SpotOn+

Center for Proton Therapy :: Paul Scherrer Institut :: #17_5/2019

Dear Reader,

it is my distinct pleasure to inform you that PSI will organize a Symposium on Proton Therapy on August 29th 2019 before the annual meeting of SASRO in Lausanne. This is the first dedicated scientific meeting on protons in Switzerland. You find the program of this symposium on the last page of this newsletter. Registration is free but compulsory via the website of SASRO's annual meeting (https://medicongress.vivenio.de/event/#/?event=SASRO). The aim of this proton therapy symposium is to inform the Swiss Radiation Oncology community of the status of this selective treatment modality in respect to cancer management. It will come as a timely gathering as proton therapy centers are opening in Europe. It is foreseen that by 2022, ca. 30 particle centers will be in operation in Europe. This will give the European Particle Therapy Network (EPTN; https://www.estro.org/Science/EPTN) the possibility to perform prospective clinical trials to generate high-quality level I-II evidence regarding the benefit of protons over photons for a limited number of patients with specific indications. A meeting in Luxembourg in October 2018 at the Directorate-General for Health/European Commission concluded that "International collaboration was essential given the still very limited number of patients", and it should be recommended that all new proton therapy centers should contribute to reinforce the international knowledge base. At this occasion, a temporary subgroup on proton therapy was created and a clear mandate was given by the EU DG-Santé commission and the European Investment Bank to this working-group which includes EPTN (a task force of ESTRO), the EORTC and a number of cancer centers. A number of prospective trials are currently accruing patients (i.e. low-grade glioma in Essen, D, and brain tumors in Dresden, D) or should be launched in the not too distant future, for head and neck cancers (TORPEDO trial, UK; DAHANCA 35, DK; IMPERATOR trial, NL), oesophageal and breast cancers. Thanks to the input of the EORTC, a prospective database will be activated Q4 2019 to register patients treated with protons within the framework of the E2RADIatE project (protocol EORTC 18033). This endeavour will generate critical data on the outcome of patients treated with protons. In the meantime, we have to select patients for this treatment modality based on retrospective data, such as those generated by PSI. In this newsletter you will find the joint analysis between PSI and the Institute Curie Proton Therapy (Orsay,F) assessing the outcome of skull base chondrosarcoma patients. This is an extremely rare tumor and only a joint analysis could bring some meaningful information to the oncology/neurosurgery community. Two hundred and fifty-one patients were treated with protons with or without photons to a median dose of 70 GyRBE (range, 62-76). With a mean follow-up time of 87.3 months, treatment failures were observed in only 15 (6%) patients. These data suggest very strongly that optimal tumor resection (leaving the patient functionally unimpaired), as in chordoma, should be pursued. The last article of this newsletter details the delivery monitoring systems that are controlling the delivery of radiation and log the data for offline analysis.

That being said, I am looking forward to seeing you at the proton therapy symposium this summer. Please stay tuned for our next edition for some results stemming from our ongoing clinical/research program.

Yours sincerely,
Prof. Damien Charles Weber,
Chairman of CPT
Paul Scherrer Institute

Radio-Oncology News

Long term outcome of skull-base chondrosarcoma patients treated with high-dose proton therapy

Introduction

Chondrosarcoma (ChSa) is a rare bone tumor that accounts for approximately 0.15% of intracranial malignancy and up to 6% of all skull base tumors. The therapeutic strategy usually involves cytoreductive surgery, with or without postoperative radiation therapy (RT), which is usually administered with protons or carbon ions due to the relative radio-resistance of this tumor. This study is a pooled analysis from two centers that evaluated the long term outcome of skull base ChSa patients treated with protons, with or without photon therapy (PT) and assessed prognostic factors for patient's outcome.

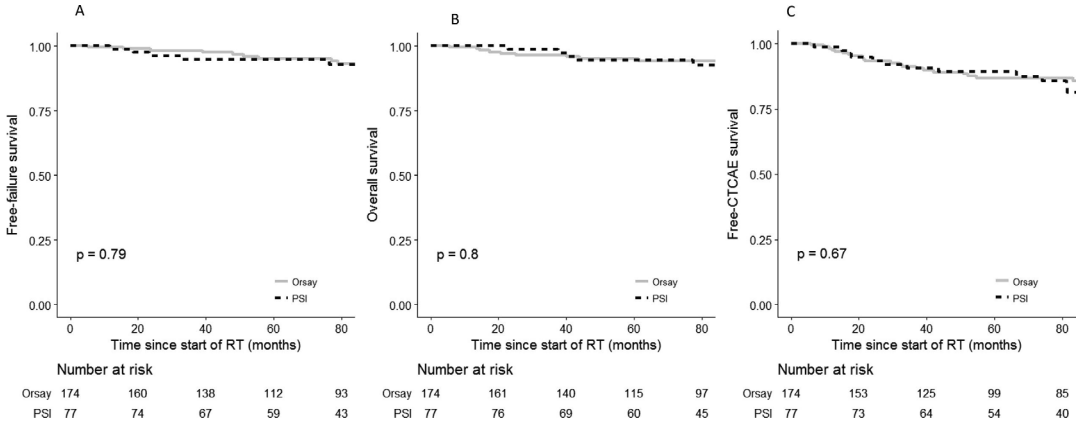
Materials&Methods

Between 1996 and 2015, 77 and 174 (total, *n* = 251) patients with histologically proven diagnosis of skull-base ChSa were treated with curative intent at the Paul Scherrer Institut (PSI; protons only) and the Institut Curie Proton Therapy center-Orsay (ICPO; protons ± photons), respectively. PSI and ICPO are the two most experienced proton centers in Europe and have been treating patients with protons since 1984 and 1989, respectively. Treatment planning was performed respecting pre-defined dose constraints with the PSIPlan and ISIS 3D/ISOgray treatment planning systems at PSI and ICPTO, respectively. The median planning dose was 70.0 (range, 64.0–76.0) and 70.2 (range, 62.0–71.2) GyRBE at PSI and ICPTO, respectively. The gross tumor volume (GTV) was delineated on the planning computed tomography with the help of the pre- and/or postoperative MRI scans. Radiologic criteria for local tumor control were defined as stable or reduced tumor volume on consecutive MRI ± CT scans compared with pre-PT images.

Results

The median follow-up for all patients was 87.3 months. Treatment failure was observed in 15 (6.0%) patients: local failure only occurred in 11 patients 5.3–140.8 months after PT (median, 43.6). Three patients presented with distant failure only, 15.7–79.7 months after PT (median, 39.7). One patient presented with a sequential distant and local failure, 55.6 and 67.6 months after PT, respectively. Patients failed in lymph node (*n* = 1), lung (n = 1), distant brain (*n* = 1) and vertebra (*n* = 2). The estimated 7-year failure-free survival (FFS) was 93.1% (95% CI: 89.6 to 96.7). Noteworthy, all but one patient presented with brainstem or optic apparatus compression prior to PT. There was an even split between male and female gender among patients with treatment failure. In univariate analysis, the failure rate was significantly influenced by the tumor volume and the optic pathway compression. The 7-year FFS was 96.4% vs. 87.4% for patients with tumor volume ≤25 and ›25 ml, respectively ($p = 0.006$). The 7-year FFS of patients with and without compression was 89.5% vs. 96.0% ($p = 0.027$). In total, 25 (10%) patients died during the follow-up period. Ten (40.0%) patients died as a result of tumor progression. The estimated 7-year overall survival (OS) was 93.6% (95% CI: 89.6 to 96.7). In univariate analysis, OS was significantly influenced by the tumor volume, age and number of surgery (higher risk for bigger volumes, older age or multiple surgeries). The occurrence of a local and/or distant failure was significantly associated with the risk of death (HR 126.0, 95% CI 38.3 to 414.5; $p < 0.0001$) and was thus an independent predictor of death. A full multivariate analysis was not performed because of the low number of failures relative to the prognostic parameters.

Acute radiation-induced toxicity was manageable and was limited to asthenia, focal temporary alopecia and erythema. Thirty nine late grade ≥3 radiation-induced toxicities were observed in 38 (15.1%) patients. The estimated 7-year toxicity free survival was 84.2% (95% CI: 79.3 to 89.5). In univariate analysis, the only two prognostic factors were tumor volume and age (higher risk for bigger volumes and older age).



Failure-free- (A) overall- (B) and toxicity-free (C) survival for ChSa patients treated with PT.

Conclusion

Local or distant control of this skull base tumor impacts overall survival. Surgery designed to achieve removal of the tumor with a relatively low risk of disability, followed by high-dose proton beam therapy, appears to achieve the best long-term results in skull base ChSa. Hearing loss and brain necrosis were observed in a number of patients after PT which comes with a non-trivial, albeit acceptable, toxicity rate that may affect the QoL of these patients. After the delivery of radiation, long term surveillance is warranted.

Results of this collaboration project were published recently (Weber et al. *Long term outcome of skull-base chondrosarcoma patients treated with high-dose proton therapy with or without conventional radiation therapy; 2018)*

Physics News

PSI monitors system for proton dose delivery

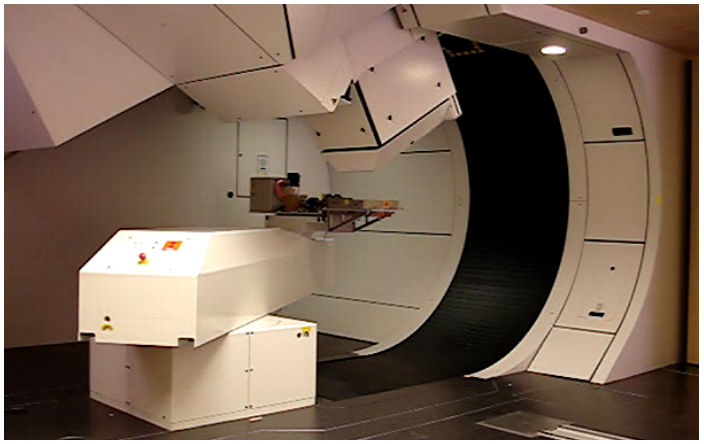


Figure 1 shows the Gantry 2 with a replica of the nozzle position detector to execute some quality assurance measurements.

The Paul Scherrer Institute (PSI) was the first center to use the proton spot scanning technology for treatment of cancer, a highly effective and precise delivery technique for proton irradiation. The technique consists of delivering the desired number of protons accelerated at the same kinetic energy precisely to defined spots within the patient. By using fast and powerful electromagnets, the protons are delivered spot-by-spot into the tumor volume in the patients. Protons of the same kinetic energy slow down at the same pace through matter and are stopped completely at a calculated distance inside a given target volume. A strong magnet at the accelerator allows to start and stop the protons delivery, creating packets of dose with the same characteristics. The dose being delivered has a lateral profile of a pencil, with a relative maximum at the tip, giving the name to the delivery: spot scanning.

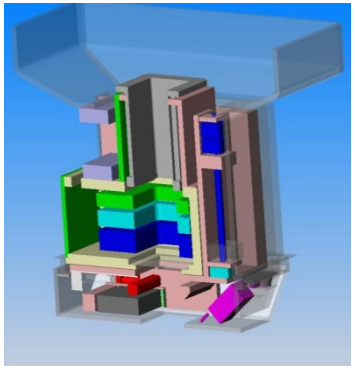


Figure 2 shows the cross section of the Gantry 2 nozzle. The light blue and green box are the dose measurement monitor and the dark blue is the position sensitive monitor.

Given the precision with which the dose is being delivered, an accurate monitoring system is crucial to the spot scanning technique. PSI has more than 20 years of experience in proton monitoring techniques for spot-scanning systems, with the development of the Gantry 1 in the 1990s. Ten years later, with the PROSCAN project the Gantry 1 technology was improved to be integrated into the new Gantry 2, where patients treatment started in 2013.
The delivery monitoring systems developed at PSI are supervising the treatment and log the information produced by the detector for offline analysis. The monitors record many parameters, such as dose delivered and the protons position. The safety of the patient is at the core of the beam monitoring system and all precautions have been taken to prevent any unwanted dose delivery to occur during a treatment.

The dose delivered to the patient is measured by two redundant ionization chambers in the gantry nozzle. The idea to have two redundant monitors is linked to the control system delivering the treatment: the system is divided in two main components, one responsible to delivering the treatment (TDS) and one verifying the delivery of the treatment (TVS). A specific monitor is attributed to each subsystem and the ratio between the dose measured between the TDS and TVS is constantly verified, ensuring the right dose is delivered to the patient and otherwise interrupting the proton beam delivery.
To ensure the monitors accuracy, the monitor response is calibrated using a Faraday's Cup. By measuring the charge deposited by protons stopping in a brass block, the exact number of protons can be precisely evaluated and it is used to calibrate the monitor response for a given kinetic energy. This calibration is repeated every three years in order to guarantee the stability of the system, and over 20 years of irradiation for the Gantry 1, variations less than 3% were observed. Finally, the dose delivery is also checked daily by using calibrated ionization chambers.

In addition to the dose delivered to the patient, the size and position of the proton spots is controlled by a stripped ionization chamber and it is the last significant element found in the proton path before reaching the patient. This monitor is a key component of the TVS dose delivery subsystem. The detector measurements precision is also part of the different daily checks and it is done by measuring the beam profile and position at the iso-center with an independent position sensitive detector.
The physicists process all data produced by the different monitoring units to determine the quality of treatment. According to strict tolerance and action level on the results of the data analysis, they proceed with required maintenance when necessary. The extensive daily quality insurance procedures insure the highest quality of treatment. The proton treatments delivered at the PSI since more than 20 years have been using the highest precision and care, in a typical Swiss tradition.
This work was presented at the OMA workshop at CERN, Geneva in June 2018.

For any further information, please refer to CPT

Dr. Francis Gagnon-Moisan
+41 56 310 53 83
francis.gagnon@psi.ch

Proton Therapy Symposium

29th August 2019 at SASRO venue, 09:00 – 11:30

Agenda

8:00 – 9:00	**Registration and Coffee**	
9:00 – 9:10	Welcome & Opening	Prof. Damien Weber, Head and Chairman of the Center for Proton Therapy at PSI; Prof. Jean Bourhis, Head of the Radio-Oncology Department at the Centre Hospitalier Universitaire Vaudois
9:10 – 10:30	**Clinical**	**Chair: Prof. Damien Weber**
9:10 – 9:30	Proton Therapy in Switzerland and Europe	Prof. Damien Weber
9:30 – 10:00	Indications for protons	Dr. Marc Walser, Senior Radiation Oncologist at CPT/PSI
10:00 – 10:30	Clinical case studies	Alessandra Bolsi, Senior Medical Physicist at CPT/PSI; Dr. Sébastien Tran, Radiation Oncologist at CPT/PSI
10:30 – 11:20	**Physics & Medical Physics**	**Chair: Prof. Tony Lomax, Chief Medical Physicist at CPT/PSI**
10:30 – 10:50	Rapid referrals: from Papyrus to the XXI century	Prof. Tony Lomax
10:50 – 11:05	Advanced delivery	Dr. David Meer, Senior Scientist Technology Development at CPT/PSI
11:05 – 11:20	Medical physics research and development	Dr. Francesca Albertini, Senior Medical Physicist at CPT/PSI;
11:20 – 11:30	**Summary & Closing Remarks**	**Prof. Damien Weber; Prof. Jean Bourhis**

SASRO 2019
https://www.sasro.ch/2019

Free online registration for Symposium
https://medicongress.vivenio.de/event/#/?event=SASRO

Proton Therapy in Switzerland and Europe

The European research endeavor/strategy for particle therapy in Europe will be discussed during the symposium. Prospective trials worldwide for brain tumors highlights the current limitations when performing prospective trials using protons and a number of issues associated with clinical research and particle therapy will be further detailed during the meeting.

Indications for protons

Indications for proton therapy in Switzerland is entity based. It results from PSI application to Federal Office of Public Health (FOPH) in 2009. This list www.psi.ch/en/protontherapy/indications assembles eye tumors, brain tumors including skull base tumors, head and neck malignancies as well as sarcomas and of course all pediatric tumors.

Medical physics research and development

We will review the current research topics at the centre for proton therapy, including motion imaging and management, optical tracking for eye treatments, daily adapted therapy and proton FLASH irradiations. In addition, we will review the history of electronic patient referrals and how this could develop in the future.

Imprint

Editor
Dr. Ulrike Kliebsch

Chairman
Prof. Damien C. Weber

Chief Medical Physicist
Prof. Tony Lomax

Contact

Center for Proton Therapy
CH-5232 Villigen PSI
protonentherapie@psi.ch
www.protonentherapie.ch
Tel. +41 56 310 35 24
Fax +41 56 310 35 15

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