unclear.

In February 2020, WP6 held a workshop in Manchester, UK, with local co-organisation by professor of proton therapy physics Karen Kirkby and team at the University of Manchester and support by the European research project INSPIRE (https://protonsinspire.eu/). It was arranged as an open meeting for everybody with an interest in the clinical impact of the RBE in proton therapy and experimental particle radiobiology, and 44 participants from eight countries and 13 centres were present at the two-day meeting.
The first day of the meeting was focused on RBE and radiobiology, the clinical perspective and use of a variable RBE in proton therapy. This subject was addressed in four sessions:
(1) Clinical problem – significance of elevated RBE in proton therapy
(2) Current clinical practice – strategy to overcome the problem
(3) Back-translation from clinics to radiobiology research
(4) How can we implement variable RBE in clinical treatment planning?

During these sessions, both the current experimental and clinical data were presented and discussed. Representatives from clinical centres that were involved in patient treatment laid out the current clinical practice regarding the risk of a variable RBE in their centres. This overview revealed different strategies that ranged from delivery of more than one field, through placement of the distal edge of the field outside any organ at risk, to the evaluation of the LET distribution of treatment plans for individual patients.
On the second day of the workshop, an overview was conducted of current radiobiological research at the different centres, based on incoming abstracts. A summary of the workshop was published in the radiobiology corner of the July 2020 ESTRO newsletter.

To follow up on the workshop, WP6 and Armin Lühr, the coordinator of the INSPIRE WP9 on mathematical modelling and simulation, are conducting a survey on current clinical practice regarding RBE in European proton therapy centres. The questions in the survey cover treatment planning, prescription and RBE strategies, and aim to form an overview on whether RBE and LET are taken into account in clinical practice in European proton therapy centres and, if so, how this is done in practice. All European centres are invited to take part in the survey; currently 23 centres have completed the online questionnaire. The data will be published after it has been collected and analysed.

https://www.estro.org/About/Newsroom/Newsletter/Radiobiology/%C2%AC%C2%AC%C2%ACRadiobiology-of-protons-the-clinical-perspectiv

WP7: Health economy

Health economic profiling of particle therapy is pivotal for its positioning within the portfolio of alternative radiotherapeutic modalities. However, so far, no assessment has been completed on a European level as it seems to be difficult to obtain the permission of centres to disclose the relevant financial and operational data. Results of health economic profiling, however, should enable the establishment of transparency of resource consumption information in comparison with that used in alternative modalities or combinations thereof. It adds corresponding information to the clinical outcomes that are observed in clinical trials and register studies.
The WP7 team has developed a methodological inventory that can be used for various assessments. These assessments can be adapted to national health technology assessment (HTA) requirements if needed.

The methodological inventory of the WP7 entails:

(1) top-down and bottom-up costing procedures, which are explained here.
   a. Top-down procedures are typically used by payers or HTA organisations to assess technologies that are based on estimates, including investment and operational costs (personnel, maintenance, energy consumption etc.). Together with the number of patients who are treated and assumptions about the delivered fractions, the approach enables the calculation of robust costing estimates.
   b. Bottom-up costing is more demanding in terms of the resources that are required to pursue the analysis, since it involves mapping of workflows/processes and cycle times. However, the approach delivers a more comprehensive and precise view on costing. The accounting approach called activity-based costing supports the assessment by a two-stage procedure that assigns indirect resource costs (equipment, personnel) to the actual treatments, through the intermediary of the activities or process steps that are performed in each diagnosis-related radiotherapy treatment.

(2) surveys of items that can be tailored and deployed in costing analysis.

(3) the potential support of research by the WP7 team through application of modelling and scenario techniques. This would be in regard to the impact of innovation and technological modifications.

Together with clinical outcome data, patient-reported outcome and health-related quality-of-life assessments, comprehensive health economic assessments are feasible. Therefore, the WP7 team encourages EPTN members to get in contact to explore potential support in this respect.

An online meeting was held in December 2019 to investigate whether there was interest among members to start a small group that would collaborate on the evaluation of the ESTRO health economics in radiation oncology (HERO) costing model in the context of proton beam therapy. Participants attended from Marburg and Dresden in Germany, Villigen in Switzerland and Manchester in the UK, as well as Noemie Defourny, Yolande Lievens and Chiara Gasparotto who represented ESTRO-HERO.
There was interest in testing the model, and login details were made available. The initial intent was to meet again at ESTRO in April 2020 for initial feedback. However, due to the Covid-19pandemic, this was cancelled. Moreover, concerns were raised regarding the privacy and integrity of the tool if it was web-based, whereas in some centres the use of their data outside the university clinic servers/network could offer a challenge.

Recently, Professor Kirkby and Dr Thomas Mee, research associate in proton therapy at the University of Manchester, have shown renewed interest in testing the model. Ms Defourny is also working in Manchester on the costing of PBT, so the first collaboration between ESTRO-HERO/EPTN WP7 and the group in Manchester will be set up to evaluate the applicability of the model to PBT, before enlarging the collaboration with other partners in EPTN WP7.

WP	Title	Coordinators
1	Clinical	Hans Langendijk (Groningen, The Netherlands)-Leader Roberto Orecchia (Milano, Italy) Karin Hausterman (Leuven, Belgium) Daniel Zips (Tuebingen, Germany) Jacques Balosso (Grenoble, France) Esther Troost (Dresden, Germany)
2	Dose assessment, quality assurance, dummy runs, technology inventory	Oliver Jäckel (Heidelberg, Germany) Sairos Safai (Villigen, Switzerland) Stefan Menkel (Dresden, Germany)
3	Education	Morten Høyer (Aarhus, Denmark) Marco Schwarz (Trento, Italy)
4	Image guidance in particle therapy	Aswin Hoffmann (Dresden, Germany) Alessandra Bolsi (Villigen, Switzerland)
5	TPS in particle therapy	Håkan Nyström (Uppsala, Sweden) Tony Lomax (Villigen, Switzerland)
6	Radiobiology, RBE	Manjit Dosanjh (Geneva, Switzerland) Bleddyn Jones (Oxford, UK) Jörg Pawelke (Dresden, Germany) Martin Pruschy (Zurich, Switzerland) Brita S. Sørensen (Aarhus, Denmark)
7	Health economy	Yolande Lievens (Ghent, Belgium) Klaus Nagels (Bayreuth, Germany)

INSPIRE

The INSPIRE project (Grant agreement 730983) is funded through the European Union's Horizon 2020 research and innovation programme and is aimed at the integration of proton therapy research activity across Europe. For more information visit INSPIRE's web site https://protonsinspire.eu/.

Like all integration activities, INSPIRE provides transnational access (TNA) so that researchers across Europe can access the facilities of its beneficiaries. INSPIRE also conducts joint research activities to enhance further its research capabilities and make them available to its users. INSPIRE's networking activities are designed to enhance collaboration, training and innovation opportunities across Europe and also to ensure that potential users of INSPIRE's research capabilities are kept informed of what is on offer. Highlights of INSPIRE's work over the past year were:

- It hosted the Particle Therapy Co-operative Group meeting (PTCOG58) in Manchester in 2019; attracted over 1350 delegates from all over the world – largest conference ever held in particle therapy

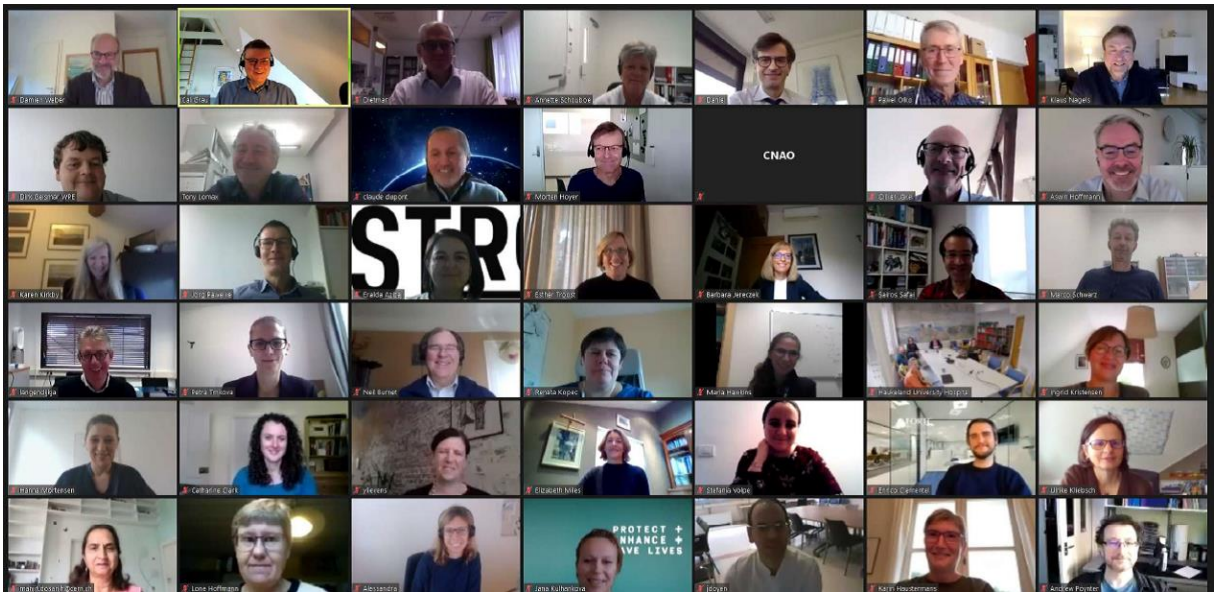
- The group joined analytical research infrastructure in Europe (ARIE) and wrote a position paper on how a common complementary approach would help to address the societal challenges of the horizon Europe missions framework
- It conducted a huge range of public engagement and training activities: https://protonsinspire.eu/news
- It made available outputs (publications, software etc.) through INSPIRE's open access portal: https://protonsinspire.eu/publications
- INSPIRE has made a major contribution to work with industry. Examples include joint work to produce a new proton therapy FLASH ready nozzle, in which project research went through basic research and technology readiness level 1 (TRL 1) to a commercial prototype (TRL 8). Another example is production of the proton-therapy normal-tissue complication probability (NTCP) database, which has gone from TRL 2 to TRL 6 during collaboration with INSPIRE. Another project that was conducted through TNA has involved collaboration with a European metrology programme for innovation and research (EMPIR) project called ultra-high dose pulse (UHDPulse) and a small business and has enabled the development of a new detector (TRL4 - TRL7).
- In TNA, INSPIRE is working on 32 different projects in 11 different countries across Europe and these include collaboration with the USA.
- Highlights of joint research activities that have not been mentioned so far include a paper that features INSPIRE's capabilities: https://doi.org/10.3389/fphy.2020.565055
- INSPIRE was involved in an inter-comparison radiobiology experiment that incorporated a phantom and enabled measurements to be taken at different TNA providers at different positions along the Bragg peak
- It took part in a pan-European study on harmonisation of the definition of LET and RBE for proton therapy. Major papers were presented at ESTRO, PTCOG and at the EPTN WS6 meeting in Manchester in February 2020.
- It has been part of an initiative on proton therapy FLASH, through work on dosimetry, treatment planning and establishment of the parameter space for FLASH.
- It has worked with the organisers of the first and second FLASH workshops (Institut Curie and Lausanne University Hospital (CHUV)) and Kenes Group, which is a leading professional conference organiser, to develop the flash radiotherapy and particle therapy conference. This meeting will incorporate the third FLASH workshop and will be held over 1-3 December 2021 in Vienna, Austria.

Ongoing trials

In the UK, the toxicity reduction using proton beam therapy for orophangeal cancer (TORPEDO) trial is open and recruiting volunteers to take part. To date, 11 patients have been recruited. New trials that are expected to open soon are:
ARACHNID: durvalumab (MEDI4736)+ tremelimumab in combination with different radiotherapy modalities for advanced hepatocellular carcinoma
PARABLE: proton beam therapy in patients with breast cancer to evaluate early and late-effects
APPROACH: proton beam radiotherapy and molecularly defined good prognosis glioma
PROTEUS: PBT vs. photon chemoradiation as preoperative treatment of oesophageal cancer
NIPRO: nivolumab with proton beam therapy in patients >70 years old with oropharyngeal cancer

In Denmark, the DAHANCA 35 trial of proton vs. photon therapy for head and neck cancer and the Danish Breast Cancer Group proton trial have been launched, and the PROTECT international trial for oesophageal cancer is in preparation.

The date for the next EPTN meeting will be decided and communicated at a later timepoint.



Faces from the online meeting